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Vitamin D and health: is it the 'sunshine superstar' or just 'media hype'?

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Vitamin D is a unique nutrient, since the main source is not diet but rather the action of sunlight on the skin (in both humans and animals). Vitamin D regulates more than 200 genes; and whilst it has been traditionally known to play a major role in musculoskeletal health, more recent research has shown the importance of vitamin D to other health outcomes, including diabetes & cancer and immune function but controversies remain as to the exact nature and extent of the majority of these relationships; and whether associations are in the causal pathway. In relation to vitamin D and risk of acute respiratory tract infections (ARTI), data suggest that overall, there may be some benefit from daily, low-dose vitamin D in reducing risk, even though the size of any potential benefit may be small. In the COVID-19 pandemic, minority ethnic groups have been shown to be at increased risk of more severe outcomes compared to their white European counterparts which has been associated with low vitamin D status, although causation has yet to be determined. Using data from NDNS and the UK Biobank cohort, stark ethnic differences in vitamin D status have emerged, with dark-skinned population groups at more risk of low vitamin D status (serum levels <25/30 nmol/l) compared to white European groups. Furthermore, studies have also shown that South Asian population sub-groups living in the UK have much less seasonal variation in vitamin D status than is evident in White population subgroups. Recent data suggest that dark-skinned populations may need at least twice the currently recommended daily intake of vitamin D in order to reach an adequate serum 25 (OH)D concentration throughout the year, an area in which further research is urgently warranted.

There are two forms of vitamin D: Vitamin D₂ (ergocalciferol) is found in a small variety of fungi and plants that contain the steroid ergosterol. When exposed to UV radiation at wavelengths of 240–300nm, the ergosterol is transformed to ergocalciferol. Vitamin D₃ (cholecalciferol) is also synthesised via UV irradiation. Historically, vitamin D₂ and vitamin D₃ have been considered equally efficacious in improving vitamin D status. However, in the largest (to date) randomised, controlled trial comparing the two forms of vitamin D, results showed that vitamin D₃ was more than twice as effective as vitamin D₂ at raising total 25(OH)D status, when given in a low dose that is both physiologically relevant and in line with public health guidance. In further analysis of these samples, an in-depth examination of changes in the human blood transcriptome following supplementation with

physiological doses of vitamin D2 and D3 has been recently published. Whilst overlap in the repertoire of differentially expressed genes was present in the vitamin D2 or vitamin D3-dependent effects identified, most changes were specific to either one vitamin or the other. Of particular interest was that following vitamin D3 supplementation, the majority of changes in gene expression reflected a down-regulation in the activity of genes, many encoding pathways of the innate and adaptive immune systems - thus potentially shifting the immune system to a more tolerogenic status. These unique findings certainly warrant further investigation of the respective physiological roles of D2 and D3.

Despite the change in advice regarding vitamin D supplementation in the UK in 2016, the latest NDNS data (years 2016-2019) for the UK shows that 19%, 16% and 13% of children aged 11 to 18 years, adults aged 19 to 64 years and adults aged 65 years and over, respectively, had serum 25(OH)D concentrations below 25 nmol/L. Understanding of vitamin D's role in health has developed extensively over the past 100 years but (many) unanswered questions remain. Not least of these, are which policies are needed to irradicate vitamin D related health inequalities around the world. The spread of the SARS-CoV-2 virus has attracted a huge interest in vitamin D; and in particular claims on social media and the world-wide web that vitamin D is the 'magic-bullet' "cure". This lecture will review our current (global) knowledge in Vitamin D and Health; and will address whether it is *truly* a 'sunshine superstar' or whether it is all just 'media hype'!