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Dietary protein content and the diet's net acid load: opposing effects on bone health[1,2]

Anthony Sebastian

In this issue of the Journal, Alexy et al (1) report on a study they performed in children and adolescents, the results of which relate to the subject of the long-term relative effects on bone health of the protein content of the diet compared with that of the diet's net load of acid in the body. We consider their findings of potential importance not only for children and adolescents but also for adults because of the controversy that prevails about whether dietary protein has an anabolic or catabolic effect on bone. Their findings may provide insight into the interplay of circumstances that determine when dietary protein has a beneficial or detrimental effect on bone.

Alexy et al collected dietary intake data over 4 y in 229 healthy children and adolescents aged 6–18 y. After 4 y, they analyzed the diet composition data in relation to proximal forearm bone variables, measured by quantitative computed tomography. After adjustment for potential confounders, they found significant associations of protein intake with improved bone variables, including bone cortex area and—importantly during growth—with bone mineral content. At the same time, they found significant negative associations of the diet's net acid load with those variables. Higher long-term protein intakes were thus associated with the bone variables as an anabolic factor, whereas higher long-term diet-dependent net acid loads were associated with those variables as a catabolic factor. The net effect proved anabolic but was apparently short of protein's anabolic potential because of the catabolic effect of the positive net acid load.

On the basis of the findings of Alexy et al, we speculate that dietary modifications designed to maintain a protein-rich diet and eliminate a net acid load to the body would improve bone health axially and peripherally in children, adolescents, and young adults and would promote the achievement of their genetic potential for peak bone mass. Alexy et al's findings provide both a rationale and an incentive to explore these possibilities interventionally. From the findings of the Framingham Osteoporosis Study in adults, Tucker et al (2) likewise speculated on the relative effects of the diet's protein content and acid load on bone.

We should not find it surprising that dietary protein has a magnitude-dependent anabolic effect on bone, because protein supplies the amino acid substrates for building bone matrix. In animals, dietary essential amino acid supplementation increases bone trabecular architecture, cortical thickness, and bone strength. Moreover, in humans, essential amino acid supplementation increases circulating concentrations of insulin-like growth hormone I (IGF-I) (3), a recognized bone growth–promoting factor. High-protein diets likewise typically increase circulating IGF-I concentrations (4). Cross-sectional studies in postmenopausal women have shown a positive association of circulating IGF-I concentrations with bone mineral density and subnormal IGF-I concentrations in patients with osteoporosis; the lowest concentrations were in those persons who had sustained fractures. Other studies have shown that short-term (2 mo) administration of recombinant human IGF-I improves bone mass gain during recovery from hip fracture. Thus, protein-induced increases in IGF-I concentrations may account, at least in part, for the anabolic effect of dietary protein on bone.

Furthermore, we should not find it surprising that the diet's net acid load has a magnitude-dependent catabolic effect on bone. The diet's positive net acid load induces low-grade metabolic acidosis (5), and, in postmenopausal women, the administration of alkalinizing salts of potassium that reduce that net acid load and ameliorate the systemic acidosis improves calcium and phosphorus balance (6) and reduces bone resorption markers (6, 7).

The observation by Alexy et al that a catabolic effect on bone related to the magnitude of the diet's net acid load can at least partially offset the anabolic effect of higher dietary protein intakes inspires a hypothesis to explain why some studies suggest beneficial bone effects with higher protein intakes (2, 8, 9), whereas others suggest detrimental bone effects (10, 11). We hypothesize that the balance between the amount of protein in the diet (anabolic effect) and the net acid load of the diet (catabolic effect) in part determines whether the diet as a whole has a net anabolic or catabolic effect on bone.

If a lower dietary net acid load permits greater anabolic effects of protein on bone, we might want to consider whether a negative dietary net acid load (ie, net base-producing diets) might optimize the anabolic effects of dietary protein on bone. The metabolic alkalosis expected with a net base-producing diet itself has an anabolic effect on bone (12), and the metabolic acidosis expected with a net acid-producing diet, in addition to producing negative effects on the body's calcium economy, reduces serum IGF-I concentrations (13). Therefore, the combination of a net base-producing, alkalosis-producing diet and a high-protein diet

[1] From the Department of Medicine, Division of Nephrology, and the Moffitt/Mt-Zion General Clinical Research Center, University of California, San Francisco, San Francisco, CA.

[2] Reprints not available. Address correspondence to A Sebastian, 40 Crags Court, San Francisco, CA 94131. E-mail: anthony_sebastian@msn.com.

might optimize peak bone mass achievement during development and greatly mitigate or eliminate age-related decreases in bone mass. Indeed, from an evolutionary perspective, natural selection may have designed human physiology to best fit a dietary environment of high protein consumption and net base production (14).

For Americans and peoples of industrialized countries to achieve the combination of a high-protein diet and a net base-producing diet, a considerable change in food consumption patterns would be required (14). This change would involve the consumption of greatly increased amounts of bicarbonate precursor–rich plant source foods—such as leafy green vegetables, stalks, roots and tubers, and fruit—and the consumption of greatly reduced amounts of energy-dense, nutrient-limited foods—such as fats and oils and refined carbohydrates—and net acid-producing cereal grains (14). Such a diet would resemble that of prehistoric hunter-gatherers. How to become a 21st century urban hunter-gatherer requires considerations beyond the scope of this review (15).

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