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Dear Readers,

In this issue we are returning to the subject of childhood vitamin D deficiency, the prevalence of which has begun to rise again in some countries, as has been documented even in the UK. According to the article by the author whom we asked to prepare an update on this topic, certain risk factors such as ethnic composition and overweight have changed and become more frequent.

Recently, in Europe, there has been an increase in populations with darker skin and different cultural habits such as wearing full-body garments for religious reasons. Both of these factors are known to hinder endogenous vitamin D production by reducing exposure to sunlight. Moreover, the prevalence of overweight has risen to include 30% of the paediatric population. This condition is also a significant risk factor for vitamin D deficiency since it is known that persons with obesity require supplementation with higher doses. Therefore, to provide for adequate bone development, but also plausible extra-skeletal benefits, it should be remembered that it is important to ensure adequate vitamin D status in children during all stages of growth. This requires supplementation, especially in the first years of life, and particularly if the mother was vitamin D deficient during pregnancy.

The author has further emphasised that in a paediatric age it is likely that high bolus doses can induce the expression of catabolic enzymes that inactivate vitamin D, which we also hypothesised based on the results of our recent pharmacokinetics study<sup>1</sup>. Thus, vitamin D supplements should be taken daily rather than in monthly or weekly bolus doses. In an earlier issue of this journal<sup>2</sup>, we also provided pharmacokinetic and pharmacodynamic justification in support of the exclusive benefits, and especially extra-skeletal advantages, conferred by daily administration of vitamin D<sup>3</sup>.

For the other article, I asked the authors to focus on a possible correlation between vitamin D deficiency and complex regional pain syndrome (CRPS), also termed algodystrophy. This is because it was recently shown that patients with distal radius fractures complicated by CRPS had significantly lower plasma concentrations of vitamin D than those who had not experienced this complication. Based on the available evidence, as you will see, the authors acknowledge that vitamin D deficiency may lead to an increased risk of CRPS for essentially two reasons. The first is because deficiency may lead to an increase in fracture events, especially intra-articular fractures, which tend to induce the syndrome, and which can also be due to the associated risk of falling. The second is likely related to the fact that vitamin D deficiency is a predisposing condition for neuroinflammation and proinflammatory immunological status, both of which are involved in the pathogenesis of CRPS.

As evidence of a possible causal link between vitamin D levels and proinflammatory cytokines, some investigations have demonstrated that vitamin D supplementation is able to reduce serum concentrations of TNF- $\alpha$  and IL-6, as well as IL-17<sup>3</sup>. Thus, there arises the

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hypothesis that vitamin D supplementation may contribute to an additional or faster benefit than the recognised approach to treating algodystrophy with neridronate. It is likely that vitamin D supplementation also helps to reduce the side effects of amino-bisphosphonates in the acute phase, since these would be modulated by serum levels of 25(OH)D <sup>4</sup>.

What are your thoughts?

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