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Dr Rolf Vollmer

First Vice President and Treasurer of DGZI

The right measures at the right time

It was certainly one of the more memorable press conferences in recent dental history that Henry Schein held online on late Thursday afternoon at the end of February. Stanley M. Bergman, chairman of the board and CEO of Henry Schein, elaborated on questions about moral duties and entrepreneurial responsibility in times of a global health crisis. All over the world, people are losing trust in their governments, according to Bergman. It has become apparent that businesses are able to react more swiftly to the challenges posed by the pandemic than are governmental institutions owing to their innovation strength and flexibility. Procurement of validated personal protective equipment and especially vaccine development come to mind here. Bergman spoke in favour of global efforts to improve material and infrastructural requirements of healthcare systems to better fight the current and future pandemics.

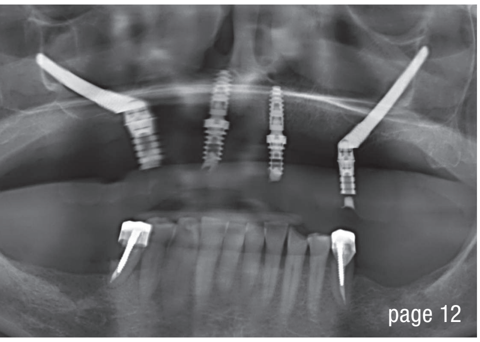
In Germany, political entities and expert dental associations quickly switched to crisis mode, implementing improved hygiene guidelines in order to maintain dental care during lockdown. In an unprecedented response, it was the dental practices themselves who streamlined their patient management, readjusted their already outstanding hygiene protocols and implemented infection protection in shift operations, and thus strongly consolidated patients' trust in dental care. In doing so, Germany-based dentists set an international example.

The latest numbers from the German statutory occupational accident insurance association for non-state healthcare and welfare institutions in the Berufsgenossenschaft für Gesundheitsdienst und Wohlfahrtspflege (BGW) prove that, not only patients, but also practice staff are well protected against infections by consistent hygiene measures. In 2020, the BGW recorded 19,774 reportable occupational suspected cases of SARS-CoV-2—only 85 of which were related to the dental profession. Of course, these figures only hold true for Germany. Nevertheless, they bolster dental offices worldwide, because they indicate that, for dentists and their staff, a sustainable way out of the crisis with comparatively few infections is possible by appropriate crisis management in combination with a high standard of hygiene.

In this spirit, I wish you pleasant reading of the new implants—**international magazine of** oral implantology, continuously safe practice management and a great deal of courage to support your patients. After all, implantology is an integral part of sustainable healthcare!

Yours,

Dr Rolf Vollmer



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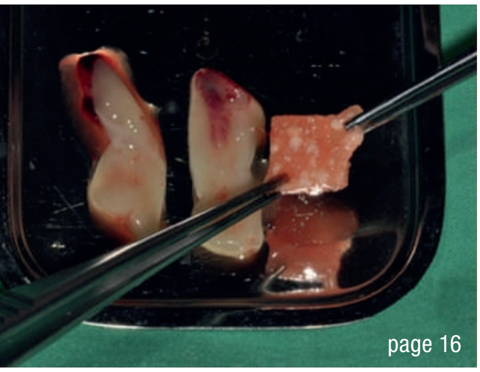

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The key role of vitamin D in immune health and regeneration

The evidence for supplementation

Prof. Shahram Ghanaati, Dr Karl Ulrich Volz & Dr Sarah Al-Maawi, Germany & Switzerland

