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

The Balance of Bone Health: Tipping the Scales in Favor of Potassium-Rich, Bicarbonate-Rich Foods[1,2]

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Abstract

Public health nutrition strategies to develop and maintain bone health throughout the lifecycle as well as to prevent osteoporosis in later life are urgently needed. In the United States, ~10 million Americans have osteoporosis, with costs estimated at $17.9 billion per year and costs in Europe well in excess of €13.9 billion. This review article outlines the current evidence available in the literature linking potassium-rich, bicarbonate-rich foods to osteoporosis prevention. The health-related benefits of a high intake of potassium-rich, bicarbonate-rich foods (e.g., fruits and vegetables) on disease prevention (e.g., cancer, heart disease) have been gaining increasing attention in the literature, and there is growing belief, from a variety of observational, experimental, clinical, and intervention studies, that a positive link exists between potassium-rich, bicarbonate-rich foods and indices of bone health. However, observational studies are not hypothesis proving and can only suggest the potential mechanisms of action. We now urgently need data from randomized controlled trials to determine for certain whether a potassium-rich, bicarbonate-rich diet or supplement is important to the skeleton. A 1-mo dietary intervention study involving 23- to 76-y-old men and women has shown that a diet high in bicarbonate (high fruits and vegetables) and potassium (high in milk and dairy products) (Dietary Approaches to Stopping Hypertension) significantly reduces bone turnover. Longer-term dietary studies are critical. In addition, the mechanisms underlying a positive effect of a potassium-rich, bicarbonate-rich diet on bone need to be fully determined. These currently include, but are not limited to, *1*) the potential role of the skeleton in acid-base homeostasis; *2*) other nutrient or dietary components found in abundance in fruits and vegetables such as vitamin K, β-carotene, and vitamin C; and *3*) other as yet ''unidentified'' dietary components. The road ahead is a challenging one. J. Nutr. 138: 172S–177S, 2008.

General introduction and review objectives

There are few foods that are good sources of both potassium and bicarbonate in the Western diet. **Table 1** illustrates a variety of foods and food groups that supply pertinent amounts of potassium in the diet, with milk and dairy products being good sources. However, only fruits and vegetables are suppliers of a potassium-rich, bicarbonate-rich combination (1) [and hence have a negative potential renal acid load (PRAL)[3] value]. In the past, our main approach to examining the relation between nutrition and bone health has been to focus on specific (or a variety of) nutrients commonly consumed in the human diet (2,3). An important alternative approach is the consideration of the "foods" we consume rather than the nutrients contained within them; hence, we should focus on the concept of food-specific effects on the diet rather than nutrient-specific effects. Across nations and countries, there is a general consensus regarding the proportions of food groups we should be eating.

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[3] Abbreviations used: APOSS, Aberdeen Prospective Osteoporosis Screening Study; BMD, bone mineral density; DASH, Dietary Approaches to Stopping Hypertension; NEAP, net endogenous acid production; PRAL, potential renal acid load.

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TABLE 1 PRAL values of a variety of foods and food groups[1]

Food/Food group	PRAL	Food/Food group	PRAL
	mEq/100 g edible portion		*mEq/100 g edible portion*
Fruits and fruit juices		Milk, dairy products and eggs	
Apples	−2.2	Milk (whole, pasteurised)	0.7
Bananas	−5.5	Yoghurt (whole milk, plain)	1.5
Raisins	−21.0	Cheddar cheese (reduced fat)	26.4
Grape juice	−1.0	Cottage cheese	8.7
Lemon juice	−2.5	Eggs (yolk)	23.4
Vegetables		Meat, meat products and fish	
Spinach	−14.0	Beef (lean only)	7.8
Broccoli	−1.2	Chicken (meat only)	8.7
Carrots	−4.9	Pork (lean only)	7.9
Potatoes	−4.0	Liver sausage	10.6
Grain products		Beverages	
Bread (white wheat)	3.7	Coca Cola	0.4
Oat flakes	10.7	Coffee (infusion)	−1.4
Rice (brown)	12.5	Tea (Indian infusion)	−0.3
Spaghetti (white)	6.5	White wine	−1.2
Cornflakes	6.0	Red wine	−2.4

[1] Reproduced from Remer and Manz (1).

