THE NUTRITION X-CHANGE

1 VITAMIN D: THE SUNSHINE VITAMIN

A LOOK AT THE EFFICACY, IMPORTANCE AND SUPPLEMENTATION OF VITAMIN D.

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Vitamin D – The Sunshine Vitamin

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Practical Implications

- Vitamin D is crucial for maintaining many aspects of human health that affect athletic performance including; bone health, muscle function and repair and immune health.
- The main way we get vitamin D is from sunlight exposure (80-90%) with only the remaining 10-20% coming from the diet
- Many athletes present with vitamin D deficiency especially in the winter months, which has been shown to have negative effects on muscle and immune function.
- The measurement of vitamin D concentration is somewhat complicated. Emerging evidence suggests that the ethnicity of an athlete may be an important consideration when interpreting measured vitamin D concentrations. Routine measurement in ethnically diverse athletes may therefore be limited and perhaps reserved for symptomatic athletes.
- During winter months, supplementation with 1000-2000IU per day has been shown to have no side effects and corrects deficiencies.
- Seeking sensible summer sun exposure (15 minutes of exposure to arms and legs without burning) will maintain vitamin D concentrations in the summer months.

High dose supplementation (10,000IU per day) increases vitamin D catabolism which can have negative side effects and should be avoided.

Background

The last decade has witnessed a remarkable rise in research and general interest in vitamin D with many sports teams now supplementing with vitamin D as part of their regular nutrition strategies. This growth in interest has been largely triggered by a growing understanding of the crucial biological roles of vitamin D combined with a realisation that many individuals, especially those living away from the equator, show clinical vitamin D deficiencies (Chen et al., 2007) -see Figure 1. Importantly, studies have shown that athletes are not immune to this risk of deficiency (Close et al., 2013b) with significant declines observed in vitamin D levels in the winter months (Morton et al., 2012). Vitamin D is termed the 'sunshine vitamin', given that the primary route of synthesis is in the skin via sunlight (or more specifically, ultraviolet B radiation) exposure. Indeed 80-90% of our vitamin D is obtained via sunlight with as little as 10-20% coming from dietary sources (see Table 1 for dietary sources of vitamin D).

Vitamin D metabolism

A basic understanding of vitamin D metabolism is essential to fully appreciate the actions of vitamin D as well as the various markers used to assess vitamin D concentration and responses to supplementation (a simple schematic representation of this can be seen in Figure 2). Briefly, UVB radiation converts 7-dehydrocholesterol in the skin to pre-cholecalciferol (also termed pre-vitamin D3). [With dermal synthesis, excessive pre-cholecalciferol production is converted into inert photo products to

