Calcium balance and acid-base status of women as affected by increased protein intake and by sodium bicarbonate ingestion[1-3]

Josephine Lutz, PhD

ABSTRACT Six women, aged 38 to 62 yr, participated in a 40-day metabolic study to investigate the effect of level of protein intake and of sodium bicarbonate ingestion on urinary calcium, net calcium balance, net renal acid excretion, and arterialized venous blood pH and bicarbonate ion concentration. The diet contained 44 g protein during the first 16 days and 102 g during the remaining 24 days. During the last 10 days of the study, 5.85 g of sodium bicarbonate was ingested concomitantly with the higher protein intake. Calcium, phosphorus, and magnesium intakes were held constant at 500, 900, and 300 mg, respectively. The increase in protein intake significantly increased urinary calcium and net renal acid excretion and the mean net calcium balance became negative. The ingestion of sodium bicarbonate alkalinized the urine and reversed the increase in urinary calcium associated with the higher protein intake; the mean net calcium balance became positive. The arterialized venous blood pH and bicarbonate ion concentrations were not significantly affected by dietary treatments. The results suggest that the ingestion of a small amount of sodium bicarbonate may be an effective way to increase calcium retention in women with protein-induced hypercalciuria. *Am J Clin Nutr* 1984;39:281–288.

KEY WORDS Protein intake, dietary calcium, acid-base equilibrium, bones, aging, osteoporosis, women, menopause, bicarbonate

Introduction

The calciuretic effect of increases in protein intake at controlled levels of calcium and phosphorus intakes is well established (1). Dependent upon the levels of calcium and phosphorus ingested, an increase in protein intake may increase urinary calcium to the extent that calcium balance is adversely affected. Johnson et al (2) suggested that the calcium lost from the body with higher protein intakes was coming from bone and that lifelong ingestion of higher protein intakes might play a role in the causation of osteoporosis. Wachman and Bernstein (3) hypothesized that bone dissolution is a possible mechanism to buffer the fixed acid load imposed by ingestion of an acid-ash diet in man.

In a previous study with postmenopausal women, urinary calcium doubled and net renal acid excretion increased 3½-fold when protein intake was increased from 50 to 110 g while calcium and phosphorus intakes were maintained constant at 700 and 1080 mg, respectively (4). The total renal acid excretion increased gradually after the change to the higher protein diet, suggesting the possibility that a transitory retention of hydrogen ions by the body had occurred. However, systemic acid-base indices were not evaluated in that study.

The objectives of this present study were: *1*) to determine whether a decrease in blood pH and bicarbonate ion concentration could

[1] From the Clinical Science Center, University of Wisconsin-Madison, School of Nursing, Madison, WI 53792.

[2] Supported in part by Grant 120187 of the University of Wisconsin-Madison Graduate School and by USPH NIH Grant P30 AM26659 awarded to the University of Wisconsin-Madison Clinical Nutrition Research Unit.

[3] Address reprint requests to: Dr. Josephine Lutz, K6/366 Clinical Science Center, University of Wisconsin-Madison School of Nursing, Madison, WI 53792.

Received June 27, 1983.
Accepted for publication September 20, 1983.

be detected when protein intake was increased, and *2*) to determine whether ingestion of sodium bicarbonate concomitantly with the higher protein intake would be effective in correcting changes in urinary calcium and acid induced by the higher protein intake.

The protein intakes selected for the study were within the range of those commonly consumed by older women in our society. The calcium intake of 500 mg used approximates the median calcium intake of women in the United States (5). Seventy mEq of sodium bicarbonate was chosen for ingestion with the higher protein intake since the results of the previous study had indicated that this amount would be sufficient to neutralize most of the urinary acid excreted (4).

