Phosphorus - Essential to Bone Health

Calcium and Phosphorus are essential to human life. In vivo, the ionic forms of calcium and phosphorus combine to form calcium phosphate. First as dicalcium phosphate [$CaHPO_4$, monetite or DCP] and on through sequential synthetic reactions to become tricalcium phosphate [$Ca_{10}(OH)_2(PO_4)_6$, hydroxyapatite or TCP]. During the process of bone hardening or aging, the Ca:P ratio gradually increases from 1:1 to 1.67. Hydroxyapatite is the predominate mineral of the bone with smaller quantities of intermediate calcium phosphates and some calcium carbonate present.

There are several stages of human life when the calcium and phosphorus requirements are most critical. First, in utero, followed by childhood anabolism, and later during puberty when there is a strong requirement for growth hormone. Bone mineralization only slows after the epiphyseal plate has closed. It is believed that greatest peak bone mass laid down in the formative years leads to the greatest old age skeletal resilience and integrity. In women, calcium and phosphorus requirements are greatest during pregnancy, lactation and in post-menopause when the protective effect of estrogen is depleted.

In humans, peak bone mass is evident between 20 to 35 years of age and is thought to be stable during this time in both sexes. With age, bone mass is gradually depleted with the impact most serious in post-menopausal women [(especially at trabecular-rich sites as the spine or wrist), (Cashman, 2002)].

Reductions in bone density are classified as osteopenia, borderline low density bone mass, and osteoporosis, which are evidenced by low bone mass and microarchitectural deterioration of the bone tissue. In the U.S., it is estimated that there are 10 million adults suffering from osteoporosis with an additional 18 million people suffering from osteopenia. In women, after age 50, it is estimated that these states will lead to a risk of 17.5% hip; 15.6% spine and 16.0% forearm fractures; and a lifetime risk of fragility of 40% in women and 13% in men. Eighty percent of women over 75 years of age stated that they preferred death to a serious hip fracture and the confinement to a nursing home (National Institutes of Health, 2000). Many hip fractures of the elderly, unfortunately, result in a high degree in mortality within six months of the incident. With the increase in life expectancy and the generation of aging baby boomers, osteoporosis, unless arrested, will lead to a serious increase in fractured bones and potentially mortality.

Importance of Phosphorus in Bone Health

The major component and an essential ingredient of human bones and teeth is a mineral form of calcium and phosphorus called hydroxyapatite. It is hydroxyapatite that gives bones and teeth their rigidity. While calcium is the most prevalent element in bone, bone diseases (such as osteoporosis) are due to more than just a lack of calcium. Several other nutrients and minerals, including phosphorus, are also critical to maintaining healthy bones. The challenge of promoting bone health in this country is an important initiative, for the well-being of both the developing and the aging populations, and all of the factors involved must be considered.

Phosphorus is an essential nutrient for human and animal life. It is fundamental to growth, maintenance, and repair of all body tissues, and is necessary, along with calcium and magnesium, for proper growth and formation of bones in infants and children. Sufficient phosphorus intake is important throughout life to ensure the proper balance of essential minerals in order to promote remineralization of bones and teeth to keep them in a healthy state.

About 85% of adult body phosphorus is found in the bones, with the remaining 15% found in the soft tissues (IOM, 1997). Recommendations from the National Academy of Sciences provide a dietary phosphorus level that individuals should try to meet (the RDA – Recommended Dietary Allowance). While the RDA levels depend on age, the daily recommendation is 1250 mg for youth age 9 to 18 years, and 700 mg for adults 19 years and older (IOM, 1997).

Osteoporosis is a common form of bone disease, and is characterized by low bone mass and deterioration of the bone structure. While many osteoporosis prevention studies have focused on calcium, the emphasis for some of these studies has now shifted toward the importance of the balance of calcium and phosphorus in treatment for this disease. In order to ensure the most efficient use of the calcium ingested to prevent osteoporosis, it is also important to consume at least 700 milligrams of phosphorus daily. If the ratio of calcium-to-phosphorus is too high, proper bone growth cannot occur.

Research has shown that intake of high daily levels (1000 to 1500 mg) of calcium to prevent or treat osteoporosis can bind up to 500 mg of phosphorus, making it unavailable to the body (Heaney, 2004). Typical diets contain adequate levels of phosphorus, due to its availability in many common food sources, so that this is not always a serious problem. There are some people, such as women over 60 years of age and those who have poor nutrition, who may not normally consume the RDA of 700 mg phosphorus. It has been documented that 10% to 15% of older women have intakes of less than 70% of the recommended daily allowance of phosphorus (Heaney, 2004). Low phosphorus intake is more common among the elderly, which is also the group that is more prone to suffer from osteoporosis. Ensuring that this population group has an appropriate intake of phosphorus should be an important part of treatment of this bone disease (Heaney, 2004). For these people, calcium supplements which do not contain phosphorus will not provide adequate help with osteoporosis, since the building of new bone mass requires appropriate levels of both minerals.

Other researchers demonstrated in a controlled study among elderly women that a daily supplement of 1200 mg of calcium from calcium phosphate, along with adequate levels of Vitamin D, led to a reduction in bone loss and helped maintain optimum bone mass. These authors concluded that a favorable ratio of calcium to phosphorus had a positive effect on calcium utilization (Chapuy et al, 1992). Phosphorus and calcium have been shown to be co-dependent for bone health.

