VITAMIN D
UpDates

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EDITORIAL

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Dear Readers,
In this issue, two topics are discussed in depth, as usual by expert Authors who are working on them.
The first topic concerns an update on the possible role of vitamin D in atopic dermatitis. It is known that the skin is a central organ for vitamin D metabolism, representing both the site of its synthesis and a target organ. Vitamin D regulates both the proliferation and differentiation of keratinocytes and it is also involved in regulating the synthesis of ceramides, which are a key component of the corneocyte lipid envelope, thus helping to protect the skin from pathogenic chemical, physical and microbiological agents. Vitamin D also performs several actions on the skin's immune system, including induction of antimicrobial peptide synthesis, inhibition of antigen presentation by Langerhans cells and induction of regulatory T lymphocytes. So, patients with atopic dermatitis show genetic and acquired alterations in the formation and regulation of their skin barrier and a dysregulation in their immune response. Hence the possible role of vitamin D deficiency in the pathogenesis of certain inflammatory and immune-mediated skin diseases such as atopic dermatitis and the opportunity to exclude or treat it in affected patients.
The second topic addressed in this issue concerns recent epidemiological and clinical evidence indicating that some benefits of vitamin D supplementation, whether skeletal or extra-skeletal, may be limited to the daily dosage. Recent studies, including those from our School [1], have in fact shown pharmacokinetic and pharmacodynamic characteristics that justify the preferential choice of a daily supplementation strategy over that of boluses. Indeed, we showed that a daily dose, often considered less functional, is more effective than boluses (with the same cumulative dose) in restoring and increasing normal 25(OH)D levels. The explanation for this phenomenon must be sought in vitamin D's different anabolism-catabolism in relation to its supplementation schedule. Vitamin D boluses rapidly saturate 25-hydroxylase, which is responsible for the conversion of vitamin D_3 and D_2 to 25(OH)D, resulting in the induction of 24-25-hydroxylase, the enzyme responsible for the catabolism of vitamin D to 24-25(OH)D (the inactivated form). In other words, 25-hydroxylase saturation would limit the conversion of cholecalciferol boluses to the semi-active form, resulting in fewer biological effects. The 25(OH) hydroxylase reminds me of an oven where bread is baked daily, which needs a daily supply of flour to maximise production but would not benefit from an intermittent supply of flour, even if in surplus.

However, there is another possible though intriguing motivation for dosing with a daily strategy: the potential extra-skeletal immunomodulatory effect of vitamin D would in fact appear to be attributable to the direct activity of the 25(OH)D precursor, that is, cholecalciferol or vitamin D_3 on immune cells [2]. Actually, after exposure to a foreign pathogen, T lymphocytes express the vitamin D receptor, which, in the presence of adequate levels of vitamin D_3, transduces a signal of lymphocyte proliferation and the activation of adaptive immunity. Therefore, this particular immunological effect seems to be mediated by the "inactive" vitamin D precursor and not by the forms that are biologically active on mineral and bone metabolism. Hence, this effect appears to be independent of 25(OH)D concentrations, but more closely linked to the availability of

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vitamin D_3 in the bloodstream. Consequently, daily doses could have the distinct advantage of maintaining stably high levels of vitamin D in the circulation, whose very short serum half-life, on the order of a single day, is well known. On the other hand, it is also known that many, if not all, cells have the hydroxylase activity required for intracellular activation of vitamin D.

Do you want to bet that we are on the verge of discovering, as recently hypothesised [3], that the serum concentration of cholecalciferol is actually better than that of 25(OH)D in expressing an adequate vitamin D level? Happy reading!

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