This proportion may be displayed in different formats (e.g., the United Kingdom and Australia use a plate; the United States and Singapore use a pyramid; Finland uses a plate and pyramid combination) (**Fig. 1**), but in essence, the message is the same (4,5). There is general agreement that fruits and vegetables should be consumed in adequate amounts, with requirements varying according to age and energy needs (www.fruitsandveggiesmatter.gov) for the optimization of health. In addition, the U.S. Dietary Guidelines recommend 3 servings of dairy per day for the age group 9 y and above to meet potassium requirements (5).

Using a food-specific approach to the prevention of osteoporosis represents a particularly attractive method. We urgently need diets for all individuals, particularly young and older women, that are balanced in key food groups and deliver an abundance of important nutrients. If we can prove that such diets have a positive effect on bone health in the long term [e.g., Dietary Approaches to Stopping Hypertension (DASH)-type diets], there will be wide implications for clinicians to use key public health nutrition messages that can be followed by patients, with the potential of other health-related benefits.

FIGURE 1 A food-based approach to dietary recommendations. An example of the pyramid model (5).

The objective of this article is to outline the evidence, as it currently stands in the literature, linking potassium-rich, bicarbonate-rich foods (i.e., fruits and vegetables or dietary alkali) to osteoporosis prevention. The published cross-sectional, observational and longitudinal studies in men and women of all age groups are discussed together with the available clinical studies. The biological mechanisms for a link between dietary alkali and the skeleton are reviewed in depth. Estimating levels of dietary acidity and their link to bone health are also reviewed. The article concludes with a detailed focus on research areas that require urgent attention.

Review methodology

Articles that have been published over the last 3 decades (up to early 2006) have been included in this review and have been selected on the basis of their original study design. Publications have been identified from a number of sources including searches on key online databases including Medline, Ovid, and PubMed as well as the use of the Proceedings from each of the 6 International Symposiums on Nutritional Aspects of Osteoporosis (Lausanne, Switzerland 1991–2006 and the 2nd International Symposium on Acid-Base Balance (Munich, Germany 2006).

Evidence for a beneficial effect of fruits and vegetables alkali on indices of bone health

Cross-sectional/longitudinal, observational studies. Observational studies are at best hypothesis generating and not (as is the case with intervention studies) hypothesis proving. However, they still provide useful background information for links between diet and disease. Of interest to the bone field is the number of population-based studies published in the latter part of the 20th century, and more recently between 2001 and 2006, which have demonstrated a consistent, beneficial effect of fruit and vegetable intake on indices of bone health across a wide range of age groups including young boys and girls (6–10), premenopausal women (11–13), perimenopausal and postmenopausal women (14,15), and elderly men and women (16).

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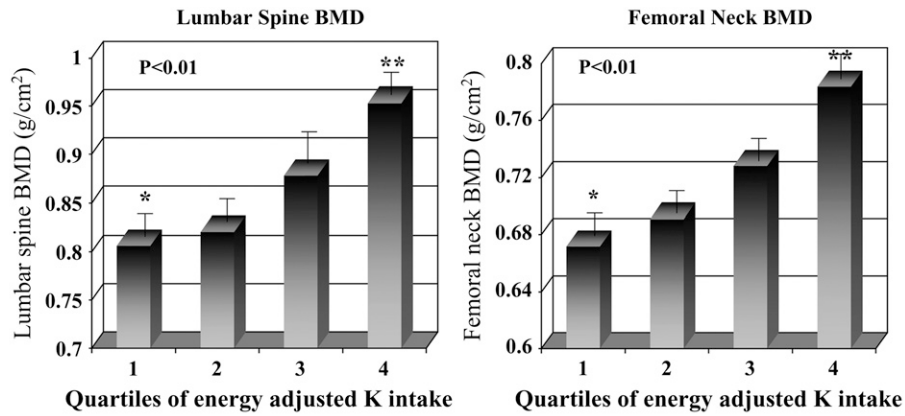

FIGURE 2 Potassium intake and BMD in 994 women; baseline values are shown for the lumbar spine and femoral neck BMD from the APOSS Reproduced from (11).