Additional animal studies have demonstrated the importance of phosphorus, in conjunction with calcium, for bone development (Shapiro and Heaney, 2003). These results showed that calcium and phosphorus are co-dependent, and that both minerals are critical to support soft tissue and bone growth.

Concerns have been raised in the past that a high phosphorus intake could possibly interfere with calcium nutrition by reducing its absorption (Calvo and Park, 1996). These have been shown to merely be theoretical concerns, however. Research studies done to evaluate the effect of higher phosphate content (and lower calcium-to-phosphorus ratio) of the diet showed that the calcium absorption was not lowered. As long as the calcium intake levels are adequate, even higher phosphorus levels will not interfere with the calcium absorption (Heaney and Recker, 1982). An appropriate balance of calcium and phosphorus levels is a key for maintaining healthy bones.

Bioavailability of Phosphorus in the Diet

When evaluating the levels of phosphorus and other minerals present in the diet, it is important to understand the amount of this total phosphorus that is actually bioavailable to the groups for which the diet is being developed.

Most food sources exhibit good phosphorus bioavailability. One major exception, however, is the storage form of phosphate utilized in whole grains and plant seeds (such as cereal grains, beans, peas, and nuts) (IOM, 1997). This storage form is in a complex called phytic acid (myo-inositol 1,2,3,4,5,6-hexakis phosphate), and its salt - phytate. Phosphorus in this form is poorly available to monogastric species of mammals, such as humans, because they lack phytase, the enzyme that hydrolyzes the ortho-phosphate groups from the phytate molecule (Cromwell et al, 1993; Greinier and Jany, 1992). It has been found that in general, about two-thirds of the phosphorus in grains is phytate bound, and therefore not available to humans. (Sugiura et al, 1999).

Most inorganic forms of phosphorus, such as those found in many supplements and as ingredients in many foods, are readily ionizable and available for absorption following ingestion. Even phosphates that are less soluble in neutral pH conditions, such as most calcium phosphates, will dissolve in the acidic pH found in the stomach during digestion. The subsequent absorption across the intestinal wall into the blood allows both the phosphorus and the associated cation, (e.g., calcium in calcium phosphates), to be available physiologically. In addition, other soluble forms of phosphate (such as phosphate salts of organic acids) found in the diet are also bioavailable to humans through their eventual absorption into the blood system.

The Impact of Diet on Calcium and Phosphorus in Health

It is estimated that 150 mg of calcium is accumulated each day during active skeletal growth and maturation with an average of 700 mg calcium per day entering and leaving the bones in adulthood. Ninety-nine percent of the body's calcium is stored in the bone and 80 to 90% of its phosphate (Driesens and Verbeek, 1990). About 99% of the human body's calcium is in the bone mass. Eighty percent of the human body's phosphorus is in the bone mass and is turned over at a range of 480 to 1440 mg per day (Williams, 1993). Therefore, it is of paramount importance to have a constant supply of both calcium and phosphorus in the diet for skeletal integrity.

Absorption of calcium is very inefficient in the normal human, as only an estimated 10 to 30% of calcium is absorbed and 20 to 70% of dietary calcium is excreted in the feces. It is important to note here that results from animal studies cannot always be equated with reactions of the human, as growing rats will absorb almost 100% of dietary calcium (Hegsted, 1968); do not undergo epiphyseal plate closure and excrete only 1 to 2% of their calcium intake in urine (Zemel, 1985) and that humans in deficient mineral states develop more efficient absorptive mechanisms (Fairweather-Tait et al., 1995; Barger-Lux and Heaney, 1993). Phosphorus is thought to be more efficiently absorbed than calcium however; approximately 30% of phosphorus is excreted in the feces and the bulk is excreted in the urine.

Food grade phosphates are not 100% bioavailable. Generalizations should not be made only on the basis of the amount of calcium and phosphorus consumed, as some food sources are better than others and excellent sources may be less often consumed than poor sources of calcium and phosphorus. Further, osteoblasts are responsible for the laying down of bone and osteoclasts are those agents responsible for resorption.

Infant Nutrition

Mize et al. (1995), evaluated the effect of three different levels of phosphorus (90, 106 or 120 mg P/100 kcal) in combination with high calcium (180 mg/100 kcal) intakes in very low birth weight 715 to 1510 g) infants (n=35) during a one week trial. The results indicated phosphorus available for soft tissue was significantly higher in the 106 and 120 P supplements and was sufficient to support soft tissue accretion. Total absorbed phosphorus and phosphorus tubular reabsorption were each affected by phosphorus intake. It was concluded that the historic formula calcium to phosphorus ratio of 2:1 was suboptimal and that a ratio of 1.6:1 to 1.8:1 would be more desirable.

Specker et al (1997) evaluated the effect of either low or moderate calcium and phosphorus formulas versus breast feeding on the bone mass content (BMC) in infants from two weeks to six months of age followed by feeding of either moderate or high mineral formulas versus cow's milk for an additional six months. Feedings are summarized in Table 1.