A healthy immune system is the basis of general good health and a good immune defence. It has been proved that individual habits, nutrition and the environment have an influence on our health.[1] A balanced and healthy diet in particular is the key to a healthy human body. An unbalanced diet can seriously impair the immune system and increase the risk of chronic disease as a result.[1] In the last decade, chronic diseases such as diabetes mellitus, obesity and cardiovascular disease have surged sharply in various countries. A major reason for this is an increasingly unhealthy living environment and increasingly unhealthy lifestyle choices, especially in industrialised countries.[2] The role of food components and especially vitamins has become increasingly important in various areas. In 1928, the German biochemist Adolf Windaus was awarded the Nobel Prize in Chemistry for his work on the correlation between sterols and vitamins, which sparked further research interest in vitamin D.[3]

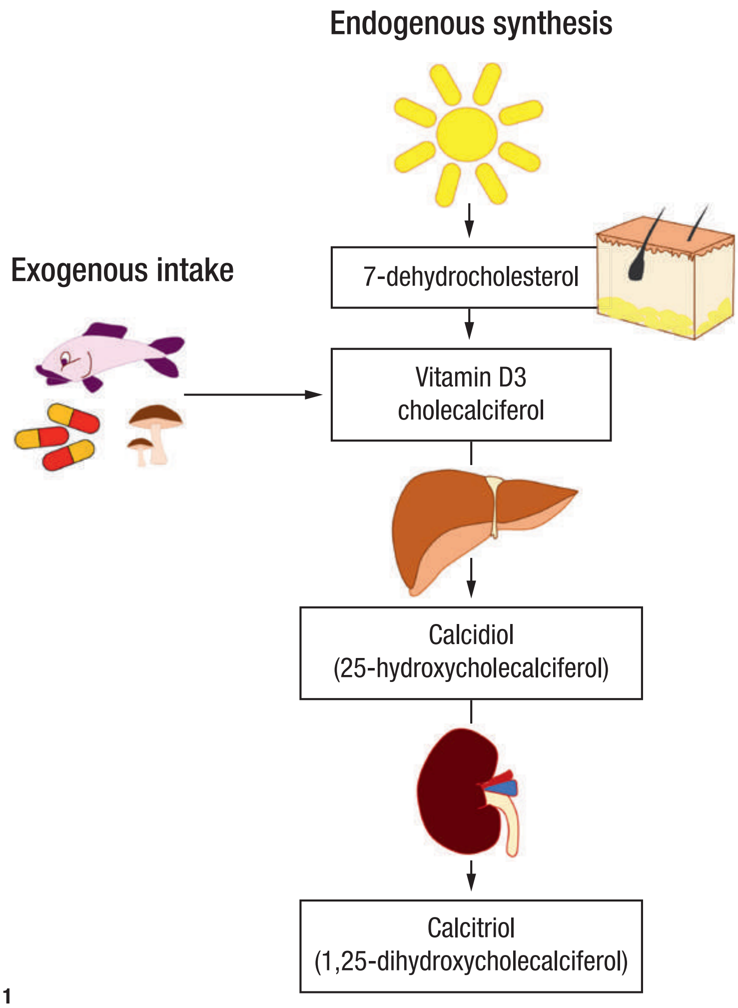

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Fig. 1: Diagram for endogenous synthesis and exogenous vitamin D3 intake.

Vitamin D can be produced in a physiological way in the human body. Sunlight is essential for this endogenous synthesis, which takes place primarily in the skin, where 7-dehydrocholesterol is converted into cholecalciferol (vitamin D3) by UVB rays. In order to reach its biologically active form, cholecalciferol undergoes further conversion steps in the liver (calcidiol) and in the kidney (calcitriol). The latter is the biologically active form of vitamin D and acts as a transcription factor. After binding to the vitamin D receptor, calcitriol regulates the expression of various proteins in the cell. The physiological mode of action of calcitriol therefore resembles that of a hormone and not that of a vitamin. That is why vitamin D, as a precursor of calcitriol, should rather be regarded as a prohormone (Fig. 1).[4,5] The connection between vitamin D and parathyroid hormone was recognised shortly after its discovery. Within this context, the regulatory effect of vitamin D on the mineral balance of the body and in particular the regulation of calcium and phosphate levels was emphasised.[6–8] Furthermore, it was established quite early on that vitamin D plays an important role in mineralisation and bone formation. Consequently, many studies have focused on the influence of vitamin D on skeletal health and the treatment of diseases such as osteoporosis. These findings have contributed to vitamin D being primarily associated with bone health in the public perception.

