Issues and Opinions in Nutrition

Excess Dietary Protein Can Adversely Affect Bone[1,2]

Uriel S. Barzel[3] and Linda K. Massey*[4]

*Division of Endocrinology and Metabolism, Department of Medicine, Montefiore Medical Center and The Albert Einstein College of Medicine, Bronx, NY 10467 and *Food Science and Human Nutrition, Washington State University, Spokane, WA 99201*

ABSTRACT   The average American diet, which is high in protein and low in fruits and vegetables, generates a large amount of acid, mainly as sulfates and phosphates. The kidneys respond to this dietary acid challenge with net acid excretion, as well as ammonium and titratable acid excretion. Concurrently, the skeleton supplies buffer by active resorption of bone. Indeed, calciuria is directly related to net acid excretion. Different food proteins differ greatly in their potential acid load, and therefore in their acidogenic effect. A diet high in acid-ash proteins causes excessive calcium loss because of its acidogenic content. The addition of exogenous buffers, as chemical salts or as fruits and vegetables, to a high protein diet results in a less acid urine, a reduction in net acid excretion, reduced ammonium and titratable acid excretion, and decreased calciuria. Bone resorption may be halted, and bone accretion may actually occur. Alkali buffers, whether chemical salts or dietary fruits and vegetables high in potassium, reverse acid-induced obligatory urinary calcium loss. We conclude that excessive dietary protein from foods with high potential renal acid load adversely affects bone, unless buffered by the consumption of alkali-rich foods or supplements.   J. Nutr. 128: 1051–1053, 1998.

KEY WORDS: • *humans* • *protein* • *bone* • *acid* • *potassium*

This paper will discuss the effects of dietary protein on acid-base metabolism and ultimately on urinary calcium and bone. Although important, heredity, exercise and dietary calcium and phosphate per se will not be considered. Because the factors discussed are not related to sex hormones, findings apply equally to both genders.

Bone is a very large ion exchange buffer system. Green and Kleeman (1991) reported that 80% of total body carbonate is in the hydration shell, the water surrounding bone, as are 80% of citrate and 35% of sodium, which can serve to buffer excess acid. Ninety-nine percent of the calcium is in bone. Bone responds to acid by an acellular, physicochemical reaction with the rapid release of carbonate, citrate and sodium from the hydration shell. In response to chronic acid stress such as is imposed by an acid-ash diet, cellular responses mobilize bone and calcium as a buffer.

An acid-ash diet is a diet that creates acid in the process of its metabolism. The average American diet, which is high in protein and low in fruits and vegetable, can generate over 100 mEq of acid daily, mainly as phosphate and sulfate (Remer and Manz 1994). Acid generated by diet is excreted in the urine. Foods such as fish and meat have a high potential renal acid load (PRAL) (**Table 1**). Many grain products and cheeses

also have a high PRAL. In contrast, milk and non-cheese dairy products such as yogurt have a low PRAL. Fruits and vegetables have a negative PRAL, which means that they supply alkali-ash.

An example of a food product that yields high levels of acid for the body to dispose of is a cola drink. Phosphoric acid is one of the ingredients listed on the cola container. The pH of cola is ~3.0, ranging from 2.8 to 3.2. The human kidney can excrete urine with a pH no lower than 5. If one ingests and fully absorbs a beverage with a pH of 3, one has to dilute it 100-fold to achieve a urinary pH of 5. Thus, a can containing 330 mL of cola would result in 33 L of urine! This does not happen because the body buffers the acid of the soft drink. For full buffering, 1 L of cola requires some four tablets of Tums, which contain 16 mEq of carbonate as the calcium salt.

A relevant comparison of the metabolic effects of acid phosphate and neutral phosphate was published by Lau et al. (1979). Young healthy adults consumed identical diets plus 2 g of phosphate, either acidic or neutral. The total phosphate ingested was identical, but the acid phosphate group ingested an excess of 24 mEq H^+. Net urinary acid and calcium excretion were measured. Urinary calcium excretion per day was 52 mg greater in subjects consuming acid phosphate than in those ingesting neutral phosphate. Clearly, it is not how much phosphate is consumed that affects urinary calcium, but whether it is in a chemically neutral or acid form.

