VITAMIN D
UpDates

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EDITORIAL

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In this issue you will find an update on the relationship between vitamin D and two major topics: autoimmune diseases and pain.
Vitamin D is said to have immunomodulating effects. What does that mean? Trying to provide as simple an answer as possible, I believe that vitamin D's three main immunological functions should be acknowledged: the bactericidal function, the inflammatory response attenuation function and that of promoting immune tolerance [1].
The first role, also in chronological order, is as a bactericide, as was discovered 170 years ago, when cod liver oil was used to treat tuberculosis. Although, the key mechanism was only described by the scientific community 40 years ago with the identification of vitamin D receptors in leukocytes and when it was shown that vitamin D-activating enzymes could also be found in the monocyte-macrophage line. The second function is vitamin D's ability to attenuate the inflammatory response by inhibiting proinflammatory cytokines and by stimulating those with anti-inflammatory action at the level of T lymphocytes, thus reducing possible clinical manifestations of chronic inflammatory diseases or possible damage from "friendly fire". Vitamin D's third important immunological function is how it promotes immune tolerance, by being able to slow down dendrite cell maturation and antigen presentation, as well as by inhibiting the survival, proliferation, differentiation, and antibody production of B lymphocytes.
Hence the pathophysiological rationale for understanding the risk of incurring autoimmune diseases under conditions of vitamin D deficiency also arises. In this regard, as is well known, numerous epidemiological studies have described a high prevalence of vitamin D deficiency in several autoimmune diseases, including above all, multiple sclerosis, type 1 diabetes, psoriasis, Crohn's disease and many rheumatological diseases (especially rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, systemic sclerosis, and lupus). However, these observations were unable to document any certain cause and effect correlation. Long-term longitudinal studies, preferably prospective, which explore the correlation between vitamin D status or vitamin D supplementation and the incidence of autoimmune diseases, are needed to prove this.
As you will read in this issue, it has indeed recently been observed that daily supplementation with 2000 IU of vitamin D was associated with a significant reduction in the risk of incurring autoimmune diseases [2]. This important result confirms the clinical significance of the pathophysiological assumptions, being the causal relationship. It further supports the belief that prevention of vitamin D deficiency can in effect also reduce the risk of autoimmune diseases.
The other contribution in this issue is a review of the possible role of vitamin D in pain, the main clinical expression of many diseases, especially rheumatological and oncological. Here too, the author has first of all taken care to summarise the main physiopathological assumptions that might underlie this finding, specifically identifying them in the presence of certain vitamin D receptors in the neurons of the central and peripheral pathways involved in pain detection and processing. This includes vitamin D's ability to modulate the expression of various pain-related genes, also in the presence of enzymatic activities assigned to vitamin D activation at a neuronal level, and then vitamin D's capacity to interact or interfere with neurotrophic factors or algogenic cytokines or other neuro-immunomodulators.

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Although there is a rationale for expecting a positive effect of vitamin D in pain control, as you will see, the results of the studies conducted to date are inconsistent and discordant. Nevertheless, as the author acknowledges, there are many justifications for such discrepancies. These include the still uncertain definition and determination of what vitamin D deficiency is and its variability, the many genetic polymorphisms that can affect a "functional" vitamin D deficiency as well as different individual pharmacokinetics or pharmacodynamics, personal heterogeneity, and variability in the perception of pain, which tend to compromise any accurate assessments, and which render urgent the search for the biomarkers of pain. Thus, the need for further clinical studies and translational research in this field as well is revealed.

What are your thoughts?
Happy reading!

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