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New Reference Values for Vitamin D

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Vitamin D · Dietary intake · Endogenous synthesis · Vitamin D status · Reference value

Abstract
In the recent past, many studies have been published on the association between vitamin D and bone health or the risk of various chronic diseases. Thus, the D-A-CH reference values [D-A-CH arises from the initial letters of the common country identification for the countries Germany (D), Austria (A) and Switzerland (CH)] for the intake of vitamin D have been revised based on a critical review by the German Nutrition Society. Both dietary intake and endogenous synthesis contribute to the body's vitamin D status. Since different factors modulate the extent of endogenous vitamin D formation, quantification is hardly possible. Therefore, the new reference values for vitamin D intake are specified for a situation in which endogenous synthesis is completely missing. Based on the findings of the critical review, serum 25-hydroxyvitamin D concentrations of 50 nmol/l or higher are considered an indicator of an optimal vitamin D status. When endogenous synthesis is missing, adequate vitamin D intake is estimated as 20 μg per day for children, adolescents and adults. Dietary vitamin D intake from habitual diet is not sufficient to achieve this value. This gap has to be covered by endogenous vitamin D synthesis and/or additional intake of vitamin D. It is clearly stated that the desired vitamin D supply can be achieved without using vitamin D supplements by frequent sun exposure.

Introduction

Currently, no other vitamin is of greater interest to the scientific community and general public than vitamin D. A unique characteristic of vitamin D is that it is not only obtained from food, but the human body can also produce vitamin D itself if the skin is exposed to sunlight (UVB).

The great interest in vitamin D is based on a large number of studies that not only confirm the known association between vitamin D and bone health but also hypothesize a role of this vitamin in the prevention of various chronic diseases. In light of this new yet unsettled research, the German Nutrition Society (Deutsche Gesellschaft für Ernährung e. V., DGE) has recently conducted a critical review of 'Vitamin D and prevention of selected chronic diseases' [1] (only available in German; www.dge.de). The evidence judgement in this critical review was accomplished according to the methodological approach of the DGE guidelines on evidence-based nutrition. Based upon this review and other recently published systematic reviews or meta-analyses, the DGE has revised the reference values for the intake of vitamin D.

The Nutrition Societies in Germany, Austria and Switzerland edit the 'Reference Values for Nutrient Intake' together. Currently, these reference values are under revision, whereby Vitamin D was the first nutrient to be revised.

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Vitamin D Intake and Status of the German Population

Reflecting both vitamin D intake and endogenous synthesis, the serum concentration of 25-hydroxyvitamin D [25(OH)D] is an established biomarker for determining vitamin D supply [2, 3]. Because the contribution of vitamin D intake from habitual diet to the overall vitamin D supply is limited, its recording does not allow for valid conclusions on the vitamin D status of a person.

According to data from the National Nutrition Survey II, the median vitamin D intake of adults living in Germany was 2–4 μg per day [4]. In children, the median intake was 1–2 μg per day [5]. The median 25(OH)D serum concentration in children and adolescents was 41.9 nmol/l (5% percentile (P5) - 95% percentile (P95) 13.9–96.3 nmol/l), and in adults (18 to under 65 years), it was 46.2 nmol/l (P5–P95 15.5–123.0 nmol/l); at age 65–79 years, the median 25(OH)D serum concentration was 39.1 nmol/l (P5–P95 15.3–104.0 nmol/l) [Mensink, pers. commun.].

According to data from the Robert Koch Institute, 15.5% of children and adolescents and 14.3% of adults (aged 18–79 years) had 25(OH)D serum levels of less than 25 nmol/l [1]. About 62% of boys and 64% of girls aged 1–17 years as well as 57 and 58% of 18- to 79-year-old men and women, respectively, showed 25(OH)D serum concentrations of less than 50 nmol/l [1].