Similar findings were reported by Breslau et al. (1988). They compared vegetarian, ovovegetarian and animal protein diets. Although total protein, phosphorus, sodium, potassium and calcium content of all of these diets was not different, the animal protein diet contained 6.8 mmol more sulfate. Urinary

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JN **THE JOURNAL OF NUTRITION**

TABLE 1

Average potential renal acid loads (PRAL) of certain food groups and combined foods[1]

Food group	PRAL
	mEq/100 g edible portion
Beverages	
Alkali-rich and low phosphorus[2]	−1.7
Alkali-poor and low phosphorus[3]	0
Fats and oils	0
Fish	7.9
Fruits and fruit juices[4]	−3.1
Grain products[5]	
Bread	3.5
Flour	7.0
Noodles, spaghetti	6.7
Meat and meat products	9.5
Milk and dairy products	
Milk and non-cheese products[6]	1.0
Cheeses with lower protein content[7]	8.0
Cheeses with higher protein content[8]	23.6
Vegetables[9]	−2.8

[1] Data represent the arithmetic means of the PRAL values of the respective foods [Table 1, Remer and Manz (1995)].
[2] Beverages (phosphorus <30 mg/100 g) with several times higher sodium + potassium content compared with chloride; for example, red wine, white wine, certain mineral waters and coffee.
[3] Beverages (phosphorus <30 mg/100 g) with similar sodium + potassium vs. chloride content. Cocoa (alkali- and phosphorus-rich) also falls in this PRAL category. Because of a medium phosphorus content (e.g., 28 mg/100 g), some European pale beers have a relatively high PRAL value (~1 mEq/100 g).
[4] Without dried fruits.
[5] Irrespective of the type of flour (whole meal or white, plain).
[6] Primarily whey based.
[7] Less than 15 g protein/100 g.
[8] More than 15 g protein/100 g.
[9] Without asparagus (very low alkali excess) and spinach (very high alkali excess).

pH was more acidic, 6.17 vs. 6.55, and net acid excretion was 27 mEq/d higher in those consuming the animal protein diet; both urinary phosphate and sulfate were higher. Daily urinary calcium was 47 mg higher when those young adults were consuming an animal protein diet vs. the vegetarian diet.

The effect of a higher protein, acid-ash diet has also been shown in elderly people who participated in a study in which they ate 0.8 or 2 g protein/kg body weight (Licata et al. 1981). Urinary calcium nearly doubled with the higher protein diet, increasing from 90 ± 17 to 171 ± 22 mg/d. Calcium balance was positive (+40 ± 35 mg/d) when subjects consumed the low protein diet but negative (−64 ± 35 mg/d) when they consumed the high protein diet.

Recently, Appel et al. (1997) reported the effect of a high fruit and vegetable diet in an 8-wk study of >350 people. Dietary protein was a constant percentage of energy, whereas dietary calcium was somewhat lower in the control diet (443 vs. 534 mg/d), and dietary potassium and magnesium were higher in the experimental diet (4700 vs. 1700 mg/d and 423 vs. 176 mg/d, respectively). An increase in fruit and vegetable intake from 3.6 to 9.5 daily servings decreased urinary calcium from 157 ± 7 to 110 ± 7 mg/d, a drop of 47 ± 6 mg/d, whereas urinary calcium of controls dropped only 14 ± 6 mg/d. This was not an effect of salt, because urinary sodium decreased by only 232 mg/d (7%) in the intervention group, and increased by 142 mg/d (5%) in the control group. Fruits and vegetables are the major source of buffer in the diet (Table 1).

Population studies further confirm the effect of urinary acidity on urinary calcium excretion. Hu et al. (1993) studied women in five different Chinese counties. Urinary calcium excretion was lower when the urine was more alkaline; more acidic urine was associated with a higher urinary calcium.

Strong evidence that the effects of high protein diets are mediated through changes in acid-base balance comes from studies in which the acid loads of dietary protein are neutralized with bicarbonate. Only two studies with this design have been published to date. Lutz (1984) supplemented a high protein diet (102 g) with bicarbonate and looked at the effect on urinary calcium and calcium balance. Subjects were in negative calcium balance while consuming 102 g protein/d, but the bicarbonate supplement decreased urinary calcium by 66 mg/d and balance was slightly positive. Subjects had similar calcium balances when consuming either the high protein (102 g) diet plus bicarbonate or a moderate protein (44 g) diet. A more elaborate study was conducted by Sebastian et al. (1994) who studied a 96-g protein diet in women. During $KHCO_3$ supplementation, urinary calcium fell and calcium balance was more positive.

A study in adult rats assessed bone formation and resorption by microradiography (Barzel and Jowsey 1969). Rats fed ammonium chloride for 1 y had increased resorption of bone and decreased amounts of femoral bone, ~15–20%. A similar effect was also seen when the rats consumed a low calcium diet. Bone resorption was increased in rats consuming ammonium chloride regardless of the calcium content of the diet, and total bone was smaller than in the controls fed the same diet. Rats fed a low calcium diet who received bicarbonate experienced high bone formation and deposited about the same amount of bone content as rats fed a regular calcium diet. Ammonium chloride as a source of acid caused bone resorption and decreased total bone, whereas bicarbonate increased bone formation and increased total bone, thus protecting the rat's skeleton from the negative effects of a low calcium diet. More recently, the effects of acid ingestion on rat bones were duplicated with histomorphometry and bone markers by Myburgh et al. (1989).

