CALCIUM NUTRITION AND SKELETAL AND ALVEOLAR BONE HEALTH

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INTRODUCTION

Osteoporosis has become a major orthopedic disorder in about 25% of postmenopausal women of Anglo-Saxon origin which in the U.S. results annually in some 5,000,000 spontaneous fractures. The disease exists in pre-clinical and clinical stages in 45% of the 28 million women of 45+ years. Spinal compression fractures occur in approximately 25% of women of 60 or more years. Hip fractures result in more than 30% of women after age 65. After 80 years of age, 15% will die within 3 months from indirect sequelae. Concomitant alveolar bone loss of the mandible occurs in most patients over 45 years of age. By age 60 almost 40% will have lost all their teeth. Loss of teeth is a major cause of malnutrition in the elderly.

The foregoing data and century end population projection of some 40 million of the 65+ age group make it imperative that effective modalities be developed, established and applied as soon as possible for the prevention and management of fractures.

CLINICAL ASPECTS OF BONE LOSS

Severe skeletal bone loss in mature women and men may exist long before it is manifested by clinical symptoms or biochemical changes or outward physical changes. In most instances, advanced osteoporosis is first revealed by the occurrence of spontaneous fractures of the hip, spine and long bones in postmenopausal women. Typical age associated structural changes in the vertebral mass results in a gradual loss of height and kyphosis which may cause progressive and persistent pain in the lumbar region of the spine are shown in Figure 1. Progressive deformation of the spine due to loss of height causes displacement of viscera and consequent malabsorption of nutrients. The concomitant loss of alveolar bone with aging frequently results in the loss of teeth. However, dental problems due to alveolar bone loss often occur in middle aged and younger women whose dietary during pregnancies failed to meet the added needs of the fetus.

Assuming relatively normal bone formation in the young we can then examine the effects of age and other factors which cause skeletal bone loss (Figure 2). In the first instance, it is essential to discuss the difference between osteomalacia

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Figure 1. Relationships of aging to skeletal and alveolar bone loss.

and osteoporosis. Osteomalacia, adult rickets, is characterized by decreased bone density primarily due to loss of calcium of the protein matrix, hence bone of abnormal calcium:protein ratio. This disease results from a lack of vitamin D which is needed by the body to utilize calcium bone formation. Osteomalacia occurs in geographic areas with limited sunshine and/or vitamin D intake. Osteoporosis, on the other hand, is defined as decreased bone density due to loss of total substance without change in chemical composition. This is the predominant form of bone loss in pre- and postmenopausal women in the U.S.
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Figure 2. Major causes of bone loss.

which is associated with a high incidence of fractures.

Alveolar bone experiences active exchange with the vascular nutrient supply, as do all other bone and soft tissues elsewhere in the body. It is a dynamic bone that has a remodeling rate considerably greater than that of the flat bones of the skull, which may be the reason why osteoporosis resulting from deficiencies of calcium, phosphorus, and vitamin D is seen first in the alveolar bone.

Radiometric detection of bone loss—One of the persistent obstacles in probing this insidious disease entity has been the lack of simple objective methods for detection of bone loss in patients before it becomes a clinical fait accompli. Invasive procedures such as isotope tracer methods, measurements of serum and urine calcium levels, or calcium balance determinations have proved less than adequate for the detection of asymptomatic bone loss. These considerations and the subjective shortcomings of conventional visual examination of radiographs for the diagnosis of osteoporosis and other biomedical problems prompted us to develop a simple and inexpensive radiographic method for quantitative evaluation of bone loss in terms of measurement of density of the mid-radius site of the right and left hand, 5-2 phalanx (1, 2). Selection of 5-2 phalanx is based on ready accessibility of the structure and a substantial amount of compact skeletal tissue with minimal interference from soft tissue. These characteristics give x-ray densitometry of this bone high preference for determination of skeletal bone health for surveys of a large population (3).

The fact that poor dentition is one of the principal causes of malnutrition of the elderly stresses the need to examine modalities which may minimize tooth loss. Difficulties in chewing with dentures often causes people to favor consumption of less nutritious foods than those eaten by persons with healthy natural teeth. The serious clinical and economic implications of this nutritional problem prompted us to develop a practical and quantitative method for detection of alveolar bone loss.