However, some studies have shown the positive effect of vitamin D on the immune system too and thus on the general health of the body. Several studies have shown that vitamin D has a preventive effect on chronic diseases such as diabetes mellitus, hypertension and cardiovascular disease.[9] Studies also report its potential anti-inflammatory and antiviral effects.[10] In this context, it has been shown that vitamin D supplementation in pupils could reduce the incidence rate of influenza virus infection.[11] These rather new findings and the immunomodulatory effects of vitamin D demonstrate the importance of maintaining healthy vitamin D levels in the body. Since endogenous vitamin D synthesis is compromised by relatively short exposure to sunlight in most countries, the need for exogenous supply is becoming increasingly important. However, the intake of vitamin D through food seems to be insufficient in the general population, which has contributed to a global vitamin D deficiency pandemic.[12] This pandemic has already been documented and reported in numerous studies in various countries.[13] Nevertheless, its importance is still mostly under-estimated in most countries.

The concept of supplementation with vitamin D preparations was first introduced in the 1940s. Today, 90 years later, there are still no uniform recommendations regarding the dose to be taken. One of the reasons for this is the historical development and the association of vitamin D with bone health and the new knowledge about its further extensive capabilities. Although there is a growing amount of data on the non-skeletal effects of vitamin D and its preventive role in many chronic diseases, current dose recommendations are still based solely on bone requirements. Another issue is the difficulty in standardising methods for the determination of serum vitamin D levels. This review therefore focuses on the non-skeletal effects of vitamin D and its supplementation dose based on randomised controlled clinical trials. It provides an overview of the new findings and treatment protocols.

Immune system booster in the case of chronic and infectious disease

There is increasing interest in the study of the immune system-supporting mechanisms of vitamin D. Interestingly, the majority of body cells express vitamin D receptors on their surfaces, which emphasises the multimodal action of vitamin D. Owing to its regulatory effect, the active form of vitamin D as a hormone can intervene in the synthesis of various cytokines and regulate them according to their condition.[14] It has been shown that vitamin D inhibits the production of pro-inflammatory cytokines, whereas it up-regulates the synthesis of anti-inflammatory signal molecules.[5] In this way, it exerts its immunomodulatory effect and supports the differentiation of lymphocytes into Th2 cells and regulatory T cells.[14] This could explain its potential preventive influence in chronic and infectious diseases. However, these mechanisms of action still remain largely unexplained for the respective indications.

The correlation between vitamin D levels and the prevalence of various chronic diseases has been shown in several clinical studies. A meta-analysis of 25 prospective cohort studies has shown that low vitamin D levels increase the risk of developing cardiovascular disease. In about 10,000 patients, the risk of cardiovascular disease was about 44 % higher than in people with healthy vitamin D levels.[15] Another study showed a correlation between vitamin D levels and the development of hypertension. It examined 8,155 patients suffering from hypertension and vitamin D deficiency. After the vitamin D deficiency had been eliminated, 71 % of the patients no longer showed any symptoms or had measurably high blood pressure.[16] A positive influence of vitamin D has also been demonstrated in the development of Type 2 diabetes mellitus. It was shown that the number of patients in a prediabetic stage and with a vitamin D deficiency was significantly lower than in the untreated group, once the vitamin D deficiency had been eliminated.[17]

