Letters to the Editor

Physiologic norm for vitamin D supported, not challenged

Dear Editor:

The results presented in your recent article, ''25-Hydroxyvitamin D in African-origin populations at varying latitudes challenges the construct of a physiologic norm'' (1), provide excellent evidence in support of the theory that human skin color is an evolutionary adaptation to UV light as well as for its corollary, that health disparities should be expected in any population with diverse skin colors and that in populations living far from the equator, these disparities can be ameliorated by optimizing individual 25-hydroxyvitamin D [25(OH)D] concentrations.

However, the title of the article is both puzzling and troublesome. The findings of this study do not appear to include anything that challenges the construct of a physiologic norm for 25(OH)D. In fact, the authors specifically state, ''Given the evolutionary framework outlined above, the inference would seem unavoidable that the population distribution of 25(OH)D observed in Americans of European descent and Ghanaians represents the physiologic norm for the species.''

In the following sentence, the authors reference research published in another journal (2). They state, ''However, recently published data, as noted above, show that variation in vitamin D–binding protein accounts for most of the variation in total serum 25(OH)D between US blacks and whites.'' This is not an accurate paraphrasing of the other research, which actually states, ''Levels of vitamin D–binding protein only partially explained racial differences in levels of total 25(OH)D; other factors, including skin pigmentation and other polymorphisms, probably contribute to low levels of total 25(OH)D in blacks.''

The appropriate title for the research reported in this article is ''25-Hydroxyvitamin D in African-origin populations at varying latitudes supports the construct of a physiologic norm.''

The author did not declare any conflicts of interest.

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2. Powe CE, Evans MK, Wenger J, Zonderman AB, Berg AH, Nalls M, Tamez H, Zhang D, Bhan I, Karumanchi SA, et al. Vitamin D-binding protein and vitamin D status of black Americans and white Americans. N Engl J Med 2013;369:1991–2000.

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Reply to T Weishaar

Dear Editor:

We appreciate Weishaar's interest in our recent publication (1) and fully agree that much remains to be learned about both the complex role of the vitamin D–hormone system in human health and the evolutionary process that shaped geographic patterns in human populations. The point of our article was to demonstrate that, although concentrations of total 25-hydroxyvitamin D [25(OH)D] vary markedly among populations whose evolutionary history is tied to equatorial regions, there do not appear to be adverse consequences associated with ''low'' 25(OH)D, certainly in terms of the best-documented health outcomes, such as bone health and levels of parathyroid hormone. These data are only compatible with the hypothesis that it is bioavailable 25(OH)D that is necessary for healthy functioning of this system, and that the focus on total 25(OH)D has been misleading. This suggests that research assessing the risk of lower total 25(OH)D is not adequately informative about physiologic effects. Although it is true that we state that the concentrations of total 25(OH)D (i.e., the sum of bound and unbound hormone) seen in Europeans and Ghanaians must in some sense be the ''norm,'' we argue that deviation from this norm is unlikely to have adverse consequences (i.e., it is the unbound fraction that accounts for physiologic consequences); why the bound fraction should vary among continental populations is not easily explained.

This perspective was summarized in the Discussion of our article: ''Why levels of binding protein would vary by latitude is not understood. Furthermore, it is even more difficult to explain why evolutionary selection on skin color would have been driven by a positive survival advantage for 'sufficient' 25(OH)D if the variation by latitude reflects only the bound form of the hormone.''

With regard to the second issue related to our interpretation of the article by Powe et al. (2), it is correct that genetic variants in binding protein appeared to explain only 79% of the black-white difference in their data. However, in agreement with our article, in their Abstract, Powe et al. state, ''Community-dwelling black Americans, as compared with whites, had low levels of total 25-hydroxyvitamin D and vitamin D–binding protein, resulting in similar concentrations of estimated bioavailable 25-hydroxyvitamin D. Racial differences in the prevalence of common genetic polymorphisms provide a likely explanation for this observation.'' This evidence is seen most clearly in the authors' Figure 2c and Figure 3b. It should also be noted that the sample size included in the study by Powe et al. was somewhat limited when one attempts to assess complex effects such as genotype-phenotype variation across groups.