Table 6. Disintegration and dissolution of commercial calcium carbonate tablets—(October 1987)—controls

Product	Strength (mg)	Lot number	Expiration date	Disintegration time (minutes)	Amount dissolved in 30 minutes (percent)
Os-Cal	500 (OS)[1]	55548	1/89	7	104
Caltrate-D	600	168-528	12/89	12	77
Tums[2]	200	0766-0740-52	12/91		102
Giant Natural	600	21593	1/90	7	107

[1]OS = oyster shell.
[2]Broken into pieces before testing.

Summary

1. There is a serious problem with the quality of many calcium supplements in the marketplace today, and FDA should immmediately address this issue.
2. Consumers should insist that the calcium supplements that they buy meet USP standards.
3. Calcium supplements (carbonates, phosphates) are best administered at mealtime. They should always be taken with a full glass of water, juice, or other liquid to enhance solubility.
4. The use of calcium salts (in which solubility is pH-dependent), particularly tribasic calcium phosphate, should be avoided in achlorhydric patients.

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Panel Session: Nutrition/Exercise

Is Osteoporosis a Pediatric Disease? Peak Bone Mass Attainment in the Adolescent Female

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Synopsis

Osteoporosis in the elderly woman is determined by the amount of peak bone mass in adolescence, the premenopausal maintenance of such peak bone mass, and the rate of postmenopausal bone mass loss. The majority of research efforts in the past have been directed at defining the pathogenesis and treatment of postmenopausal osteoporotic bone loss. A comparatively new, and potentially fertile, area of research deals with factors responsible for attaining and augmenting peak bone mass in the adolescent female.

Determinants of peak bone mass include genetic, nutritional, weight loading (exercise), and environmental factors. Nutritional factors, especially calcium, are potentially most amenable to therapeutic manipulation. Current data suggest that calcium deficiency exists in the adolescent female; and, although the current data are preliminary and not conclusive, they suggest that increasing calcium intake may be of value in increasing peak bone mass. However, assurance of compliance in the teenage female population in increasing calcium intake is difficult; relating a disease of the elderly, such as

osteoporosis, to a teenage female population, a population that may experience the disease 40–50 years later, is frequently frustrating. Nevertheless, increased attention must be directed toward increasing calcium intake in this population of females.

The amount of bone mass in adolescence may determine the amount of bone mass postmenopausally; a high or low peak bone mass may, therefore, contribute to protection against, or risk of, subsequent fracture. The ultimate target population for osteoporosis prophylaxis may indeed be the young, rather than the elderly, female.

THE EPIDEMIOLOGIC DETERMINANTS of postmenopausal osteopenia, and postmenopausal osteoporosis with fracture, include the amount of peak bone mass in adolescence, the maintenance of such peak bone mass premenopausally, and the rate of bone mass loss, principally postmenopausally (fig. 1). While the age of attaining peak bone mass is undefined (is it in the third decade, the second decade?), a number of determinants of peak bone mass can be identified, including nutritional, genetic, mechanical loading (including exercise), and environmental factors (fig. 2).

Genetic Factors

As Matkovic and Chesnut (*1*) have noted in ongoing studies of 31 healthy Caucasian females originally age 14, peak bone mass attainment is under the genetic influence of both parents. Similar correlations have been reported by Lutz (*2*) in 26-year-old daughters and their mothers. In addition, by age 14, young females have already achieved about 90 percent of their mothers' values for height and for bone mass, as determined by radiographic and photon absorptiometric techniques (*1*). However, such studies essentially measure the degree of family resemblance, and do not strictly define the strength of the genetic component of that resemblance.

Studies in monozygotic and dizygotic twins more precisely define a possible contribution of genetic factors (determinants) to bone mass. An increased intrapair (within the twin pair) variance in dizygotic twins, compared with monozygotic twins, presumably indicates a significant genetic contribution to the observed variation.