Table 1. Mineral and Protein Content of Different Feeding Regimens

Time	Ca (mg/l)	P (mg/l)	Ca:P Ratio	Protein (g/l)
Feeding group first six mos.				
Human milk	300	150	2.0	10.5
Low mineral	430	240	1.8	16.2
Moderate mineral	510	390	1.3	14.5
Feeding group during the second six mos.				
Moderate mineral	510	390	1.3	14.5
High mineral	1350	900	1.5	19.8
Cow milk	1230	960	1.3	33.9

The results indicated that bone mass accretion was significantly greater ($P<0.001$) at six months in those infants fed the moderate mineral formula versus either the low mineral formula or the breast milk. The BMC at six months among the formula-fed infants was correlated with both average dietary phosphorus intake ($P< 0.001$) and the average dietary calcium intake ($P< 0.001$) during the first six months. The relationships between BMC and these minerals remained significant even after controlling for caloric intake ($P= 0.004$ for phosphorus; $P= 0.02$ for calcium). Speck et al (1997) concluded that it was not possible to determine the independent effects of dietary calcium and phosphorus on BMC because of the strong correlation of these minerals with each other ($P< 0.001$).

From six to twelve months the BMC was similar among the treatment groups. It is interesting to note, however, that infants fed human milk during the first six months of life had a greater gain in bone mass during the second six months of life when they were provided a moderate to high mineral formula than infants previously fed low or moderate mineral formulas. This indicates that a higher level of phosphorus than that in breast milk may be required for bone mass accretion and that perhaps a lower Ca:P ratio is optimal. It should also be noted that there were no reported harmful effects of moderate to high mineral consumption.

It is interesting to observe the trend that organic food consumption has increased and that the population tends to consider it more healthful. Very few phosphates are currently permitted in organic food. The following two case studies are illustrative of the assumption that organic and vegan diets are healthier.

Two cases of infant malnutrition have recently been reported (Carvalho et al., 2002). Diagnoses were delayed due to a low degree of suspicion. The first patient was admitted with severe Kwashiorkor. After 13 months of breast feeding he was perceived to be milk intolerant and was switched to a rice beverage (1.5 l/d) with small amounts (ca. two tsp.) of solid foods. Serum phosphorus was reported to be 2.2 mg/dl (normal 4.5 to 6.9 mg/dl). Therapy for Kwashiorkor was instituted along with potassium, phosphorus, mulivitamins, zinc and folic acid. Subsequent treatment was phased into toddler formula followed by a milk-based pediatric nutritional supplement. He made an uncomplicated recovery.

The second case involved a 17 month old child with rickets. He was initially breastfed with vegan infant foods introduced at four months. At 10 months, he was weaned and began a soy beverage (without Vitamin D or calcium), which his parents drank in place of milk. The patient then consumed a vegan diet and included regular foods as tofu, sweet potatoes, potatoes, spaghetti, fig bars, infant cereal, bananas, strawberries and other fruits and vegetables. The diet was adequate in fat (108% RDA), carbohydrate (117% RDA), protein (335% RDA). Analysis indicated that Vitamin D was absent (0% RDA). The only significant source of calcium was derived from the infant cereal, which provided 450 mg/d calcium. The serum alkaline phosphatase (1879 U/l, normal as 150 to 420 U/l) was markedly elevated, phosphorus (1.7 mg/dl, normal as 4.5 to 6.9 mg/dl) was low and calcium (8.9 mg/dl, normal 8 to 10.3 mg/dl) was in the low, normal range. The 25-hydroxy-Vitamin D (7.7 pg/ml, normal 8.9 to 46.7 pg/ml) level was low, despite the initiation of 30% of the recommended dose of multivitamins one month prior to admission. Parathyroid hormone (114 pg/ml, normal 10 to 65 pg/ml) level was considerably elevated and, in view of the low, normal calcium level, was consistent with secondary hyperparathyroidism. Radiologic evaluation revealed a diffuse profound osteopenia and osteomalacia. They metaphyses of the long bones were frayed and the epiphyseal plates were widened. In addition, he had a pathologic fracture of the left ulna. These observations are diagnostic of advanced rickets. The low 25-hydroxy-Vitamin D level along with the history of a deficient diet supported a nutritional cause (Carvalho et al., 2001).

These two cases are of importance, as they are indicative of both calcium and phosphorus deficiency. In case one, it is critical to note that severe hypophosphatemia has been linked to a high mortality. Rice beverages are typically not processed with phosphates. Therapy included the introduction of toddler formula with a milk-based pediatric nutrient supplement, which would contain calcium and phosphorus. In industrialized countries it is common that presumptive lactose intolerance leads to avoidance of dairy products and thus calcium and phosphorus.

In case two, the toddler was fed a vegan diet, which is often assumed to be healthier. Carvalho et al. (2001) cite the work of Dagnelie (1990), which reported a high incidence of rickets in those consuming diets of minimally processed foods. Further more these diets often contain high fiber, which can absorb vital minerals and thus render them biologically unavailable (Weber et al., 1993). Here, the soy milk did not contain significant levels of calcium as it was only determined to be present in the infant cereal. It is not uncommon to use calcium sulfate in soy protein processing during the protein extraction step. Commercial soy beverages may sometimes contain added calcium but phosphorus may not be added if the supplementation source is calcium carbonate, which is used, in least cost formulations. Even if the solid foods listed are consumed and broccoli, green beans, applesauce and carrots added to the diet at a level of two tablespoons each per day, the contribution of calcium and phosphorus would be 53 and 104 mg/d, respectively (USDA database). Calcium and phosphorus were clearly deficient due to the observed and profound osteopenia, osteomalacia, the frayed long bones, widened epiphyseal plate and fractured left ulna.