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which could be correlated with skeletal bone loss. To this end, a method was developed similar in principal to the determination of radiodensity of phalanx 5-2. Briefly stated conventional x-rays of the left and right molar 1 and 2 areas are taken at a fixed distance, angle and exposure time with an aluminum reference standard.

Figure 3. Age-sex relationships of alveolar bone and phalanx 5-2 bone densities.
The results of an extensive survey of the radiodensity of alveolar M1, M2, and phalanx 5-2 structures of "healthy normal" females and males ranging in age from 15 to 75 years are shown in Figure 3. The graphics demonstrate that alveolar bone density values, by reason of the greater bone mass involved, are significantly higher for both sexes than the corresponding 5-2 phalanx coefficients. The data also show that the parallel rise and fall of bone density in both sites is diagnostic of the rate of bone loss with age in females and males. The lower density coefficients of these osseous structure in females as compared to that of males is reflected in the far greater incidence of tooth loss and hip, spinal and long bone fractures in females of 40+ years.

**CLINICAL INVESTIGATIONS**

**Calcium intake and bone status** - Among common foods, milk and cheese are the richest sources of calcium. Most other foods contribute much smaller amounts or none. The 1959 USDA survey of 5,500 "normal" females showed that in the age group of 45 years and over, the estimated average calcium consumption approximated 450 mg per day - about 50% below the 1974 RDA of 800 mg per day (Figure 4).

![Figure 4. Calcium consumption and fracture incidence in females.](image)

Our radiodensitometric measurements of 4,280 "healthy normal" females from 15-95 years of age revealed that progres-
sive bone loss after 40 years appears to be a culmination of life long inadequate intake of calcium and the onset of menopause. The relationship found between incidences of disabling fractures of long bones, spine and hips of 313 women of 55+ years and their coefficient of phalanx 5-2 bone density revealed that subnormal bone densities occurred primarily in those whose average calcium consumption of 50% or less than the USRDA of 800 mg per day. From these measurements it can be deduced that a phalanx bone density of 115 mils - optimal mean - is associated with minimal fracture risk and may serve as a dependable parameter for the competence of the major skeletal sites of fractures in women.

In order to quantify the relationship of the amount of calcium intake needed for optimal skeletal bone status serial measurements of daily calcium intake from the major food sources and phalanx 5-2 measurements of 52 "healthy normal" pre- and postmenopausal women were collected and assembled graphically in Figure 5A. It is clear from these results that bone densities rose to age optimal levels as calcium intake approached 800 mg per day or more. These data support the conclusion that a daily intake of 800-1000 mg of calcium is necessary to maintain optimal bone health - and minimal fracture risk - in women of 53+ years. The results of a comparable study with 136 females 36-65 years to ascertain diet-

![Figure 5. Calcium intake and phalanx 5-2 (A) and alveolar bone (B) densities of females 36-65 years of age.](image-url)
ary calcium needs for the maintenance of optimal alveolar bone density shown in Figure 5B indicate the similarity to skeletal bone needs, namely, 800-1000 mg of calcium per day.

These data indicated that alveolar bone density is closely related to a dietary calcium intake of 800-1000 mg per day which apparently can only be achieved by ample amounts of dairy products or calcium supplements. Glickman (4) postulated that alveolar bone loss is the "crux of the problem" in periodontal disease. Although animal and some human data lend support to this point of view, there has long been a need to document this important concept in man. Application of quantitative radiography during periodic dental examinations and analyses of a dietary record appears to be the means of choice for early detection of alveolar bone loss and to evaluate the efficacy of dietary or therapeutic measures. Improvement in bone density found in the longitudinal studies with the "healthy normal" women of 26-78 years of age with an average dietary intake of 400 mg of calcium per day strongly support the preventative advantages of the administration of 600-850 mg of calcium per day as a safe, effective and practical means to achieve the reversal of incipient or advanced osteoporosis in pre- and postmenopausal females.

