VITAMIN D - "SOLAR VITAMIN"

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SUMMARY

The discovery that sunlight can cure rickets was first scientifically confirmed in 1919. Shortly thereafter, in 1924, it was found that inactive lipids in the diet and skin are converted into antirachitic substances under the influence of UV light. Vitamin D (Vit D), also known as the "sunshine vitamin," was first identified in 1931. In recent decades, it has regained the focus of interest among the broader scientific community and dermatologists. Specifically, certain dermatoses have been associated with low Vit D levels, leading to its supplementation in patients. On the other hand, some dermatoses worsen with sun exposure, necessitating strict avoidance of sunlight and the therapeutic use of Vit D preparations. We are witnessing a growing number of cases of melanoma and non-melanoma skin cancers, with excessive sun exposure being the primary etiological factor in most cases. This paper provides a literature review on the historical discovery of Vit D and presents findings from studies examining Vit D levels not only in various dermatoses but also in other diseases. The number of studies, as well as the spectrum of diseases in which the role of Vit D is being investigated, continues to increase.

Keywords: Vitamin D, sunshine vitamin, antirachitic substance, calcium, phosphorus, skin.

SRPSKI

VITAMIN D- "SUNČANI VITAMIN"

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SAŽETAK

Da sunčeva svetlost može izlečiti rahitis prvi put je naučno otkriveno 1919. godine. Uskoro, 1924. godine utvrđeno je da se inaktivni lipidi u ishrani i koži pod dejstvom UV svetla pretvaraju u antirahitične supstance. Vitamin D (vit D), takođe poznat kao "sunčani", prvi put je otkriven 1931. godine. Ovaj vitamin se u poslednjim decenijama ponovo nalazi u žiži interesovanja i šire naučne zajednice i dermatologa. Naime, postoje dermatoze kod kojih je utvrđen nizak nivo Vit D, i kod pacijenata se primenjuje njegova suplementacija. Sa druge strane, postoje dermatoze koje se pogoršavaju sa izlaganjem sunčevom svetlu, pa im se zabranjuje izlaganje suncu. Kod njih se u terapijske svrhe moraju primeniti preparati Vit D. Svedoci smo sve većeg broja obolelih od melanomskih i nemelanomskih karcinoma kože. Kod većine njih etiološki agens je prekomerno izlaganje suncu. U ovom radu iznosimo pregled literature u vezi istorijata otkrića Vit D i rezultate studija ispitivanja novoa Vit D ne samo kod različiti h dermatoza, već i drugih bolesti. Studija je sve više, kao i spektra bolesti kod kojih se ispituje uloga Vit D. Tako da je Vit D sa pravom ponovo u žiži naučnog interesovanja.

Ključne reči: Vitamin D, sunčani vitamin, antirahitična supstanca, kalcijum, fosfor, koža.

INTRODUCTION

History

The first scientific discoveries related to the antirachitic effect of sunlight date back to 1919, as noted by Bergqvist and Ezzedine. A few years later (1924), it was discovered that inactive lipids in the diet and skin could be converted by UV light into substances with antirachitic effects (1). Vitamin D (vit D), also known as the "sunshine vitamin," was first identified in 1931. In recent decades, this vitamin has once again become a focal point of interest for the broader scientific community and dermatologists (1, 2, 3, 4).

The primary source of vitamin D is skin exposure to sunlight and the action of ultraviolet B (UVB) rays, accounting for over 80% of the total vitamin D produced. Exposure of even a small skin area to UVB rays is sufficient for vitamin D synthesis. There are only a few natural sources of vitamin D: cod liver oil, cheese, mackerel, salmon, egg yolk, beef liver, and tuna (3, 5). Supplementation through external intake of vitamin D can be achieved via various supplements or medications, as well as cosmetic products, primarily in the form of oil-based solutions (alcoholic, sucrose, or glycol types) and capsules for external use (5, 6). Maintaining higher serum vitamin D levels significantly improves the prognosis of numerous systemic diseases. However, determining the necessary concentration is challenging due to various factors affecting absorption (7).

