Comments

Vitamin D and host resistance to infection? Putting the cart in front of the horse: authors reply

We appreciate the interest in our review and the comments made by Drs Grant, Goldstein and Mascitelli on our manuscript 'Vitamin D and host resistance to infection? Putting the cart in front of the horse'.[1] However, we disagree with the premise of their comments and their characterization of our review. While it is correct that we based our conclusions on our knowledge of animal experiments and the mechanisms underlying the effects of vitamin D on immune function, we did not overlook relevant human studies.

Careful examination of the Aloia study that was referred to as a successful randomized controlled trial of vitamin D supplementation reveals that it was a letter to the editor, where the authors did a secondary analysis of a randomized control trial that was negative for the original outcomes (i.e. bone mineral changes).[2] The letter to the editor did not contain enough information to evaluate the analysis presented and since letters to the editor are not peer-reviewed, this reference should not be used as such. The Urashima *et al.*[3] study was a randomized control study using vitamin D supplementation and very carefully looked at the incidence of influenza A and B. The cases of influenza A in the vitamin D group were 18 of 167, while the placebo group had 31 of 167. Indeed, there were significantly fewer cases in the vitamin D group; however, influenza B cases were 39 of 167 in the vitamin D group and 28 of 167 in the placebo group.[3] The increase in cases in the vitamin D-supplemented group was not significantly different. Dr Grant and colleagues state that 'No effect of vitamin D was found for type B influenza, which is generally less common than type A influenza'.[3] However, in this case this may be misleading since in these children there were more cases of type B influenza (67 cases) than type A influenza (49 cases).[3] In addition, if you add the cases of type A and B influenza together the vitamin D-treated children had 57 cases and the placebo group had 59 cases.[3] Lastly, there is no evidence that the immune response to type A or type B influenza differs in a way that would explain vitamin D influencing one strain versus another. The review article by Dr Cannell and colleagues does not provide any new data on the topic and is largely a hypothesis that needs to be tested.[4] We conclude that these two human studies fail to provide 'ample' evidence that vitamin D reduces the risk of human infection with influenza.

As for the other references cited by Dr Grant and colleagues, they fail to provide new and/or direct evidence to support a role for vitamin D in humans infected with influenza and or other infections. Associations between season and vitamin D and/or UV light and the 1918–1919 pandemic are not especially helpful.[5] UV light does increase vitamin D production in the skin, but has a number of other effects that should be independently tested. In addition, UV light is immunosuppressive and this immunosuppression still exists in mice that are deficient in the ability to use vitamin D.[6] Similarly, review articles and expert opinions do not provide new data and, therefore, our original conclusion that there is no evidence to support the anti-infective effects of vitamin D does not overlook human studies. We, therefore, maintain our conclusion that there is to date no published, peer-reviewed evidence in any system to directly support a role for vitamin D and host resistance to infection. Unfortunately, the various letters to the editors, reviews, etc. that suggest a connection are no substitute for direct proof. The hypotheses have been proposed and now the critical experiments need to be performed in all areas (cells, animals and humans) to either prove or disprove the hypothesis. While healthy debate is good, over-interpretation of the current peer reviewed data only serves to confuse the public and other scientists who work in the area of vitamin D nutrition.

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REFERENCES

1 Bruce D, Ooi JH, Yu S, Cantorna MT. Vitamin D and host resistance to infection? Putting the cart in front of the horse. *Exp Biol Med (Maywood)* 2010;**235**:921–7
2 Aloia JF, Li-Ng M. Re: epidemic influenza and vitamin D. *Epidemiol Infect* 2007;**135**:1095–6; author reply 1097–8
3 Urashima M, Segawa T, Okazaki M, Kurihara M, Wada Y, Ida H. Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren. *Am J Clin Nutr* 2010;**91**:1255–60
4 Cannell JJ, Zasloff M, Garland CF, Scragg R, Giovannucci E. On the epidemiology of influenza. *Virol J* 2008;**5**:29
5 Grant WB, Giovannucci E. The possible roles of solar ultraviolet-B radiation and vitamin D in reducing case-fatality rates from the 1918–1919 influenza pandemic in the United States. *Dermatoendocrinology* 2009;**1**:215–9
6 Becklund BR, Severson KS, Vang SV, DeLuca HF. UV radiation suppresses experimental autoimmune encephalomyelitis independent of vitamin D production. *Proc Natl Acad Sci USA* 2010;**107**:6418–23