Furthermore, the potential of an anti-infectious or antiviral effect of vitamin D has been increasingly investigated in recent years. As a result, vitamin D has gained greater significance as a preventive or adjuvant therapy.[11,18] A systematic review has shown that a vitamin D deficiency is associated with a higher viral load in hepatitis B patients.[19] Furthermore, it was shown that vitamin D can inhibit a herpesvirus infection through its anti-inflammatory and supportive defence effect.[20] In addition, studies have shown that vitamin D supplementation reduces the prevalence of influenza infections during influenza outbreaks.[21] Another meta-analysis showed that the number of certain vitamin D receptor polymorphisms involved in processing of vitamin D correlates with an increased risk of a viral infection. Based on the vitamin D-mediated improved immune defence and its potential role as an antiviral agent, its importance in the prevention of viral diseases is increasingly being investigated. Especially in the COVID-19 pandemic, vitamin D supplementation can play an important role in preventing and defeating infection.[22]

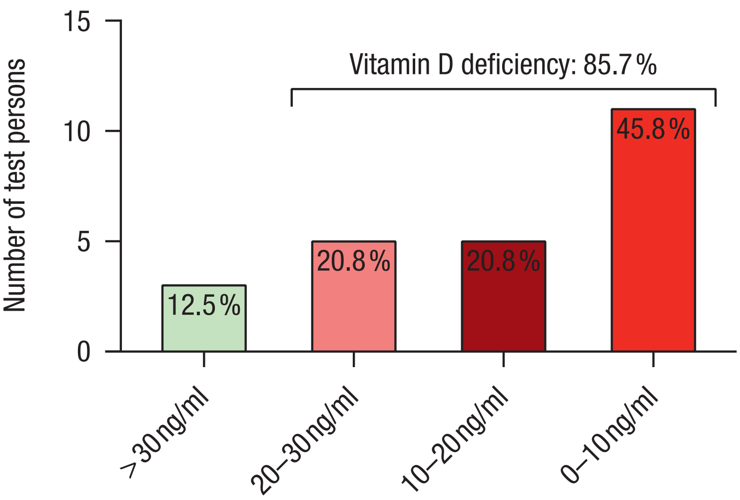

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Fig. 2: Distribution of vitamin D levels according to a pilot study conducted by the Clinic for Oral and Maxillofacial Plastic Surgery at Goethe University Frankfurt am Main.

Determination of vitamin D levels and definition of hypovitaminosis

Vitamin D is a lipophilic molecule that is transported in the blood by carrier proteins. Approximately 80 % of these molecules are bound to the vitamin D binding protein in this manner. A further 10–15 % are bound to albumin and the rest circulates freely in the blood. The determination of the vitamin D level as part of a routine examination involves measuring the total concentration of all these forms. The 25(OH)D serum concentration is widely recognised as a reliable marker of vitamin D levels.[12] Similar to other vitamins and blood components, the vitamin D concentration is usually expressed in nanograms per millilitre (ng/ml) or in nanomoles per litre (nmol/l). Both units are used, depending on the individual testing laboratory. Here, it must be noted that 1 nmol/l equals 0.4 ng/ml. The definition of a healthy vitamin D level and thus hypovitaminosis is a matter of much debate. In the literature, a vitamin D level of less than 30 ng/ml (75 nmol/l) is considered a vitamin D deficiency (hypovitaminosis).[13,19,23,24] In various countries, studies have reported a general vitamin D deficiency. Observational studies have documented that the prevalence of vitamin D levels of below 20 ng/ml (50 nmol/l) is as much as 24 % in the US, 37 % in Canada and 40 % in Europe.[13,24] The German Robert Koch Institute reported that 58 % of 18- to 79-year-olds in Germany have a level of below 20 ng/ml (50 nmol/l).[25] This vitamin D deficiency pandemic was recognised as such several years ago. However, not much has been done in terms of supplementation and defining a sufficient dose. A pilot study examined the vitamin D levels of medical staff in the clinic for oral and maxillofacial plastic surgery at Goethe University in Frankfurt am Main in Germany. Out of 24 participants, 85.7 % had a vitamin D deficiency with a value below 30 ng/ml, whereas 45.8 % even had a value of below 10 ng/ml (Fig. 2). It is important to emphasise that a healthy vitamin D value is considered to be between 40 ng/ml and 60 ng/ml.