Food selection patterns are typically dictated in children, however, they may reflect the actions of their parents or guardians. Fisher et al. (2004) evaluated the intake of calcium on 192 non-Hispanic girls ranging between five to nine years and their mothers based on 24 hr. recall and beverage choices. At age 9, the girl's bone mineral status was assessed and showed that calcium intake ($P< 0.0001$). Girls that met the AI (adequate intake) for calcium tended to have higher energy intakes ($P< 0.0001$) but were not heavier and consumed almost twice the amount of milk as those who failed to meet the AI. Milk consumption with age (from 5 to 9) tended to decrease less ($P< 0.01$) over the years and sweetened beverages were consumed 18% les ($P< 0.01$) than with those girls not meeting the AI. Girls who met the AI were served milk more frequently than were girls who consumed less than the AI ($P<0.0001$) and had mothers who drank milk more frequently ($P< 0.01$) than did the mothers of the girls who consumed less than the AI. These researchers concluded that calcium intake predicts bone mineral status during middle childhood and reflected mother-daughter beverage choice patterns that are established well before the rapid growth and bone mineralization observed in adolescence. Since these observations related to milk consumption, clearly there would be a concurrent consumption of calcium and phosphorus.

Storey et al. (2004) analyzed data from the USDA Continuing Survey of Food Intake by Individuals (CSFII) 1994-96 and 1998. Among the interesting results are that boys steadily increase calcium consumption with age although it begins to fall below the AI in the 9 to 13 and 14 to 18 year age groups to 79% and 89% of the AI, respectively. For girls, average total calcium consumption increased in patterns, but decreased to a greater extent in the 9 to 13 and 14 to 18 year age groups, 65% and 54%, respectively. These trends related directly to reduced milk consumption with age and consequently calcium and phosphorus intake. These effects were modest for Caucasian and African American females and profound for Hispanic females. Furthermore, these researchers noted that there was a weak but positive correlation between total beverage (milk, fruit juice, soft drink) and calcium intake and that calcium intake based upon beverage consumption explained only 2 to 3% of the variance in intake for each age group. The authors concluded that carbonated soft drink consumption among adolescent girls was modest and did not appear to be linked to decreased calcium intake.

Diets of Canadian men and women were evaluated for 24 hour recall and the quantities of food consumed were documented. Three groups of men ([18 to 34 y], [35 to 49 y], [50 to 65 y]) consumed an average of 1192, 940 and 851 mg Ca/d, respectively without supplements. Calcium supplements contributed 47 to 73 mg Ca/d among the three age groups. Women in the same three age groups consumed an average of 757, 737 and 712 mg Ca/d within the respective age groups. Calcium supplementation within the three groups contributed 55, 116 and 203 mg Ca/d with the respective age groups. Only the 18 to 34 y men consumed Ca at levels within the AI. Women 50 to 65 compensated for low dietary Ca the most through supplementation (Johnson-Down el al., 2003).

With high Ca, more men tended to consume fluid milk; cheese; cream, ice cream, milk desserts and yogurt; and ready to eat cereals. In women, Ca intake was associated with higher consumption of the same food groups as men plus fruit. It is interesting to note that men with higher Ca consumption tended to have increased intake of fluid milk and non-carbonated beverages. High Ca consuming women tended to consume 5.5 times (15.1 versus 2.7 oz.) more milk and 25% less (15 versus 18.9 oz.) carbonated beverage per day than the low Ca consumers. Although the low Ca consumers tended to partake of soy beverages this would not approach the difference in the consumption of milk. The high Ca consumers tended to eat more dairy products, which would be indicative of calcium and phosphorus consumption.

Ethnic dietary preferences, beliefs, mineral intake and bone status among adolescent Israeli Jewish and Arab high school girls (mean age 14.5 years) were evaluated (Rozen et al., 2001). Two thousand girls completed a semi-quantitative food frequency questionnaire and a personal history questionnaire. Average calcium intake was determined to be 1,260 mg/d, however, 20% had a calcium intake below 800 mg/d and bone mineral content and density was determined on these subjects. The low calcium diets were also shown to be deficient in phosphorus (95.2%), magnesium (84.8%), iron (90.5%) and zinc (100%). The low calcium consumption was almost equally divided between the Jewish and Arab girls and more alarming 6.4% and 7.3% of each group consumed less than 500 mg calcium per day. Low calcium consumption was related with low caloric intake (<1,200 calories/d) and high protein levels in efforts to "diet". Israel is reported to have the highest levels of girls on weight reduction diets. The WHO (as cited by Rozen, 2001) has reported that only 50% of dieters tend to drink milk once a day. The Arab diet typically contains more than 50% fruits and vegetables, which contribute oxalates and hydrates which form insoluble complexes with calcium, phosphorus, magnesium and iron. Although, bone mineral content and density was reported to fall within the normal ranges, however, it is unknown if peak bone accretion will be achieved within those lacking in the essential bone building minerals.

