

**LE Magazine March 1999**

## ABSTRACTS

**Calcium Absorption  
Strengthening Bones With The Correct Nutrients**

## Factors relating to calcium absorption

### ***Absorbability of calcium sources: the limited role of solubility***

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*Calcif Tissue Int 1990 May;46(5):300-4*

(Fractional absorption of seven chemically defined calcium sources was measured in normal adult women under standardized load conditions. Solubility of the sources in water at neutral pH ranged from a low of 0.04 mM to a high of 1500 mM. The relationship of solubility to absorbability was weak. In the range from 0.1 to 10 mM, within which most calcium supplement sources fall, there was no detectable effect of solubility on absorption. Data from four food sources are presented for comparison. Absorbability of food calcium was not clearly related to absorbability of the dominant chemical form in the food concerned. These findings suggests that (1) even under controlled, chemically defined conditions, solubility of a source has very little influence on its absorbability; and (2) absorbability of calcium from food sources is determined mainly by other food components.

## **A low-boron diet and calcium-loss prevention**

### ***Effect of dietary boron on mineral, estrogen, and testosterone metabolism in postmenopausal women***

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FASEB J 1987 Nov;1(5):394-7

A study was done to examine the effects of aluminum, magnesium, and boron on major mineral metabolism in postmenopausal women. This communication describes some of the effects of dietary boron on 12 women between the ages of 48 and 82 housed in a metabolic unit. A boron supplement of 3 mg/day markedly affected several indices of mineral metabolism of seven women consuming a low-magnesium diet and five women consuming a diet adequate in magnesium; the women had consumed a conventional diet supplying about 0.25 mg boron/day for 119 days.

Boron supplementation markedly reduced the urinary excretion of calcium and magnesium; the depression seemed more marked when dietary magnesium was low. Boron supplementation depressed the urinary excretion of phosphorus by the low-magnesium, but not by the adequate-magnesium, women. Boron supplementation markedly elevated the serum concentrations of 17 beta-estradiol and testosterone; the elevation seemed more marked when dietary magnesium was low. Neither high dietary aluminum (1000 mg/day) nor an interaction between boron and aluminum affected the variables presented. The findings suggest that supplementation of a low-boron diet with an amount of boron commonly found in diets high in fruits and vegetables induces changes in postmenopausal women consistent with the prevention of calcium loss and bone demineralization.

## **Anabolic effects on bone**

### ***Therapeutic efficacy of 1alpha,25-dihydroxyvitamin D3 and calcium in osteopenic ovariectomized rats: evidence for a direct anabolic effect of 1alpha, 25-dihydroxyvitamin D3 on bone***

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*Endocrinology 1998 Oct;139(10):4319-28*

It is an important question for clinical therapy of osteoporosis with vitamin D metabolites whether these compounds exert their beneficial effects on the skeleton indirectly through an increase in intestinal calcium absorption or whether there is also a major direct component of action on bone.

In this study, female 6-month-old Fischer rats were either ovariectomized (OVX) or sham operated. One month before surgery, all rats were placed on a diet containing 0.25% calcium and were kept on this diet throughout the study. Beginning 3 months post-OVX, groups of OVX rats orally received vehicle, a calcium supplement, low dose (0.025 microg/ kg x day) or high dose (0.1 microg/kg x day) 1alpha,25-dihydroxyvitamin D3 [1,25-(OH)2D3], or combinations of low and high dose 1,25-(OH)2D3 with the calcium supplement. By 3 months postsurgery, pretreatment OVX controls had lost 74% and 37% of tibial and vertebral cancellous bone, respectively. Two-way factorial ANOVA showed that a 3-month treatment of osteopenic OVX rats with 1,25-(OH)2D3 dose dependently increased vertebral and tibial cancellous bone mass ( $P < 0.001$  and  $P = 0.021$ , respectively) and trabecular width ( $P < 0.001$ ). Furthermore, 1,25 (OH) 2 D3 increased serum calcium ( $P = 0.028$ ) and urinary calcium excretion ( $P < 0.001$ ) and reduced serum PTH levels ( $P < 0.001$ ), osteoclast numbers ( $P < 0.001$ ), and urinary collagen cross-links excretion ( $P < 0.001$ ). Calcium supplementation alone was without therapeutic effect, and there was no significant two-way interaction between the individual treatment effects of 1,25-(OH)2D3 and calcium on bone mass. These data indicate that the anabolic effects of 1,25-(OH)2D3 in osteopenic OVX rats are mediated through a direct activity on bone.