Materials and methods

Subjects

Two women volunteers aged 38 and 40 yr and four aged 59 to 62 yr were selected for the study. Relevant information about the subjects is given in **Table 1**. All subjects described themselves as being healthy and none was taking medications. The subjects were selected on the basis of reliability and interest in the scientific aspects of the study. All understood the purpose of the study and their obligations as subjects. Calculated values from 3-day dietary records obtained before the start of the study indicated that the mean daily intakes of energy and certain nutrients of the subjects were as follows: energy, 1600 kcal; protein, 68 g; calcium 980 mg; and phosphorus, 1270 mg. This study was approved from an ethical standpoint by the University of Wisconsin-Madison Center for Health Sciences Committee for the Protection of Human Subjects.

Study conditions

The study, 40 days in length, was a repeated measures design in which each subject received all three dietary treatments and each acted as her own control. During the first experimental period, lasting 16 days, the subjects consumed a diet containing 44 g protein; the first 8 days of this period were considered an adaptation period. During the second experimental period, lasting 14 days, the diet contained 102 g protein. During the third experimental period, lasting 10 days, 5.85 g (70 mEq) of sodium bicarbonate, taken in three equally divided doses after each meal, were ingested concomitantly with the 102-g protein diet.

TABLE 1
Information about subjects

Subject	Age	Ht	Wt
	yr	*cm*	*kg*
1	60	165	61
2	62	165	59
3	38	157	55
4	40	165	71
5	59	157	55
6	60	168	61

Except for the dietary restrictions, subjects were free to continue their own activities; all were active and resided in their own homes throughout the study. They came to the metabolic unit each morning for breakfast and foods for lunch and dinner were weighed or measured into disposable containers for consumption at home. Distilled water and tea and coffee prepared with distilled water were permitted as desired but the amounts of tea and coffee consumed were measured and recorded.

Diet

The low protein diet provided 7 g nitrogen daily and the moderate protein diet, 16.3 g. One menu was used throughout the study. The basal menu contained the following foods in g: orange juice, 100; peaches, 100; creamed cheese, 20; grape juice, 150; turkey roll, 50; mayonnaise, 15; applesauce, 100; shortbread cookies, 14; tomato juice, 150; dry rice, 20; ground round steak, 50; carrots, 30; celery, 30; onion, 10; frozen peas, 80; pears, 100; butter, 30; jelly, 28; 0.4 g sodium chloride; and bread. The bread used during the lower protein period was made with 80 g flour, 23 g wheat starch, 12.5 g corn starch, 10 g sugar, 22 g vegetable shortening, 3 g sodium chloride, 3 g yeast, 10 mg zinc as zinc sulfate, and 3 g Metamucil powder, a source of fiber. The nitrogen content of the diet was increased by addition to the bread of 45 g wheat gluten, 8 g casein, and 24 g lactalbumin. The caloric content of the bread consumed during the higher protein periods was maintained in the same manner as that consumed during the lower protein period by deletion of the starch and by decreasing the vegetable shortening to 10 g. During the period when sodium bicarbonate was ingested, a molar equivalent amount of sodium chloride was deleted from the diet so as to maintain sodium intake constant; sodium chloride was omitted from the bread and food and unsalted butter was substituted for salted. Based on calculations, the sodium content of the diet was 2500 mg. The basal diet provided approximately 1840 kcal. Because of differences in energy requirements among the women, some adjustments in intakes of unsalted butter, rice, jelly, and sugar were permitted so as to maintain constant body weight. The lower protein diet provided 211, 140, and 683 mg of calcium, magnesium, and phosphorus, respectively, whereas the higher protein diet provided 270, 156, and 882 mg. Supplements of calcium gluconate, magnesium gluconate, and potassium dihydrogen phosphate raised the daily intakes of calcium, magnesium, and phosphorus to approximately 500, 300, and 900 mg, respectively. A multivitamin and mineral supplement (Paladac with minerals, Parke-Davis, Morris Plains, NJ) was taken daily to assure that major nutrient needs were met; each tablet contained 23 mg calcium, 17 mg phosphorus, and 1 mg magnesium.

Sample collections and analyses

Daily urine composites were made from 24-h urine collections for each subject and aliquots acidified with hydrochloric acid. An 8-day urine composite was prepared for experimental period one; two 7-day composites, for period two; and a 10-day composite, for period three. Feces collected throughout the study were separated into 8, 7, or 10-day composites. Brilliant Blue Dye was used as a fecal marker. Compliance in 24-h urine collections was monitored by consistency of urinary creatinine.