Merilees et al. (2000) studied the effect of high calcium intake (1160 mg/d) from dairy foods on bone density, bone mineral content, serum lipid and anthropometric measurements on 91 post-pubertal teenage (15 to 18 y.o.) girls over a two year period with one year follow-up. The group consuming dairy foods showed significantly higher ($P < 0.001$) calcium, phosphorus and protein with no significant difference in height, weight, lean body and fat mass. Bone mineral density increased ($P < 0.05$) in the trochanter (4.6%), lumbar spine (1.5%) and femoral neck (4.8%) of those consuming the high dairy diet. BMC increased in the trochanter ($P < 0.05$) and to some extent in the lumbar spine. The dairy supplemented regimen did not adversely impact body weight, fat and lean mass or serum lipids. Twelve months after the study, the girls had returned to their baseline diets indicating that self-selection of dairy foods may be hard to achieve.

It is well known that fractional calcium absorption is greatest during early adolescence and sound dietary practices can preclude skeletal deterioration later in life. Despite this fact, personal choices are not the only factors impacting calcium and phosphorus intake. Taha et al. (2001) evaluated the effect of religious law, exercise, sun exposure and diet on 30 male and 20 female ultra-Orthodox Jewish adolescents (15 to 19 years). Mean calcium consumption was 908 ± 506 mg/d; phosphorus was 1329 ± 606 mg/d and Vitamin D was 286 ± 173 IU/d. Twenty-seven percent of the boys showed lumbar BMD values equivalent to adult osteoporosis and overall, the boys tended to have profoundly lower lumbar BMD than the girls. Although an actual cause for such a high incidence of low lumbar BMD was not determined, it is presumed that avoidance of dairy and meat in combination; limited exposure to the sun and limited weight bearing activity could be factors.

Calcium and Phosphorus in Pediatric Disease and Injury

Vargas et al. (2003) evaluated bone mineralization in 23 children and adolescents (10.9± 2.9 years) with Type I Diabetes. Average bone mineral density was normal (-0.75± 1.01), however; it was determined that 39.1% of the patients had osteopenia. Serum C peptide was significantly (P< 0.05) elevated in those with osteopenia (n=9) to non-osteopenic (n=14) patients. BMI and C peptide also correlated with bone mineral density.

Severe burn injury (53.1% surface area; 44.2% full-thickness) and serum calcium, magnesium and phosphorus homeostasis was evaluated in 41 pediatric (6.5±0.8 years) patients (Wray et al., 2002). The observations were that hypovitaminosis D observed in burn injury correlated with serum calcium and phosphorus abnormalities.

Calcium and Phosphorus in Osteoporosis

Popovtzer et al. (1976) evaluated the effect of alternating calcium and phosphorus infusions for a period of one year on five patients with severe osteoporosis. The results indicated a thickening of the cortical bone, lasting relief from bone pain and the rate of spontaneous bone fractures decreased from at least one per year to none during the year following treatment. Silverberg et al. (1986) extended this work to demonstrate that two grams of elemental phosphorus given daily stimulated bone remodeling.

Goldsmith et al. (1976) evaluated the effect of phosphorus via inorganic phosphate supplementation in seven postmenopausal women with osteoporosis. Bone density was in the fifth percentile for all but one patient and the percentage of bone surface involved with resporption was higher than normal. In all patients, calcium balance became more positive or less negative. Density of the midradius increased slightly in all patients.

Tranquilli et al. (1994) evaluated the dietary habits of 194 postmenopausal women, with no history of HRT, of which 70 were osteoporotic and 124 served a controls. Dietary recall and forearm bone mineral content (BMC) were evaluated. Statistical analysis (P < 0.05) showed a strong correlation between reduced dietary intake of calcium, phosphorus and magnesium in osteoporotic women and BMC. Calcium and magnesium intake were below the RDA in normal women.

Molimard et al. (1985) provided seven elderly patients either a dietary regimen with 1500 mg Ca/d or a diet containing 500 mg Ca/d supplemented with 1000 mg Ca in the form of either dicalcium phosphate or tricalcium phosphate. It was determined that calcium balance remained positive under the calcium phosphate treatment. The authors also noted that the calcium phosphates were inexpensive, stable and well tolerated by patients and should be evaluated for therapy in mass prevention of osteoporosis.

Numerous intervention studies and longitudinal studies have been conducted in recent years. Fardellone et al. (1998) evaluated 116 healthy postmenopausal women fed either a placebo or 1200 mg calcium carbonate (in two separate daily doses) over a period of 60 days. A significant increase in urinary excretion of pyridinoline was observed when the dietary calcium intake was lower than the median value. Calcium supplementation resulted in a significant increase in 24 h urinary calcium (39%, P = 0.02) and a significant reduction of bone alkaline phosphatase at 2 mos. and of all bone-resorption markers (hydroxyproline, pyridinoline and deoxypyridinloine) at one and two months without significant changes in 44 to 68 PTH fragments or iPTH concentrations. Two months of calcium supplementation in postmenopausal women was efficient in reducing markers of bone turnover, with a greater effect in women with a low dietary calcium intake.

