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The Importance of Calcium, Potassium, and Acid-Base Homeostasis in Bone Health and Osteoporosis Prevention

Nutrient Effects on the Calcium Economy: Emphasizing the Potassium Controversy[1,2]

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Abstract

The calcium economy is a dynamic state influenced by fluxes in dietary calcium intake, intestinal calcium absorption, and renal calcium conservation. The relationship of selected bone-related nutrients to these calcium fluxes exhibits both constructive and destructive interactions that affect the overall state of calcium balance. The basis of the calcium requirement and the impact of vitamin D, protein, phosphorus, sodium, and caffeine on the calcium economy are reviewed. Against this background, emerging data on potassium are presented. Data from balance studies of healthy white women at midlife were reviewed to assess the effect of diet potassium on the calcium economy under steady-state conditions. Potassium was inversely associated with both urinary calcium excretion and intestinal calcium absorption, yielding no significant net change in calcium balance. In the population reported on here, dairy, meat, and cereal grains together contributed 56%, and fruits and vegetables 44%, of total dietary potassium. To the extent that fruit and vegetable potassium is a surrogate for high bicarbonate, this cohort did not have a dietary intake pattern allowing for measurement or interpretation of the potential effect of a high-bicarbonate-containing diet on long-term steady-state calcium balance. Potassium itself is uniformly well absorbed regardless of the dietary source. Mean 24-h urinary potassium averaged 92% of dietary intake. According to nationwide food consumption surveys, milk is the number 1 single food source of potassium in all age groups in the United States. J. Nutr. 138: 166S–171S, 2008.

Introduction

The skeleton is a complex organ system, and osteoporosis a complex and multifactorial condition of bone pathology. Calcium homeostasis is but 1 factor impacting skeletal health and disease. Although suboptimal calcium intakes and negative calcium balance may ultimately result in osteoporosis, not all osteoporosis occurs as a direct result of calcium deficiency. Nevertheless, it is generally agreed that the progression of osteoporosis may be exacerbated by negative calcium balance.

Maintaining calcium homeostasis is a dynamic process influenced by fluxes in dietary calcium intake, intestinal calcium absorption, and renal calcium conservation that, taken together, determine the calcium economy. Many factors affect these processes, including thyroid and renal function, serum 25-hydroxyvitamin D and parathyroid hormone concentrations, and diet and nutritional status.

The relation of nutrition to the calcium economy exhibits both constructive and destructive interactions that affect the overall state of calcium balance. This article presents the basis for the calcium requirement in adults, with a summary of nutritional factors that influence the adult calcium economy toward positive or negative balance by discussing selected bone-related nutrients in regard to their impact on intestinal calcium absorption and renal calcium excretion. In particular, an emerging role for potassium and its accompanying anion in relation to the calcium economy is presented, along with data quantifying the dietary intake and bioavailability of potassium from various food sources.

Selected bone-related nutrients

Numerous observational studies and clinical trials have been conducted to elucidate the effect of various macro- and micronutrients on calcium balance. The bone-related nutrients, identified as calcium, phosphorus, vitamin D, magnesium, and fluoride, formed the first group of nutrients subject to review when the Food and Nutrition Board of the Institutes of Medicine began its latest review, in the mid-1990s, of the 45 nutrients for which recommendations are established. These 5 nutrients were

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categorized together as the so-called bone-related nutrients because the index disease associated with a deficiency is primarily a bone, or hard tissue, endpoint. An adequate intake (AI) of fluoride prevents tooth decay, for example; and an AI of vitamin D prevents rickets in children.

Calcium likewise had been reviewed primarily for its role in the development and maintenance of a healthy skeleton, and the body of science that attended calcium in the mid-1990s was sufficient to warrant an increase in the calcium recommendation, up from the previous RDA for adults of 800 mg/d established in 1989 to the current (50 y) AI recommendation of 1200 mg/d (1).

Contributions of sound science notwithstanding, the 1-nutrient–1-disease paradigm for nutrient recommendation was the prevailing model well into the 1990s. However, by the time the fifth and final group of nutrient recommendations was established and published by the Institute of Medicine a decade later, a new paradigm had emerged. Rather than addressing nutrient requirements on the basis of the minimum amount needed to prevent the index disease, the reference value, as in the case of potassium for example, was derived on the basis of reducing chronic disease and promoting the greatest public health benefit (2). The result was an increase in the potassium recommendation, up from an estimated minimum requirement of 2000 mg/d, to the current (14 y) AI of 4700 mg/d (3). This broader context of potassium's health-promoting function included an emerging constructive role for potassium in the calcium economy.

