Letter to the Editor,

Regarding Chan et al, Dairy products, calcium, and prostate cancer risk in the Physicians' Health Study. Am J Clin Nutr 2001' 74: 549-554

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Dear Sir:

Since it affects decisions a man may make to optimize his nutrient intake, or the strategy of a physician to treat prostate cancer, I want to comment on the recent paper by Chan et al (1). They report that high intakes of dairy products or calcium increase the risk of prostate cancer, and propose that anything that lowers circulating 1,25(OH)2D – particularly consumption of calcium or dairy products – could increase the risk of prostate cancer. They state, "epidemiologic studies suggest that 1,25(OH)2D may protect against prostate cancer" (1). The epidemiologic studies cited to support this statement (references 27, 29, 31 in Chan et al) do not offer support for it, and the other references they cited, relating to VDR genetics, or in vitro results, were not appropriate.

The epidemiologic evidence relating prostate cancer to vitamin D or 25(OH)D is based on ecologic studies demonstrating an inverse correlation between ultraviolet light exposure and prostate cancer mortality rates in the U.S. (2). UV light affects systemic levels of 25(OH)D (3), but it has practically no effect on 1,25(OH)2D. Except for Corder et al (4), no study supports a role for systemic 1,25(OH)2D in prostate cancer. Those authors reported that pre-diagnostic 1,25(OH)2D levels were lower in prostate cancer cases by a statistically significant, but mechanistically implausible, 4.6 pmol/L (1.83 pg/mL) (4).

Likewise, presentation of results by Chan et al seems to be selective in terms of the effect of calcium intake on the 1,25(OH)2D level. They only show a significant difference between the lowest and highest quartiles of calcium intake. However, the full effect of calcium intake on prostate cancer was already evident in the third quartile – men averaging just one glass of milk daily, but apparently with no effect on 1,25(OH)2D (1).

There is a mechanism to explain why UV light might prevent prostate cancer. Schwartz et al (5), and now others (6;7), have shown that prostate cells synthesize their own 1,25(OH)2D from 25(OH)D. More importantly, the desirable in vitro effects of 1,25(OH)2D on prostate cells are produced using just 25(OH)D (6).

Chan et al leave readers wondering whether the benefits of dietary calcium to lower blood pressure and prevent osteoporosis need to be balanced against the risk of prostate cancer. Dietary calcium and circulating 1,25(OH)2D do not correlate with prostate cancer prevalence when circulating 25(OH)D is higher. Giovannucci attributed the lack of a relationship between 1,25(OH)2D and prostate cancer in Hawaii to their higher 25(OH)D level (8;9). This would also account for why calcium intake does not affect prostate cancer in Milan, Italy (10). When circulating 25(OH)D is high enough, then the prostate can produce the 1,25(OH)2D needed to regulate proliferation and differentiation of its cells. In contrast, when circulating 25(OH)D is so low that the prostate cannot produce enough of its own 1,25(OH)2D, then a higher circulating 1,25(OH)2D (attainable by restricting calcium intake) might become relevant to the biology of the prostate gland.

When the mechanisms are considered in the context of 1,25(OH)2D as a paracrine hormone of the prostate, then the health implication becomes clear –

ensure that the 25(OH)D concentration is optimal for the requirements of its paracrine role, and to attain this, men need far more vitamin D than the current AI for this nutrient (3).

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