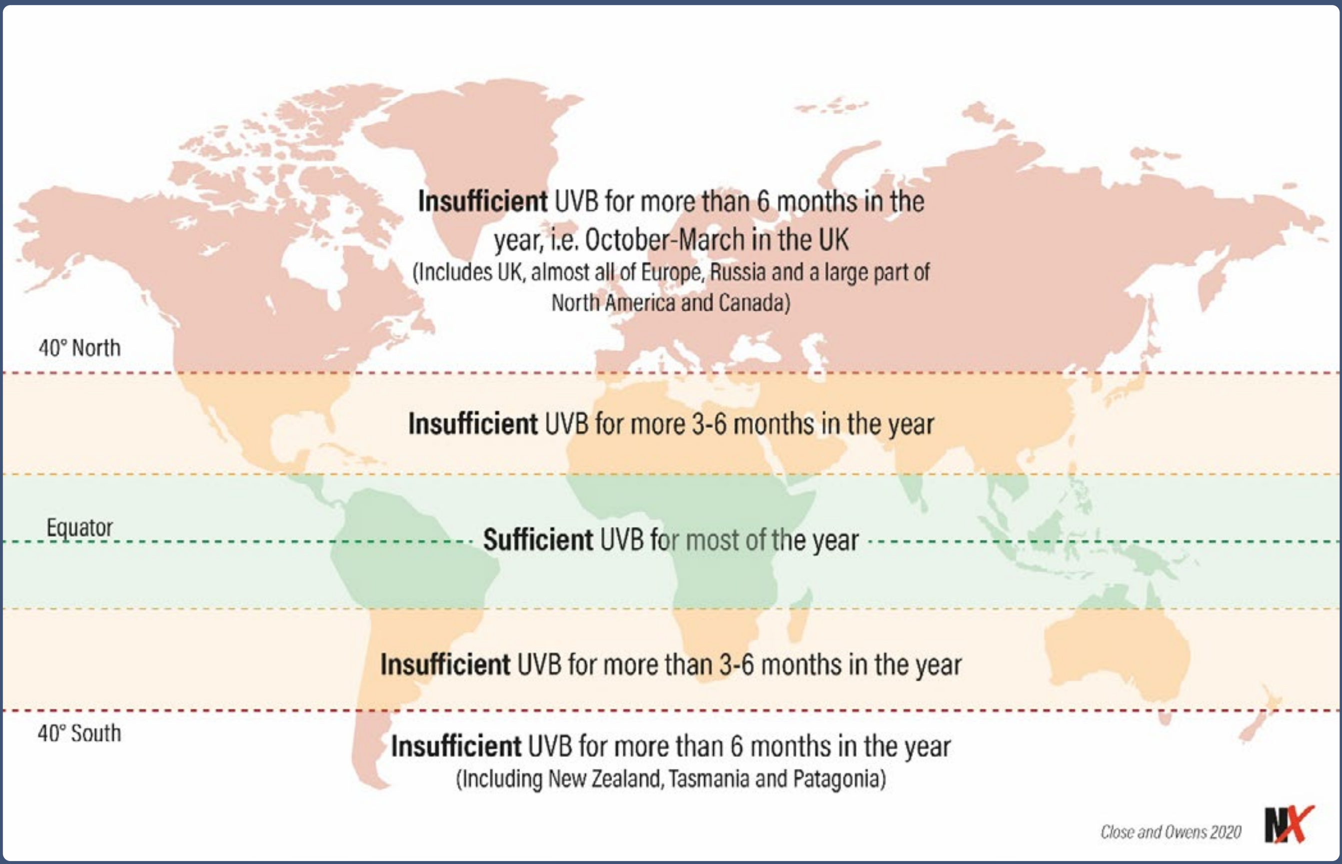

Figure 1. Effects of Geographical location on annual UVB exposure and therefore ability to synthesise vitamin D.

prevent toxicity. This is a key regulatory mechanism that is not available when supplementing vitamin D]. Pre-cholecalciferol is next converted in the skin to cholecalciferol, known as vitamin D3. Vitamin D3 then enters the circulation bound to vitamin D-binding protein (DBP) and is converted to 25-hydroxyvitamin D (25[OH]D in the liver. It is 25[OH]D that is routinely used as a measure of blood vitamin D concentrations. 25[OH]D is then further hydroxylated in the kidneys to the active form of vitamin D, termed 1,25 dihydroxyvitamin D (1,25[OH]2D) which is transported in circulation to target tissues expressing the vitamin D receptor (VDR) subsequently regulating gene transcription (Hamilton et al., 2010). Interestingly, many non-renal tissues (e.g. epithelia, placenta, brain, endocrine glands, immune cells and bone) in the human body are also capable of converting 25[OH]D into 1,25[OH]2D likely in a tissue-specific manner.

Measurement and classification of vitamin D status

One of the main areas of confusion with vitamin D is the measurement and classification of deficiency according to blood concentrations. Blood is typically collected via venepuncture although more recently 'blood spots' from a simple finger prick have been validated which has obvious logistical benefits. There are then a number of methods to assess 25[OH]D to determine vitamin D status, although it is generally accepted that a form of mass spectrometry, HPLC-MS, is the most valid and reliable method (Snellman et al., 2010) and should be the assay of choice. Dependent upon the country of analysis, circulating concentrations of vitamin D may be expressed in different units, these being ng.ml-1 and nmol.L-1, (where 1 ng.ml-1 = 2.496 nmol.L-1). Given that the SI unit for vitamin D is nmol.L-1 this value will be used throughout the article.

Following laboratory analysis of the blood, a quantitative value (typically of 25[OH]D) is given, which is used to indicate vitamin status. There is currently a great deal of controversy with regards

