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Editorial: Attainment of Peak Bone Mass

Most physicians are aware of the inexorable loss of bone that accompanies aging. Osteoporosis is one consequence of this loss. The bone density of elderly women, who manifest osteoporotic fractures, depends on both the rate of loss and the initial bone mass. Attention to the factors that lead to the development of peak bone mass, which is the highest value that an individual attains during her lifetime, is warranted. The large variance of normal bone density is often not appreciated. A normal 30-yr-old woman in the bottom decile for bone density could have the same density as an 80-yr-old woman in the top decile. The variance does not appear to increase with aging; and because the normal range in young women is already so broad, inequities must be present during growth. Not surprisingly, the list of factors relating to peak bone mass is similar to the list of risk factors for postmenopausal osteoporosis, including race, sex, heredity, diet, hormonal factors, activity, weight, and drugs or diseases that lead to bone loss. Unfortunately, these factors are not understood, not well studied, and not at all independent.

There is no consensus on the age at which peak bone mass occurs. Longitudinal measurements of bone density through adolescence and early adult years are not available. Some cross-sectional studies have found no increase in bone density after age 20, whereas others, with larger numbers of subjects, find the bone density increases until about age 35, then starts a downward trend (1). Thus, it appears that the density of the bone continues to increase for at least a decade after the maximum height has been attained.

Hereditary and racial factors are probably the most important determinants of peak bone density. Black children have higher bone density than white children (2). The bone density of teenage girls is correlated to the densities of the fathers and mothers (3). Twin studies have given the best data about the influence of heredity on bone mass. Pocock *et al.* (4) showed that bone density was significantly better correlated in monozygotic than in dizygotic twins. How the genetic message governs the bone density is unknown. Bone density is related to body size, muscle mass, and hormone levels, all of which are also under genetic control, but these known factors do not sufficiently explain the observed variance in bone density.

Body size is related to bone mass. Obese women, black or white, have higher bone density than women closer to their ideal body weight (5), and women with anorexia have low bone density. It is not clear if weight *per se* influences bone mass, or whether the changes are mediated by associated hormonal differences. Within the normal range of weight, some investigators find a positive correlation with bone density and other do not. One reason may be the technique used to measure the bone. Projectional methods (such as photon absorptiometry) do not measure a geometric density, and larger bones will have higher measurements than smaller bones with equal density. The true three-dimensional density of bone can be noninvasively measured only by computed tomography. Studies using this technique show no correlation between height or weight and bone density (6).

Dietary factors are of great interest and importance because they can be modified. There is considerable controversy about the efficacy of calcium in postmenopausal women, about whom there is a plethora of contradictory data. From adolescents there is hardly any data, despite the fact that most investigators think this is a crucial time for bone development. Surveys which compare the bone density of elderly women to the recalled calcium intake during their youth have not yielded consistent results, perhaps because the recall of remote dietary intake is inaccurate. The recommended daily allowance of calcium has been set at 1200 mg/day, but many American teenage girls avoid dairy products in attempts to keep slim and fashionable, failing to meet the RDA. Matkovic *et al.* (3) recently studied 18 teenage girls whose customary calcium intakes varied from 250 to 1700 mg daily, and found a positive correlation between calcium balance and calcium intake ($r = 0.67$). In a 2-yr longitudinal study they did not find a difference in change in bone mass in a group with an intake of 750 mg/day compared to 1640 mg/day, but the number of subjects was small. Larger studies are definitely needed.

Hormonal factors appear to play a major role in the attainment of peak bone mass. Estrogen deficiency has serious detrimental effects on the bone mass. Oopherectomy results in a rapid loss of bone, and women with various causes of secondary amenorrhea have low bone density. It is not known if excess levels of estrogen result

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in increased bone mass. The side effects of estrogen would prohibit the direct study of administering supraphysiological estrogen doses to normal women for the duration necessary to demonstrate a change in bone mass. Although estrogen receptors have recently been found on the surface of osteoblasts, the physiological role of estrogen has not been determined. In females, androgens may also be important. Buchanan *et al.* (7) found independent significant correlations between bone density and estrogen or androgens in 30 young women with various exercise and menstrual histories. In another study, they demonstrated that young women with excess androgens (recruited from an electrolysis center) had higher bone densities than normal women, and this difference was abolished by controlling for androstenedione (8).

Activity also influences bone mass. Elegant animal studies have shown that bone responds to compressive forces by increasing bone mass (9). The converse is also true: bedrest leads to rapid bone loss. Again, the physiological mechanisms are unknown, especially the transmission of the signal (bone stress) to the cells responsible for remodeling bone. Cross-sectional data shows that bone mass is higher in athletes, but the factors that enable excellent athletic performance could be associated with bone density, so that athletes could have higher bone density on a hereditary basis. In an interesting prospective study, military recruits who completed intensive training for 14 weeks increased bone density of the tibia by 8–12%. However, 41% of the young men who started the training developed stress fractures (make-it-or-break-it). In that study the bone density initially was similar in the two groups (10). Although some investigators disagree, most longitudinal studies of adult women have shown that exercise can improve bone mass. Aerobic exercise may not have the same effects on bone as exercise that compresses bone; Davee *et al.* (11) found that college women who participated in muscle-building exercise had higher bone density than those who performed aerobic exercises. This could explain some of the discrepancies in studies of the effect of exercise on bone density.