In addition to calcium, vitamin D, phosphorus, and potassium, protein, sodium, and caffeine have been conclusively studied for their effect on bone health. These 6 nutrients, plus caffeine, will be considered for their impact on the calcium economy.

Calcium requirements

Calcium requirements have been determined to be that intake above which no further calcium can be *retained* (1). Maximal calcium retention is a function of the quantities of calcium ingested, absorbed, and excreted. In adults, the amount of calcium absorbed from the gastrointestinal tract must be quantitatively equal to all calcium losses from the body to achieve a calcium steady state that affords protection to the skeleton. However, to achieve positive calcium balance and maximal calcium retention, the quantity of calcium absorbed by the GI tract must *exceed* all calcium losses, thereby providing the substrate necessary to maximize skeletal size and strength for bone growth in childhood and adolescence and maintenance in adulthood.

Absorption of calcium is known to be relatively inefficient, although it is important to note that unabsorbed calcium yields beneficial results in the gut by blocking absorption of potentially harmful byproducts of digestion. In healthy adults, at typical calcium intakes, gross absorption averages in the range of 25–35% of ingested calcium. Heaney et al. (4) have shown a full range of normal absorption in women to be 15–45%.

Calcium excretion occurs through renal losses as well as losses through the bowel (feces), skin, hair, and nails. These obligatory calcium losses can easily exceed absorbed calcium at prevailing calcium intakes. Therefore, dietary intake has to be high enough to ensure that the rate of absorption introduces enough calcium into the system to offset obligatory losses and avoid skeletal damage.

Even at low calcium intakes, there is always an obligatory loss of calcium in the urine and feces. Usual 24-h calcium excretion via urine and feces is ~160–200 mg and increases by a factor of 5–10% as calcium intake increases (5). Calcium losses through skin, hair, and nails must also be taken into account. Estimates of these daily calcium losses, which are unrelated to calcium intake, fall in the range of 40–80 mg (6). Substantial dermal calcium losses can be much higher under conditions of heavy sweating. Klesges et al. (7) have reported a mean dermal calcium loss of over 200 mg during a 2-h basketball practice session in college athletes. Also affecting calcium loss is menopause, which is accompanied by a sustained rise in obligatory urinary calcium of ~30 mg daily (8).

On the basis of the median value of each calcium excretion variable (urine/feces, 180 mg; skin/hair, 60 mg; menopause, 30 mg) plus a conservative estimate of 30 mg calcium lost in sweat, a cumulative daily calcium loss of 300 mg would be considered typical for most adult women and would require a calcium intake of 1200 mg/d, absorbed at 25% efficiency, to offset loss. At a calcium intake of 1000 mg/d, a 30% absorption efficiency rate would be required, whereas a calcium intake of 850 mg/d would require an absorption efficiency rate of 35% merely to offset daily obligatory calcium losses. In contrast, median calcium intakes among U.S. women continue to be <700 mg/d (9), an intake that even under optimal calcium absorption efficiency is not adequate to offset the most conservative calcium excretion values, let alone to achieve maximal calcium retention.

The target intake of dietary calcium to achieve the desirable maximal retention and afford optimal calcium accretion in bone is difficult to estimate because of a host of other factors that play a role in the calcium economy. The considerable interindividual variation in both calcium absorption and excretion that occurs can partially be attributed to the effects of various other nutrients on the calcium economy. Therefore, any nutrition-associated improvement in intestinal calcium absorption or reduction in urinary calcium excretion could produce an important calcium advantage for women with low calcium intakes, assuming no offsetting adjustments of other calcium fluxes.

Nutrient impact on intestinal calcium absorption and renal calcium excretion

Vitamin D. The calcium economy depends most critically on vitamin D. A primary factor affecting calcium absorption is the vitamin D status of the individual. Serum 25-hydroxyvitamin D concentration (25OHD) is the accepted functional indicator of vitamin D status (1). It has long been recognized that vitamin D is necessary for the active transport of calcium across the intestinal mucosa; however, the vitamin D status that fully optimizes calcium absorption has only recently been identified and quantified. Heaney et al. have shown that intestinal calcium absorption improved by 68% when serum 25OHD was raised from 50 nmol/L to >80 nmol/L in postmenopausal women (10). Although both values fall within the current laboratory reference range for "normal" serum 25OHD status, these results indicate that calcium absorption efficiency is suboptimal at the lower end of the reference range.