Heaney and Nordin (2002) described results from a longitudinal study of 191 Roman Catholic nuns (subset 1) over a period of 25 years and a cohort group (88 women and 5 men) from the United Kingdom who tended to consume nonphosphate calcium supplements (subset 2). The results indicated that subset 1 tended to consume 696 mg Ca and 1101 mg P per day which was similar to the results obtained for women 50 to 59 y.o as described in National Health and Nutrition Examination Survey III (NHANESIII). The second subset consumed an average each of 1100 mg each of Ca and P. Evaluation of fecal composites indicated that the higher the intake of calcium, the more phosphorus is excreted in the feces. This is indicative of not phosphorus resorbed from the bone, but of calcium binding excess phosphorus in the gut and then excreted. Since data from NHANESIII indicated that an appreciable number of individuals consumed less than 70% of the RDA for phosphorus and this was concentrated around the elderly with an estimated 15% of those 80 y.o and older and 10% of those from 60 to 80 y.o. Heaney and Nordin (2002) postulated that the later life phosphorus RDA should be increased to a level (1250 mg P/d) more typical for adolescence when bone mineralization is the greatest. If this is the case, an estimated 25 to 50% of women 60 to 80 y.o. would now have deficient phosphorus intakes suboptimal for current antiosteoporosis agents. In the current circumstances, absorbed phosphorus may be too low to support both soft tissue phosphorus needs and new bone mineralization which consumes mineral at a Ca:P molar ratio of approximately 1.6:1.

Calcium and Phosphorus in Combination

Several researchers (Abrams and Atkinson, 2003; Anderson and Garner, 1995; Calvo and Park, 1996) have speculated that high dietary phosphorus is routinely consumed. It is presumed that elevated levels are due to the consumption of food ingredients (phosphate salts) and phosphoric acid in carbonated cola type beverages. In their evaluation of calcium, magnesium, phosphorus and Vitamin D fortification of foods, Abrams and Atkinson (2003) concluded that, "it is unlikely that phosphorus supplementation is needed for most population groups because of the relatively high usual dietary phosphorus intakes, primarily from phosphate salts added to carbonated beverages and as food preservatives". It is interesting to note that phosphoric acid is used in only carbonated, cola-type beverages. At the levels used, the phosphorus contribution ranges from 30 to 40 mg P per 12 oz. Serving (one can). Smith et al (1989) conducted an eight week study in which 10 healthy premenopausal women consumed 1.4 liters of diet cola (diet Coke) each day. The consumption of 1.4 liters of diet cola resulted in similar mean serum levels of calcium, ionized calcium, phosphorus, alkaline phosphatase, parathyroid hormone, 1,25-dihydroxvitamin D_3, and osteocalcin when compared with controls not consuming cola. Twenty-four hour urine volume, creatinine clearance, calcium-creatinine ratio and phosphorus-creatinine ration were similar among cola consumers and controls.

Furthermore, no phosphates are used as food preservatives at the present time. Phosphates are Generally Recognized As Safe (GRAS) food ingredients, so identified by the U.S. FDA. They are permitted in a wide variety of food products and impart many positive attributes. Processed meat products are one example in which phosphates are used to bind pieces for restructured products (delicatessen chicken breast), develop and stabilize emulsions (frankfurters and bologna) and work synergistically with sodium chloride to reduce the NaCl requirement and to reduce cook-cool losses (ham and like cured meats).

High protein diets have often been associated with a hypercalciuric effect. It has been demonstrated that sulfur containing amino acids are actually the stimulus for enhanced urinary excretion of calcium (Whiting et al., 1997; Kaneko et al., 1990). Both studies evaluated the impact of high and low protein diets on calcium balance and the Japanese study compared meat and dairy proteins against diets high in soy protein isolate (SPI). All diets contained soy products, which could have contributed some phytoestrogen activity. SPI diets were used as an internal control as the high protein soy diets contained added sulfur amino acids. It was concluded in each study that catabolism of the sulfur amino acids resulted in a rise in acid secretion into the urine mediated by oxidation of with the formation of sulfate and hydrogen ions. Acid stress inhibits renal tubular reabsorption of calcium. Added dietary potassium could alleviate the hypercalciuric effect of protein.

Subsequent studies on the impact of protein on calcium retention and balance have shown some other interesting effects. Kerstetter et al. (1998) demonstrated depressed calcium absorption when a low protein diet was consumed while Heaney (2000) and Roughead et al. (2002) showed that feeding trials conducted over a longer time frame, the hypercalciuric effect of high protein was attenuated and in fact coingested phosphorus would offset the hypercalciuric effect of protein, possibly through a PTH-mediated mechanism.

IFAC poundage data has consistently demonstrated that consumption (corrected for non-food uses of food-grade phosphates used in dentifrices, pet food, personal care products etc.) of food grade phosphates has grown with the population in the U.S. and has not increased across the population as a whole.

Barger-Lux and Heaney (1993) studied 28 healthy, premenopausal women before and after low (5 mmol/d; 200 mg/d) and high (70 mmol/d; 2000 mg/d) calcium dietary regimes. The results indicated that there is considerable variation in the apparent capacity to conserve calcium among women with low intakes. None of the subjects consumed diets high in phosphorus. It was concluded that calcium restriction can evoke a persistent PTH response in the absence of a high phosphorus intake.

Hegsted (2001) questioned the low rate of bone fracture in Asian countries where calcium consumption is low. In these countries, the consumption of soy based products is high which would lead one to conclude the beneficial impact of dietary phytoestrogens.

Johnson-Down et al. (2003) indicated that expanding the authority to allow Canadian food processors greater latitude for calcium supplementation could lead 6 to 7% of adult men to consume greater than the upper limit (UL) of calcium. Heaney (2000) noted the dramatic decline in milk consumption. Heaney et al. (1982) determined that a daily intake of 2.5 g elemental calcium is quite safe in all people except those with sarcoidosis, active tuberculosis, or other absorptive hypercalciuric syndromes. Spencer et al. (1984) reported that calcium balance was not adversely affected by the high intake of phosphorus up to 2000 mg/d during calcium intake of 200, 800 or 2000 mg/d.