Externally or internally applied vitamin D supplementation is highly beneficial for sensitive, capillary, and mature, aging skin. Studies to date have shown polymorphisms in vitamin D receptors, which are significantly more common in patients with atopic dermatitis. These findings suggest a crucial role of vitamin D in the pathogenesis of the disease. Additionally, experimental research conclusions indicate that the human antimicrobial peptide LL-37 is often insufficiently expressed in patients with atopic dermatitis. The deficiency of this peptide disrupts the re-epithelialization process. Clinical studies confirm that vitamin D supplementation increases LL-37 expression in these patients and reduces disease severity (5, 6).

Since obtaining sufficient amounts of vitamin D solely from natural dietary sources has proven inadequate, many countries have begun fortifying foods with vitamin D, particularly orange juice, milk, yogurt, and cereals. Additionally, various forms of vitamin D supplements are widely available over-the-counter in the form of vitamin D3 and D2, with or without calcium, at affordable prices. Vitamin D supplements also safely increase serum vitamin D levels, although not as effectively or quickly as sunlight exposure (3).

Synthesis of Vitamin D and Its Metabolites

The function of keratinocytes in relation to vitamin D is unique because they not only serve as the primary source of vitamin D for the body (containing the precursor 7-dehydrocholesterol (7-DHC)), but they also metabolize the produced vitamin D into active metabolites through enzymatic mechanisms. This process is referred to as the photoendocrine system of vitamin D. It should be emphasized that vitamin D itself regulates the proliferation and differentiation of keratinocytes (1,7).

From the vitamin D precursor, 7-DHC, exposure to UVB rays of shorter wavelengths opens the B-ring of the steroid, forming previtamin D3. After thermal isomerization is completed, cholecalciferol (vitamin D3) is formed. Two separate hydroxylation reactions occur to produce the active form of vitamin D, 1,25-dihydroxyvitamin D (1,25(OH)D). The first hydroxylation reaction takes place in the liver, resulting in 25hydroxyvitamin D (25(OH)D), the primary circulating form of vitamin D. Its concentration can be measured in serum to determine vitamin D status. The second hydroxylation reaction occurs predominantly in the kidneys, although many other cells, such as keratinocytes, use the same enzymes to produce 1,25(OH)D. The kidneys facilitate the uptake of 25(OH)D3 using a vitamin D-binding protein. If glomerular filtration decreases due to chronic kidney disease, serum vitamin D levels also decline. 25(OH)D regulates cell proliferation, immune response, and serum calcium and phosphorus levels. Inhibition of cAMP protein 1,25(OH)2D3 enhances the production induced by growth of mycobacteria (7,14,15).

Apart from cholecalciferol (vitamin D3), vitamin D is also available as ergocalciferol (vitamin D2). Its hormonal role is expressed as dihydroxycholecalciferol (calcitriol) (16). Sun exposure provides vitamin D in the form of D3. Dietary sources can supply both forms, which are officially considered equivalent and interchangeable, though this is only partially accurate. D2 and D3 differ in their efficacy in raising serum 25-hydroxyvitamin D levels, as the metabolites of vitamin D2 do not bind to the vitamin D-binding protein in plasma with the same efficiency, and this ability is reduced. Additionally, vitamin D2 has a non-physiological metabolism and a shorter shelf life. However, in current practice, vitamin D preparations are more frequently used in the form of vitamin D2 rather than vitamin D3 (3).

In addition to the production of previtamin D3, further UVB exposure leads to the production of two isomeric forms of vitamin D, which do not affect calcium homeostasis. During UVB exposure, the skin converts approximately 15% of 7-dehydrocholesterol into previtamin D3. Studies have shown that UVB exposure of the skin not only results in the production of previtamin D3 but also generates two isomers of vitamin D and some other metabolites if UVB exposure continues. Importantly, none of these metabolites have activity in calcium modulation, ensuring the safe production of vitamin D under UVB radiation. Any additional previtamin D3 is broken down. The formation of vitamin D3 in the skin offers multiple benefits to the body, even from the isomerized degradation metabolites, compared to dietary supplementation of vitamin D3. It is now known that the effects of these degradation photoproducts may be beneficial in the prevention of tumors (including skin cancers) and their genesis, as well as exerting antiproliferative effects on keratinocytes (6,7). According to the Clinical Practice Guidelines of the US Endocrine Society, vitamin D deficiency is defined as serum 25-OH D levels <50 nmol/L (below 20 ng/mL). Vitamin D insufficiency is defined as serum 25-OH D levels between 50 and 75 nmol/L (21-29 ng/mL) (2). The gold standard for analyzing vitamin D status is the measurement of its main circulating metabolite, 25-hydroxyvitamin D3 (25(OH)D3), using high-performance liquid chromatography (HPLC) or liquid

chromatography-tandem mass spectrometry (LC-MS/MS) (17).