Reference Values for Vitamin D Intake

Infants

Regular exogenous vitamin D supplementation is very important during infancy. Breast milk usually contains very low and insufficient concentrations of vitamin D [6, 7]. Furthermore, infants should not be exposed to direct sunlight, as their skin's protective mechanism has not yet developed. Therefore, continuous administration of a vitamin D supplement is generally recommended.

A daily vitamin D intake between 2.5 and 5 μg was shown to protect infants from rickets [8]. However, recent research shows that this does not ensure a 25(OH)D serum concentration of at least 30 nmol/l in all infants [9]. Currently, 30 nmol/l is the concentration that is deemed necessary for reliable rickets prophylaxis [10, 11]. Scientific associations consider a 25(OH)D serum concentration of at least 50 nmol/l in infants – the same as in adults – to be desirable [9, 12, 13]. This cannot generally be achieved by a vitamin D intake of 5 μg per day [14–16]. In contrast, intake of 10 μg of vitamin D per day resulted in a 25(OH)D serum concentration of more than 50 nmol/l [17, 18]. Based upon these studies, the estimated value of adequate vitamin D intake during infancy is set to 10 μg per day.

Children

In small children, rickets occurs very rarely after sufficient vitamin D supply during infancy. As in infants, for children a 25(OH)D serum concentration of at least 50 nmol/l is considered necessary [9, 12, 13, 19]. Intake of 5–10 μg of vitamin D per day in children resulted in a 25(OH)D serum concentration of more than 50 nmol/l [20]. However, a higher intake of vitamin D of about 20 μg per day is required to guarantee a 25(OH)D serum concentration of more than 50 nmol/l in almost all children without UVB light exposure [21]. Therefore, the estimated value of adequate vitamin D intake with missing endogenous synthesis in children is set to 20 μg per day.

Adolescents and Adults under 65 Years

Maximum bone mass is only achieved around the third decade of life. After that, maintenance of bone mass is the main concern. The quantity of vitamin D that is required for achieving and maintaining maximum bone mass is not known exactly. Internationally, with respect to bone health, a 25(OH)D serum concentration of at least 50 nmol/l is considered to be desirable [1, 2]. The reference values for vitamin D published by the US Institute of Medicine [12] are based on new calculations regarding the distribution of the 'vitamin D requirement curve' in the general public. According to this, a 25(OH)D serum concentration of 40 nmol/l in adults meets the requirements for vitamin D on average (assessed by calcium absorption and bone mineral content). With additional consideration of the variation in the population, 50 nmol/l is the calculated serum concentration at which the vitamin D requirement with regard to bone health is met in 97.5% of the population.

Cashman et al. [22] showed that 50% of the Irish population (the study was performed at the 51st and 55th degrees of latitude, which is about the latitude of Germany) achieved a 25(OH)D serum concentration of more than 50 nmol/l during winter months with a supplementary vitamin D intake of 10 μg per day. About 90–95% of the population achieved this with a supplementary intake of about 20 μg per day. Therefore, the estimated value of adequate vitamin D intake – while endogenous synthesis is lacking – is set to 20 μg per day for both adolescents and adults.

Adults above 65 Years of Age

Among those 65 years and older, the main objective is minimizing age-related loss of bone mass to reduce the risk of fractures as a clinical manifestation of osteoporosis. It has to be taken into account that vitamin D is also associated with muscle function [23–25] and thus with the risk of falls and fractures.

In several studies, protective effects with regard to functional impairment of the musculoskeletal system, falls, fractures and premature death were achieved in this age group through vitamin D supplementation of 10–20 μg per day [1, 26–30]. In this population, an intake of 20 μg of vitamin D per day leads to a 25(OH)D serum concentration of more than 50 nmol/l in 90–95%, which corresponds to a serum value of 75 nmol/l in about 50% of the population [31].