Studies by Smith and co-workers (*3*) demonstrated that juvenile dizygotic twins have a significantly greater variation in intrapair difference in bone mass and bone width at the wrist, as obtained by single photon absorptiometry (SPA) measurements, compared with monozygotic twins of similar ages. Such intrapair differences were found in these studies to increase with age, as noted in the bone mass and bone width of *adult* monozygotic and dizygotic twins, suggesting that in these adult twins, environmental, as well as genetic, interactions contribute to such observed variations in bone mass at later ages. Also, Pocock and co-workers (*4*) described a significantly higher correlation of bone mass measurements at the lumbar spine within the twin pair of adult monozygotic twins, compared with adult dizygotic twins; similar data were reported in the same study at the proximal femur and the forearm, although the authors felt that a lesser genetic contribution might be in evidence at these sites, compared with the spine. Dequeker and co-workers (*5*) also noted similar findings, although they observed that a genetic effect on spinal bone mass appeared to be predominantly in twins younger than 25 years, and could not be conclusively demonstrated in adult twins.

Therefore, it appears reasonable to conclude that there is a significant genetic contribution to peak bone mass attainment, and to postulate that genetic factors, either alone or in interaction with environmental variables, may predispose an individual to the development of osteoporosis. The relative contribution of genetic factors to peak bone mass, compared with the other previously noted determinants, is, of course, unknown.

Nutritional Factors

For defining the role of nutritional factors in determining peak bone mass, few data are available for adolescents, and the data that are available relate primarily to calcium. A Recommended Daily Allowance (RDA) of 1,200 milligrams (mg) of calcium per day for females between the ages of 11 and 18 years is advised; however, the Health and Nutrition Examination Survey data (*6*) showed an intake in females aged 11–24 years of 700–950 mg calcium per day, and Matkovic and co-workers (*7*) found an intake of 1,015 mg per day in 31, 14-year-old females. However, in the latter sample, the range of calcium intakes was 296–1,801 mg per day, with 26 percent of the subjects ingesting < 800 mg per day. The RDA is probably not met by the majority of teenaged females.

In the ongoing study by Matkovic and co-workers (*7*), a significant ($_P < .01$) linear correlation of 0.78

Figure 1. Determinants of postmenopausal osteopenia and osteoporotic fracture

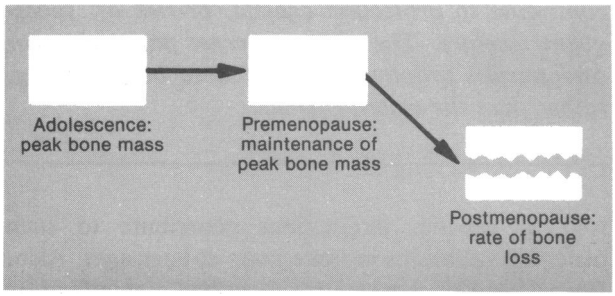
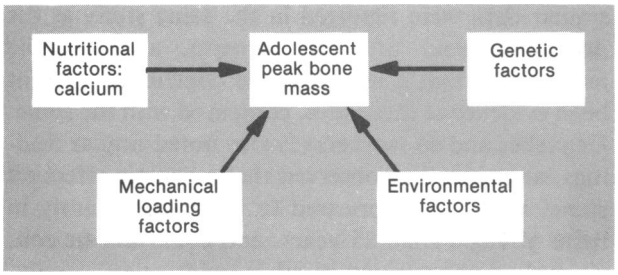


Figure 2. Determinants of adolescent peak bone mass



existed between calcium intake and calcium retention (as defined by calcium balance) in adolescent females aged 14 years, with the greater calcium retention (+543 mg per day), at a calcium intake of 1,506 mg per day. In addition, at age 14, calcium balance was positive in this female group at a calcium intake of 575 mg per day or greater—perhaps less than might have been anticipated from the RDA. Also, in adolescent females age 14, calcium balance was significantly more positive, at comparable levels of calcium intake, when the calcium source was calcium carbonate, rather than milk. Such a discrepancy in calcium balance between calcium sources is presumably due to the phosphate in milk; phosphate intake was significantly higher in the group receiving milk as their calcium source, and a significantly negative correlation existed between phosphate intake and calcium absorption (*7*).