Protein. Studies using purified protein or protein hydrolysates have consistently shown a representative 1-mg rise in urinary calcium excretion for each 1 g of ingested protein (11,12). Others, however, taking protein in its whole food context ingested as meat and/or dairy, have shown no rise in urinary calcium (13–15). Kerstetter et al. (16) found high protein intakes actually enhance calcium absorption. The protein ingested as meat and dairy foods is accompanied by phosphorus and potassium, which may counter a protein effect on urinary calcium, as both phosphorus and potassium tend to be hypocalciuric (14,17).

The value of adequate protein on skeletal tissue cannot be overstated. Protein is a major bulk constituent of bone and must be regularly supplied by the diet. Under conditions of calcium repletion, Dawson-Hughes et al. (18) showed bone gain with high animal protein intake but no bone effect with a low protein intake, whereas a high protein intake under conditions of calcium deficiency showed worsening bone status. The true effect of either nutrient on the calcium economy can best be demonstrated under conditions of full repletion of each, a criterion that is often disregarded under study conditions testing isolated nutrients.

Phosphorus. Bone mineral is predominantly calcium phosphate. Adequate dietary phosphorus is essential for bone building. Ingested phosphorus, however, alters the operation of the calcium economy. Dietary phosphorus reduces urinary calcium losses (14). Rafferty et al. have shown that calcium supplements and fortificants containing phosphorus (e.g., tricalcium phosphate, dicalcium phosphate) have a diminishing effect on calcium absorption when tested against dairy milk in the same subjects (K. Rafferty, G. Walters, R.P. Heaney, unpublished data). Milk also contains phosphorus, but a synergistic effect of other nutrients in milk (e.g., calcium, protein, potassium, magnesium) may lead them to act together to improve absorption of dairy calcium relative to phosphate-containing calcium supplements.

Caffeine. As reported by Barger-Lux and Heaney (19,20), the influence of caffeine on short-term increases in urinary calcium is attributed to the diuretic effect of caffeine, with loss of calcium accompanying a temporary increase in sodium excretion. Apart from the acute diuretic effect, there is no discernable effect of caffeine on 24-h urinary calcium excretion. The reported negative effect of caffeine on calcium absorption is quite small and may be offset by the addition of 1–2 tablespoons (15–30 mL) of milk to 1 cup of caffeine-containing coffee. In calcium-replete individuals, there is no evidence that caffeine has any negative effect on the calcium economy.

Sodium. There is a sustained consensus that excessive dietary sodium intake as sodium chloride (NaCl) elevates urinary calcium excretion, presumably because sodium competes with calcium for reabsorption in the renal tubules (21,22). A representative value has urinary calcium excretion increasing ~20 mg for each 1000-mg increase in dietary sodium at prevailing calcium intakes (23). However, at calcium intakes at or above recommended levels, adaptive increases in absorbed calcium offset the increased urinary loss. Furthermore, potassium intakes at recommended levels effectively negate NaCl-induced calciuria (21).

How much of the hypercalciuric effect of NaCl can be attributed to the coexisting chloride anion is not fully known. For example, replacement of sodium chloride with the bicarbonate or citrate forms of sodium reversed the urinary calcium excretion (24). These findings indicate that the net effect of dietary minerals such as sodium and potassium can be modulated by the accompanying anions as well as by replete dietary intakes of calcium and potassium.

Potassium and the calcium economy

Against this background, it is of interest to examine the effect of potassium on the calcium economy. In healthy adults, potassium bicarbonate has been shown to be hypocalciuric (17,25). A potassium-associated reduction in urinary calcium excretion could produce an important calcium advantage for women with high potassium intakes, assuming no offsetting adjustments of other calcium fluxes. This potential advantage was examined in the analysis of a large balance study database to assess potassium effects on the calcium economy under steady-state conditions.

Known as the Omaha Nun Study, and originally funded by the NIH for 27 consecutive years as a prospective investigation of calcium metabolism and bone health, the study obtained 8-d inpatient metabolic measurements of nitrogen, phosphorus, and calcium balance in 191 healthy women through midlife under steady-state conditions. In this longitudinal study, fractional calcium absorption was measured at 5-y intervals yielding 644 absorption values over a period of more than 30 y.

