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Elderly Women Need Dietary Protein to Maintain Bone Mass

Excess dietary protein is considered a risk factor for osteoporosis owing to the potential for renal acid load. Researchers who conducted a recent prospective study of older adults reported that animal protein had a protective role for bone, especially in elderly women, whereas plant protein was negatively associated with bone mineral density. An interaction between protein and calcium suggested protein alone was not the important factor. Other studies confirm the beneficial effect of increasing dietary protein intake in older women to reduce bone mineral density loss and risk of fracture, suggesting that emphasis should be placed on promoting adequate protein intake in elderly women.

Key Words: animal protein, plant protein, net acid production, bone mineral density, osteoporosis

Scientists have long known that excess dietary protein raises net acid excretion, thereby causing a rise in urinary calcium excretion, and leading to bone loss.[1,2] Whereas it has been difficult to define the amount of dietary protein that qualifies as "excess," the common perception is that the typical North American diet, high in animal protein, is sufficient to evoke changes in calcium metabolism and result in bone loss and subsequent osteoporotic fractures.[3,4] Recent studies have challenged this popular view of dietary protein, however, particularly for elderly women. A review of the recent studies on how protein intake affects bone mineral density (BMD) or hip fracture incidence in elderly women shows near consensus that increasing protein intake is not harmful but beneficial to bone health (in the range of usual intake) of the women studied.

Of the six prospective studies relating dietary protein to bone health (measured as BMD or fracture incidence) in older American women, only Feskanich et al.[5] found a significant increase in fracture risk, and this risk was seen only for protein intakes greater than 95 g/day, which corresponds with intakes of less than 10% of protein intake for U.S. women 50 years and older.[6] (Table 1) The other five studies involving subjects with mean protein intakes between 68 and 79 grams/day, found that the higher protein intakes were associated with reduced fracture risk,[7] higher BMD,[8] or reduced BMD loss.[9–11] Mean calcium intakes did not reach the Adequate Intake level of 1200 mg[12] in any study. The calcium-to-protein ratio of subjects in studies showing a protective effect of protein was higher than in the study showing an adverse effect, suggesting that the calcium-to-protein ratio may be important when considering protein effects on bone.[13]

The debate concerning protein and its effect on bone has also raised the issue of the type of protein; animal protein is thought to provide more potential renal acid load than plant-based protein. Likewise, Sellmeyer et al.[8] found that a greater ratio of plant-based to animal protein was beneficial in reducing BMD loss and hip fracture risk in elderly women. As shown in Table 1, however, most of the recent studies of elderly women found no benefit of plant-based protein over animal protein,[10] or an advantage of animal protein over plant-based protein.[7,9,11] One study has suggested that consumption of plant-based protein may cause loss of bone because there was a negative association between vegetable protein and BMD in elderly female subjects, but not in male subjects.[11] In this study, Promislow et al. examined protein intake and BMD in 1526 men and women aged 55 to 92 years who were participants in the Rancho Bernardo cohort.[11] This group of subjects has been studied by these authors since the early 1970s. Between

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Table 1. Summary of Recent Studies Examining the Effect of Total Protein, Animal Protein, and Plant Protein Intakes on Bone Health in Elderly Women

Study	Promislow et al. (2002)[11]	Munger et al. (1999)[7]	Hannan et al. (2000)[9]	Dawson-Hughes et al. (2002)[10]	Sellmeyer et al. (2001)[8]	Feskanich et al. (1996)[5]
Duration (years)	4	3	4	3	~7	12
Number of subjects	960	32,006	615	342	1035	85,900
Subjects	Rancho Bernardo cohort*	Iowa (randomly selected)	Framingham cohort*	Boston volunteers*	Study of Osteoporosis Fractures cohort	Nurses' Health Study cohort
Age (years)	71 (mean)	61 (mean)	75 (mean)	≥65	>65	46–71
Protein intake (g)	71	78	68	79	50	79.6
Calcium intake (mg)	985	1150	810†	1346	853	718
Calcium-to-protein ratio	14:1	15:1	11:1	17:1	17:1	9:1
Conclusions‡	$\uparrow$ p $\uparrow$ BMD $\uparrow$ ap $\uparrow$ BMD $\uparrow$ pp $\downarrow$ BMD	$\uparrow$ p $\downarrow$ Fx $\uparrow$ ap $\downarrow$ Fx $\uparrow$ pp $\uparrow$ Fx	$\uparrow$ p $\uparrow$ BMD $\uparrow$ ap $\uparrow$ BMD $\uparrow$ pp $\leftrightarrow$ BMD	$\uparrow$ p $\uparrow$ BMD $\uparrow$ ap $\leftrightarrow$ BMD $\uparrow$ pp $\leftrightarrow$ BMD	$\uparrow$ p $\uparrow$ BMD $\uparrow$ ap $\uparrow$ Fx $\uparrow$ pp $\downarrow$ Fx	$\uparrow$ p $\uparrow$ Fx $\uparrow$ ap $\uparrow$ Fx $\uparrow$ pp $\leftrightarrow$ Fx