Paradoxically, however, bone mass changes in wrist and spine, over a 2-year period in the same 14-year-old female population, indicated a trend toward a more positive effect on bone mass using milk as compared to calcium carbonate, with significant increases from baseline at these skeletal sites in the milk group, compared with the same sites in the calcium carbonate group over 20 months of follow-up (*8*). However, changes over time between the group receiving milk, the group receiving calcium carbonate, and a control group were not significant. In this ongoing study, however, the study population is quite small, with 8 subjects in the control group, 9 in the milk group, and 11 in the calcium carbonate supplement group. Such small numbers may not be sufficient for statistical power to determine differences among the groups (that is, a Type II error may be demonstrated). Such paradoxical findings of differing effects of calcium sources on calcium balance, and on bone mass, again demonstrate that the relationship between nutrition, specifically calcium intake, and peak bone mass remains unclear. Nevertheless, at this time it appears reasonable to assume that calcium deficiency exists in the majority of adolescent females, at least as defined by the RDA. The role of calcium intake, and of different calcium sources, in attaining peak bone mass, remains to be fully defined, but is probably positive.

The role of other nutrients in attaining peak bone mass needs to be elucidated; excessive phosphorus, protein, and caffeine ingestion, in combination with other risk factors, may have a deleterious effect. Also, in terms of nutritional factors, anorexia is a condition that exerts an extremely negative effect on bone mass in the adolescent. Such an effect is seen at both cortical and trabecular bone mass sites, as has been shown by Rigotti and co-workers (*9*), who noted a reduction in trabecular bone at the spine, with subsequent compression fractures, in anorexic females, as well as a reduction in predominantly cortical bone mass as assessed by SPA measurement of the wrist.

Mechanical Loading Factor

The third determinant of bone mass is exercise and mechanical loading factors. While exercise would presumably have a positive effect on peak bone mass attainment, no data are available to substantiate such a presumption in the adolescent female group. However, amenorrhea, specifically exercise-induced amenorrhea, is associated with a detrimental effect on bone mass at predominantly trabecular bone sites. As Chan and coworkers (*10*) have shown, the amenorrheic exercising female at age 24 may have the spinal bone mass, as determined by dual photon absorptiometry, of a 50-year-old female. Such a negative effect of amenorrhea, of whatever cause, could be extrapolated to the young adolescent female as well.

Environmental Factors

Environmental factors that have a deleterious effect on adolescent peak bone mass attainment are

primarily smoking and alcohol ingestion. Whether such environmental factors as industrial pollutants will prove to have a negative effect on bone mass development in teenage females remains to be elucidated.

Other Factors

Included in this category of determinants of peak bone mass attainment are various medications associated with osteopenia, such as cortisone, and medical conditions also associated with bone loss, including immobility, hyperthyroidism, hyperparathyroidism, and amenorrhea. Lactation may also be included in this category, because it can have a detrimental effect upon bone mass in the lactating adolescent mother, and probably a negative effect on peak bone mass attainment as well. Chan and co-workers (*11*) noted that bone mass, as ascertained by SPA measurements of the wrist, was significantly lower in lactating adolescents as compared with nonlactating adolescents, and also compared with lactating adults, over 14 weeks of lactation. In addition, increasing calcium intake may ameliorate somewhat this deleterious effect on bone mass, as shown in studies with various calcium intakes over a similar 14-week period of lactation (*11*).

Questions on Adolescent Bone Mass

1. How to identify at-risk adolescent females? In 1987, the assumption that deficient peak bone mass attainment in adolescent females may contribute to subsequent postmenopausal osteopenia appears quite reasonable, although data supporting such an assumption remain preliminary. If such an assumption is conclusively proven in the future, how are such at-risk adolescent females to be identified? First, although a deficient bone mass at multiple skeletal sites in the teenage years may extrapolate to a deficient bone mass after menopause, it is obviously not appropriate at this time to recommend quantitative bone mass screening for vast numbers of adolescent females, particularly given the controversy surrounding bone mass quantitation even in the elderly. Second, while assessment of risk factors, such as a family history of osteoporosis, low calcium intake, and so forth, may eventually prove to be markers for subsequent bone loss, no studies are yet available to confirm such an expectation. Third, the findings of Matkovic and Chesnut (*1*), and Lutz (*2*), which noted a strong resemblance between parents' bone mass and their daughters' bone mass, have potential application for recognition of risk of inadequate bone mass in the daughters, since their data suggest that adolescent and middle-aged females at risk could be identified through their mothers' bone mass measurements. Such a possibility requires further study. Lastly, Pocock and coworkers (*4*) have hypothesized that a single gene or set of genes may determine bone mass at multiple skeletal sites, and that potential DNA studies could genetically identify individuals at risk. This would be a fertile area for future research, but at present remains only a hypothesis.