Inpatient diets were individually designed by the unit dietitian to match within 5% each subject's usual diet in energy, protein, calcium, and phosphorus. The protein, phosphorus, and calcium intakes of the subjects were determined by chemical analysis of duplicate weighed diets. The median nutrient intake values for the group also closely matched the NHANES III dietary intake medians for this population of 59 g protein, 617 mg calcium, 2342 mg potassium, and 1000 mg phosphorus/d (9).

All urine was collected and measured for creatinine, calcium, phosphorus, nitrogen, and potassium; stool collections were analyzed for calcium, and dual isotopic calcium tracer studies yielded measurement of fractional calcium absorption. The study itself has been characterized elsewhere in regard to the calcium requirement of middle-aged women (26). Rafferty et al. reported on their investigation of the association between dietary potassium intake, fractional calcium absorption, and urinary calcium excretion in this same cohort of women, studied on diets to which they had adapted over periods of years (27). Potassium intakes varied among subjects by ~4-fold (1170 – 4524 mg/d.) The potassium value was derived from food tables and measured against urinary potassium measured values. **Figure 1** sets forth the inpatient diet potassium against the prestudy diet potassium as obtained from 7-d weighed and measured food records on a subset of 123 women, showing that a usual potassium intake was achieved.

An inverse relation between dietary potassium and urinary calcium was found, such that for each 1000 mg potassium ingested, 11 mg calcium was conserved. This is slightly lower than, although similar to, an accepted representative effect size reported by others of 15 mg calcium conserved for each 1000 mg of potassium ingested (27). However, a calcium balance effect was not found, largely because the reduced calciuria was offset by a reduction in intestinal calcium absorption, effectively eliminating any appreciable net balance change.

A possible mechanism for this negative potassium effect on intestinal calcium absorption has been described by Jaeger (28),

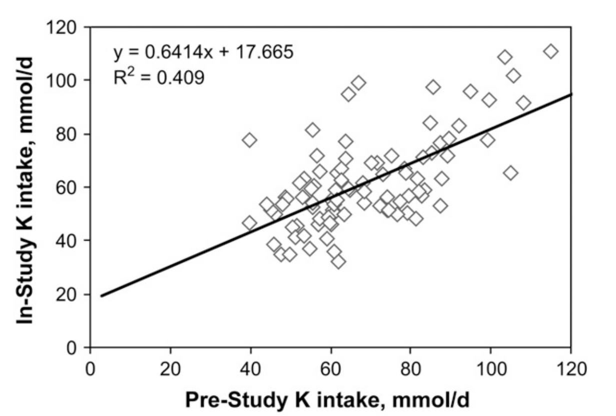

FIGURE 1 Inpatient diet K against the prestudy diet K as obtained from 7-d weighed and measured food records on a cohort of 123 women. In-study K intakes approximated prestudy usual intakes. The potassium values were derived from food tables (1 mmol K = 39 mg).

who noted that potassium loading caused renal phosphate retention, which lowered 1,25-dihydroxycholecalciferol synthesis and would be expected to reduce calcium absorption.

At the median intakes of this study population, potassium food sources were primarily dairy, meat, and cereal grains (56%) with a lesser amount of potassium obtained from fruits and vegetables (44%). To the extent that fruit and vegetable potassium is a surrogate for high bicarbonate, this cohort did not have a dietary intake pattern allowing for measurement or interpretation of the potential effect of a high-bicarbonate-containing diet on long-term steady-state calcium balance.

Potassium bioavailability

Potassium absorption was also measured, prompted by the concurrent release of the first printing of the USDA's 2005 *Dietary Guidelines for Americans,* scientific section on potassium and sodium, which contained the statement: "Although meat, milk, and cereal products contain potassium, the form of potassium in these foods is not as readily available for absorption (29)."

Median potassium intake under study was 2404 mg/d, closely matching the NHANES III potassium intake for women at midlife (9). Mean 24-h urinary potassium averaged 92% of dietary intake (**Fig. 2**). Because, under steady-state conditions, urinary potassium is equal to absorbed potassium, it follows that mean potassium absorption in these women was nearly complete.