Zemel and Linkswiler (1981) supplemented basal diets with combinations of either high (1194 mg) or low (399 mg) calcium plus either low (835 mg) or high (1835 mg) phosphorus using calcium gluconate and either monosodium phosphate or sodium hexametaphosphate. The results indicated that there was negative calcium balance when the low calcium and phosphorus diets were consumed. Calcium balance became positive when under the low calcium high phosphorus regimen was consumed (Table 2). Calcium equilibrium was achieved when the high calcium high phosphorus diets were consumed ($P < 0.05$). The combined supplement of calcium and orthophosphate caused decreases in the excretion of both cyclic AMP and hydroxyproline suggesting a decrease in PTH-mediated bone resorption.

Table 2. Absorption, Excretion and Retention of Phosphorus as Affected by Calcium and Orthophosphates (mg/d)

Diet	Intake	Apparent Absorption	Urinary Excretion	Retention
Low Ca Low P	835[a]	486[a]	679[a]	-193[a]
Low Ca High P (ortho)	1835[b]	1307[b]	1416[b]	-109[b]
High Ca High P (ortho)	1835[b]	1239[b]	1197[b]	+42[c]

Nonmatching superscripts in each column denote significant ($P < 0.05$) differences.

Misconceptions Related to Supplements

It is commonly presumed by the consumer that mineral supplements can be taken at will; solubility is correlated with the quality of the mineral and that all sources are equivalent. Kobrin et al. (1989) reported two case studies in which in-patients were administered calcium carbonate tablets with end stage renal disease to control hyperphosphatemia. In one case, despite the increased dosage, the hyperphosphatemia persisted and abdominal pain was reported. A plain abdominal roentgenogram was ordered and revealed the presence of tablet shaped opacities at various locations from the stomach to the rectum. In the second case, a female underwent a parathydroidectomy for severe hyperparathyroidism. She subsequently developed hypocalcemia and was placed on calcitrol and calcium carbonate tablets. She remained hypocalcemic despite progressively increased calcium supplementation and noted the passage of tablets in her feces. Again, an abdominal roentgenogram disclosed clumps of tablet-shaped opacities at various sites along the intestinal tract.

Despite USP standards for disintegration, the calcium carbonate tablets failed to dissolve. Since they would require an acidic environment to facilitate dissolution, neither patient was achlorhydric nor hypochlorhydric. Dissolution could also be retarded by over compression; formulation without starch or an acid insoluble coating.

Mason et al. (1992), described simple tests that could be used by the consumer to determine the rate of dissolution. This involves adding a tablet to 200 ml vinegar and stirring each five minutes to observe disintegration within a 30 minute time frame.

Heaney et al. (1990), evaluated the effect of solubility on absorbability of a variety of calcium supplements. It was concluded that a false sense of security could be derived from solubility studies since they are a poor reflection of absorbability and more importantly absorbability of calcium from food sources is predominantly determined by other food sources. This would support the premise that calcium and phosphorus supplementation to food would be most desirable for optimal bioavailability.

Dietary Intake of Phosphorus in the US Population

Estimates of usual intakes of phosphorus derived by the Institute of Medicine (IOM, 1997) show that a significant proportion of the US population may not be meeting the Daily Recommended Intake levels for phosphorus. The estimates in the IOM 1997 report are based on the 1994 USDA Continuing Survey of Food Intakes by Individuals (CSFII). To further explore this, more recent food consumption data to derive estimates of dietary intakes of phosphorus (i.e., intakes associated with food and beverage consumption only, excluding intakes from supplements) for the total US population and the same subpopulations (21 subpopulations) considered in the IOM 1997 report was examined.

Intake estimates were derived from the National Health and Nutrition Examination Survey (NHANES) 1999-2000 and 2000-2001. The NHANES survey is a complex multistage probability sample of the civilian US population. It is designed to give annual samples that are nationally representative of the US population. The survey collects 1-day food intake data, in addition to nutrition, demographic, and health information. The NHANES survey over-samples minorities, low-income groups, and children, and statistical weights are provided by the National Center for Health Statistics (NCHS) to adjust for the differential probabilities of selection. The NHANES surveys are administered in different locations in the US over the 2-year period and involve interviews, a physical exam, and laboratory tests done on location in mobile vehicles. The dietary component of the surveys integrates USDA's Continuing Survey of Food intakes by Individuals (CSFII) into NHANES.

Participants included 9,965 subjects in the 1999-2000 survey and 11,039 subjects in the 2000-2001 survey. The dietary intakes presented below include only those individuals identified by NHANES as having complete and reliable dietary records (N=18,725).