Nitrogen contents of all foods and calcium, magnesium, and phosphorus contents of all foods and excreta were determined as previously described (4). Net balance was calculated as intake minus urinary and fecal losses. Average values for the 8, 14, and 10 days of the three experimental periods were used in these calculations.

Urinary pH, titratable acid, ammonium, and bicarbonate ion concentrations were determined on 3 days of each experimental period, using methods previously described (4). Net renal acid excretion was calculated in the conventional manner as the sum of total titratable acid plus ammonium ion concentration minus bicarbonate ion concentration. The bicarbonate ion concentration was calculated from the urinary carbon dioxide content using the Henderson-Hasselbalch equation and a pK_1 of 6.1; the carbon dioxide content was measured with a Natelson microgasometer (6). Total titratable acid was defined as the sum of titratable acid due to organic acids and that due to urinary phosphate using the method of Lemann and Lennon (7).

Four sets of arterialized venous blood were obtained from subjects after an overnight fast and analyzed for pH and PCO_2. One set was obtained at the end of the first and third experimental periods and two sets one midway and one at the end of the second period. Blood was obtained and analyzed for two subjects on 3 consecutive days. The blood was drawn using an indwelling needle in a dorsal hand vein with the hand heated to approximately 43°C, while the subjects were comfortably reclining. At each testing session, six 3-ml blood samples were slowly drawn into heparinized syringes over a period of 20 min; the capped syringes were immediately placed in ice and analyzed within 2 h using conventional electrodes (Radiometer, Copenhagen) at 37°C and calibrated with tonometered blood. The results of the last four of the six blood samples obtained for each subject at each testing session were used in the calculations. Blood bicarbonate ion concentrations were calculated using the Henderson-Hasselbalch equation with the conventional values for pK_1 and CO_2 solubility (6.10 and 0.0301). A close agreement in acid-base values has been reported between brachial arterial and arterialized venous blood (8).

Statistical analysis

A repeated measures analysis of variance approach was applied to study the effects of diet and age of subjects for each of the measurement variables. One grouping factor was used to classify subjects according to age into younger (40 yr) and older (approximately 60 yr); the within group factors were dietary treatment and sampling time. Comparisons between the means of paired observations at different dietary treatments were evaluated using the Scheffé test, and the joint relationship between the variables, using Pearson's product moment correlation. The level of significance chosen was $p \leq 0.05$.

Results

Effect of dietary protein on mineral balance

The effects of the three dietary treatments on mean urinary and fecal calcium and net calcium balance are presented in Table 2. Since there was no significant difference in any of these factors between the younger and older women, these data were pooled. The mean urinary calcium increased 94%, from 96 to 186 mg, with the increase in protein intake from 44 to 102 g and decreased 32% to 126 mg when sodium bicarbonate was ingested concomitantly with the 102-g protein diet. The mean fecal calcium decreased from 412 to 396 mg with the increase in protein intake and decreased slightly further to 376 mg when sodium bicarbonate was taken with the higher protein intake. The overall difference in fecal calcium due to dietary treatment was not statistically significant. The mean net calcium balance was positive (8 mg) at 44 g of protein intake, and became negative (−68 mg) with the increased protein intake; the difference approached significance ($p < 0.10$). All but one subject achieved calcium balance when protein intake was 44 g; none, when it was 102 g. When sodium bicarbonate was added to the higher protein diet, the mean net calcium balance again became positive, 21 mg; this value was significantly different from that obtained during the second dietary period ($p < 0.05$) but not significantly different from that of the first period. All but one of the subjects achieved positive calcium balance during this dietary period.

The women were in negative net phosphorus balance when protein intake was 44 g and in positive balance when it was 102 g. The mean values were −14, 9, and 30 mg for the three dietary periods, respectively. The women achieved magnesium balance during all three dietary treatments; the mean values were 24, 8, and 28 mg, respectively.

