products, levels of pesticides and heavy metals in infant formulas are at a minimum. It is therefore unlikely that infant formulas are contaminated with concentrations of pollutants, such as polychlorinated biphenyls, that are likely to cause adverse consequences.

In conclusion, the data from any systematic review and meta-analysis is only as robust as the data from the trials reviewed. We were fortunate to have completed a collaborative review with data from high-quality trials conducted both by industry and by academia. We found no evidence that LCPUFA supplementation of infant formula influences the growth of term infants in either a positive or a negative way (1). The challenge now is to assemble new and existing data in robust systematic reviews of other health effects of LCPUFA supplementation in formula-fed infants.

The authors had no conflict of interest.

Maria Makrides
Robert A Gibson

Child Health Research Institute
Women’s Youth and Children’s Health Service
Department of Pediatrics
University of Adelaide
72 King William Road
North Adelaide SA 5006
Australia
E-mail: makridesm@mail.wch.sa.gov.au

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LETTERS TO THE EDITOR

Protein consumption as an important predictor of lower-limb bone mass in elderly women

Dear Sir:

In a recent Journal article, Devine et al (1) offered further evidence in humans of a bone anabolic effect related to an increase in dietary protein intake from amounts below to amounts above currently recommended intakes—to wit, an anabolic effect that occurs despite the potentially offsetting catabolic effect of greater endogenous acid production due to higher protein intake.

In a cross-sectional study of elderly women, the investigators reported significantly more positive bone status with protein intakes of >87 g/d than with intakes of <66 g/d, the highest and lowest tertiles of protein intake, respectively. It is important, however, that they did not report the average values of protein intake in these 2 groups or the within-group distribution of values. We would like to have that information because of the possibility that the healthier bone status in subjects with higher protein consumption reflects primarily beneficial bone effects in those subjects only when they are compared with subjects who are consuming decidedly suboptimal protein intakes. In the low-protein group, a major unmet need of bone for a protein anabolic effect may render this bone particularly responsive to the catabolic effect of the dietary positive net acid load, even though the net acid load may be reduced by the lower protein intake. With little countervailing protein anabolic effect, the catabolic effect of any degree of positive dietary net acid load may prevail unchecked, taking its toll over the years.

In the overall study group examined by Devine et al (n = 1077), in which protein intakes ranged from 25 to 136 g/d and averaged (± SD) 80.5 ± 56 g/d, the subjects in the lowest tertile group, who consumed <66 g protein/d, had an average protein intake between 25 and 65 g/d, and thus this group presumably included many subjects with decidedly suboptimal habitual protein intakes. Moreover, the investigators found significantly different positive bone effects of dietary protein between the lowest and highest tertiles of protein intakes but not between the middle and highest tertiles, which may suggest that there is a prerequisite for a decidedly suboptimal protein intake in the comparison group against which higher protein intakes are associated with improved bone health.

Extrapolating interventionally, I would suggest that a person’s bone, when avid for protein’s anabolic effect because of the person’s habitually suboptimal protein intake, will experience a net anabolic effect when the person consumes a greater amount of protein, despite an accompanying greater acid load from the higher protein intake. (Indeed, the acid load may increase little, because the protein-deficient body retains rather than catabolizes the additional protein.) Increasing protein intake from, say, 40 to 110 g/d may have a net anabolic effect on bone because the habitual low protein consumption has made the bone particularly receptive to protein’s anabolic effect, thus providing a greater counterbalance to the catabolic effect of the potentially higher net acid load. But increasing protein intake by equal increments—from, say, 80 to 150 g/d—may have a net catabolic effect on bone because the habitual higher protein consumption has made the bone less receptive to protein’s anabolic effect, thus providing a lesser counterbalance to the catabolic effect of the potentially higher net acid load.

Devine et al may have estimated the dietary net acid load for each subject, as they did for dietary protein content. With that information and on dividing their subjects into 2 groups, they may have found, on multivariate analysis, an independent negative determinant in dietary net acid load that had a lesser effect (ie, a lower standardized regression coefficient) than did protein in the group with protein intakes between the lowest and the median and a greater effect than did protein in the group with protein intakes between the median and the highest.

