Does Excess Dietary Protein Adversely Affect Bone?
Symposium Overview1,2

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This commentary and the following two reviews present the proceedings of the symposium of the Nutrition Working Group of the American Society for Bone and Mineral Research, in Cincinnati, OH on September 10, 1997. The purpose of the symposium is to assist nutrition and medical research professionals in understanding the complex issues involved in this topic; such understanding will lead to better-designed experiments that will enable us and our colleagues to make appropriate dietary recommendations to reduce the future incidence of osteoporotic fractures.

Linda Massey introduced the symposium topic by reviewing the types of research evidence that have been presented on both sides of the debate. The calcuiotic effect of protein consumption has been known since 1920. A review of 19 human studies confirmed that within 2–4 h after humans consume protein, urinary calcium is increased (Kerstetter and Allen 1990). Dietary protein increases glomerular filtration rate and decreases fractional renal reabsorption (Benabe and Martinez-Maldonado 1991); these changes have been proposed to be mediated by changes in acid load (Barzel 1995) or increases in insulin (Kerstetter and Allen 1990).

Serious attention to the possible effects of excessive dietary protein on human bone arose from the classic studies of Hellen Linkswiler and her students beginning about 1970. When purified protein supplements are added to diets, calcium balance usually becomes more negative, suggesting that bone may be affected. However when increased protein is added as foods, particularly meat or dairy products, decreased calcium balance is not always seen (Hunt et al. 1995), especially in young healthy people (Pannemans et al. 1997). This is due to other components of protein-containing foods that have also been shown to alter the urinary excretion of calcium and thus potentially calcium balance. These include phosphate (Remer and Manz 1994, Spencer et al. 1988), sulfate (Remer and Manz 1994) and potassium (Sebastian et al. 1994), as well as calcium (Heaney 1993).

The acid load of high animal protein diets and the alkaline load of high plant diets have been proposed as major factors in overall calcium balance (Barzel 1995). The potential renal acid load (PRAL) of diets can be predicted from knowing dietary composition. Remer and Manz (1995) have calculated the PRAL of 114 frequently consumed foods based on 100-g servings. Fruits and vegetables have negative values, meaning they reduce acid excretion; milk and yogurt yield about 1 mEq, whereas meats, fish, poultry, cheeses and even some grain products potentially yield 7 mEq or more acid per 100-g serving.

Epidemiologic studies have added to our knowledge, but we do not yet know how much and what source of protein is protective of our bones. Cross-cultural comparisons associate long-term consumption of higher animal protein with increased hip fracture rates (Abelow et al. 1996); however Feskanch et al. (1996) found no association between adult protein intake and hip fractures in the U.S. Nurses’ Health Study. Before recommending vegan diets, however, we must consider that Chiu et al. (1997) have recently shown that postmenopausal Taiwanese women who have consumed long-term traditional vegan diets were more likely to have bone densities below the fracture threshold. Even in vegan diets, increased protein intake was associated with increased bone density. Yet another study of Chinese women showed that the acid-base status of the total diet determined urinary calcium excretion; no significant associations, either positive or negative, were shown with dairy products (Hu et al. 1993). In western countries, postmenopausal lacto-ovo-vegetarian women do not have different bone densities than omnivorous women with the same lifestyle (Tesar et al. 1992).

Another experimental approach is to look at the effects of pH on bone cells in cultures. Even very small changes in pH within normal ranges greatly affect osteoclast and osteoblast calcium metabolism (Arnett and Spowage 1996).

Finally, we must consider the protein needs of the elderly, the group at most risk of fracture. Certainly inadequate intake of protein leads to muscle atrophy, which in turn leads to increased risk of falls at minimum and possibly decreased bone density. Protein supplementation may also reduce further bone loss in elderly patients with hip fracture (Bonjour et al. 1996).

Barzel and Massey (1998) presented evidence that the symposium title question has a positive answer unless the acid produced by protein metabolism is buffered. Bone ions serve the body as a buffer system as well as providing physical support. Modern diets contain and/or generate ~50–100 mEq acid/d, which must be neutralized. When young people were fed acid phosphate vs. neutral (potassium) phosphate, urinary calcium was higher. Elderly adults given 2 g/(kg-d) protein were in negative calcium balance, but in positive balance when receiving a lower protein intake. The recently published DASH study (Appel et al. 1997) showed that the addition of

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fruits and vegetables to a diet decreased urinary calcium excretion from 157 to 110 mg/d, even though dietary protein and calcium were constant. Fruits and vegetables are major sources of buffer (alkali) in the diet.

Further evidence that the effects of high protein diets are mediated through changes in acid-base metabolism comes from studies in which acid loads of dietary protein are neutralized with bicarbonate. The effects of adding buffer to a high protein diet are that urine pH rises, ammonia excretion increases and calcium increases. When the body is challenged with an acid load, the kidneys try to excrete more urine and will rob the skeleton of additional buffer that is needed. A more elaborate study of similar design found that during KHCO₃ supplementation of a diet containing 90 g protein/d, urinary calcium fell and calcium balance was more positive. Minute changes in blood pH and CO₂ levels were noted; several investigators have documented that osteoblasts and osteoclasts respond to very small changes in pH when growing in culture. Even a small drop in pH (~0.02 units) will cause a tremendous burst in bone resorption.