TABLE 2
Effect of dietary treatment on urinary and fecal calcium and net calcium balance

Subject	44 g protein				Dietary treatment 102 g protein				102 g protein + $NaHCO_3$			
	I*	U*	F*	B*	I*	U*	F*	B*	I*	U*	F*	B*
	mg/day											
1	516	65	416	35	515	147	385	−17	524	96	488	−60
2	510	78	432	0	509	188	386	−65	519	120	307	92
3	520	122	316	82	520	183	404	−67	528	151	325	52
4	519	125	461	−67	517	196	434	−113	523	146	365	12
5	506	81	424	1	502	192	318	−8	512	106	379	27
6	526	103	423	0	526	212	450	−136	538	139	394	5
Mean ± SEM	516	96	412	8	515	186	396	−68	524	126	376	21
	±2	±10†§	±20	±20	±3	±9†‡	±19	±21‖	±4	±9‡§	±26	±20‖

* I, intake; U, urinary loss; F, fecal loss; B, net balance. Values are the means of 8, 14, or 10 days for the 44 g protein, 102 g protein, or 102 g protein with sodium bicarbonate periods, respectively.
The pairs of values with the same symbol are significantly different: † or ‡ $p < 0.001$; § $p < 0.01$; ‖ $p < 0.05$.

Urinary acid excretion

Figure 1 shows the changes in urinary pH and calcium, and in the excretion of total titratable acid, ammonium ion, and net renal acid that occurred as the result of dietary treatment. All indices mentioned above were significantly affected by dietary treatment.

With the increase in protein intake from 44 to 102 g, the following changes were observed in mean values for the 3 days of each period when urinary acid indices were measured. Urinary pH decreased 0.8 U; total titratable acid increased 10 mEq and appeared to remain stable with time; ammonium ion concentration more than doubled, increasing with time; and net renal acid excretion paralleled the change in ammonium ion increasing from 32 to 71 mEq.

When 70 mEq of sodium bicarbonate was added to the 102-g protein diet, the mean urinary pH increased from 5.3 to 6.9; total titratable acid decreased to 6 mEq, again appearing to have stabilized; ammonium ion concentration decreased from 46 to 21 mEq and net renal acid excretion decreased 85% from 71 to 11 mEq. The mean net renal acid excretion averaged 10 mEq less than the ammonium ion concentration during this period, a reflection of the large amount of bicarbonate ion being excreted. The mean urinary calcium decreased gradually after the addition of bicarbonate to the diet from 196 mg on the last day of the second dietary period to 144, 114, and 111 on the 2nd, 6th, and 10th day of the third dietary period.

The mean urinary calcium and acidity values separated according to age of the subjects are presented in **Table 3**. The small number of subjects prevents drawing definite conclusions about statistically significant differences due to age. The mean urinary pH was consistently higher for the younger women. Total titratable acid values were variable, increasing less with the increase in protein intake for the two younger women and decreasing more with the addition of sodium bicarbonate to the diet. The two younger women excreted more ammonium ion throughout the study than did the older group. Although the younger women excreted a greater amount of net renal acid during the first two treatment periods than did the older women, the average increase in net renal acid excretion with the increase in protein intake was approximately the same, 40 and 38 mEq. Net renal acid decreased more for the younger than for the older women when sodium bicarbonate was added to the higher protein diet.

Arterialized blood pH and bicarbonate ion concentrations

The mean values obtained for arterialized venous blood pH and bicarbonate ion concentrations are presented in **Table 4**. Although the mean values decreased with the increase in protein intake and increased with the addition of sodium bicarbonate to the higher protein diet, the absolute differences