* Although these studies included male and female subjects, only female subject data are reported.
† Mean intake of both male and female subjects.
‡ For comparative purposes, a reduced rate of BMD loss is treated as a gain in BMD.
NS = not significant, p = total protein, ap = animal protein, pp = plant protein, BMD = bone mineral density, Fx = fracture, $\uparrow$ = higher, $\downarrow$ = lower, $\leftrightarrow$ = no effect.

1988 and 1992, subjects underwent a bone scan using dual-energy x-ray absorptiometry (Hologic QDR) and completed a food-frequency questionnaire and a medical history. Approximately 4 years later (1992–1996), 65% of subjects had a second bone scan. The authors reported analyses of the prospective data in which dietary data at baseline were related to bone density measurements taken 4 years later. BMD data were adjusted for age and body mass index (BMI, kg/m^2) in all analyses and was presented as absolute BMD or as rate of loss in BMD per annum. Dietary protein intakes were adjusted for energy intake.

Promislow et al.[11] initially examined the effect of protein intake on BMD (Table 2). For women, there was a significant positive rise in BMD as total protein increased at all three bone sites measured; this represented an increase in BMD of approximately 0.01 g/cm^2 per 15-gram rise in protein intake. This apparent beneficial effect of protein was mirrored when animal protein was used in the analyses instead of total protein. There was a fall in BMD when only vegetable protein was considered in the model, however, such that for every 5-gram intake of vegetable protein, there was a fall in BMD of approximately 0.01 g/cm^2. With multiple linear regression (Table 2), the beneficial effect of total protein was lost after adding the following covariates: calcium intake, years since menopause, exercise, diabetes state, and use of estrogen, steroids, alcohol, thiazides, or thyroid hormones. The positive effect of animal protein on BMD remained for hip and whole body, whereas the negative effect of vegetable protein remained for hip and spine. For men, there were no significant relationships between BMD and protein when analyzed using linear regression. The relationship between protein and BMD was not linear for men except for a negative effect of vegetable protein intake on BMD at all measured bone sites and only using multiple linear regression (which included the same covariates as for women excluding years since menopause and estrogen use); the latter relationship held true whether or not a quadratic term was entered into the multiple linear regression model.

Promislow et al. then examined whether calcium intake modified the protein-BMD relationships that were found for women.[11] Figure 1 depicts the interaction of animal protein intake and calcium intake and the subsequent effect on bone (spine). For both total protein and animal protein intakes, a high calcium intake had no effect on BMD, except at the spine where a decline in BMD occurred as protein intake increased; at low calcium intakes, however, as protein intake increased, so did BMD. This interaction was significant for femoral neck and spine, using either total protein or animal protein in the model. The effect of vegetable protein on BMD, as modified by calcium intake, is depicted in Figure 2. A significant interaction was found only for total-body BMD. At high calcium intakes, there was a

Table 2. Effect of Protein Intake on Bone Mineral Density at Three Different Bone Sites in Older Women Using Linear and Multiple Linear Regression Analyses

	Linear Regression			Multiple Linear Regression		
Dietary Factor	**Hip**	**Spine**	**Whole Body**	**Hip**	**Spine**	**Whole Body**
Total Protein	↑	↑	↑↑	↔	↔	↔
Animal Protein	↑↑	↑	↑↑	↑	↑	↑
Vegetable Protein	↓	↑	↔	↓↓	↑	↔

Direction of influence indicated by arrows where positive beta coefficient shown as ↑, negative beta coefficient shown as ↓, and no significant effect ($P > 0.08$) shown as ↔. From Promislow et al.[11]

negative effect of vegetable protein intake on BMD; at low calcium intakes, there was a positive effect on total-body BMD. At all other bone sites there was no apparent increase in BMD with an increase in vegetable protein intake. This pattern of interaction between protein and calcium on BMD was not observed in other studies. Dawson-Hughes and Harris[10] reported the opposite effect; in their study, higher intakes of protein spared bone loss only in a calcium-supplemented group of elderly men and women, whereas those in the placebo group (with an average calcium intake of 871 mg) did not show any protein effect (positive or otherwise) on BMD.