## Trace mineral intake and bone loss

### *Spinal bone loss in postmenopausal women supplemented with calcium and trace minerals*

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*J Nutr 1994 Jul;124(7):1060-4*

The effects of calcium supplementation (as calcium citrate malate, 1000 mg elemental Ca/d) with and without the addition of zinc (15.0 mg/d), manganese (5.0 mg/d) and copper (2.5 mg/d) on spinal bone loss (L2-L4 vertebrae) was evaluated in healthy older postmenopausal women (n = 59, mean age 66 y) in a 2-y, double-blind, placebo-controlled trial. Changes (mean +/- SEM) in bone density were -3.53 +/- 1.24% (placebo), -1.89 +/- 1.40% (trace minerals only), -1.25 +/- 1.46% (calcium only) and 1.48 +/- 1.40% (calcium plus trace minerals). Bone loss relative to base-line value was significant (P = 0.0061) in the placebo group but not in the groups receiving trace minerals alone, calcium alone, or calcium plus trace minerals. The only significant group difference occurred between the placebo group and the group receiving calcium plus trace minerals (P = 0.0099). These data suggest that bone loss in calcium-supplemented, older postmenopausal women can be further arrested by concomitant increases in trace mineral intake.

## Calcium Malabsorption in older males

### *Age-related decline of bone mass and intestinal calcium absorption in normal males*

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*Calcif Tissue Int* 1998 Sep;63(3):197-201

Although about 25% of all hip fractures occur in men, little is known about the pattern of their age-related bone loss and its main determinants. The aim of this cross-sectional study was to evaluate the age-related changes of intestinal calcium absorption, bone mass, and bone turnover in normal men. In 70 normal males (age 17-91 years), we measured spinal and forearm bone density (FBD) (by DXA), fractional intestinal calcium absorption (by oral test), serum immunoreactive parathyroid hormone (PTH), dietary calcium intake (diet records), biochemical markers of bone turnover (serum alkaline phosphatase (ALP), osteocalcin, urine calcium, creatinine, and hydroxyproline), and 1,25(OH)<sub>2</sub>D<sub>3</sub> serum levels. Vertebral bone density (VBD) showed a modest decline before age 50 and a greater decline after age 50, whereas FBD presented a significant decrease with advancing age starting at age 40, suggesting a predominant age-related cortical bone loss. Intestinal calcium absorption (47CaFA) and serum 1,25 (OH)<sub>2</sub>D<sub>3</sub> also presented an age-related decline similar to FBD. Simple correlation analysis revealed that age was significantly related to 47CaFA ( $r = 0.60$ ), calcium intake ( $r = 0.32$ ), VBD and FBD ( $r = 0.79$  and  $0.63$ , respectively), serum 1,25(OH)<sub>2</sub>D<sub>3</sub> ( $r = 0.69$ ), and serum iPTH ( $r = 0.72$ ). No significant correlation was found between age and biochemical markers of bone remodeling. Partial correlation and stepwise variable selection analyses, using 47CaFA and bone mass as dependent variables, showed that in normal males, serum 1,25(OH)<sub>2</sub>D<sub>3</sub> and dietary calcium intake were the main contributors (64%) to 47CaFA variability, whereas only age accounted for 63% of VBD and age and dietary calcium accounted for 45% of FBD variability. These results indicate that bone loss in men accelerates after age 50 years and that among other factors, intestinal calcium malabsorption and 1,25 (OH)<sub>2</sub>D<sub>3</sub> serum levels play a role.

## Lowering risk of heart disease and osteoporosis

### *Folic acid responsive postmenopausal homocysteinemia*

Brattstrom LE, Hultberg BL, Hardebo JE  
*Metabolism* 1985 Nov;34(11):1073-7

Homocysteinemia is associated with juvenile arteriosclerosis, recurrent thromboembolic complications and osteoporosis. Plasma homocysteine, measured as homocysteine-cysteine mixed disulfide (MDS), has in other than homocysteinemics been reported to be higher in patients with coronary heart or cerebrovascular disease than in controls, and higher in men than in premenopausal women. Here, in groups of normal men and normal premenopausal and postmenopausal women, we measured plasma MDS in the fasting state and four hours after a methionine load (100 mg/kg body weight), before and after four weeks of folic acid therapy at 5 mg daily. In their fasting plasma, postmenopausal women (n = 5) had significantly (P less than 0.05) higher MDS concentrations than premenopausal women (n = 5) and younger men (n = 5). After the methionine load MDS concentrations in postmenopausal women rose markedly, reaching levels significantly higher than those in younger men (P less than 0.05), and with no overlap with values in premenopausal women (P less than 0.01), or in older men (n = 5, P less than 0.01). Folic acid therapy resulted in substantial reductions (n = 15, P less than 0.01) of MDS concentrations both before the methionine load (-31%) and after (-28%), though subjects had initially had normal concentrations of serum and erythrocyte folates. We speculate that moderate homocysteinemia might contribute to postmenopausal arteriosclerosis and osteoporosis. Should this prove to be the case, folic acid might be a useful prophylactic.