Aging kidneys cannot excrete hydrogen ions as well as young kidneys; thus older people have higher blood H⁺ and lower blood bicarbonate. The elderly may be more sensitive to the effects of dietary protein and may require more buffer.

Heaney (1998) presented evidence that the title question has a negative answer if dietary calcium is adequate. Because most nutrients have adverse effects at either too low or too high intakes, the question he addressed was the following: are protein intakes at the upper end of the range likely to be found in the population harmful? Cross-cultural studies of protein intake and hip fractures are misleading because only average intakes are presented; only when differences in fracture rate can be found within an ethnic or national group will an observational study yield plausible conclusions. In most observational studies, as protein intake went up, so did calcium intake. When adjustment for calcium intake was made, most of the time the positive association between protein intake and fractures disappeared.

More useful evidence comes from metabolic studies. It is repeatedly observed that increasing protein intake increases calcium excretion. When data from many experiments are summarized, the relationship of protein intake to urinary calcium has a slope of +0.51, which means that a doubling of protein intake produces about a 50% increase in urinary calcium. This is clear for purified proteins. When protein is fed as foods and is accompanied by phosphate, the increase in urinary calcium is blunted. However, endogenous calcium excretion is increased, leaving the same net negative balance. Other experiments support this conclusion.

This negative effect of increasing protein could be expected to adversely affect bone. The reason it may not is that increased protein in self-selected diets is usually accompanied by increased calcium. Although increased protein increases obligatory loss of urinary calcium, the body may adapt to these losses by absorbing more calcium. Eating an extra five ounces of beef every day will cause an increase in urinary calcium of about 40 mg calcium; however, intestinal calcium absorption will increase about 0.0018. At an intake of 250 mg calcium/d, this is only 4.5 mg calcium, and surely bone will be lost to maintain serum calcium levels. However, at an intake of 1500 mg calcium/d, an additional 27 mg calcium will be absorbed from the diet.

As a consequence of these considerations, it is more useful to evaluate diets not on total protein intake per se, but on their calcium-to-protein ratios. A dietary calcium-to-protein ratio ≥20:1 (mg/g) probably provides adequate protection for the skeleton.

Several investigators presented new data relevant to the program topic at a special poster session before the speakers’ presentations. Mona Calvo and Youngmee Park of the FDA presented protein, calcium and protein/calcium intake data from the 1989–91 USDA CSFII survey. Median protein intakes exceeded the Recommended Daily Allowance (RDA) for all age groups; at the 90th percentile, protein consumption was about 50% greater than the RDA. However, the Ca/protein ratio was most favorable at the 90th percentile of protein intake because the higher protein intake came mostly from adding milk and other dairy products while keeping meat, fish and poultry intake at the same level. Vegetarians had about the same protein intake as omnivores at the various percentile standards. Benefits of a vegetarian diet are more likely to be due to its higher potassium content and lower potential renal acid load composition than its protein content. Even at the 90th percentile of Ca intake, women did not consume the 1000 mg/d recommended in the 1997 Dietary Reference Intake (RDI). No age group of women and only the 19- to 24-y-old males consumed protein and calcium in a ratio recommended by the 1997 RDI and RDA.

Jane Kerstetter and her colleagues at the University of Connecticut compared low and high protein intakes, 0.7 vs. 2.1 g/kg body weight by young women. Although reduced urinary calcium was seen after consumption of the low protein intakes, it was associated with a reduced intestinal calcium absorption, 19 vs. 26%. Reduction of protein intakes appears also to be affecting calcium metabolism and therefore possibly bone.

Marion Hannan and her colleagues of the Framingham Osteoporosis Study reported that men and women (ages 69–91 y) who consumed the lowest quintile of protein intakes had increased rates of femoral bone loss compared with the three higher quartiles. Women with the highest %protein intake had no bone loss over the 3- to 4-y study period. Both of these studies reemphasized the need for adequate dietary protein for bone health.

A number of interesting points and conclusions came from the discussion. For example, the beneficial effects of calcium salts on bone have generally been attributed to the calcium ion. The anion accompanying calcium in many studies was carbonate, and citrate has also been studied. Both of these anions are important buffers. Neither the comparative effect of the anion accompanying calcium on bone nor the effect of calcium salt supplementation on acid-base balance has been well studied. Calcium salt supplementation may be beneficial because it serves both as a buffer and to improve dietary calcium adequacy.

The debate over whether plant protein is less detrimental than animal protein may be minimized by recognizing that it is the total diet that determines the effect on bone. All high protein foods do not generate equal PRAL per 100 g serving. Several plant foods including nuts, legumes and some grain products have PRAL equivalent to muscle foods such as meat, poultry and fish. Hard cheeses have PRAL higher than meat, but milk and its non-cheese products (e.g., yogurt or ice cream) have a low PRAL. Fruits and vegetable consumption buffers the acid generated by dietary protein. Even if the major source of dietary protein is meat, adverse effects may be counterbalanced by generous amounts of calcium from other foods such as milk and increased consumption of fruits and vegetables, especially those rich in calcium. For a longer review on protein intake and calcium homeostasis, the reader is referred to the 1994 review by Kerstetter and Allen.
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LITERATURE CITED


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