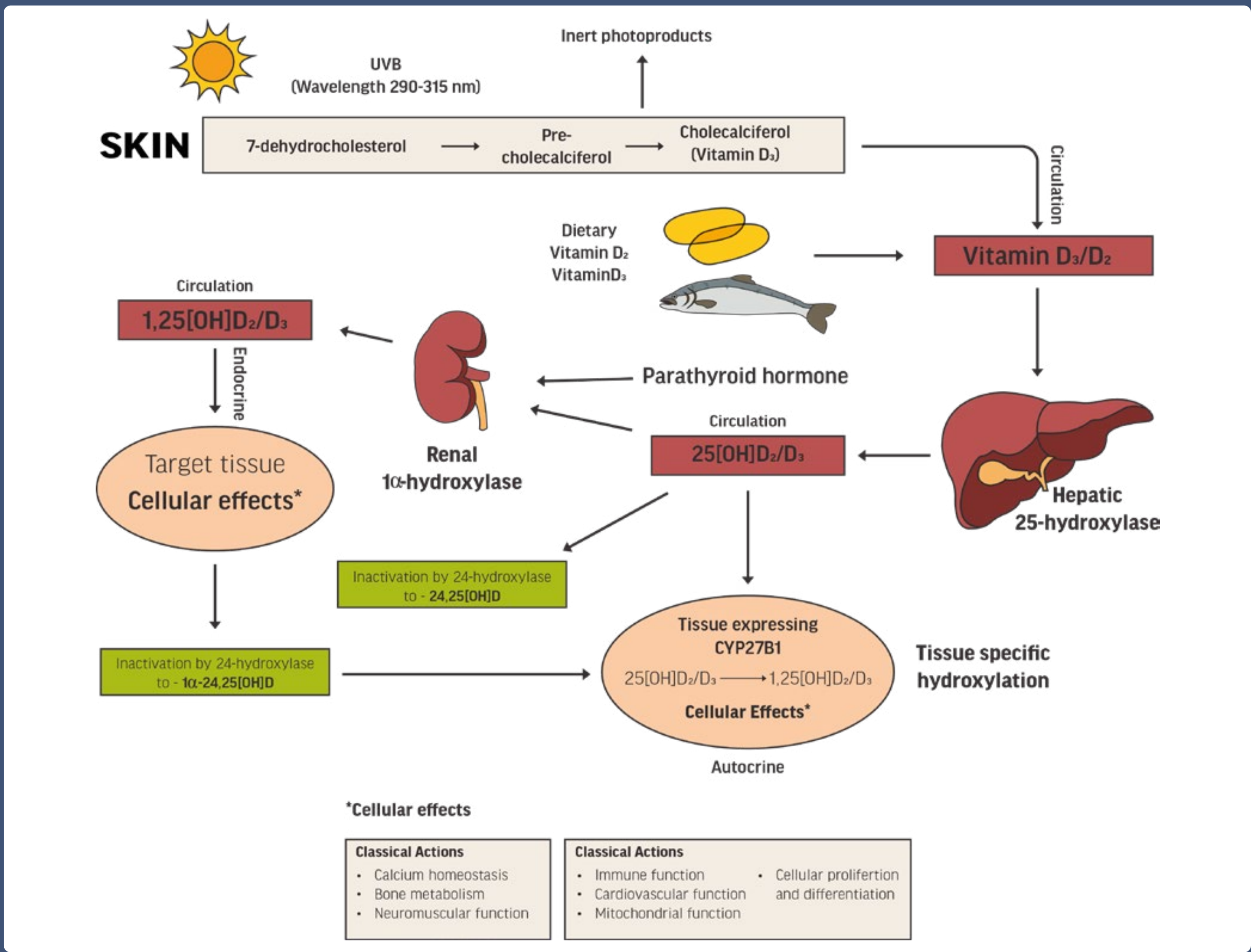

Figure 2. Vitamin D synthetic and metabolic pathways. Vitamin D obtained is from UVB stimulated photosynthetic reactions or dietary intake (Redrawn from Owens and Close, 2013).

to what the thresholds for defining sufficiency and deficiency should be (Zittermann, 2003). Traditionally, values greater than 50nmol.l-1 have been defined as sufficient although recent data has refuted this and raised the question of an optimal vitamin status. Whilst it is still too early to suggest that there may be an optimal status for athletic performance, emerging evidence has suggested that immune function (He et al., 2013) and muscle regeneration (Owens et al., 2015) may both be enhanced when vitamin D concentrations are greater than 75nmol.l-1. Table 1 summarises the National Academy of Medicine (NAM), formerly called the Institute of Medicine (IoM) classification of vitamin D status with the addition of a potential 'optimal' and 'too high' range based on the authors own research.

Benefits of vitamin for athletes

The benefits of vitamin D are multifactorial and have been covered in detail in the scientific literature e.g. (Owens, Allison and Close, 2018). What is clear however, and contrary to popular belief, is that the major benefits of vitamin D come from maintaining an adequate status (possibly 75-100nmol.l-1 as discussed earlier) as opposed to ergogenic potential from achieving supra-physiological concentrations. From an athletic perspective, the 3 main benefits of maintaining adequate vitamin D status are upon bone tissue, muscle function/remodelling, and immune support.