Baseline findings of the Aberdeen Prospective Osteoporosis Screening Study (APOSS) have shown specific associations between nutrients found in abundance in fruits and vegetables and both axial and peripheral bone mass and markers of bone resorption. Women ($n = 994$) in the lowest quartile of intake for potassium, magnesium, fiber, vitamin C, and β-carotene had significantly lower lumbar spine and femoral neck bone mineral density (BMD) (11) (**Fig. 2**). In a second study, women ($n = 62$) with low intakes of these same nutrients were found to have lower forearm bone mass and higher bone resorption (12), findings that were independent of important confounding factors. With financial assistance, initially from the Department of Health/MRC and more recently the Food Standards Agency (formerly MAFF), APOSS has shown a consistent longitudinal beneficial effect of fruit and vegetable nutrients on bone loss in premenopausal women (13) (**Table 2, Fig. 3**).

Attempts are under way to clarify the extent of the effect of fruits and vegetables and potassium and bicarbonate intake on bone health. An ongoing systematic review of published articles in the field that includes a total of 4500 subjects suggests that the risk of low BMD attributable to potassium intake is ~1% (S. A. Lanham-New and D. J. Torgerson, unpublished data). A much more detailed analysis is now urgently required to investigate which specific types of fruits and vegetables have the most direct impact on the skeleton and what quantities are required to be consumed daily for a maximum effect.

Dietary intervention studies. There are only a few published intervention studies investigating the link between dietary potassium and bicarbonate and the skeleton, and this is certainly an area where a great deal more work is required.

TABLE 2 Correlation coefficients between fruit and vegetable nutrients on spine and hip bone density and hip bone loss in APOSS premenopausal women[1]

	Premenopausal women, $n = 146$			
	FN[2] BMD	Lumbar spine BMD	Change in FN BMD (Unadjusted)	Change in FN BMD (Adjusted)*
Potassium	+0.154	+0.146	+0.208	+0.252**
Magnesium	+0.094	+0.161	+0.252	+0.219*
Vitamin C	+0.118	+0.171	+0.206	+0.216*

[1] Data are means. Adjusted for age, weight, annual percentage weight change, height, smoking, and physical activity. Reproduced from Macdonald et al. (13).
[2] FN, femoral neck. * $P < 0.01$; ** $P < 0.001$.

The DASH trial was the first to indicate a link between a dietary alkali load and bone. The DASH diet comprises careful selection of low-fat dairy products, reduced amounts of meat, and a high consumption of whole grains and fruits and vegetables. In contrast, the control diet in the DASH trial reflected a typical Westernized diet that is higher in fat and low in dairy, fruit, and vegetable products. The DASH diet (17) was associated with a significant decline in blood pressure compared with baseline measurements. However, of particular interest to the bone field was the observation that increasing fruit and vegetable intake from 3.6 to 9.5 daily servings decreased the urinary calcium excretion from 157 to 110 mg/d. The authors of this article speculated that the lack of rise in calcium excretion following an extra 800 mg of calcium from dairy was probably a result of the "high fiber content of the diet possibly impeding calcium absorption." However, an alternative theory for this finding was that the higher fruit and vegetable diet reduced the "acid load" compared with the control diet (18) and conserved calcium for bone retention.

Lin et al. (19) have reported that compared with the control diet, the DASH diet significantly reduced both bone formation by 8–10% and bone resorption by 16–18% (measured by osteocalcin and C-terminal peptide, respectively) (19). The DASH-Sodium trial investigated 3 levels of sodium (50, 100, and 150 mmol) in concert with the control and DASH diets (20). No differences in bone turnover were attributed to the varying sodium levels. Further evidence of a positive dietary effect of potassium and bicarbonate-rich foods has been studied by Burckhardt et al. (21), who examined the effect of dietary modification on calcium

