Part 3: Minerals

Calcium

Function

While the structural importance of calcium (and phosphorus) in bones and teeth has been known for centuries, more recent studies have shown that all cells require calcium (Allen and Wood 1999; Arnaud and Sanchez 1996). Not only does dietary calcium have a substantial impact on osteoporosis—a relatively recent finding on a disease that has plagued humans since the prehistoric era—but it also plays crucial roles in cell membrane function and signal transduction. Nerve and muscle cell functions are critically dependent on calcium and the plasma concentration of calcium. Calcium absorption and utilization, in turn, are dependent on and strongly influenced by phosphorus, vitamin D, parathyroid hormone, calcitonin, and estrogen.

The role of dietary calcium in reducing the risk or delaying the onset of osteoporosis is now well recognized (Food and Drug Administration 1994). Because bone loss accompanies the aging process, sufficient calcium intake during early adulthood increases peak bone mass, thereby reducing the risk of osteoporosis decades later (Heaney et al. 2000). Increases in calcium intake in postmenopausal women delay calcium loss from bone, thus lowering the risk of bone density's declining to osteoporotic levels. Calcium intakes of 1,000 to 2,000 mg per day have been shown to increase bone mass or slow the decline in bone density and reduce the risk of osteoporosis (Food and Drug Administration 1994).

Safety Evidence

A number of hypotheses for adverse effects of excess calcium intake have been investigated over the years. These purported effects have included kidney stones (nephrolithiasis) (Johnson et al. 1979), hypercalcemia with renal insufficiency (milk-alkali syndrome) (Junor and Catto 1976; Orwoll 1982), and harmful calcium interactions with other minerals (Spencer et al. 1965; Clarkson et al. 1967; Schiller et al. 1989). The evidence supporting increased risk of kidney stones with high calcium intake has been contradicted by other, more credible evidence (Food and Nutrition Board 1997). It is true that high intake may induce constipation and may also put some otherwise healthy hypercalciuric men at risk of urinary stone formation. In general, however, higher calcium intake has been associated with *decreased* risk of kidney stones (Curhan et al. 1993). High dietary calcium levels can influence the bioavailability and absorption of many trace elements—particularly the divalent cautions, such as magnesium,

manganese, and zinc—but it is unlikely that these impacts are commonly severe enough to have clinical impact (Greger 1988). The intestinal interactions have been studied primarily in animals.

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The FNB evaluated the various potential adverse effects of excess calcium intake and concluded that milk-alkali syndrome was the only one with dose-response data that could support a risk assessment (Food and Nutrition Board 1997). For this effect, FNB identified a LOAEL of 5 g per day and selected a UF of 2 to derive a UL of 2.5 g per day for adults. The FNB recognized that the data from patients with kidney stones was not likely to be meaningful for normal adults, and thus did not utilize some data (Burtis et al. 1994), which might have indicated a LOAEL of 1,685 mg per day.

The EC SCF reviewed all known effects of high calcium intake and concluded that a total intake of 2,500 mg showed no adverse effect; therefore, EC SCF's NOAEL is 2,500 mg (Scientific Committee on Food 2003). Because of the robustness of the database, EC SCF applied a UF of 1 to derive a UL of 2,500 mg for total intake from all sources.

Concluding that the available data were insufficient to set an SUL, UK EVM instead determined a GL of calcium intake at which milk-alkali syndrome, constipation, and bloating would be avoided (Expert Group on Vitamins and Minerals 2003). The report recognized that few side effects have occurred in clinical trials with 1,600 or 2,000 mg of supplemental calcium (Hofstad et al. 1998; Levine et al. 1997; Bonithon-Kopp et al. 2000). Based on a mean dietary calcium intake of 830 mg per day in the UK, UK EVM set the GL for supplemental calcium at 1,500 mg per day, stating that such a supplemental level "would not be expected to result in any adverse effect."

CRN ULS for Calcium

A wide range of clinical and epidemiological studies discussed by FNB, EC SCF and UK EVM have shown no adverse effects with calcium supplements of 1,600 mg or less. Specifically relevant and well-conducted clinical trials have shown no adverse effects with calcium supplements containing 1,200 mg (Baron et al. 1999) and 1,600 mg (Hofstad et al. 1998). From these studies, CRN identifies 1,600 mg as the supplemental calcium NOAEL, but also agrees with UK EVM that a 1,500 mg GL for supplements is prudent, largely because fortified foods and dairy products are plentiful alternative sources for substantial calcium intake. Thus, the CRN ULS for calcium is set at 1,500 mg per day for adults.

Comparison of Safety Values for Calcium

CRN ULS	1,500 mg
US FNB UL	2,500 mg
EC SCF UL	2,500 mg
EC supplement maximum	Not established (as of May 2004)
UK EVM GL, supplement	1,500 mg

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