In the critical review of the DGE on vitamin D and prevention of chronic diseases [1], the available scientific evidence regarding the association between vitamin D supply and the risk of falls and fractures was judged with the highest strength of evidence, that is 'convincing' evidence. A significant reduction in falls and fractures occurred in elderly subjects with vitamin D supplementation and an optimal vitamin D status, respectively. There is 'probable' evidence that good vitamin D supply among the elderly lowers the risk of functional impairment of the musculoskeletal system (muscle strength, physical mobility, balance) and reduces the risk of premature death. On the basis of this review and a scientific opinion of the European Food Safety Authority [32], the estimated value of adequate vitamin D intake with missing endogenous synthesis is set to 20 μg per day in elderly people 65 years of age and older.

Other scientific associations have set comparable reference values for elderly people. The International Osteoporosis Foundation [33] recommends a vitamin D supply of 20–25 μg per day for older adults, and the Institute of Medicine [12] recommends 20 μg per day.

Pregnancy and Lactation

During pregnancy, an adequate supply of vitamin D is especially important, as the maternal serum concentration of 25(OH)D influences the fetal 25(OH)D concentration [9, 15].

The vitamin D concentration in breast milk is correlated with the mother's supply of vitamin D [15, 16, 34]. However, very high maternal intake of up to 160 μg per day would be necessary to influence the breast milk's vitamin D content [17, 35]. Because the side effects of very high vitamin D intake are not well known [36], such a high vitamin D intake is not recommended. Thus, the estimated value of adequate vitamin D intake with missing endogenous synthesis during pregnancy and lactation is set to 20 μg per day, as in adolescents and adults.

Contribution of Endogenous Synthesis to Vitamin D Supply

Vitamin D synthesis in the skin is determined by geographic, climatic and cultural factors, including latitude, season, time of day, sunshine, clothing and time spent outdoors. Other influences include the use of sunscreens, skin pigmentation and skin thickness; the latter decreases with increasing age [37–39].

During the summer months, it is possible to achieve the desired 25(OH)D serum level through endogenous synthesis [40]. However, in Germany, the UV Index[1] is lower than 3 for about 6 months of the year and therefore sufficient vitamin D synthesis is not guaranteed [41]. Exposure of the body in swimwear to the minimal erythema dose of sunlight, that is the UV dose that causes just visible reddening of the skin, is estimated to be equivalent to an oral intake of about 250–635 μg of vitamin D [40]. Because of this, some authors recommend that adults at a geographic latitude of 50–75 degrees N should expose a quarter of their body surface (face, hands and parts of arms and legs) to the sun daily between 12 and 3 p.m. for the following times: June to August, skin type I (skin types according to Fitzpatrick [42]), 5–10 min; skin type II, 10–15 min; March to May, skin type I, 10–20 min; skin type II, 15–25 min; September to October, skin type I, 10–20 min; skin type II, 15–25 min. From 10 a.m. to 12 p.m. and from 3 to 6 p.m., the exposure time can be doubled [43]. According to a US study, from April to October, an individual with skin type III in Boston (Boston is at a similar latitude to Barcelona, i.e. 42nd degree of latitude) has to stay in the sun for 3–8 min at noon, exposing a quarter of the body surface, to produce 10 μg of vitamin D [44].

The contribution of endogenous synthesis to vitamin D supply through UVB light exposure, especially during physical activity outdoors and with sufficient areas of un-

[1] The UV Index is the internationally agreed unit for the highest intensity of sunburn-causing UV radiation from the sun during the day on a horizontal plane. The higher the UV Index, the sooner sunburn can occur in unprotected skin. A UV Index of 3–5 is regarded as medium irradiance. The UV Index in the equatorial region is about 12 at sea level with a clear sky; in Germany during summer it is up to 8 (www.bfs.de/de/uv/uv2/uv_messnetz/uvi, accessed 15 February 2012).

covered skin, has to be investigated further. On the one hand, UVB exposure is necessary for vitamin D synthesis, while on the other hand it increases the risk of skin cancer. For this reason, an increased use of sunscreen products has been recommended [41]. However, the application of day creams with UV protection factor and sunscreens significantly reduces vitamin D synthesis in the skin [45]. An appropriate balance of UV exposure is necessary to minimize the risk of skin cancer while using UVB light for the induction of endogenous vitamin D synthesis [46].