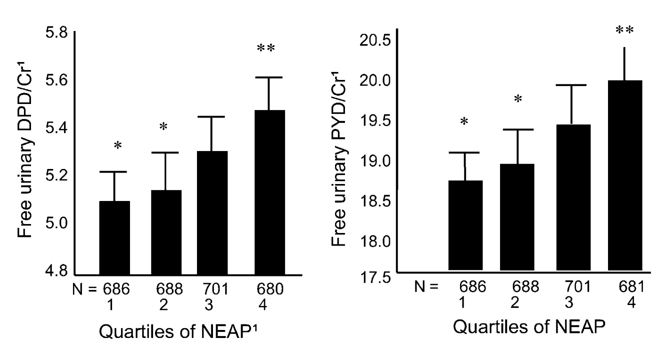

FIGURE 3 Effect of dietary acidity on bone resorption markers: *significantly different; ** $P < 0.002$. Reproduced from (37).
Biomarkers: DPD/Cr, de-oxypyridinoline/creatinine; PYD/Cr, pyridinoline/creatinine.
[1]NEAP, net endogenous non-carbonic acid production.

and bone metabolism. The "acid-forming" diet increased urinary calcium excretion by 74% and bone resorption by 19%, as measured by C-terminal peptide excretion, in comparison to the alkali-forming diet, both at baseline and after an oral calcium load.

Clinical studies. The clinical application of the effect of normal endogenous acid production on bone is of great interest, with extensive work in human subjects and at the cellular level. **Table 3** shows the seminal work by Sebastian et al. (22) demonstrating that potassium bicarbonate administration resulted in a decrease in urinary calcium and phosphorus, with overall calcium balance becoming less negative (or more positive). Changes were also seen in markers of bone metabolism, with a reduction in urinary excretion of hydroxyproline (marker of bone resorption) and an increased excretion of serum osteocalcin (marker of bone formation). Further studies are required to examine the effect of potassium bicarbonate supplementation in women consuming moderate amounts of protein (23).

More recently, short-term potassium citrate supplementation studies have shown a beneficial effect on bone turnover markers (24,25), but preliminary data from the APOSS potassium citrate intervention study indicate that these results are not mirrored over the long term in the healthy adult population (26). Interestingly, a recent Swiss study suggests a strong beneficial effect of alkali supplementation in osteopenic women (27).

Potential reasons behind the link between a potassium-rich, bicarbonate-rich diet and bone

On a daily basis, humans eat substances that both generate and consume protons. As a net result, adult humans on a normal Western diet generate ~1 mEq/kg body weight of acid per day. Of course, the more acid precursors a diet contains, the greater the degree of systemic acidity (28). Hence, in the West, there are good data to show that we consume a very acidic diet. Clear mechanisms exist for a deleterious effect of acid on bone. Novel work in the 1980s by Arnett and Dempster (29) demonstrated a direct enhancement of osteoclastic activity following a reduction in extracellular pH. This effect was shown to be independent of the influence of parathyroid hormone (**Fig. 4**). Osteoclasts and osteoblasts appear to respond independently to small changes in pH in the culture medium in which they are growing. Work by Arnett and Spowage (30) and work by Bushinsky (31) have shown evidence that a small drop in pH, close to the physiological range, causes a tremendous burst in bone resorption (30,31). Metabolic acidosis has also been shown to stimulate resorption by activating mature osteoclasts already present in calvarial bone rather than by inducing formation of new osteoclasts (32).

It is also important to note that the positive associations found between fruit and vegetable consumption and bone may be related to some other, yet unidentified, "dietary" component rather than to an alkali-excess effect (33). We know that vitamin K, vitamin C, flavonoids, and carotene are found extensively in fruits and vegetables, and these nutrients have been shown to be important to the skeleton. Furthermore, there are animal data to show that vegetables, herbs, and salads commonly consumed in the human diet affect bone resorption in rats by a mechanism that is not mediated by their base excess but possibly through pharmacologically active compounds (34).