Estimated Total Intakes

One-day intakes of phosphorus were calculated for each individual in the NHANES 1999-2000 and 2000-2001 surveys with complete and reliable dietary records. Following NCHS guidance[1], the four-year statistical weights provided by NHANES for use when combining results from the two NHANES surveys were used in the assessment. The mean and selected percentiles (1st, 5th, 10th, 25th, 50th, 75th, 90th, 95th, and 99th) of the distribution of dietary intakes of phosphorus were calculated for the 21 selected age groups. These estimates are provided in Table 3, along with the unweighted number of subjects in each subgroup. The intakes refer to phosphorus from foods, and do not include potential intakes from supplement uses[2]. Mean phosphorus intakes derived from the NHANES 1999-2000 and 2001-2002 surveys are fairly consistent with the values reported by IOM. However, the ranges of percentile values derived from NHANES were larger than those reported by IOM. This difference is most likely due to fact that the NHANES data are for 1 day of intake, while the previous set of estimates were based on two-day averages. The CSFII survey collected dietary intake information for two days; intake estimates were adjusted for intra-individual variability to reflect "long-term" intakes in the IOM report. The derivation of the IOM ***usual*** intake estimates used advanced statistical techniques to adjust for within and between subject variability. This method requires at least two intake estimates per person (the 1994 CSFII recorded intakes on 3 consecutive days) and cannot be used in the case of the NHANES data since the NHANES survey recorded consumption for only one 24 hour period.

Data available from the NHANES survey do not allow for the identification of lactating females, therefore this population group was omitted from the analysis.

Table 3

Table 1. Daily phosphorous intakes (mg) for the US Population. Estimates derived using the 1999-2000 and 2001-2002 NHANES data. Mean and percentile estimates are derived using the 4-year statistical weights provided with the data tapes.

			Percentiles								
Age Group	N value	Mean	1	5	10	25	50	75	90	95	99
0-6 months	565	318.3	0.0	0.0	0.0	119.0	288.6	452.1	643.0	771.3	1268.2
7-12 months	414	629.0	61.3	131.4	214.5	385.9	540.6	810.0	1126.4	1388.3	1939.0
1-3 years	1446	1033.4	252.7	385.1	512.1	709.4	992.1	1300.3	1585.9	1814.0	2328.3
4-8 years	1735	1117.4	253.9	466.9	599.0	811.6	1062.4	1341.0	1724.0	1974.9	2505.2
9-13 males	1116	1357.7	330.6	529.1	658.1	917.6	1235.9	1676.9	2154.6	2595.6	3730.2
14-18 males	1413	1596.1	281.4	566.0	720.4	1022.1	1467.5	1992.9	2583.9	3130.1	4326.1
19-30 males	1008	1639.1	302.4	567.5	698.6	1042.5	1517.4	2084.8	2700.2	3107.2	4234.1
31-50 males	1436	1633.7	259.0	657.6	818.7	1093.0	1511.4	2015.8	2586.8	2975.2	4104.0
51-70 males	1289	1421.4	311.1	567.0	717.1	1029.6	1353.6	1740.6	2157.6	2460.1	3596.2
>70 males	752	1239.0	286.9	496.1	648.7	857.2	1160.4	1532.0	1929.7	2175.9	2638.1
9-13 females	1166	1158.2	263.9	458.8	554.0	776.4	1068.0	1424.7	1924.5	2290.4	2913.5
14-18 females	1379	1095.2	149.2	346.6	471.4	684.5	973.3	1385.0	1804.9	2125.7	3248.8
19-30 females	1336	1182.3	204.6	393.9	526.8	798.0	1100.5	1474.8	1927.2	2171.2	3159.0
31-50 females	1594	1163.1	277.7	483.2	600.2	801.3	1092.3	1451.7	1831.6	2113.3	2795.7
51-70 females	1300	1076.5	225.0	420.9	526.1	735.6	1007.2	1308.9	1722.7	1949.4	2489.9
>70 females	776	942.0	203.6	366.2	466.1	636.1	881.9	1158.7	1533.7	1721.1	2214.6
<8 years	4160	1013.2	0.0	276.1	425.3	680.1	982.1	1297.3	1632.0	1880.7	2456.6
9+ years male	7014	1535.9	299.7	578.5	732.1	1021.5	1413.7	1914.1	2461.7	2855.5	4006.1
9+ years female	7551	1122.0	224.3	431.9	542.4	752.4	1042.7	1388.4	1800.2	2098.1	2780.8
Pregnant females	647	1403.7	333.8	483.6	687.1	968.9	1280.8	1795.2	2208.8	2522.6	3446.1
Total population	18725	1283.6	222.1	446.5	579.8	832.5	1168.9	1605.5	2118.9	2483.1	3430.3

As summarized in Table 4, from the data it appears that the total number of females with phosphorus intake below the RDI have declined since 1994 as "women 31-70" is demographically a large group, but 25% remain below RDI which is a significant number. Perhaps alarmingly, the data indicate more females in the prime bone-building years of 9-18 have daily intakes less than the RDI.

Table 4. Percent of US Females below 1000mg P per day (current RDI)

Age	1994 CSII Data	NHANES data 1999-2000 2000-2001	Change
9-13	10%	25%	**+15%** (deficiency is increasing)
14-18	25	50	**+25%**
19-30	25	25	0%
31-50	50	25	-25%(deficiency is declining)
51-70	50	25	-25%
>70	50	50	0%

[1] http://www.cdc.gov/nchs/data/nhanes/nhanes_general_guidelines_june_04.pdf
[2] Supplement data has currently been released for only NHANES 1999-2000. Respondents were asked about supplement use (prescription and over the counter) for the past 30 days, including the product name, dose, frequency, and history of usage. Supplement compositions, including ingredients and their percentage, are linked to respondents to determine how much additional intakes result from these products.

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