The investigators possibly could have made that analysis from their data. They may have estimated the dietary net acid load for each subject by using data from the same food-frequency questionnaire that they used for estimating dietary protein and calcium content.
Presumably, the food-frequency questionnaire could also have provided estimates of dietary potassium intake for each subject, in which case the investigators could have used the Frassetto algorithm (dietary net acid load = 0.91 × protein intake in g/d − 0.57 × potassium intake in mEq/d + 21) (2) to obtain an estimated value for dietary net acid load for each subject.

In performing such an analysis, Devine et al may contribute quantitative estimates of the degrees of opposing anabolic and catabolic bone effects of dietary protein in elderly subjects over the range of protein intakes observed, and they may confirm in adults the findings of Alexy et al (3) in children and adolescents, also recently reported in the Journal. In an editorial accompanying that article, we (4) further discussed the subject of the opposing anabolic and catabolic bone effects of dietary protein and suggested a way to maximize protein’s anabolic effect by supplying diets that are both protein-rich and net base–producing.

The author had no conflict of interest.

Anthony Sebastian

Department of Medicine
University of California, San Francisco
Moffitt/MZ General Clinical Research Center
40 Crags Court
San Francisco, CA 94131
E-mail: anthony_sebastian@msn.com

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Reply to A Sebastian

Dear Sir:

We thank Dr Sebastian for his interest in and comments on our investigation of dietary protein intake and bone health in elderly women.

The first question raised by Sebastian related to the average values of protein intake and within-group distribution of 2 of the protein groups, ie, the low- (<66 g/d) and high- (>87 g/d) protein groups. The low-protein group had an average protein intake of 54 ± 9 g/d (range: 23.05–65.95 g/d), and the high-protein group had an average protein intake of 111 ± 25 g (range: 87.03–258.33 g/d). Sebastian suggested that the low-protein group may have suboptimal protein intakes, a possibility that is supported in part by these data, because approximately one-third of the low-protein group had a protein intake below the Australian recommendation of 0.75 g protein/kg body wt (1), whereas none of the high-protein group had less than the recommended intake.

Sebastian suggested that the subjects in the low-protein group, who consumed suboptimal amounts of protein, may be susceptible to the catabolic effect of the positive dietary net acid load. As suggested, we estimated the dietary net acid load by using the Frassetto algorithm (2). As rightly stated by Sebastian, the net acid load indeed was significantly lower in the low-protein group than in the high-protein group (38 ± 7 and 66 ± 18 mEq/d, respectively). Furthermore, we found that the net acid load in the whole group was positively related to bone density at all hip sites and measurements of quantitative ultrasound (broadband ultrasound attenuation and stiffness), which reflected increasing bone density with increasing protein intake. With the use of multiple regression analysis, protein intake was the only significant determinant of bone density or broadband ultrasound attenuation after we accounted for dietary net acid load in the model. This suggests that, in our population, net acid balance was not a critical factor in measuring bone density and that protein intake was beneficial regardless of the net acid load it induced. This possibility was further borne out by an analysis within each tertile of protein intake (ie, low, medium, and high protein intake), which found, in a linear correlation, that no association existed with any measure of bone density or net acid load.

Sebastian went on to hypothesize that we may see an independent negative effect of dietary net acid load on bone density that is greater in those persons with protein intakes below the median (ie, the low-protein group) than in those with intakes above the median (ie, the high-protein group). Using multivariate analysis, we did not, however, see a negative effect of net acid load on bone density in the low-protein group when protein intake was dichotomized to above or below the median (56.3 g/d), nor did we see a negative effect of net acid load on bone density in either the medium- or high-protein group.

Sebastian discussed the possibility that the anabolic effect is greater in bone when low habitual intakes are increased from 40 to 110 g/d rather than when moderate intakes are increased from 80 to 150 g/d. He speculated that, across this range of protein intakes, bone may respond more readily to protein, which offsets the catabolic effect of the potentially higher net acid loads. As ascertained from our data, we did not see a negative relation between the amount of dietary net acid load and the bone mass in any tertile of intake. Essentially, in our population, net acid balance was not a critical factor in measuring bone density.

The authors had no conflicts of interest.

Amanda Devine
Ian M Dick
Richard L Prince

School of Medicine and Pharmacology
University of Western Australia
Perth
Australia
E-mail: adevine@cyllene.uwa.edu.au

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