Comparison of calcium supplements - The foregoing observations suggested the need to ascertain the relative counter-osteoporotic efficacy of a supplement of 750 mg of calcium with 375 I.U. of vitamin D₂ and one which provides ample quantities of essential trace minerals and vitamins. To this end, a radiometric evaluation was undertaken of a vitamin-mineral supplement which in addition to calcium and vitamin D₂ provides all known micronutrients at USRDA levels shown in Table 1. The test panel consisted of 12 "healthy normal" females (39-65 years of age) whose habitual diets contained 200 to 450 mg of calcium per day. Periodic radiographic measurements disclosed that within 9-11 months of daily supplementation with this product the rate of bone density improvement was 2 to 3 times greater than that found for 11 females (38-66 years of age) receiving 700-800 mg of calcium per day alone with comparable dietary habits. A summation of the bone density status before and after 12 months of supplementation with the two calcium supplements are shown in Figure 6. The clinical significance of these limited data with respect to desirability of calcium supplementation with essential micronutrients is clear.

Longitudinal evaluation of calcium supplements - Analyses of results of longitudinal studies of 3-12 years duration with 619 "healthy normal" females initially 35-65 years of age strongly supports the administration of 700-800 mg of calcium daily derived from various compounds as a safe and effective modality for the correction of incipient or advanced osteoporosis. Generally, little or no improvement was noted for the first 6-9 months of supplementation; and age norms were frequently attained within 12 to 36 months of supplementation. However, deterioration of improvements soon followed voluntary cessation of the supplements by some subjects and improved after resumption to the program. During the course of the
Table 1
COMPOSITION OF VITAMIN-MINERAL SUPPLEMENT (VM)
Percent of U.S. Recommended Dietary Allowances

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>%USRDA</th>
<th>Nutrient</th>
<th>%USRDA</th>
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<tbody>
<tr>
<td>Calcium</td>
<td>60</td>
<td>Vitamin C</td>
<td>150</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>30</td>
<td>Folic acid</td>
<td>100</td>
</tr>
<tr>
<td>Magnesium</td>
<td>50</td>
<td>Niacin</td>
<td>100</td>
</tr>
<tr>
<td>Zinc</td>
<td>100</td>
<td>Riboflavin</td>
<td>140</td>
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<tr>
<td>Iron</td>
<td>100</td>
<td>Thiamin</td>
<td>140</td>
</tr>
<tr>
<td>Iodine</td>
<td>100</td>
<td>Vitamin B₆</td>
<td>100</td>
</tr>
<tr>
<td>Copper</td>
<td>100</td>
<td>Vitamin B₁₂</td>
<td>150</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>100</td>
<td>Pantothenic acid</td>
<td>100</td>
</tr>
<tr>
<td>Vitamin D₂</td>
<td>100</td>
<td>Biotin</td>
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<tr>
<td>Vitamin E</td>
<td>100</td>
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</table>

Figure 6. Comparison of bone density improvements in women with calcium intake from diet and supplements with and without micronutrients (Table 1).

In longitudinal trials we found a significant regression of achieved bone density improvements primarily in the 45+ age group in the face of continuation of the supplements. Of the several causitive factors responsible for the remission in bone density, the known reduced intake of micronutrients...
essential for optimal metabolism and bone remodeling by the elderly seemed the most likely. This probability has been documented by the Ten State Study which revealed the incidence of a consumption of 50% below the RDA for calcium, iron and vitamins A, D, C, thiamin, riboflavin and niacin by women of 45 years or more (5,6).

The phalanx 5-2 bone studies proved helpful in the development of a protocol to quantitate the efficacy of calcium supplements in overcoming alveolar bone loss associated with chronic inadequate dietary calcium intake. Initially, 12 dental patients were selected for the study whose alveolar bone and phalanx 5-2 bone densities fell far below their age mean and whose calcium intake was found by analyses of their habitual diet to average 30-40% below the USRDA of 1000 mg per day. A supplement of 4 tablets per day provided 600 mg of calcium with micronutrients was given for a test period of 24-36 months. Densitometric measurements of both sites were done at 3 or 4 month intervals depending on the availability of the patients. The results of the study summarized graphically in Figure 7 show that use of calcium supplements in females with a low dietary calcium intake provides a practical modality for the reversal of bone loss in skeletal and alveolar bone. The greater response of +31.5% of alveolar bone to

![Figure 7](image-url)

Figure 7. Effect of calcium supplementation of low calcium diets (310-460 mg/day) on 5-2 phalanx and alveolar bone density of 12 healthy normal females 36-62 years of age. The supplement provided 600 mg of calcium with micronutrients.
calcium with microvitamin supplementation compared to +15.3% of phalanx bone is indicative of its greater metabolic activity. These and other measurements have shown that alveolar bone is a dynamic structure with a remodeling rate far greater than trabecular or cortical bone. These characteristics explain, in part, why incipient bone loss related to dietary deficiencies of calcium and other nutrients are first reflected in alveolar bone loss.