Current guidelines for vitamin D supplementation

Given that, in most cases, endogenous synthesis of vitamin D is insufficient owing to limited exposure to sunlight, the body's vitamin D intake should also come from food or dietary supplements. The amount of vitamin D absorbed can be expressed in two units: micrograms (µg) and international units (IU). One microgram equals 40 international units (1 µg equals 40 IU). These units must be considered when administering vitamin D. Since in most cases vitamin D intake via food is insufficient for the body's needs, supplementation with vitamin D preparations is an utmost necessity. In the literature, the current recommendations for doses to be administered are largely inconsistent and are mainly based on the estimated requirements of maintaining optimal bone health. The recommendations range from 400 IU/day to 4,000 IU/day. The European Food Safety Authority recommends a dose of 600 IU/day for healthy adults.[22] A similar recommendation, a dose of 400 IU/day, has been published by the Scientific Advisory Committee on Nutrition in the UK.[26] The Institute of Medicine Committee in the US recommends a dose of 600 IU/day for adults under 70 years of age and a dose of 800 IU/day for those over that age.[27] The American Association of Clinical Endocrinology recommends a dose of 1,000–4,000 IU/day.[28] The recently updated reference values of 2012 from the German

Category	Dose	Administration duration	Initial concentration	Targeted concentration	Side effects
Prevention in pupils[21]	1,200 IU/day	12 months	Not specified	Not specified	None
Cancer, cardiovascular disease[30]	2,000 IU/day	12 months	29.8 ng/ml	41.8 ng/ml	None
Diabetes mellitus[17]	4,000 IU/day	12 months	28.0 ng/ml	52.3 ng/ml	None
	4,000 IU/day	24 months	28.0 ng/ml	54.3 ng/ml	None
Ventilated patients in intensive care[31]	50,000 IU/day	5 days	23.2 ng/ml	45.0 ± 20.0 ng/ml	None
	100,000 IU/day	5 days	20.0 ng/ml	55.0 ± 14.0 ng/ml	None
Test persons with a vitamin D deficiency[32]	25,000 IU/fortnight	2 months	7.6 ng/ml	19.0 ng/ml	None
	25,000 IU/week	1.5 months	8.0 ng/ml	25.0 ng/ml	None
	25,000 IU/week	2 months	8.4 ng/ml	35.6 ng/ml	None
Test persons with a vitamin D deficiency[33]	1,000 IU/day	5 months	28.8 ng/ml	33.6 ng/ml	None
	5,000 IU/day		27.0 ng/ml	64.0 ng/ml	None
	10,000 IU/day		26.0 ng/ml	89.6 ng/ml	None
Breast cancer patients with bone metastasis[34]	7,000 IU/day	4 months	< 20.0 ng/ml	Not specified	None
Psychiatric clinic[24,35]	5,000 IU/day	12 months	24.0 ng/ml	68.0 ng/ml	None
	10,000 IU/day	12 months	25.0 ng/ml	96.0 ng/ml	None
Test persons with a vitamin D deficiency[36]	100,000 IU/month (3,000 IU/day)	36 months	24.4 ng/ml	54.0 ng/ml	None
Multiple sclerosis[37]	20,000 IU/day	12 months	21.6 ng/ml	44.0 ng/ml	None
Multiple sclerosis[38]	50,000 IU/week (7,142 IU/day)	6 months	15.3 ng/ml	33.7 ng/ml	None
Asthma, rheumatic arthritis, rickets, tuberculosis in the 1930s and 1940s[24,39]	60,000–600,000 IU/day	Not specified	Not specified	Not specified	Hypercalcaemia as a result of overphysiological vitamin D concentrations

Table 1: Overview of the vitamin D doses administered in selected randomised clinical studies.