'The ultimate target population for osteoporosis prophylaxis may indeed be the young, rather than the elderly, female.'

2. What level of calcium intake is needed to improve calcium balance, and to increase adolescent bone mass? There are conflicting data, in that the RDA of 1,200 mg per day indicates that this amount of calcium is necessary to achieve positive calcium balance in young female populations, although the studies of Matkovic and coworkers (*7*) in 14-year-old females indicate that positive calcium balance may occur, admittedly in a small subset of persons, at a calcium intake as low as 600 mg per day. Further studies are needed in this female population; for the present it appears reasonable to adhere to the 1,200 mg per day RDA.

3. What approaches should be used to encourage adolescent females to increase their calcium intake? From a practical standpoint, even if it is eventually proven that increasing calcium intake has a beneficial effect on peak bone mass attainment, and that such peak bone mass attainment translates to protection against postmenopausal fracture, it may be difficult to achieve increased calcium intake in adolescent females. Relating a disease of the elderly, such as osteoporosis, to a teentage population, a population that may experience the disease 40–50 years later, is extremely difficult. Promoting an awareness of osteoporosis, and of a potential prophylactic benefit of calcium (if so proven), to the adolescent female may be unrewarding for compliance in increasing the intake of calcium. Recognition of the difficulties above may justify, pragmatically if not nutritionally, the supplementation with calcium of foods accepted and eaten by adolescent females, including carbonated beverages, fruit juices, and other foodstuffs.

4. What messages should be given to the consumer regarding adolescent peak bone mass attainment? The current data indicate that calcium intake is defi-

cient in the adolescent female, that low parental bone mass may lead to a daughter's low bone mass, and that such a low bone mass in the daughter could result in a future risk for osteoporosis. Also, in spite of the conflicting data in this area, the hypothesis of improving peak bone mass with increasing calcium intake remains tenable, and a 1,200 mg per day intake in adolescent females appears justified. Lastly, anorexia, and exercise-induced amenorrhea, will have extremely deleterious effects on bone.

Conclusions

In conclusion, this is a new and exciting area of osteoporosis research that at present has produced only preliminary data. As further studies on this subject are completed, the observation made by Dent (*12*) 15 years ago may be confirmed; that is, that senile osteoporosis is a pediatric disease.

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Panel Session: Nutrition/Exercise

The Role of Exercise in Preventing Osteoporosis

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Synopsis

Evidence from a variety of sources indicates that exercise can increase the mineral content of bone, raising the expectation that exercise programs may be effective therapy for the treatment of osteoporosis, and the prevention of hip and spinal fractures. Indeed, prospective studies demonstrate that primarily weight-bearing exercise prevents the age-related decline in axial skeletal mass and, in some instances, increases bone mineral content. Optimal changes in the skeleton in response to exercise are seen in those women with adequate intake of dietary calcium. Neither hormonal status nor age appears to preclude the skeletal benefits of exercise. The design of an exercise program must consider the physical condition of the participants, their current levels of activity, their compliance, and the objectives of the program. Generic programs that are not designed for individuals' needs and limitations, and that are not adequately supervised, will result in a high rate of musculoskeletal complications and noncompliance.

Unfortunately, additional studies are necessary before we can construct an optimum exercise prescription for bone health which addresses duration, frequency, intensity, and type of exercise. Of concern is the fact that gains in bone mass achieved with exercise are lost following their discontinuation in postmenopausal women, underscoring the concept that the level of physical activity is a major and