The foregoing results caused us to compare the bioavailability of calcium for remodeling alveolar bone with the addition of the vitamin trace mineral complex in mature healthy normal females. The results of this on-going investigation are shown in Figure 8. These limited data indicate that alveolar bone density improvement with calcium in combination with the vitamin trace mineral complex greatly improved the counterosteoporotic efficacy of the calcium supplement - not only in terms of a shorter test period but also in the greater level of bone density improvement. These results have encouraged us to expand the test panel which currently includes 35 females (41-59 years) under the care of two practicing dentists who have cooperated in this program for 7 years.

The development during the past 20 years of non-invasive techniques for quantitative determination of bone density has made it possible to ascertain not only the prevalence and incidence of osteoporosis but also evaluate the counterosteoo-
porotic efficacy of various nutrients and medications. The availability of these procedures have made it possible to compare the rate of age related osteoporosis of different bone structures (Figure 9).

![Graph showing percentage with osteoporosis vs age ranges]

**Figure 9.** Comparison of incidence of osteoporosis of dorso-lumbar spine in 2088 women (6) and alveolar bone loss in 2320 women (2).

**DISCUSSION**

Currently, none of the four drug types, sodium fluoride, anabolic steroids, calcitonin and estrogens, employed alone or to supplement the counterosteoporotic activity of calcium and vitamin D, have been approved by the FDA. All four have been reported to be primarily inhibitors of bone resorption rather than stimulators of bone formation and do little to alter the prevailing osteoporotic conditions.

**Fluoride** - The only proven benefit of fluoride administration is its role in preventing dental caries. Earlier reports of its usefulness in the treatment of osteoporosis remain controversial. Riggs *et al.* (7) postulated that a combination of fluoride, calcium and vitamin D would increase bone formation in osteoporosis and protect against skeletal fragility. Unfortunately, the pharmacologic dose of fluoride, 22-48 mg per day required to produce a response to therapy.
proved to be highly toxic - causing hematemesis, anemias, neurologic disturbances and joint pain. Because fluoridic bone has increased crystallinity and may have decreased elasticity, increased bone mass after therapy does not necessarily signify increased bone strength. The fracture rate in fluoride, calcium-vitamin D, treated patients has been found to be 8 times greater than that of untreated patients (8). In consideration of these pharmacologic and morphologic problems, fluoride has not been approved for treatment of osteoporosis by the FDA.

Anabolic Steroids - Although synthetic steroids possessing high anabolic and reduced androgenic activity have been available for clinical purposes about 40 years, there is little unanimity regarding their role in this therapeutic armamentarium in their treatment of osteoporosis. Improvements in protein metabolism suggested that these agents would also stimulate total bone formation. Although, nitrogen and calcium retention was observed with administration of the various available synthetic steroids in elderly osteoporotic females, bone turnover measurements revealed no consistent effect on bone formation. The masculinizing effects and increased libido produced by these steroids limited periods in which medication was or can be administered (9). Early calcium balance studies by Albanese and associates (10) and neutron activation data recently reported by Chestnut (11) suggest that stanozolol administration may induce significant bone resorption activity. However, it should be noted that in view of prevailing therapeutic uncertainties the FDA continues to classify anabolic steroids as: "Probably effective as adjunctive but not primary therapy in senile or postmenopausal osteoporosis." Equal or greater consideration should be given to diet, calcium balance, physiotherapy and good general health promoting measures. Final classification of less than effective indications requires further investigations (9).