Roles of Vitamin D

Vitamin D is a liposoluble steroid hormone with a key role in calcium and phosphate homeostasis and maintaining bone health by promoting the absorption of calcium and phosphorus and ensuring their adequate concentrations. Vitamin D is essential for the growth and remodeling of osteoblasts and osteoclasts, leading to a positive correlation between vitamin D status and bone health (18). Endogenously produced 1,25(OH)D maintains calcium homeostasis, as osteoblasts require calcium ions for collagen matrix synthesis. Vitamin D deficiency is associated with elevated parathyroid hormone levels, which help maintain calcium balance in the serum and bones. Parathyroid hormone extracts calcium from the bones into the bloodstream and expels phosphorus through urine. Hypervitaminosis D can result in hypercalciuria and hypercalcemia, accompanied by symptoms such as weakness, headaches, confusion, and polyuria. Although achieving hypervitaminosis D requires a high intake of vitamin D, toxicity is rare because the kidneys perform the final regulatory mechanism during hydroxylation. However, the effects of vitamin D are not limited to bones. It acts on nearly all organ systems in the human body. Vitamin D is essential for other physiological functions and is considered a crucial component for muscle performance and immunity (2, 3, 5, 7, 8, 9, 10). Given its role in regulating numerous cellular functions, vitamin D plays a versatile role in almost all organs and organ systems, influencing the cardiovascular, neurological, immune, and endocrine systems (parathyroid glands, pancreas), as well as reproductive organs (placenta, uterus, ovaries, and testes). Vitamin D is significant in the development of autoimmune diseases and infections, playing a crucial role in defense against opportunistic infections (1, 11, 12, 13). Vitamin D deficiency increases the risk of ischemic stroke and is also associated with type 2 diabetes (14). Recent meta-analyses suggest that several diseases, including type 2 diabetes, cancer, depression, COVID-19, and acute respiratory infections, can be mitigated or prevented with vitamin D supplementation. Thus, vitamin D can serve as a dietary-based prevention and treatment strategy. For vitamin D to exert its effects, it must bind to its nuclear receptor (VDR), which is distributed across most human tissues. Research has shown that VDR also functions as a tumor suppressor, and inhibition of its expression is associated with melanoma progression (7).

Factors That Reduce Vitamin D Production

Several factors can diminish vitamin D production. Skin type

according to the Fitzpatrick scale can negatively affect the ability to maintain vitamin D production. It has been observed that as the Fitzpatrick skin type progresses from I to VI, from lighter to darker skin, vitamin D production decreases. Based on this, it can be concluded that darker skin requires higher doses of UV radiation to produce the same level of vitamin D that lighter skin generates. This is likely because the higher melanin content characteristic of darker skin provides greater protection from UV radiation compared to lighter skin. Fitzpatrick skin types I and II have lower minimal erythema doses (the amount of UV radiation required to cause sunburn) compared to types V and VI. As a result, UV radiation penetrates more effectively, stimulating greater vitamin D production in skin types I and II. Supporting this, an experimental study showed that 30 minutes of exposure in lower Fitzpatrick phototypes converted 3% of skin 7dehydrocholesterol (7-DHC) into previtamin D3, while higher Fitzpatrick phototypes converted only 0.3%. This characteristic of lower Fitzpatrick skin types also increases the risk of skin cancer and other UV-induced dermatoses (7).

Some studies have provided interesting data indicating that individuals with higher Fitzpatrick skin types may have vitamin D deficiencies because melanin competes with 7-DHC for UV absorption. On the other hand, individuals with lighter Fitzpatrick skin types can produce more than 50 nmol/L of 25(OH)D from just 30 minutes of daily sun exposure, whereas darker skin may require up to two hours of exposure to achieve the same production level (7).

Other factors that reduce vitamin D production include clothing and avoidance of UV radiation, which should be considered when taking a patient's medical history. Raymond-Lezman and Riskin cite a Turkish study that found women who traditionally cover most of their bodies had severe vitamin D deficiencies compared to women with greater skin exposure to sunlight (7).