Ensuring a Sufficient Vitamin D Supply

Vitamin D supply is characterized by the 25(OH)D serum concentration, which reflects both vitamin D intake and endogenous synthesis. An adequate vitamin D supply is achieved by the estimated value of adequate vitamin D intake in the absence of endogenous synthesis for the relevant age groups.

In Germany, the typical dietary intake of vitamin D is 1–2 μg per day in children [5]; in adolescents and adults, it is 2–4 μg per day [4]. In the absence of endogenous synthesis, this quantity is insufficient to reach the estimated value of adequate vitamin D intake that ensures the desired 25(OH)D serum concentration of at least 50 nmol/l. The difference between dietary vitamin D intake through habitual diet and the reference intake value has to be covered by endogenous synthesis and/or additional intake of vitamin D. With frequent exposure of uncovered skin areas (face, hands and parts of arms and legs) to sunlight, the desired 25(OH) serum concentration can be achieved without using vitamin D supplements. Individuals who spend little time outside in the sun or fully cover their skin when they go outside as well as individuals with darker skin types may be in need of a vitamin D supplement to ensure the desired 25(OH)D serum concentration.

Among individuals 65 years and older, there is greater need to take a vitamin D supplement because the vitamin D synthesis capability of the skin decreases significantly with increasing age and may be reduced by 50% [47]. In addition to the age-related reduction of skin thickness [38], a lower 7-dehydrocholesterol content is regarded as a possible reason for reduced vitamin D synthesis in aged skin [47]. The contribution of endogenous synthesis is further reduced if people stay inside most of the time, thereby reducing UVB exposure, which is often the case especially among chronically sick elderly people in need of care with restricted mobility (nursing home residents, geriatric patients).

For rickets prophylaxis, the estimated value of adequate vitamin D intake for breastfed infants and infants who are not breastfed is achieved through administration of vitamin D supplements from the first week of life to the end of the first year of life. This administration is independent of endogenous vitamin D synthesis and vitamin D intake through breast milk and infant milk formulas. The prophylaxis should be continued in the second year of life during the winter months [13]. It is possible that daily intake is above the estimated value for vitamin D in a diet with industrially manufactured infant milk and additional use of a vitamin D supplement, but in general the tolerable upper limit of 25 μg per day for infants is not exceeded.

Other Preventive Aspects

In addition to the associations mentioned above between vitamin D supply and falls, fractures and all-cause mortality among the elderly (see estimated value for adults from 65 years of age), the risks of cancer, type 2 diabetes mellitus, hypertension and cardiovascular diseases were also investigated in the DGE's critical review [1]. In the derivation of the present reference values for nutrient intake, results were only included if the evidence regarding an association with the risk of disease was judged to be 'convincing' or 'probable'[2].

There is 'probable' evidence that there is no association between the supply of vitamin D and the risk of cancer of the prostate, pancreas, endometrium, esophagus, stomach, kidney and ovary and non-Hodgkin lymphoma. There is 'possible' evidence that there is an increased risk of pancreatic cancer at very high 25(OH)D serum concentrations.

For the other diseases considered (colon cancer, breast cancer, all cancer sites, cardiovascular diseases, type 2 diabetes mellitus and hypertension), the evidence regarding an inverse association or lack of an association with vitamin D supply was judged to be 'possible' or 'insufficient'. Therefore, preventive effects regarding these diseases have yet to be confirmed. The US Institute of Medicine reached similar conclusions regarding the association between vitamin D intake and the risk of the chronic diseases investigated [49].

[2] The methodological approach for evidence judgement has been described in detail in German in the guidelines of the German Nutrititon Society (www.dge.de/leitlinie). The evidence-based guideline regarding carbohydrate intake has also been published in English [48].

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