Overall, these studies show us that the effects of adding buffer to a high protein diet are as follows: *1*) urine pH falls; *2*) urinary net acid excretion, titratable acidity and ammonia excretion decrease; *3*) calciuria decreases; and *4*) total bone increases. On the other hand, when the body is challenged with a dietary acid load, the kidneys excrete more acidic urine, and the organism also turns to the skeleton for additional buffer.

The long-term consequence of a small change in calcium balance is substantial. A 50-mg increase in urinary calcium loss per day will result in a 18.25-g loss per year, or 365 g over 20 y. Because the average adult female skeleton contains 750 g calcium at its peak, this is a loss of one half of total skeletal stores! For a male with a store of 1000 g calcium, this is about one third of the total.

Both Bushinsky (1996) and Arnett and Sakhaee (1996) have documented that osteoclasts and osteoblasts respond independently to small changes in pH in the culture media in which they are growing. A small drop in pH causes a tremendous burst in bone resorption. Sebastian et al. (1994) noted small changes in blood pH and CO_2 levels that would be considered within the normal range during the potassium supplementation described above, but would be sufficient to affect bone metabolism.

Dietary salt is known to affect urinary calcium excretion.

It is generally poorly appreciated that the anion accompanying sodium is important to the overall effect of salt on calcium metabolism (Massey and Whiting 1996). When Berkelhammer et al. (1988) replaced sodium chloride with equimolar sodium acetate in patients receiving total parenteral nutrition who had marked hypercalciuria, urinary calcium decreased markedly and calcium balance became positive. The blood pH was 7.37 with sodium chloride and 7.46 with sodium acetate. It was the chloride or acetate, not the sodium, that determined the blood pH and the degree of urinary calcium excretion. They confirmed observations by others that urinary calcium paralleled total acid excretion.

The effects of dietary protein may be greater as we age. Aging kidneys cannot generate ammonium ions and excrete hydrogen ions as well as young kidneys do. High dietary acidity yields a lower blood pH in the elderly (Frassetto et al. 1996). In fact, a review of the literature reveals that older people have higher blood H^+ and lower blood bicarbonate (Frasetto and Sebastian 1996). Parathyroid hormone (PTH) levels are higher in older adults. PTH influences plasma CO_2 as well as plasma phosphate levels; the total buffering capacity is decreased when PTH is elevated (Barzel 1981). Overall, we can conclude that the elderly have decreased renal ability to excrete free acid, as well as elevated PTH, both of which promote acidosis. Therefore, the elderly may be more sensitive to the effect of acidic diets, and this would mean that they require more buffer than younger people for the same dietary acid load. When the elderly are given supplements of calcium citrate, lactate or carbonate, it is not the calcium but the accompanying anion that benefits their bones. Over time, it is the balance of dietary acid and base that determines calcium balance; remember that different food sources of protein differ greatly in their acidogenic effects (Remer and Manz 1995).

Bone and mineral investigators should look at acid-base effects of diet and use appropriate methods to quantitate these effects. The 24-h urine collection in a metabolic unit as part of total calcium balance measurement is the gold standard of acid-base research. The 24-h collection of urine in an ambulatory setting, as used by Appel et al. (1997), is a second choice method. Hu et al. (1993) used a 12-h, overnight collection in a community study. Another approach to evaluate the acid-base effect of a diet is to quantitate the net acid content of each dietary item (Remer and Manz 1995). There is also a need to develop convenient methods for quantitating urinary acid excretion. A possible simplified approach could be based on key dietary and urinary components. For example, Frassetto et al. (1997) found that the dietary protein to potassium ratio predicts net acid excretion. Net renal acid excretion, in turn, predicts urinary calcium excretion.

In summary, a diet high in acid-ash protein causes excessive urinary calcium loss because of its acid content; calciuria is directly related to urinary net acid excretion. Alkali buffers, whether chemical salts or dietary fruits and vegetables, reverse this urinary calcium loss.

Overall, the evidence leaves little doubt that excess acidity will create a reduction in total bone substance. This is normal physiology—not pathology. This is a mechanism of Homo sapiens to protect himself against acidosis. The ability to buffer the acidosis of starvation or a high meat diet gave a survival advantage in a hunter-gatherer society. Modern peoples are now eating high protein, acid-ash diets and losing their bones. The study by Appel et al. (1997) shows that increasing buffering capacity by increasing fruit and vegetable intake is a practical way to counteract the acidity generated by the dietary protein, reduce calciuria and consequently improve calcium balance.

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