The cohort was divided into halves based on median intakes for protein and calcium. Those with high protein intakes would have tended to be high in both meat and dairy, and those with high calcium intakes would have been high specifically in dairy. Potassium absorption was separately analyzed in those above and below the median intakes for the 2 nutrients. Potassium absorption remained above 90% on both sides of the protein and calcium medians (**Table 1**), and the small differences between them were not statistically significant. From the failure to find a difference at low and high meat and dairy intakes, it can be concluded that potassium is uniformly well absorbed regardless of dietary source.

With the results of this analysis provided to the USDA, the errant statement was expunged from subsequent printings of the 2005 *Dietary Guidelines for Americans* text and replaced with: "Meat, milk, and cereal products also contain potassium but may not have the same effect on acid-base metabolism (30)."

Achieving dietary potassium adequacy

Investigation into the dietary sources of potassium in this study population was undertaken to identify any significant dietary pattern variance in those with high potassium intakes compared with those with lower potassium intakes. Only 2% ($n = 11$) of the full cohort was identified as a "high-potassium" group, having a usual dietary potassium intake of >3500 mg/d (~75% of the AI of 4700 mg/d) with no 1 individual meeting the AI of 4700 mg/d. The primary dietary pattern variable that distinguished the high-potassium group from the full cohort was a high milk consumption, amounting to a difference of ~2½ cups/d (600 mL/d) (**Fig. 3**).

In their analysis of 17,959 individual respondents in the 1994–1996, 1998 Continuing Survey of Food Intake by Individuals (CSFII), Weinberg et al. (31) similarly showed that a difference of ~2⅓ cups (552 mL) of milk separated quartile 2 of dairy intake from quartile 4. As milk intake increased from 0.9 cups (216 mL)/d (quartile 2) to 3.2 cups (768 mL)/d (quartile 4), potassium also increased from 50% of the AI to 75% of the AI.

TABLE 1 Bioavailability of dietary potassium by high and low protein and calcium intakes in women through midlife obtained under steady-state conditions in metabolic balance studies

Calcium median 636 mg/d	Potassium fractional absorption	Protein median 62.8 g/d	Potassium fractional absorption
<636 ($n = 60$)	0.9447	<62.8 ($n = 59$)	0.9374
>636 ($n = 61$)	0.9128	>62.8 ($n = 59$)	0.9249

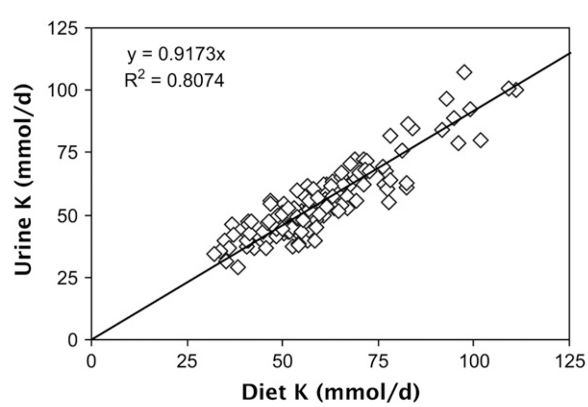

FIGURE 2 Inpatient diet K against urine K values obtained in a cohort of 123 women through midlife under metabolic conditions. Mean 24-h urinary K averaged 92% of dietary intake under steady-state conditions (1 mmol K = 39 mg).

Dietary sources of select bone-related nutrients

Nationwide nutrition and food consumption surveys are useful to identify nutrients that may be consumed at levels low enough among a population to cause concern, to quantify primary dietary sources of nutrients, and to establish public policy guiding recommendations for food consumption and fortification. NHANES 1999–2000 and CSFII 1994–1996 analyses of food sources of calcium, vitamin D, protein, phosphorus, and potassium reveal milk to be the number 1 single food contributor of each of these bone-related nutrients with the exception of protein in all age groups of both sexes (32,33). **Table 2** identifies the NHANES 1999–2000 and CSFII 1994–1996 top 3 food sources for calcium, vitamin D, protein, phosphorus, and potassium in the diets of children and adults in the U.S. population. Recognition of the contribution of dairy foods in achieving nutrient adequacy of several key nutrients, including potassium, led to an increase in the recommendation for dairy intake in the 2005 *Dietary*

