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Invited Commentary

Building skeletons during adolescence: what is the target?

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The concept that osteoporosis is a paediatric disease has been popularised over the last 20 years. The basis for this description is that achieving an optimal peak bone mass during adolescence can postpone or prevent clinical osteoporosis in older adults[1]. Although clinical data supporting this hypothesis are very limited, the theory is rational and remains an important approach to evaluation of nutritional intake during childhood and adolescence. Unfortunately, multi-decade long randomised supplementation trials are not practical and we may never be certain how variations in Ca intake during childhood and adolescence affect the risk of osteoporosis in the elderly.

In recent years, there has been an effort to understand the large variability in bone mineral accretion during growth. One key aspect of this variability is genetic variation in Ca metabolism, especially absorption efficiency and urinary excretion. It has long been clear that there are sex and racial differences in the rate at which bone is formed and mineralised. However, the physiological basis for these variations and their magnitude have only recently been systematically investigated. Increased Ca absorption efficiency in Blacks during puberty has been demonstrated as well as differences in bone formation rates among races and sexes[2,3]. Furthermore, the effects of specific genetic polymorphisms on Ca metabolism during adolescence are beginning to be evaluated[4].

Because of the variability in Ca metabolism related to genetics, diet and other factors, it is a challenge to provide estimates for Ca requirements. Currently, available values from the US and Canadian Dietary Reference Intakes provide only a single estimate of Ca requirements at each age, referred to as an adequate intake[5]. As such, there is no mean requirement identified (estimated average requirement; EAR) nor a standard deviation about that mean needed to calculate an RDA[5,6].

To determine an EAR and the variability about that value requires knowledge of the targeted amount of Ca that needs to be retained from the diet for skeletal accretion during growth. Attempts to provide new data to advance this field therefore rely on new data related to identifying this target endpoint and the components (absorption efficiency and excretion) by which one can calculate the amount of intake needed to achieve that target.

The study by Vatanparast *et al.*[7] provides important information regarding the target value for Ca accretion to the skeleton. In this case, the goal was identified as the usual average rate of Ca accretion by the skeleton during adolescence in a longitudinally followed population of adolescents in Canada. The values given are limited, however, by the population studied (Caucasians living in Canada) and may not apply to other population groups or other parts of the world. Furthermore, it must be recognised that a limitation of this approach is that these recommendations assume that the average rate of Ca accretion in the population studied is also the optimal rate of accretion. Making this assumption for adolescents is uncertain if the population is at high risk for long-term bone mineral deficiency.

The substantially lower usual Ca intake of many adolescent females in North America in relation to the calculated requirements both from the study by Vatansparast *et al.*[7] and the current adequate intake for North America[5] leads to uncertainty as to what population should be used to set targeted standards for bone mineral accretion. This situation in which Ca intakes are low relative to recommendations is different in adolescents compared with other age groups. For example, in small children, usual Ca intakes in US and Canadian diets are high relative to recommendations[5,8], and early childhood (about ages of 1–4 years) is a time of relatively slow bone Ca accretion.

Randomised clinical trials looking at long-term bone mineral accretion at different levels of Ca intake would be very helpful in understanding the ultimate goal of peak bone mass. Unfortunately, most randomised Ca supplementation trials were short term and the extremely few long-term trials have been difficult to use in this regard due to methodological limitations. It is likely that short-term trials are inadequate to fully understand the effects of Ca supplementation on peak bone mass. The effects of catch-up mineralisation in late adolescence or early adulthood have been very hard to identify[9].

It is critical to have data from multiple population groups and locations on which to base dietary recommendations, and therefore the data in the paper by Vatanparast *et al.*[7] are important additions to the data available in the mid-1990s. Longitudinal data are preferred to cross-sectional data, although overall differences in the results for peak bone mineral accretion rates are not large. It would be very helpful to have further such data from other countries and other population groups so that the process of determining average rates of bone Ca accretion can be determined for all populations.

The second half of the factorial balance equation, i.e. the amount of dietary Ca needed to meet the targeted

Ca accretion values determined by dual-energy X-ray absorptiometry, is similarly difficult to calculate. There are large differences based on sex, race and pubertal status in how much Ca is absorbed and retained from the diet. Of note is that, in the absence of severe deficiency, it does not appear that vitamin D status is a major factor in the variability in Ca absorption efficiency in adolescents[3,10,11]. Furthermore, estimates of absorption efficiency from available mass and isotopic balance studies are limited by the methodology used to obtain them and by the natural inverse relationship between Ca intake and absorption efficiency that is present in adolescents as well as adults[12]. Calculations using single absorption values, even when derived from multiple sources, may not provide a full picture of Ca absorption efficiency.

Consideration needs to be given of how to use the values for intake guidelines described. For example, Vatanparast *et al.*[7] report an estimated mean Ca intake requirement of 1200 mg/d for boys and 1000 mg/d for girls 14–18 years of age[7]. However, how to use these results is uncertain. For example, given that osteoporosis is much more prevalent in women than in men, is it helpful to recommend a greater Ca intake in adolescent boys than in girls based on these data? Is it possible that one can overinterpret small differences in average requirements over a narrow age group in a way that leads to dietary recommendations that may not reflect goals related to lifelong development of good dietary habits?

It is important to establish a research agenda for the future in this field. Recent studies have shown that dietary factors, such as prebiotics, can enhance Ca absorption in adolescents[13]. Furthermore, the potential for identifying genes that are related to Ca absorption efficiency may allow for true individualisation of recommendations. Population recommendations are certainly necessary. However, moving from having poorly understood large variances in the components of a population's Ca requirements to better understood factors of an individual's risk factors for low bone mineral accretion will ultimately be critical as individuals look to optimise their personal nutrition. As such, future research will need to focus on these genetic and dietary factors that are identifiable or modifiable in regulating peak bone mass.

Finally, we need to recognise that no nutrient, not even Ca, is an island in building and maintaining strong bones. The relationship between severe vitamin D deficiency and inadequate bone mineral accretion and rickets is well recognised, but other dietary factors need to be considered as well in terms of optimising bone health in adolescents. This includes other bone minerals, such as Mg, P and Zn. Consideration should be given to the effects Na and phytate intakes have on Ca metabolism. The effects of chronic illnesses on dietary requirements should be further investigated. Current therapies for a range of illnesses, such as cystic fibrosis and childhood leukaemias, have left us with a rapidly increasing population of children with the potential for significant lifelong health issues related to decreased bone mineral mass. Using the techniques described by Vatanparast *et al.*[7], along with studies of mineral metabolism in children who have chronic illnesses will be a major benefit to those caring for this population[14].

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