



UNIVERSITY OF LEEDS

This is a repository copy of *Letter by Kain Regarding Article, "Vitamin D Promotes Vascular Regeneration"*.

White Rose Research Online URL for this paper:  
<http://eprints.whiterose.ac.uk/84858/>

Version: Accepted Version

---

**Article:**

Kain, K (2015) Letter by Kain Regarding Article, "Vitamin D Promotes Vascular Regeneration". *Circulation*, 131 (22). e514-e514. ISSN 0009-7322

<https://doi.org/10.1161/CIRCULATIONAHA.114.013334>

---

© 2015 American Heart Association, Inc. This is an author produced version of a paper published in *Circulation*. Uploaded in accordance with the publisher's self-archiving policy.

**Reuse**

Unless indicated otherwise, fulltext items are protected by copyright with all rights reserved. The copyright exception in section 29 of the Copyright, Designs and Patents Act 1988 allows the making of a single copy solely for the purpose of non-commercial research or private study within the limits of fair dealing. The publisher or other rights-holder may allow further reproduction and re-use of this version - refer to the White Rose Research Online record for this item. Where records identify the publisher as the copyright holder, users can verify any specific terms of use on the publisher's website.

**Takedown**

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing [eprints@whiterose.ac.uk](mailto:eprints@whiterose.ac.uk) including the URL of the record and the reason for the withdrawal request.



[eprints@whiterose.ac.uk](mailto:eprints@whiterose.ac.uk)  
<https://eprints.whiterose.ac.uk/>

## Physical Activity, Ultraviolet B derived 1, 25-Vitamin D3 and Vascular Regeneration

**Kirti Kain MD, FRCP, FHEA**

University of Leeds, Leeds, LS2 9JT

### **Corresponding Author**

**Dr Kirti Kain MD FRCP FHEA**

Clinical Senior Lecturer in Cardiovascular Medicine

Division of Cardiovascular & Diabetes Research

Leeds Institute of Cardiovascular and Metabolic Medicine

University of Leeds

Clarendon Way

LEEDS LS2 9JT

UK

Fax +44 (0)113 3436603

Tel +44 (0)113 3437745

E-mail [k.kain@leeds.ac.uk](mailto:k.kain@leeds.ac.uk)

I read with interest the paper by Wong *et al* on the effects of vitamin-D supplementation on vascular repair <sup>1</sup>.

Outdoor physical-activity promotes health as well as treat chronic conditions e.g. psoriasis possibly by increasing biosynthesis and biological-activity of active hormone 1,25-dihydroxycholecalciferol (1,25-dihydroxy-vitamin-D<sub>3</sub>; 1,25-VitD<sub>3</sub>) on endothelial function and vascular repair.

The beneficial effects of physical activity on endothelial function can be mediated in a number of ways, including synthesis of molecular mediators, changes in neurohormonal release and oxidant/antioxidant balance. Physical activity can also elicit systemic molecular pathways connected with angiogenesis and chronic anti-inflammatory action with consequent modification of the endothelial function <sup>2</sup>. It is already known that Vitamin-D receptors are present in all the major cardiovascular cell types including cardiomyocytes, arterial wall cells, and immune cells. Vitamin-D deficiency is associated with vascular diseases through mechanistic changes in endothelial cells, smooth muscle cells, macrophages, dendritic cells, T cells, cardiomyocyte and aortic valve fibroblasts <sup>3</sup>. Renin-angiotensin-systems are also present locally in almost all tissues of body. Hyperglycemia, obesity and hypertension stimulate tissue renin-angiotensin-systems whereas glucagon-like peptide-1, vitamin-D, and aerobic exercise are inhibitors of tissue renin-angiotensin-systems and to some extent can prevent metabolic diseases. Angiotensin II, stimulates reactive-oxygen-species, induces tissue damage, and can be associated with most diabetic complications <sup>4</sup>.

Increasing biological activity of sunshine (Ultraviolet B (UVB) exposure) derived 1,25-VitD<sub>3</sub> is particularly relevant for South Asians (grandparents originating from India, Pakistan, Bangladesh) because they are viscerally obese, physically inactive and insulin resistant. There is an increased risk of endothelial dysfunction leading to diabetes, ischaemic heart disease and ischaemic stroke when compared with Europeans. There is no evidence that the diabetes and cardiovascular diseases status changes in South Asians with vitamin D supplementation or even with the fortification of foods with vitamin D or differences in sun exposure in different continents <sup>5</sup>.

Sunlight exposure for adequate biosynthesis of biological active 1,25-VitD<sub>3</sub> is discouraged particularly in the West because of fear of melanomas. A recent study 'Melanoma in Southern Sweden' demonstrated that avoidance of sun exposure was a risk factor for all-cause mortality. Sunburn might be an outdoor problem if a person is sunbathing (static exposure) rather than when conducting activity (motion).

Research resources are finite in these times of austerity and there are cost implications with vitamin-D supplementation at population level, as vitamin-D deficiencies are up to 70% in some population groups. Getting adequate vitamin-D from outdoor UVB exposure ought to be population-health goal. Measures to increase biological-activity of 1,25-VitD<sub>3</sub> derived from UVB exposure through outdoor-physical-activity may well have the potential to stimulate both the increased *biosynthesis* and the *bioavailability* of cholecalciferol. Moreover, there is no issue of hypervitaminosis with UVB derived vitamin-D. Optimum doses of vitamin-D supplementation are not established and high doses induce ectopic vascular calcification.

It would be interesting to study the effects of physical-activity (sub studies: outdoor versus indoor activity; in summer versus winter) on biological-activity of active hormone 1,25-VitD3 by monitoring 24-hydroxylase expression and the effect this has on the prevention of cardio-metabolic conditions such as type 2 diabetes, autoimmune diseases and neoplastic conditions.

**Acknowledgments:** University of Leeds

**Sources of Funding:** No external source

**Disclosures:** None

## References

1. Wong MS, Leisegang MS, Kruse C, Vogel J, Schurmann C, Dehne N, Weigert A, Herrmann E, Brune B, Shah AM, Steinhilber D, Offermanns S, Carmeliet G, Badenhoop K, Schroder K, Brandes RP: Vitamin d promotes vascular regeneration. *Circulation* 2014;130:976-986.
2. Di FS, Sciartilli A, Di V, V, Di BA, Gallina S: The effect of physical exercise on endothelial function. *Sports Med* 2009;39:797-812.
3. Norman PE, Powell JT: Vitamin D and cardiovascular disease. *Circ Res* 2014;114:379-393.
4. Skov J, Persson F, Frokiaer J, Christiansen JS: Tissue Renin-Angiotensin Systems: A Unifying Hypothesis of Metabolic Disease. *Front Endocrinol (Lausanne)* 2014;5:23.
5. G R, Gupta A: Vitamin D deficiency in India: prevalence, causalities and interventions. *Nutrients* 2014;6:729-775.