Bone Health. The most well-known role of vitamin D is in terms of its effects on bone mineral density. Vitamin D status is indicative of calcium absorption and bone mineralisation (Berry, Davies and Mee, 2002) and there is considerable data describing the relationship between 25[OH]D deficiency (i.e. <50nmol.L-1) and bone health, especially in non-athletic populations. It is possible that the osteogenic

Total Serum 25[OH]D	Status
< 12 nmol.L-1	Severely deficient
12 – <30 nmol.L-1	Deficient
30 – 50 nmol.L-1	Inadequate
> 50 nmol.L-1	Adequate
>75nmol.L-1	Maybe optimal for athletes?
>125nmol.L-1	Potentially too high (Owens et al)

Table 1. The National Academy of Medicine (NAM) vitamin D status classification system and suggested optimal concentrations.

A cautionary note on the emerging importance of vitamin D binding protein (DBP) and bioavailable vitamin D

In applied practice 25[OH]D is the metabolite of choice to define vitamin D status, and indeed this marker has been used to define optimal status as well as assess the risk of over supplementation. However, emerging research is now highlighting a 'paradoxical relationship' between ethnicity and vitamin D concentration, that has largely been ignored. This paradox, termed the "black athlete paradox" paradox (Brown et al., 2018) is based upon the fact that many black athletes present with deficient 25[OH]D concentrations despite demonstrating the greatest bone mineral density (BMD) and a reduced risk of fracture (Cauley et al., 2005; Hannan et al., 2008), with no obvious signs of impaired athletic performance.

One explanation for this paradox is related to the role of vitamin D binding protein (DBP) and its effects on the bioavailable vitamin D. Recall that DBP is the primary carrier of vitamin D in the circulation and this protein binds 85–90 % of circulating 25[OH]D and 1,25[OH]2D3. The remaining 10-15% of unbound 25[OH]D is considered to be bioavailable (note bioavailable vitamin D includes the 25[OH]D that is either free or bound to albumin). It is now known that there are 3 major forms of DBP which are genetically determined, each form differing in its binding affinity for 25(OH)D. We have recently demonstrated that there was no relationship between serum 25(OH)D concentration and makers of bone health (Allison et al., 2015) in an ethnically diverse group of athletes, however, when bioavailable vitamin D was assessed this fraction was able to predict bone mineral density (Allison et al., 2017). Similar suggestions have been made for measuring the ratio of 25[OH]D to 24,25[OH]D (the product of vitamin D breakdown) as a more sensitive marker of vitamin D status that total 25[OH]D alone. Given that vitamin D screening is expensive and potentially unsuitable in ethnically diverse populations, screening should perhaps be reserved for symptomatic athletes until more research is performed to determine the most suitable measurement of vitamin D status of athletes.

stimulus of weight-bearing activities associated with athletic training and performance somewhat compensates for lower vitamin D concentrations which may account for poor association between BMD and vitamin D in athletic populations. It may also be that, as discussed above, measurement of bioavailable vitamin D or the 25[OH]D:24,25[OH]D ratio could be more indicative of BMD. Taken together, it is important to ensure athletes are not clinically vitamin D deficient and it may be important to assess this in symptomatic athletes such as those prone to stress fractures.

Muscle Function. In terms of muscle function there is currently conflicting evidence with regards to the effects of vitamin D supplementation. For example, whilst no relationship between 25[OH]D status and muscle strength has been reported by some authors (Dhesi, 2004; El-Hajj Fuleihan, 2005; Annweiler et al., 2009; Ceglia et al., 2011), others, including ourselves, have found improvement in 10-m sprint times and vertical jump height following supplementation (Close et al., 2013a). The reason for this discrepancy is likely to be the baseline concentration of vitamin D prior to supplementation. Where we reported improvements in performance, mean baseline 25[OH]D concentration was well below 50 nmol.L-1 whereas in later studies from our group we did not observe any benefits with supplementation when baseline 25[OH]D was greater than 50 nmol.L-1 (Owens et al., 2013). It would appear that in terms of muscle function, problems are only observed when athletes present with very low vitamin D concentrations (for example <20nmol/L; Stockton et al., 2010) with no evidence to date suggesting that supra physiological blood concentrations (i.e. > 75nmol.L-1) offer any performance advantages including endurance performance. Therefore, it may be wise to correct deficiency rather than trying to achieve supra-physiological vitamin D concentrations in terms of basic skeletal muscle function.

There is, however, emerging evidence that increasing 25[OH]D concentrations > 75 nmol.L-1 may enhance muscle remodelling following injury. In an integrative biology study from our group, we reported that maintaining serum 25[OH]D concentrations >50nmol/L may be beneficial for skeletal muscle reparative processes. Supplementation of vitamin D improved muscle force recovery following exercise-induced muscle damage, an observation that was later supported mechanistically in cell-based studies (Owens et al., 2015). Importantly, the cell-based studies also revealed a potential for vitamin D treatment to enhance hypertrophy following injury. Taken together, available evidence suggests that increasing serum 25[OH]D may be beneficial for enhancing reparative processes and potentially for facilitating subsequent hypertrophy.