TABLE 3 Short-term effects (18 d) of potassium bicarbonate supplementation study on mineral balance and bone turnover in postmenopausal women[1]

	Before $KHCO_3$	During $KHCO_3$	Change
Ca balance, *mg/(d · 60 kg)*	−180 ± 124	−124 ± 76	+56 ± 76
P balance, *mg/(d · 60 kg)*	−208 ± 127	−161 ± 92	+47 ± 64
Serum osteocalcin, *μg/L*	5.5 ± 2.8	6.1 ± 2.8	+0.6 ± 0.48
Urinary hydroxyproline, *mg/d*	28.9 ± 12.3	26.7 ± 10.8	−2.2 ± 1.8
Net renal acid excretion, *mmol/d*	70.9 ± 10.1	12.8 ± 21.8	–58.1 ± 54.2

[1] Values are means ± SD. $P < 0.01$

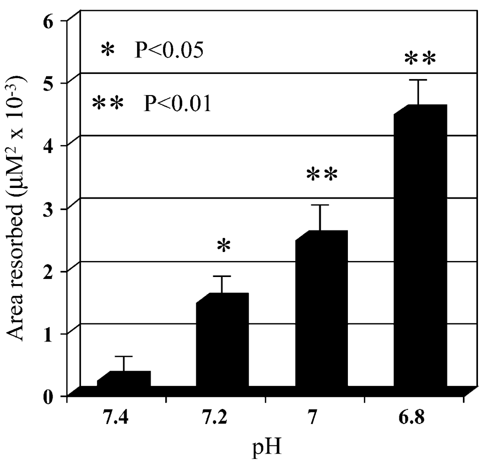

FIGURE 4 Increase in osteoclastic activity with a reduction in extracellular pH. Mean values were significantly different from that at pH 7.4: $*P < 0.05$, $**P < 0.01$. Reproduced from (29).

Dietary balance and the skeleton: concept of net endogenous acid production. Determination of the acid-base content of diets consumed by individuals and populations is a useful way to quantify the link between acid-base balance and skeletal health. As mentioned previously, on a daily basis, humans eat substances that both generate and consume protons, and, as a net result, consumption of a normal Western diet is associated with chronic, low-grade metabolic acidosis. The severity of the associated metabolic acidosis is determined in part by the net rate of endogenous noncarbonic acid production (NEAP), which varies with diet (35). In the Aberdeen studies, women with the lowest estimate of NEAP were found to have higher lumbar spine and femoral neck BMD and significantly lower urinary pyridinium cross-link excretion (marker of bone resorption) (36). Using the calculated regression equation, holding weight and height constant (using the mean values for the group), and looking at the difference in lumbar spine BMD between the minimum and maximum intakes of NEAP estimated, investigators found an 8% reduction in lumbar spine BMD. Absolute values were 0.923 g/cm^2 for the highest intake of NEAP estimate and 0.999 g/cm^2 for the lowest intake of NEAP, a difference of 0.076 g/cm^2. An increase in BMD by 1 standard deviation unit is likely to result in a 50% reduction in fracture rates. Findings for bone resorption were mirrored in the follow-up of the Aberdeen studies (37), and similar results have also been shown in the younger population (38).

Concluding remarks and areas for further research

It should not be forgotten that it is generally believed that our modern diet is vastly different from that which early humans once consumed (39). The dietary content of preagricultural man suggests intakes of sodium to be 600 mg/d and of potassium reaching 7000 mg/d, compared with current intakes of sodium and potassium of ~4000 mg/d and 2500 mg/d, respectively, in the United Kingdom, United States, and Australia. Intakes of bicarbonate and chloride show similar shifts.

Future research in this area needs to focus on a range of key aspects (40): *1*) long-term intervention trials centered specifically on potassium-rich, bicarbonate-rich foods (e.g., fruits and vegetables) as the supplementation vehicle and measurements of a range of indices of bone health and fracture risk; *2*) experimental studies (at cellular, animal, and human levels) to determine whether there are other aspects of potassium-rich, bicarbonate-rich foods that are beneficial to bone metabolism and what specific mechanisms are involved; *3*) investigation of levels of potassium-rich, bicarbonate-rich foods in relation to markers of skeletal integrity in a wide range of population groups, including the young, postmenopausal women, and the elderly. The road ahead is indeed a challenging one!

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