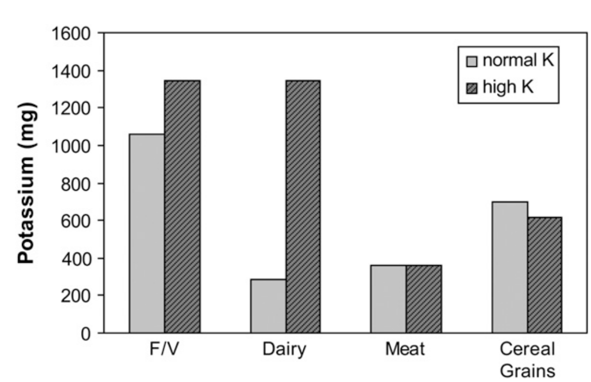

FIGURE 3 Dietary K by food group as derived from 7-d weighed and measured food records obtained from women through midlife. Mean normal K intake = 2402 mg/d; mean high K intake = 3643 mg/d.

TABLE 2 Top 3 food sources of selected bone-related nutrients in the U.S. diet as derived from nationwide food consumption surveys: NHANES 1999–2000 and the CSFII 1994–1996

Nutrient	Rank	2–5 y[1]	6–11 y[1]	12–18, y F[2]	12–18, y M[2]	Adults[3]
Calcium	1st	Milk	Milk	Milk	Milk	Milk
	2nd	Cheese	Cheese	Cheese	Cheese	Cheese
	3rd	Bread	Bread	Bread	Bread	Bread
Vitamin D	1st	Milk	Milk	Milk	Milk	Milk
	2nd	Ready-to-eat cereal	Ready-to-eat cereal	Ready-to-eat cereal	Ready-to-eat cereal	Ready-to-eat cereal
	3rd	Eggs/fish	Eggs/fish	Eggs/fish	Eggs/fish	Eggs/fish
Protein	1st	Milk	Milk	Beef	Beef	Beef
	2nd	Poultry	Beef	Poultry	Milk	Poultry
	3rd	Beef	Poultry	Cheese	Poultry	Milk
Phosphorus	1st	Milk	Milk	Milk	Milk	Milk
	2nd	Cheese	Cheese	Cheese	Cheese	Cheese
	3rd	Poultry	Bread	Beef	Beef	Beef
Potassium	1st	Milk	Milk	Milk	Milk	Milk
	2nd	Potatoes	Potatoes	Potatoes	Potatoes	Potatoes
	3rd	Juices	Tomatoes	Tomatoes	Beef	Coffee

[1] NHANES 1999–2000.
[2] NHANES 1999–2000; F = female; M = male.
[3] CSFII 1994–1996.

Guidelines for Americans to 3 servings per day for all individuals over 9 y (34).

Limitations of this study and area for further research

Although the effects of calcium, vitamin D, protein, phosphorus, sodium, and caffeine on the calcium economy are generally well established, the effect of potassium, with or without the accompanying bicarbonate anion, is less well understood. It is possible that physiological adaptation to steady-state dietary input over time may account for the difference in the outcome between a study of the effects of potassium on the calcium economy and results reported in short-term intervention trials. Also, in contrast to other studies based on a whole-foods model, in which fruits and vegetables provided the majority of the dietary potassium, this study was limited to a cohort in which the dietary potassium source was primarily milk, meat, and cereal grains, and the focus was on potassium itself rather than the accompanying anion. Fruits and vegetables are rich in both potassium and bicarbonate precursors (e.g., citrate) that metabolize to bicarbonate, whereas milk, meat, and cereal products contain fewer bicarbonate precursors.

Therefore, the failure to find a balance effect in the study reviewed here cannot be extrapolated to a diet rich in fruits and vegetables and their bicarbonate precursors. Indeed, any skeletal benefit of dietary potassium would seem to be dependent on the accompanying bicarbonate-generating anion. Further research is needed to elucidate a bicarbonate effect distinct from a potassium effect on the calcium economy.

A notable feature of the calcium economy is that adjustments of calcium absorption and excretion can diminish the impact of a high calcium intake or compensate for a low calcium intake. Quantifying various nutrient and whole-food effects on the calcium economy provides valuable data for public health professionals, clinicians, and nutritionists to counsel patients on achieving calcium balance; however, simply put, all true nutrient effects on the calcium economy can be managed either by reducing excess intake of the nutrient concerned or by increasing calcium intake. The most effective approach to improving calcium nutriture and preserving the calcium economy is to increase consumption of those foods naturally nutrient-rich in calcium, vitamin D, protein, phosphorus, and potassium. At present, the food source that best achieves such a naturally nutrient-rich designation is dairy.

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