All studies outlined in Table 1 focused on determining whether excess protein was harmful to bone and, therefore, the question of whether subjects were ingesting too little protein was not analyzed as thoroughly by the investigators. Kerstetter et al.[14] reported that protein intake at or below 0.8 g/kg body weight results in perturbations of calcium homeostasis, suggesting that low protein intake is a cause for concern. It is likely that protein requirements for bone health were not being met by some of the women in the studies shown in Table 1; assuming that researchers detected a difference in bone loss between subjects who consumed adequate amounts of protein and those who did not, this would indicate a beneficial effect of protein on BMD.

Possible mechanisms for the role of animal protein in bone health include the presence of the amino acid lysine, of which plant protein foods are poor sources. Lysine has been noted for its role in bone health.[7] However, a specific benefit of animal protein has not been demonstrated in experimental studies. When subjects were given beef or plant-based proteins, there was no difference in urinary calcium excretion between treatments, suggesting no benefit of animal over plant protein in the short-term.[15] Another possible beneficial effect of animal protein is zinc; 80% of the average intake of dietary zinc is obtained from animal sources, and zinc is better absorbed in the absence of phytate.[16] However, none of these are mechanisms that, alone, could likely produce such a large benefit to bone. Further, how could Promislow et al.[11] find adverse effects of "vegetable proteins" (their term for nonanimal proteins)? Plant-based proteins are generally recognized as being sources of alkalinity that can neutralize acid from metabolism of sulfur amino acids.[2,16] This is true for fruits or vegetables, yet some plant-based proteins such as grains, legumes, and nuts have potential renal acid load values as

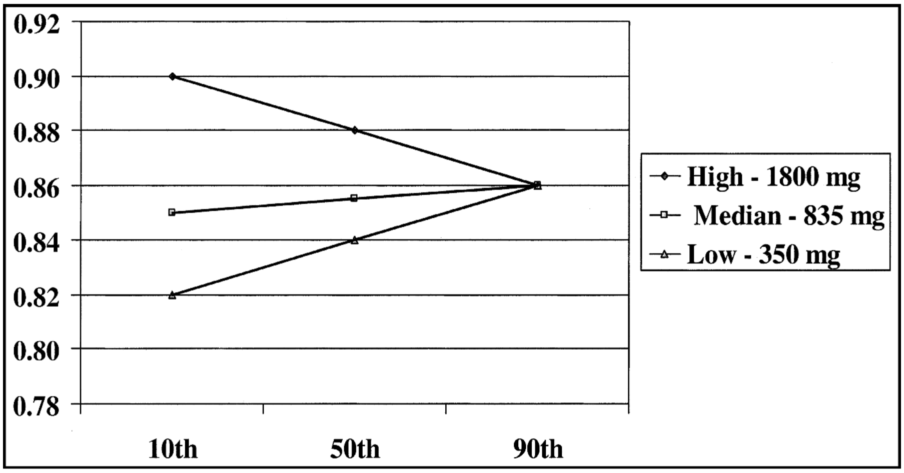

Figure 1. Stylized depiction of animal protein calcium interaction at spine in women.[11] Y-axis units are bone mineral density (g/cm^2); X-axis units are percentiles of protein intake; legend shows calcium intake tertiles.

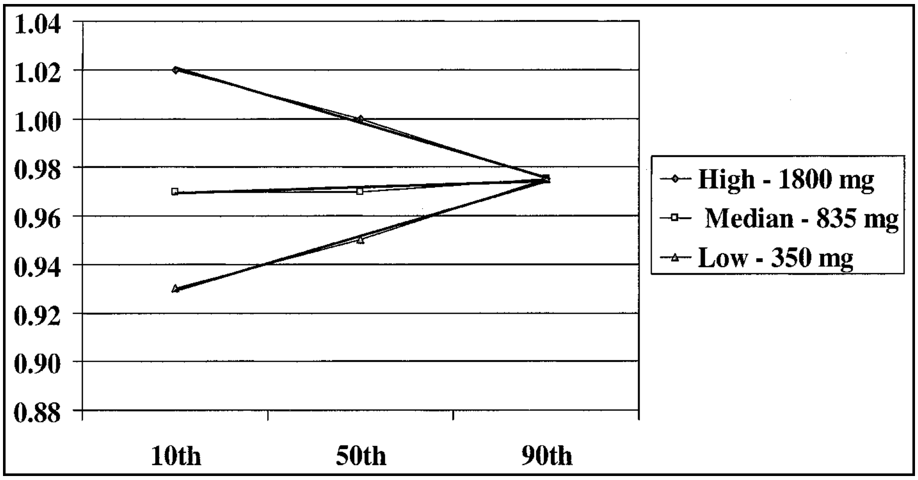

Figure 2. Stylized depiction of vegetable protein–calcium interaction at total body in women.[11] Y-axis units are bone mineral density (g/cm^2); X-axis units are percentiles of protein intake; legend shows calcium intake tertiles.

