Vitamin D Nutrition Does Not Cause Peripheral Artery Disease

To the Editor:

We wish to point out to readers who look casually through the Brief Review by Norman and Powell 1 or who have access only to its abstract that the review is not relevant to vitamin D in the context of nutrition. Furthermore, the authors failed to present evidence that suggests that vitamin D may have cardiovascular benefits.

The major difficulty with the Brief Review is that it fails to distinguish between what is physiological nutrition in humans, versus the administration to rats of pharmacological amounts of vitamin D, its derived hormone, calcitriol, or analogs. The vitamin D–nicotine (VDN) model of arteriosclerosis has been used for many years2 in rats using a huge bolus dose of vitamin D (40 000 IU/rat) along with nicotine. Per kg body weight, the vitamin D dose in animal models exceeds by 200-fold what humans can derive through sun exposure (250 to 625 micrograms/d, or 10 000 to 25 000 IU/d).

The term “vitamin D” should not have been used in such a generic sense. For example, take the sentence, “In postmenopausal women, vitamin D supplementation (two micrograms per day) increased CD3 and CD8+ subsets of lymphocytes.” 3 Despite appearances, this does not refer to either the nutrient vitamin D or to nutritional supplementation. Instead, the two micrograms relates to double the physiological replacement dose of one of the most potent hormones in our bodies, calcitriol. Those who read the sentence without checking directly the article cited3 are left the false impression that vitamin D supplementation is risky; if 2 µg affects lymphocytes, then so should the 10 µg in a multivitamin.

In the abstract and in the text they write “Vitamin D is likely to have a role in the paradoxical association between arterial calcification and osteoporosis.” 4 However, Norman and Powell fail to mention that there is no effect of vitamin D consumption on circulating levels of the calcitriol that they propose as the agent affecting arteries.5,5

Under the heading of “Vitamin D and Animal Models,” Norman and Powell stated that “Chronic less toxic treatment also results in metastatic calcification and deteriorating renal function. In general, vitamin D results in arterial wall calcification and a variety of other ‘arteriosclerotic’ changes.” However, to support this statement they cite drug company–funded research that involved molecular analogs of the vitamin D hormone given at pharmacological doses.6 None of this is pertinent to vitamin D in the context of human nutrition.

In the section headed “Epidemiological Studies of Vitamin D and Arterial Disease”, the authors report some of the literature on vitamin D and cardiac disease, but they have omitted articles which provide evidence of an inverse association between serum 25-hydroxyvitamin D and myocardial infarction.8,9 They have made no mention of the reported inverse association between vitamin D status and cardiac function.9 There is also a growing literature of an inverse association between vitamin D status and diabetes,10,11 which is a major risk factor for cardiovascular disease.

We regret writing such a critical letter, but we do not regard the recently published Brief Report as a balanced summary of the research on vitamin D and cardiovascular disease. To complicate the issue, the Brief Review is ambiguous about whether the “vitamin D” being discussed relates to nutrition, endocrinology, or pharmacology.12

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In Response:

Dialogue and controversy stimulate research, so we are pleased to respond to the comments of Vieth and Scragg, who may hold different views to ours. They are focused on the role of vitamin D in human nutrition. Our focus was the potential for vitamin D to have effects on disease processes in peripheral arteries. However, we acknowledged that vitamin D may have cardiovascular benefits.

In the Abstract we stated: “Although some vitamin D is essential for cardiovascular health, excess may have detrimental effects. . .” We then identified our perspective would not be the role of vitamin D in health by stating in the first paragraph of the article itself: “The physiological role of vitamin D in skeletal and cellular health has been reviewed elsewhere.”11 and in the last paragraph of the section entitled “Vitamin D and Peripheral Arterial Calcification” we stated: “While adequate vitamin D nutrition is essential for optimal vascular function . . .” and cited an Editorial by Michael Holick entitled “Sunlight and Vitamin D: Both Good for Cardiovascular Health.”2

We agree with Vieth and Scragg over the difference between physiological nutrition in man and experimental studies. We endeavoured to make it clear that there is a difference between dosages used in animal models and dosages relevant to human nutrition. With regards animal models, we stated that: “the majority have used short courses of potentially toxic doses of vitamin D . . .” Furthermore, we ended that paragraph with the following comment: “The relevance of any of these models to the development of cardiovascular disease in man is uncertain.” We believe this is appropriately circumspect. Furthermore, humans (particularly infants) have been exposed to excess vitamin D in the past, and this may still occur, albeit infrequently.3

We never stated or contended that vitamin D nutrition causes peripheral arterial disease but attempted to bring together newer lines of evidence to indicate where the effects of vitamin D in microenocrine loops, calcification, and immunomodulation might impact.
on the development of peripheral arterial disease. Although we used
the term “vitamin D” generically on some occasions and agree that
this lack of precision sometimes can cause ambiguity, we used
precise terminology as much as possible. For example, the term
“1α,25(OH)₂D₃” was used more than forty times in the article.

We reject the criticism, that we omitted “. . . articles which
provide evidence of an inverse association between serum 25-
hydroxyvitamin D and myocardial infarction.” In that very same
section we cited Dr Scragg’s work: “Scragg et al even reported an
inverse relationship between levels of 25(OH)D₃, and myocardial
infarction.”4 We agree that comment about the apparent inverse
relationship between vitamin D status and diabetes is relevant, but
some of this information5 was not available at the time of our review.

Our review aimed to be brief, balanced, and focused on peripheral
arterial disease, not “cardiovascular disease”; inevitably we did not
cite all the cardiovascular disease literature. Vieth and Scragg appear
to equate peripheral arterial disease with cardiovascular disease.
Peripheral arterial disease is a distinct form of cardiovascular
disease, with some distinctive risk factors and pathologies. Arterial
calcification, poor collateral circulation, and aneurysms are common
and often clinically challenging problems in peripheral arterial
disease. We would appreciate focused discussion of these problems,
rather than the attempts to subsume them into the more generalized
(topic of cardiovascular disease.

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