Estrogens - In 1940 Albright, Bloomberg and Smith (12) proposed the existence of a hormonal regulation of osteogenesis in adults based on the antagonistic action between anabolic and catabolic steroids. On the basis of this rationale and early clinical trials the estrogens have been employed for the management of osteoporosis in postmenopausal women for some 40 years. Based on analyses of available data, the National Academy of Science and the Food and Drug Administration published the opinion that "estrogen therapy in postmenopausal osteoporosis is probably effective only when used in conjunction with other therapeutic measures such as diet, calcium, physical therapy and other good health promoting measures." The problem that estrogen use by postmenopausal women may increase the risk of endometrial cancer, gallstones and possibly cardiovascular disease now causes most physicians to avoid their administration.

A number of investigations have shown that although bone loss may be retarded by estrogen treatment, there is essentially no evidence that estrogens can significantly replace bone mass previously lost. In an attempt to clarify this clinical problem, serial radiodensitometric measurements done.
with "healthy normal" women (47-67 years) 41 of whom had been prescribed estrogen therapy (0.624-1.25 mg/day) 2-5 years and 41 had not. The results of this survey showed that there is no significant difference in the range of bone density between estrogen-treated and untreated test groups (13). A subsequent densitometric study on the counterosteoporotic efficacy of calcium-vitamin D2 supplementation in postmenopausal women with histories of comparable inadequate calcium intake who had not or had received estrogen medication failed to reflect any therapeutic advantages of prior estrogen administration.

Improvements in metacarpal mineral content by Lindsay et al. (14) for bilaterally castrated females treated with estrogen, mestranol. for 5 years suffer in their clinical interpretation from lack of data on daily calcium intake and inherent metabolic differences of both his test and placebo groups from natural postmenopausal women. Recently a number of studies have been reported in which a combination therapy of estrogen, fluoride and calcium have been employed in the management of vertebral osteoporosis. The most extensive investigation (1968-1980) of these is that of Riggs and associates (15) which included 165 female patients 47-81 years of age. The administration of all three agents was statistically more effective in terms of reduced fracture incidence than any other combination. However, twenty-three of the 61 fluoride-treated patients had rheumatic symptoms (joint pain and swelling or painful plantar fascial syndrome); 9 had gastrointestinal symptoms (severe nausea and vomiting, peptic ulcer or blood-loss anemia) and 1 had both rheumatic and gastrointestinal symptoms. These reactions were not observed in the untreated patients. Hypercalcaemia and/or hypercalcuria was observed in 24% of the patients receiving 1000-3000 mg of calcium per day and 50,000 I.U. vitamin D2 weekly or bi-weekly with or without 0.625-2.5 mg of estrogens per day.

Calcium - Our results of studies undertaken to assess the relationship of daily calcium intake and bone density of 52 postmenopausal women showed that bone densities rose to age or optimal levels as calcium intake approaches 800 mg per day or more. These findings also support the concept that a daily intake of 800-1000 mg of calcium is necessary to maintain optimal bone health in pre- and postmenopausal women. If this cannot be achieved with dairy products, a calcium supplement should be given. The benefits of this latter approach has been documented by longitudinal studies with 619 women (35-75 years) for periods of 3-13 years, which show that with continuous daily supplementation with 750 mg of calcium and 375 I. U. vitamin D2, bone loss can be slowed or reversed. In the course of these trials it was found that rate and degree of bone density improvement achieved with supplementation decreased significantly with the age at which it was initiated. Longitudinal measurements of 8 test volunteers who stopped the supplements on their own initiative and later reentered the study showed significant increases in bone density during the initial supplementation period, deterioration after stoppage of the supplements and improvement in bone density on resumption of the supplements (5).
Smith and associates (16) have demonstrated that bone loss in females of 80+ years may be reversed and maintained at a higher level of bone mineral content through physical activity or calcium and vitamin D supplementation. Albanese and coworkers (17) have found that bioavailability of calcium supplements for bone remodeling may be significantly accelerated in the presence of a vitamin-trace mineral complex which approximates the U.S. Recommended Dietary Allowances (18). Lee et al. (19) have studied the effects of supplementation of the diets with calcium or calcium rich foods on bone density of elderly females with osteoporosis. This investigation demonstrated that the beneficial effects of calcium or calcium rich foods on bone density occurred in at least half of the 20 female (62.3-83.9 years) osteoporotic patients.

REFERENCES

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