high as meat.[17] Furthermore, vegetables may have additional benefit for bone health by a mechanism other than base potential. A recent study of onions, vegetable mixes, salads, and herbs indicates inhibition of bone resorption when these foods are fed to rats; this is done through an unknown mechanism independent of base excess.[18] Future studies should include characterization of the plant-based proteins.

As dietary factors tend to exhibit co-linearity with other components in the diet, dietary patterns should be considered. It may be that dietary factors associated with animal protein intake are affecting bone health. These factors include calcium and vitamin D,[7] which are highly correlated with total protein as well as animal protein intake. Calcium intake increases with consumption of animal protein-based foods such as milk, yogurt, and cheese; vitamin D, which is also essential for bone health, is found in animal protein sources such as fish, eggs, and fortified dairy products. Also, potassium, an important electrolyte in reducing the hypercalcuric effect of protein, is associated with total protein intake[19] and can be obtained in the diet from milk and seafood. Munger et al.[7] reported a positive relationship between total protein intake and animal protein intake, but a negative relationship between plant-based protein and total protein. This suggests it may be easier to maintain an adequate intake of protein when consuming animal protein sources. However, Promislow et al.[11] found a positive relationship between plant and total protein. It is possible their finding about the negative consequence of plant protein on BMD was related to an overall lower protein intake of subjects ingesting primarily plant-based foods. Further, if the plant-based protein were derived from highly refined grains, the diet of these subjects would be less nutrient dense and would have a greater potential renal acid load than expected from a diet rich in fruits and vegetables.

Salt intake is a dietary factor that deserves further consideration. Packard and Heaney[1] quantified the effects of protein and sodium on urinary calcium loss, and concluded that high sodium intake would have a greater effect on calcium loss than a diet moderately high in protein. None of the studies in Table 1 reported whether those consuming protein (or animal protein) had better diets (i.e., ones containing fewer high-salt, processed foods). Most of the subjects of the studies in Table 1 were localized in a single geographic and socioeconomic stratum, and most were volunteers; therefore dietary patterns may be unique to those groups and not generalizable. Researchers must be aware of these possible confounding factors when assessing relationships between protein and bone health.

It is therefore not clear yet whether protein, rather than co-ingested nutrients, is promoting better bone health in the elderly. The study by Dawson Hughes and Harris[10] found protein in conjunction with high calcium favors maintenance of BMD, which is different from the findings of Promislow et al.[11] who found that in the presence of high dietary calcium, protein had little effect on BMD. Despite this difference, both groups suggest that protein prevents loss of BMD in elderly subjects through an increase in insulin-like growth factor-1 (IGF-1). IGF-1 is recognized as an important factor in bone growth because it stimulates proliferation and differentiation of osteoblasts, selectively stimulates the transport of phosphate across membranes of osteoblastic cells, and inhibits the degradation of collagen produced by osteoblasts.[20] However, the role of IGF-1 in the elderly is not clear. Whereas serum IGF-1 was related to BMD in an earlier Rancho Bernardo study,[21] Dawson-Hughes and Harris[10] could not find a relationship between IGF-1 and BMD in their elderly subjects. Because IGF-1 is a reliable index of protein-energy undernutrition in the elderly,[22] improvement in hip fracture healing[23] may reflect improvement in protein status. Nevertheless, studies involving administration of recombinant human IGF-1 to osteoporotic patients suggest this hormone may play a unique role in fracture healing,[24] and thus IGF-1 remains a promising area for further research.

Whereas most of the recent prospective studies indicate that protein is beneficial for bone health of elderly women, it is not clear in what amounts, nor is it clear whether the kind of protein is important. However, there is indication that many elderly women are ingesting protein at levels below their requirement. Furthermore, the co-linear nature of other bone-related nutrients with protein needs to be considered to clarify whether protein is the primary determinant of fracture risk or BMD status. It is possible that protein intake is indicative of the consumption of other important nutrients that play a role in bone health. A review of recent prospective studies[5,7–11] indicated that the ratio of calcium to protein is a necessary criterion for bone health. Future studies should examine the whole diet to determine what dietary patterns are associated with a diet high in plant or animal protein, as it may be that this is the reason for the conflicting findings regarding the effect of the type of protein on bone health.

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