Immune Support. The third area where vitamin D is important for athletes is in the regulation of immune function. Following injury, the most time lost to training and/or competition in athletes is due to illness (Walsh, 2019). It is not a new observation that vitamin D is important for immune function with a landmark study in 2011 clearly showing that for every 10 nmol.L-1 increase in 25[OH]D there was an associated 7% reduction in infection risk (Berry et al., 2011). This benefit has also been observed in athletic populations, for example, (He et al., 2013) reported that vitamin D supplementation during 16-weeks of winter training significantly reduced infection risk.

Vitamin D supplementation

Given that the major source of vitamin D is sunlight with very little coming from our diet (See Table 2), combined with the knowledge that athletes have consistently been shown to be deficient in vitamin D in the winter months (Close et al., 2013b) it is of little surprise that vitamin D supplementation is now common in both athletes and the general population. There are two natural forms of vitamin D, these being ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3). In terms of supplementation vitamin D3 has been reported to be more effective than Vitamin D2 and should therefore be the supplement of choice.

Can you have too much of a good thing?

Whilst many scientists have recommended mega dose supplementation of vitamin D (Zittermann, 2003; Heaney, 2013), both EFSA and the US Institute of Medicine have set the safe upper limit as 4000iU per day (i.e. 100µg), and work from our lab has suggested that this dose is more than adequate to correct vitamin D deficiencies. This is an important point to stress given the premise that many athletes believe if a little of something is good a lot must be really good. We have also reported that high dose vitamin D supplements (bolus dose of 70,000iU per week equating to 10,000iU per day) in a professional squad of team sport athletes decreased PTH production and significantly increased vitamin D catabolism (Owens et al., 2017). Moreover, this increase in the inactive vitamin D metabolite outlived the decline in the active metabolites following withdrawal of supplementation, which could be potentially harmful and may explain the negative findings associated with mega dose vitamin D supplementation (Sanders et al., 2010). Indeed, recently it has been shown that long term supplementation (3 years) of high dose (10,000 IU per day) in a large group (n=311) of healthy adults reduced bone mineral density (Burt et al., 2019). We therefore believe that a moderate daily dose of vitamin D3 may be most appropriate when supplementing vitamin D; something in the region of 1000-2000IU per day.

Conclusion

Vitamin D is crucial for both athletic performance and general health. There is currently considerable debate as to what constitutes a vitamin D deficiency although there is a general agreement that concentrations less than 50nmol.l-1 can certainly result in problems - concentrations that are frequently reported in athletes during the winter months. Vitamin D deficiencies can impair muscle function and recovery, compromise immune health and risk skeletal problems and therefore it is crucial to identify deficient athletes and treat accordingly. In the summer months, sensible sun exposure is recommended (do not burn) whilst in the winter months given that solar synthesis is not possible, a supplement in the rage of 1000-2000iU per day is suggested.

Food	Vitamin D (IU) per serving
Tuna	50-200
Mackerel	540
Salmon	500
Trout	500
Eggs (found in yolk)	30
Portobella mushrooms	350
Pork	50
Fortified cereals	100
Commercial Supplements	400-10,000

Table 2. Common sources of vitamin D in food sources. Note a recommended supplement is 1000-2000IU per day.

Author bios

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Graeme is a professor of Human Physiology at Liverpool John Moores University where he combines his academic research (>125 research papers to date) with nutrition and physiology consultancy to some of the world's leading sporting organizations. He is currently the expert nutrition consultant to England Rugby, the Head of Performance Nutrition to The European Tour Golf and European Ryder Cup Team and consults to several Premier League Football clubs and players. Graeme is currently the Deputy Chair of the Sport and Exercise Nutrition Register (SENr) and is a fellow of both The European College of Sport Science and The British Association Of Sport and Exercise Sciences. Graeme is a scientific advisor to nutrition X and editor in chief of the Nutrition X-change.

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Daniel is a lecturer of Cellular and Molecular Sport and Exercise Science at Liverpool John Moores University. His research uses multi-model approaches to determine the mechanisms by which nutrition and exercise interact to modulate muscle health. Daniel has also provided nutrition and physiology support to a number of professional sports organisations during his career including; British Ski and Snowboard, England Rugby, Warrington Wolves RLFC and Heart of Midlothian FC.