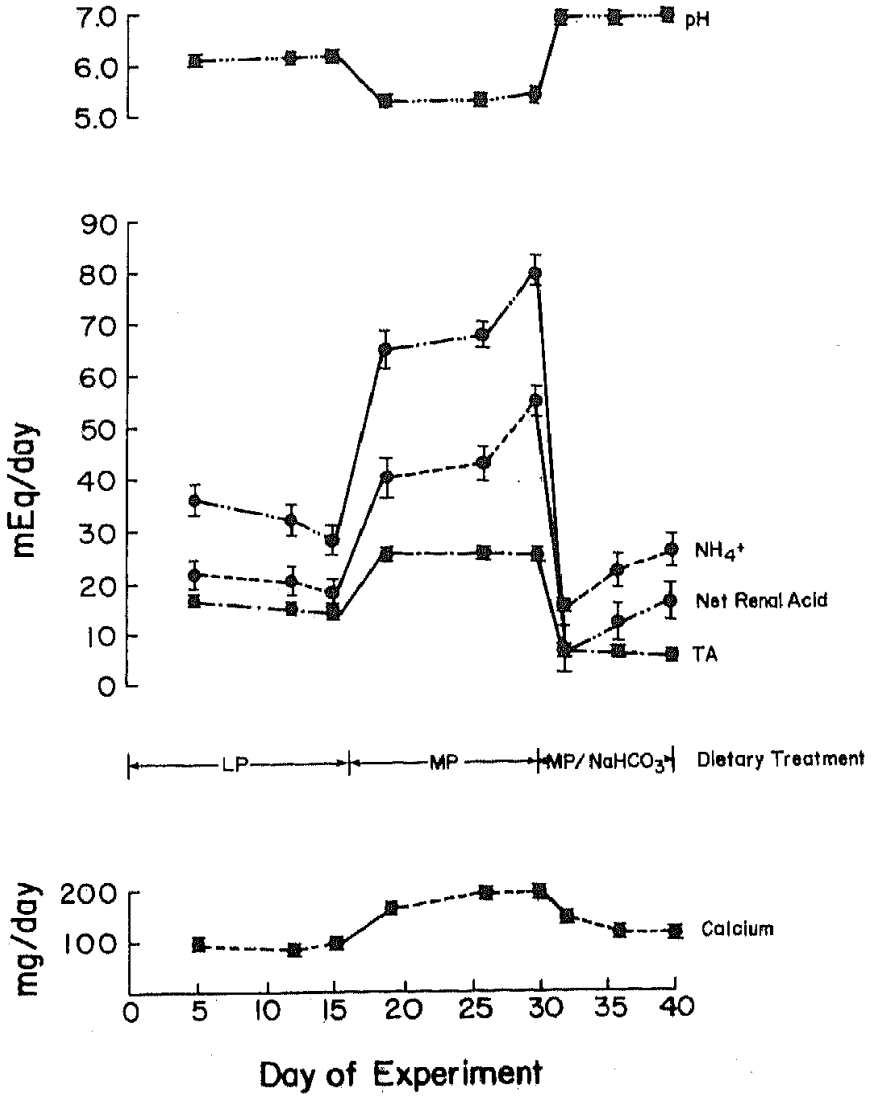

FIG 1. Renal excretion of acid and calcium of women as affected by three dietary treatments: a 44-g protein diet (*LP*, low protein), a 102-g protein diet (*MP*, moderate protein), and 5.85 g (70 mEq) sodium bicarbonate ingested concomitantly with the 102-g protein diet (MP/$NaHCO_3$). Urinary calcium and acid indices were determined on 3 days of each dietary period. The protein intake was increased on day 17; sodium bicarbonate was added to the 102-g protein diet on day 31. The *unbroken lines* connecting data obtained on days 15 and 19 and on days 30 and 32 were drawn to help the reader follow the appropriate values. *TA*, titratable acid; NH_4+, ammonium ion concentration.

were too small for statistical significance. No significant differences in arterialized venous blood pH and bicarbonate ion concentrations were obtained due to age of the subject.

Discussion

With the increase in protein intake from 44 to 102 g, as calcium and phosphorus intakes were held constant at 500 and 900 mg, the mean net calcium balance decreased from 8 to −68 mg. The deleterious effect of the modest increase in protein intake on calcium balance was mainly attributable to the increase in urinary calcium since the decrease in fecal calcium was not statistically significant. These findings are in agreement with the results of previous studies in which similar levels of protein, calcium, and phosphorus intakes have been used (1, 4). Under these conditions increased protein intake has consistently led to marked increase in urinary calcium. The effect of increased protein intake on calcium absorption has been more variable, appearing to depend upon the level of calcium intake as well as upon the level of protein intake (1, 9). Positive or less negative net calcium balance has been demonstrated with lower than with higher levels of protein intake (1, 2, 4, 9–12).

