Periodontal Disease and Breast Cancer—Letter  
William B. Grant

The recent article by Freudenheim and colleagues found a significant correlation between periodontal disease and invasive breast cancer (1). However, their discussion of potential mechanisms overlooked possibly the most important one: low vitamin D status. Low 25-hydroxyvitamin D [25(OH)D] concentration is strongly linked to breast cancer incidence in case-control studies but not prospective observational studies with follow-up times greater than 3 years (2). In a meta-analysis of 11 case-control studies from 7 different countries, the OR for 25(OH)D quantiles were found to lie on a power-law fit (arbitrary OR = 1.20 at 10 ng/mL, 0.70 at 20 ng/mL, and 0.57 at 30 ng/mL) with a correlation coefficient, r = 0.88. The reason for the difference in findings for case-control and prospective observational studies is that breast cancer develops rapidly and 25(OH)D concentrations change in time so that the correlation with 25(OH)D is attenuated in proportion to the follow-up time (2). Results for colorectal cancer were also found to degrade with increased follow-up time, but with a lower slope than for breast cancer. Support for the difference between the two types of cancer is provided by the fact that the American Cancer Society recommends mammographic screening every year for women older than 40 years but only every 5–10 years for colorectal cancer (2). Geographic ecological studies in mid-latitude countries find strong inverse correlations between solar UVB doses, the primary source of vitamin D, and breast cancer mortality rates (2). The mechanisms whereby vitamin D reduces risk of breast cancer are well known, including effects on cellular differentiation and proliferation, angiogenesis, and metastasis (2).

Periodontal disease is also causally linked to low 25(OH)D concentrations according to the criteria for causality in a biologic system proposed by A. Bradford Hill (3). One of the mechanisms is induction of cathelicidin, which has antimicrobial and anti-endotoxin properties (3). Vitamin D also reduces inflammation as demonstrated in a meta-analysis of 39 vitamin D clinical trials with biomarkers of inflammation as one of the outcomes (4). Finally, smoking lowers 25(OH)D concentrations (5).

As some of the women in the Women’s Health Initiative Study had serum 25(OH)D concentrations measured, it might be possible to obtain those measurements to verify this effect of 25(OH)D concentration. Alternatively, the geographic location of the women could be used to determine UVB doses and approximate 25(OH)D concentrations.

Disclosure of Potential Conflicts of Interest
W.B. Grant has provided expert testimony for Bio-Tech Pharmacal, Vitamin D, and Council Vitamin D Society. No potential conflicts of interest were disclosed by the other authors.

Grant Support
W.B. Grant received funding from Bio-Tech Pharmacal, Inc. and the Vitamin D Society (Woodstock, ON, Canada) and has also received funding recently from the Vitamin D Council.

Received December 30, 2015; accepted January 9, 2016; published online May 2, 2016.

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