Vitamin D3 production depends on the penetration and absorption of UVB radiation, making geographic location an important factor when determining the need for increased vitamin D intake in at-risk populations. In some regions, vitamin D is not produced during winter and spring due to latitude, regardless of skin type. Additionally, cloud cover significantly reduces UV radiation absorption, leading to vitamin D deficiency.

With the rise of air pollution following the industrial revolution, rickets incidence increased significantly. The same authors referenced a study conducted in Delhi that showed lower 25(OH)D levels in children as pollution levels rose. Similarly, in the United Kingdom, vitamin D deficiency was found to be most common in adolescent girls, likely due to reduced outdoor time. Interestingly, natural light passing through windows does not initiate vitamin D synthesis, but UV tanning beds have been shown to increase vitamin D levels (7).

Vitamin D and Various Disorders and Diseases, with Emphasis on Dermatoses

An increasing number of dermatoses are linked to vitamin D status, particularly atopic dermatitis, psoriasis, vitiligo, and skin cancers (7, 19, 20). Most studies have investigated the efficacy of the combination of calcipotriol/betamethasone dipropionate in various formulations for topical treatment of psoriasis, demonstrating good therapeutic outcomes, improvement in patients' quality of life, and clinical presentation (21, 22, 23, 24, 25).

Like other organs, the skin undergoes a phase of progressive decline in its physiological, morphological, and functional properties during aging. Aging is a natural, genetically predisposed process, but skin functions are essential for homeostasis and survival. The skin is the largest organ in our body. Together with the hypodermis (subcutaneous fat), it serves as both a source and a target organ for several hormones and neuromediators, making it an independent peripheral endocrine organ. It is crucial to emphasize that the skin has the capacity to produce prohormonal vitamin D and transform it into active metabolites. These metabolites can exert various effects on keratinocytes and fibroblasts, the primary skin cells, as well as on immune cells. These effects are mediated through the activation of the nuclear vitamin D receptor (VDR). Vitamin D plays a critical role in skin homeostasis and contributes to its barrier function. As essential components of a functional immune system, active forms of vitamin D modulate skin immunity (7).

Beyond studying vitamin D levels in different dermatoses, research is being conducted in other fields. For example, Riccardi et al. highlight that numerous epidemiological studies have shown that low circulating vitamin D concentrations negatively correlate with skin manifestations and bone abnormalities, significant clinical features of neurofibromatosis type 1 (NF1). The conclusions of these studies are anticipated to evaluate the therapeutic efficacy and role of vitamin D in NF1, based on preclinical and clinical research. Current studies show a clinical correlation between vitamin D status and NF1, providing important insights into the disease's pathogenesis and new possibilities for targeted therapy. Recent findings indicate that vitamin D or its analogs have been used to treat skin and bone lesions in NF1 patients, either alone or in combination with other therapeutic agents (8).

In research by Islam et al. (9), it was emphasized that patients with primary antiphospholipid syndrome had significantly lower serum vitamin D concentrations and poorer clinical parameters. This aligns with findings from studies on systemic lupus erythematosus (SLE) (26, 27).

Based on the above, it is suggested that vitamin D supplementation could benefit patients with primary antiphospholipid syndrome, helping to maintain clinical stability, improve overall health, and potentially reduce disease severity (9).

Vitamin D deficiency is a global health issue affecting individuals of all ages. A variety of factors contribute to deficiencies, with the most important being lack of sun exposure and poor dietary intake. It has been found that the average prevalence of vitamin D deficiency in the US population is 37.5%. This deficiency is associated with various metabolic, neoplastic, and immunological disorders, such as atherosclerosis, diabetes mellitus, autoimmune diseases, and colorectal cancer (2, 17).

Multivitamin supplements may contain either vitamin D2 or D3, but it is a noticeable trend among pharmaceutical companies to reformulate their products and introduce supplements that contain vitamin D in the D3 form, as highlighted by Mostafa and Hegazy (3).