TABLE 3
Effect of age on urinary calcium, pH, total titratable acid, ammonium ion concentration, and net renal acid excretion of women receiving three dietary treatments*

	Age group†	Dietary treatment		
		44 g protein	102 g protein	102 g protein + $NaHCO_3$
	yr			
pH	40	6.30 ± 0.10	5.68 ± 0.02	7.17 ± 0.06
	60	6.08 ± 0.06	5.18 ± 0.06	6.81 ± 0.06
Total titratable acid (mEq/24 h)	40	15 ± 1	22 ± 1	3 ± 1
	60	15 ± 0.4	27 ± 1	7 ± 1
Ammonium ion (mEq/24 h)	40	26 ± 3	56 ± 3	26 ± 4
	60	17 ± 2	41 ± 3	18 ± 2
Net renal acid (mEq/24 h)	40	38 ± 3	78 ± 3	8 ± 6
	60	29 ± 2	67 ± 2	13 ± 3
Calcium (mg/24 h)	40	110 ± 6	171 ± 6	146 ± 6
	60	83 ± 4	188 ± 10	111 ± 10

* Each value is the mean ± SEM for determinations on 3 days.
† n = two 40-yr-old women; four 60-yr-old women.

TABLE 4
Effect of dietary treatment on mean arterialized venous blood pH and bicarbonate ion concentrations

	Dietary treatment		
	44 g protein	102 g protein	102 g protein + $NaHCO_3$
pH	7.421 ±0.008	7.409 ±0.005	7.417 ±0.006
HCO_3^- (mEq/l)	24.98 ±0.57	23.66 ±0.32	25.11 ±0.50

The use of semipurified proteins on this study to increase protein intake facilitated maintaining calcium and phosphorus intakes constant at lower levels. When dealing with commonly consumed high protein foods, nitrogen and phosphorus contents vary together to a considerable extent. These two nutrients have been shown to have opposite effects on urinary calcium (1, 13), phosphorus being hypocalciuretic and protein, hypercalciuretic. Simultaneous increases in both, as might be found with self-selected diets, would be expected to lessen the effect of a change in either alone (14, 15).

The addition of 70 mEq of sodium bicarbonate to the 102-g protein diet decreased urinary calcium sufficiently so that the mean net calcium balance for the 10-day period became positive, 21 mg/day. Since urinary calcium decreased with time after the sodium bicarbonate addition to the diet as shown in Figure 1, it would be expected that calcium balance would also become more positive with time. This finding suggests the possibility that the administration of a small amount of sodium bicarbonate, approximately 1 mEq/kg body weight, might be used to increase calcium retention in individuals with protein-induced hypercalciuria. However, longer term, more extensive studies at various levels of protein, calcium, and phosphorus intakes, would be necessary before this suggestion could be implemented in clinical practice.

The hypocalciuretic effects of sodium bicarbonate have been noted previously. In studies of acid balance in humans, Lemann et al (16) noted that both fecal and urinary calcium decreased when sodium bicarbonate was administered; values for calcium balance were not reported. Reidenberg et al (17) reported that urinary calcium decreased markedly when sodium bicarbonate was administered to obese women for correction of a metabolic acidosis produced by fasting. Chan (18) reported that calcium balance became more positive when sodium bicarbonate was given to a young patient with type 1 renal distal tubular acidosis. Barzel and Jowsey (19) demonstrated that long-term ingestion of an equimolar solution of sodium and potassium bicarbonate prevented the development of calcium deprivation osteopenia in rats and increased bone formation.