## **Bone density sustenance**

### ***The role of trace minerals in osteoporosis***

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*J Am Coll Nutr 1993 Aug;12(4):384-9*

Osteoporosis is a multifactorial disease with dimensions of genetics, endocrine function, exercise and nutritional considerations. Of particular considerations are calcium (Ca) status, Vitamin D, fluoride, magnesium and other trace elements. Several trace elements, particularly copper (Cu), manganese (Mn) and zinc (Zn), are essential in bone metabolism as cofactors for specific enzymes. Our investigations regarding the role of Cu, Mn and Zn in bone metabolism include data from studies with animals on Cu- and Mn-deficient diets. We have also demonstrated cellular deficiencies using bone powder implants, as well as fundamental changes in organic matrix constituents. In clinical studies we have demonstrated the efficacy of Ca, Cu, Mn and Zn supplementation on spinal bone mineral density in postmenopausal women. Each of these studies demonstrated the necessity of trace elements for optimal bone matrix development and bone density sustenance.

## Sources of calcium in diet

### **Calcium absorption from small soft-boned fish**

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*J Trace Elem Med Biol* 1998 Nov;12(3):148-54

The prevalence of osteoporosis in developing countries is low compared to most industrialised countries despite an apparent low Ca intake. It is possible, however, that food surveys have overlooked important Ca sources in developing countries. Small fish eaten with the bones can be a rich source of Ca, even though Ca from bone may be considered unavailable for absorption. In the present study, absorption of Ca from indigenous Bengali small fish was compared with the Ca absorption from milk. Ca absorption from single meals was determined in 19 healthy men and women (21-28 y). Each subject received two meal types on two separate occasions. Both meals consisted of white wheat bread, butter and ultra pure water with the main Ca source being either small Bengali fish (397 mg Ca in total) or skimmed milk (377 mg Ca in total). The meals were extrinsically labelled with  $^{47}\text{Ca}$ , and whole-body retention was measured on day 8, 12, 15 and 19 after intake of each meal. The labelling procedure was evaluated by an in vitro method. The calculated absorption of Ca as measured with  $^{47}\text{Ca}$  whole-body retention was 23.8 +/- 5.6% from the fish meal and 21.8 +/- 6.1% from the milk meal (mean +/- SD), which was not significantly different ( $p = 0.52$ ). Even after correction for an incomplete isotope exchange, as indicated by the in vitro study, Ca absorption was similar from the two meal types. It was concluded that Ca absorption from small Bengali fish was comparable that from skimmed milk, and that these fish may represent a good source of Ca.

# **Progesterone and osteoporosis**

## ***The decrease in bone mass associated with aging and menopause***

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*J Prosthet Dent 1998 Jan;79(1):14-6*

The human skeleton accumulates bone up to approximately age 30, after which bone is gradually lost. Although estrogen replacement therapy prevents postmenopausal bone loss, it is not certain that estrogen deficiency alone is responsible for the decrease in bone mass. Progesterone deficiency could also be a factor, and progesterone replacement therapy has been shown to prevent postmenopausal bone loss associated with ovarian dysfunction. This article reviews what is known about bone remodeling and bone loss as a function of age and gender, discusses evidence from studies in rats that progesterone plays an important role in regulating bone formation, and suggests directions for future studies in predicting the success or failure of implant therapy based on the number and kinds of osteoprogenitor cells present.

## Bone formation and progesterone

### *Effects of progesterone on serum levels of IGF-1 and on femur IGF-1 mRNA in ovariectomized rats*

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J Bone Miner Res 1996 Oct;11(10):1406-12*

Local and systemic insulin-like growth factors (IGFs) may be involved in the regulation of bone formation by sex hormones. The present studies describe the *in vivo* effects of estradiol, progesterone, or both on IGF-1 mRNA abundance in bone, serum IGF-1 levels, and bone formation. Rats were sham-operated (SHAM) or ovariectomized (OVX) at 12 weeks of age and used a week later in three experiments. First, OVX rats were treated with vehicle, estradiol, and/or medroxyprogesterone (MPA) for 3 weeks, and bone formation was assessed in the tibial metaphysis. Second, OVX rats were treated in the same manner and serum IGF-1 levels measured. Third, OVX rats were treated with an injection of vehicle, estradiol, and/or progesterone, and 24 h later, levels of IGF-1 mRNA in the femur were analyzed. The mineralized surface, mineral opposition rate, and bone formation rate (BFR) were higher in OVX than in SHAM rats. The BFR was decreased in estrogen-treated but increased in MPA-treated rats compared with vehicle-treated OVX rats. Circulating levels of IGF-1 were higher in OVX than in SHAM rats but were not affected by sex hormones in a 3-week experiment, whereas these levels were not different among groups in a 24-h experiment. Northern analysis detected 7.5 and 0.8 kb IGF-1 mRNA transcripts. The abundance of IGF-1 mRNA was higher in OVX than in SHAM rats. IGF-1 transcripts 7.5 and 0.8 kb were decreased by 72 and 29%, respectively, in estrogen-treated and increased by 44 and 43%, respectively, in progesterone-treated rats compared with vehicle-treated OVX rats. We conclude that in the short term, estrogen lowers and progesterone raises bone IGF-1 mRNA and these changes are followed by coordinated changes in bone formation rate.

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