DISCUSSION

It can be said that almost a century has passed since the "discovery" of Vitamin D, first as an anti-rickets substance, and then as a liposoluble vitamin with numerous functions in our body, meaning multisystemic effects, as there is no organ and/or organ system in our body that it does not affect. Since the primary source of this vitamin is the action of UV light, it earned the name "sunshine" vitamin/hormone. Renewed interest in Vitamin D began before the Covid-19 pandemic, and during this pandemic, it seemed to be at the "peak" of attention from both the scientific community and the general public worldwide. It was at the center of both experimental and clinical research in numerous scientific studies around the world, and as the results of these studies were published, knowledge about the role of Vitamin D in various diseases and disorders spread. It is crucial for the homeostasis of calcium and phosphate, maintaining bone health. However, today, the spectrum of diseases associated with Vitamin D deficiency primarily includes skin diseases, autoimmune diseases, neurological disorders, cardiovascular diseases, and mental health issues. Research on the topical application of Vitamin D preparations in the treatment of psoriasis began in the last century. Studies published in 1975 analyzed the therapeutic applications of topically applied Vitamin D preparations. The best results in the topical treatment of psoriasis have been achieved with a combination of Calcipotriol/betamethasone dipropionate in cream or gel formulations. There is significantly less research on the topical treatment of atopic dermatitis. As previously mentioned, for all other dermatoses, oral Vitamin D preparations are recommended. The role of Vitamin D in the skin aging process is also being explored. Numerous studies are still ongoing, so new results are expected. The media has played a significant role in writing about and publishing (marketing) new Vitamin D supplementation products, whether they contain only Vitamin D or are combined with other Recently, products for topical Vitamin components. supplementation, either for therapeutic use in dermatoses (psoriasis) or for slowing the skin aging process, have increasingly appeared. Another important aspect of Vitamin D in dermatology is that some dermatoses worsen with sun exposure, so they should not be exposed to UV rays. Vitamin D preparations must be used for them. However, patients should be regularly monitored, as, as mentioned earlier, there are no universal recommendations, or precisely determined Vitamin D concentrations in the blood of the patient that are best for a specific dermatosis, taking into account factors such as gender, age, season,

etc. We are also witnessing an increase in the number of younger patients with melanoma and non-melanoma skin cancers in the last decade or two. Additionally, a deficiency of Vitamin D has been observed in melanoma patients.

According to Hernigou et al., Vitamin D became one of the most frequently used "medications" in the 20th century, as a substitute for insufficient UVB exposure for people, for various reasons. Although throughout the century, the understanding of Vitamin D metabolism has constantly grown, other diseases and disorders, not just rickets, have emerged before orthopedic surgeons. Recently, studies have been conducted on Vitamin D deficiency as a factor associated with various bone pathologies, such as fractures and prosthetic infections (4).

In the conclusion of their study, Tong et al. emphasize the need for further research to determine how much Vitamin D is necessary to maintain a healthy life. Considering the many factors that affect the amount of Vitamin D produced by UVB radiation, it must be concluded that there is no universal approach for recommendations. If a patient's Vitamin D level is below 16 ng/mL, they are at higher risk for morbidity and mortality. When the Vitamin D level is increased above 20 ng/mL, improvements in clinical condition, patient status, and disease outcomes are observed. The focus of research now also includes many projections for malignancies and high-risk diseases, as results from some studies have shown the benefits of achieving higher serum concentrations of Vitamin D. It is recommended to precisely monitor Vitamin D levels, which can help improve the quality of life for patients, reduce the burden of the disease, and extend the lives of patients. As previously stated, and as Tong et al. repeat, Vitamin D toxicity is very rare. The body has self-regulating mechanisms through the kidneys that function during Vitamin D synthesis induced by UV radiation. Patients should be monitored, and tests should be done to check for hypercalciuria and hypercalcemia with symptoms similar to hyperparathyroid hormone. If neither is present, simply reducing UVB exposure or taking supplementation will result in a reduction in calcium levels (28).

Raymond-Lezman et al. believe that the self-regulating and safe nature of Vitamin D is very important and should encourage individuals to safely increase their UV exposure while also regularly checking their skin. Patients should be educated that they must not allow sunburns to develop and should always use sunscreen as recommended by dermatologists. In this way, higher concentrations of Vitamin D can be achieved while completely reducing the risks associated with UV radiation. When UV light is not available sufficiently due to season or geographic location, Vitamin D supplementation is recommended, which will only benefit health (7).