The effects of the increase in protein in-

take on urinary pH and net renal acid excretion were similar to those obtained in the previous study (4). The acidification of the urine by the increase in protein intake and its alkalinization with sodium bicarbonate ingestion supported the premise that the increase in protein intake represented a form of acid loading and that a slight metabolic acidosis occurred in these subjects. The fact that a metabolic acidosis was not evidenced by a statistically significant change in arterialized venous blood pH and bicarbonate ion concentration could be explained by the fact that the expected changes were small and that since the blood was analyzed after an overnight fast, equilibration of blood may have occurred. The urinary changes observed on this study probably better reflected the acid-base changes that occurred. Lemann et al (20) have indicated that in healthy adults, urinary net acid excretion parallels changes in fixed acid production.

There appeared to be a discordance between urinary calcium and net renal acid excretion on this study. With the increase in protein intake, the mean net renal acid excretion increased 122% while urinary calcium increased 94%. With the addition of sodium bicarbonate to the higher protein diet, essentially all of the urinary acid was neutralized; but based on the mean values obtained for the last days of the second and the third dietary periods, urinary calcium decreased only 43%. This discordance suggested that although the net renal acid changes explained part of the increase in urinary calcium that occurred with increased protein intake, other factors may also have been involved.

The mechanism by which increases in protein intake augment urinary calcium was not investigated on this study. There is considerable evidence that a decrease in renal tubular reabsorption of calcium is involved in protein-induced hypercalciuria (1, 21, 22). It has been reported that increased protein intake augments fixed acid production by increasing the formation and urinary excretion of organic acids and the oxidation of amino acid sulfur to inorganic sulfate (20); each equivalent of sulfur amino acid metabolized produces two equivalents of hydrogen ions (23). Various explanations have been postulated for the protein-induced decrease in renal tubular calcium reabsorption: increased formation of poorly reabsorbable calcium sulfate complexes in the urine (24), a direct effect of metabolic acid on metabolic processes within renal tubular cells (25), and an enhanced delivery of sodium bicarbonate to the distal tubule (20). In this present study an increased formation of urinary calcium sulfate complexes was not a possibility since the same protein diet was consumed during the second and the third dietary periods. Either of the two other explanations are more likely.

It was of interest to compare the younger and older women in their ability to excrete the acid load imposed by ingestion of the increased protein intake. The two younger women maintained higher urinary pH throughout the study; the reason for this is not known. They were also able to excrete higher levels of ammonium ion; this was reflected in higher net renal acid excretion with the 44- and 102-g protein diets. Adler et al (26) have reported that the ability to excrete an acute acid load of ammonium chloride is impaired with aging, the impairment being proportional to the decrease in glomerular filtration rate. These investigators found that the percentage of acid excreted as ammonium ion was significantly decreased in older subjects. Their finding that the serum bicarbonate concentrations were normal despite an apparent hydrogen ion retention by the older subjects led them to speculate that some fixed source of body buffer, presumably bone, was being buffered in order to spare extracellular buffers. The similarities between the results obtained with increases in protein intake for the two age groups of women and those obtained by Adler et al (26) with ammonium chloride loading are striking. Replication of this study with more subjects would be worth while.

The author is grateful to Laurel Lebeck, MS, for technical assistance; to Audrey Chang, PhD, for statistical and computer analyses; to J Dempsey, PhD, and members of the Department of Nutritional Sciences for use of their equipment and facilities; and to David P Simpson, MD, for consultation and for suggesting the trial with sodium bicarbonate. The casein and lactalbumin were a gift from New Zealand Milk Products, Inc, Petaluma, CA 94952 and the Brilliant Blue Dye, a

gift from H. Kohnstamm and Co, Inc, Brooklyn, NY 11231.