Various factors are associated with Vitamin D status, especially skin type, gender, body mass index, physical activity, smoking, alcohol consumption, and Vitamin D receptor polymorphism. Patients with photosensitive disorders must avoid sun exposure, potentially leading to a risk of Vitamin D deficiency. It is crucial to emphasize that maintaining Vitamin D levels in the serum within normal physiological ranges is essential for patients with conditions such as atopic dermatitis, psoriasis, vitiligo, polymorphic light eruption, mycosis fungoides, alopecia areata, systemic lupus erythematosus (SLE), and melanoma (5).

It must be emphasized that today a significant portion of the urban population has a Vitamin D3 deficiency, as they do not expose their skin to the sun or spend time outdoors due to air pollution and other reasons, and as the global population ages, they lose reserves of 7dehydrocholesterol in the epidermis due to aging. As previously mentioned, the consequences of Vitamin D deficiency include bone diseases and other health issues such as malignancies, asthma, arthritis, hypertension, osteoporosis, and mental, neurological, and cardiovascular diseases. Symptoms of Vitamin D deficiency may include bone pain and muscle weakness. Vitamin D has significant applications in the cosmetic industry, as the topical use of these cosmetic preparations with Vitamin D prevents photoaging, photodamage, wrinkles, and other skin changes associated with the aging process. Topical Vitamin D preparations are also very effective in the treatment of psoriasis (6). Vitamin D supplementation (either externally or internally) can be extremely beneficial for sensitive, capillary, and mature, older skin, and is increasingly recommended for such patients. Vitamin D receptor polymorphisms are more common in patients with atopic dermatitis, leading to the conclusion of Vitamin D's key role in the pathogenesis of this common skin condition in patients of all ages. The human antimicrobial peptide LL-37 is often insufficiently expressed in individuals with atopic dermatitis, impairing the reepithelialization process. Clinical studies have shown that Vitamin D supplementation increases LL-37 expression in patients and reduces the severity of the disease, though this is still under experimental investigation (5).

Topical Vitamin D analogs exhibit significant anti-inflammatory and antiproliferative effects (inhibition of IL-2, IL-6, IL-8, IFN- γ , and IL-10 secretion, and stimulation of T-cell differentiation). This leads to inhibition of the production of psoriasis and Koebner proteins. A key element of this issue is the connection of Vitamin D's specific metabolism, simply put, with lumisterol or 7-dehydrocholesterol. These are crucial for regulating the skin's protective barrier and controlling immune functions. For Vitamin D3 to be biologically active, it must be activated by cytochrome P450 (5).

Immune-mediated dermatoses are a group of skin diseases, such as: alopecia areata, atopic dermatitis, psoriasis, systemic lupus erythematosus, and autoimmune blistering dermatoses. Vitamin D is known for its classic pleiotropic effects. Results from recent studies have shown that Vitamin D is catalyzed into its biologically active form [1,25(OH)2D], and then, in correlation with its receptor (Vitamin D receptor), plays a crucial role in many pathophysiological processes, including autoimmune and immune-related dermatoses (5).

It is well-known that the world's population is aging, industrial air pollution is high, and the number of smokers is increasing, all of which contribute to Vitamin D deficiency becoming a larger public health issue globally, especially in industrialized countries. Considering the cumulative and dosed effects of smoking on Vitamin D deficiency, the rise in smokers among the younger population is likely to lead to a significant increase in future public health burdens related to osteoporosis and other numerous cardiovascular, pulmonary, infectious, immune, and other diseases. Smoking has a significant negative impact on circulating Vitamin D levels, although this concentration can return to levels similar to those of non-smokers after quitting smoking. Given the harmful effects of smoking on Vitamin D deficiency and its associated consequences on bone health and other systems, preventing Vitamin D deficiency and smoking cessation must be prioritized, and preventive measures (education, flyers, lectures, etc.) should be implemented (10).

CONCLUSION

Given its multisystemic effects in our body, Vitamin D is rightfully at the forefront of interest for scientists, doctors, and the general public. Through various preventive measures, efforts should be made to raise awareness among the average population about the importance of maintaining physiological levels of Vitamin D, particularly among doctors. Dermatologists, in particular, must explain to their patients the impact of this vitamin on the health of our bodies. Dermatologists are already attempting to do this through various actions and activities, and indeed, further efforts are needed to educate as many people as possible, even at the school level. By doing so, we invest in the future of the nation, ensuring that it remains healthy. When diagnosing a dermatological condition, it is important to explain to patients the significance of sun exposure or avoidance, as well as the application of Vitamin D supplements.

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