References

1. Linkswiler HM, Zemel MB, Hegsted M, Schuette S. Protein-induced hypercalciuria. Fed Proc 1981;40:2429–33.
2. Johnson NE, Alcantara EN, Linkswiler H. Effect of level of protein intake on urinary and fecal calcium and calcium retention of young adult males. J Nutr 1970;100:1425–30.
3. Wachman A, Bernstein DS. Diet and osteoporosis. Lancet 1968;1:958–9.
4. Lutz J, Linkswiler HM. Calcium metabolism in postmenopausal and osteoporotic women consuming two levels of dietary protein. Am J Clin Nutr 1981;34:2178–86.
5. Heaney RP, Gallagher JC, Johnston CC, Neer R, Parfitt AM, Whedon GD. Calcium nutrition and bone health in the elderly. Am J Clin Nutr 1982;36:986–1013.
6. Natelson S. Routine use of ultramicro methods in the clinical laboratory. Am J Clin Pathol 1951;21:1153–72.
7. Lemann J Jr, Lennon EJ. A potential error in the measurement of urinary titratable acid. J Lab Clin Med 1966;67:906–13.
8. Forster HV, Dempsey JA, Thomson J, Vidruk E, Do Pico GA. Estimation of arterial PO_2, PCO_2, pH, and lactate from arterialized venous blood. J Appl Physiol 1972;32:134–7.
9. Linkswiler HM, Joyce CL, Anand CR. Calcium retention of young adult males as affected by level of protein and of calcium intake. Trans NY Acad Sci 1974;36:333–40.
10. Schuette SA, Zemel MB, Linkswiler HM. Studies on the mechanism of protein-induced hypercalciuria in older men and women. J Nutr 1980;110:305–15.
11. Hegsted M, Linkswiler HM. Long-term effects of level of protein intake on calcium metabolism in young adult women. J Nutr 1981;111:244–51.
12. Heaney RP, Recker RR. Effects of nitrogen, phosphorus, and caffeine on calcium balance in women. J Lab Clin Med 1982;99:46–55.
13. Hegsted M, Schuette SA, Zemel MB, Linkswiler HM. Urinary calcium and calcium balance in young men as affected by level of protein and phosphorus intake. J Nutr 1981;111:553–62.
14. Schuette SA, Linkswiler HM. Effects of Ca and P metabolism in humans by adding meat, meat plus milk, or purified proteins plus Ca and P to a low protein diet. J Nutr 1982;112:338–49.
15. Spencer H, Kramer L, DeBartolo M, Norris C, Osis D. Further studies on the effect of a high protein diet as meat on calcium metabolism. Am J Clin Nutr 1983;37:924–9.
16. Lemann J Jr, Lennon EJ, Goodman AD, Litzow JR, Relman AS. The net balance of acid in subjects given large loads of acid or alkali. J Clin Invest 1965;44:507–17.
17. Reidenberg MM, Haag BL, Channick BJ, Shuman CR, Wilson TGG. The response of bone to metabolic acidosis in man. Metabolism 1966;15:236–41.
18. Chan JCM. Nutrition and acid base-base metabolism. Fed Proc 1981;40:2423–8.
19. Barzel US, Jowsey J. The effects of chronic acid and alkali administration on bone turnover in adult rats. Clin Sci 1969;36:517–24.
20. Lemann J Jr, Adams ND, Gray RW. Urinary calcium excretion in human beings. N Engl J Med 1979;301:535–41.
21. Kim Y, Linkswiler HM. Effect of level of protein intake on calcium metabolism and on parathyroid and renal function in the adult human male. J Nutr 1979;109:1399–404.
22. Zemel MB, Schuette SA, Hegsted M, Linkswiler HM. Role of the sulfur-containing amino acids in protein-induced hypercalciuria in men. J Nutr 1981;111:545–52.
23. Lemann J Jr, Relman AS. The relation of sulfur metabolism to acid-base balance and electrolyte excretion: the effects of DL-methionine in normal man. J Clin Invest 1959;38:2215–23.
24. Walser M, Browder AA. Ion association. III. The effect of sulfate infusion on calcium excretion. J Clin Invest 1959;38:1404–11.
25. Lemann J Jr, Litzow JR, Lennon EJ. Studies of the mechanism by which chronic metabolic acidosis augments urinary calcium excretion in man. J Clin Invest 1967;46:1318–28.
26. Adler S, Lindeman RD, Yiengst MJ, Beard E, Shock NW. Effect of acute acid loading on urinary acid excretion by the aging human kidney. J Lab Clin Med 1968;72:278–89.