Studies of young female athletes are interesting and complicated. While the increased activity and muscle strength would be expected to increase bone mass, athletes often demonstrate weight loss, estrogen deficiency or calcium malnutrition, which could reverse the beneficial effects of exercise. Drinkwater *et al.* (12) demonstrated that elite women athletes had higher spine bone density than normal women, unless they had associated amenorrhea, in which case their bone density was significantly lower than expected for their age. Lindberg *et al.* (13) also found decreased bone density in amenorrheic athletes. Jones *et al.* (14) measured bone density at the radius, and found that amenorrheic athletes were similar to controls, but women with amenorrhea from weight loss or premature menopause were significantly lower. Marcus *et al.* (15) showed that amenorrheic runners had bone density which was lower than cyclic women, but higher than women with secondary amenorrhea who were less physically active. In a study by Buchanan *et al.* (7) the bone density was not different in normal women, eumenorrheic athletes, or athletes with oligomenorrhea. Some of the differences in results from these studies may be due to the various levels and types of activity performed by the athletes. But the cumulative data suggest that activity exerts a positive effect on bone mass, and estrogen deficiency exerts a strong negative effect. The effects may be independent. At the level of bone tissue, these findings are consistent with the hypothesis proposed by Frost (16), who postulates that bone responds to mechanical stress, and that circulating hormones modulate the magnitude of the response.

In this issue, a paper by Dhuper *et al.* (17) provides more data on the relationships between estrogen, exercise, weight, and bone density in young women. They selected adolescent girls to achieve a population with markedly different estrogen levels. About half of the subjects were dancers, who often demonstrate anorexia as well as amenorrhea. They found that the estrogen status (but not serum estradiol levels) and testosterone levels correlated with the bone mineral density of the spine, wrist, and foot. Weight also correlated with bone density in this population, and when the data were analyzed controlling for weight, there was no longer a significant correlation with estrogen. The authors also found that the girls with low bone density at the toe had the highest activity levels. Since the high activity levels were probably seen in the dancers, many of whom had low weight and low estrogen, it would appear that the strong detrimental effect of estrogen deficiency cannot be entirely reversed with exercise. These findings in adolescent girls support the conclusions from studies of amenorrheic college-aged athletes. The study also demonstrates the difficulties in determining the primary physiological signals to bone, since the factors of weight, estrogen, and exercise are so interrelated.

One of the aims of research in the bone field is to understand the factors that influence the development of bone density, with the goal of achieving optimal peak bone density in all young women. Even with our current, incomplete knowledge, we can offer some advice, so that women will not have lower bone density than their genetically determined potential. Teenagers should avoid cigarettes and excess alcohol. A diet with the recommended allowance for calcium and moderate muscle-building exercise are reasonable. For the young women with irregular periods or amenorrhea, it is logical to give

exogenous estrogen, but we lack clinical trials that demonstrate benefit.

It is disappointing that many women who follow such advice will nevertheless develop postmenopausal osteoporosis. Until we comprehend the mechanisms by which the genetic message controls bone mass, and learn to apply the knowledge to children or adolescents, we will see osteoporotic women whose peak bone mass was not high enough.

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References

1. Rodin A, Murby B, Smith MA, Caleffi M, Fentiman I, Chapman MG, Fogelman I. Premenopausal bone loss in the lumbar spine and neck of femur: a study of 225 Caucasian women. Bone. 1990;211:1–5.
2. Pollitzer WS, Anderson JJB. Ethnic and genetic differences in bone mass: a review with a hereditary *vs.* environmental perspective. Am J Clin Nutr. 1989;50:1244–1259.
3. Matkovic V, Fontana D, Tominac C, Goel P, Chesnut CH. Factors which influence peak bone mass formation: a study of calcium balance and the inheritance of bone mass in adolescent females. Am J Clin Nut. In Press.
4. Pocock NA, Eisman JA, Hopper JL, Yeates MG, Sambrook PN, Eberi S. Genetic determinants of bone mass in adults. J Clin Invest. 1987;80:706–710.
5. Liel Y, Edwards J, Shary J, Spicer KM, Gordon L, Bell NH. The effects of race and body habitus on bone mineral density of the radius, hip, and spine in premenopausal women. J Clin Endocrinol Metab. 1988;66:1247–1250.
6. Rosenthal DI, Mayo-Smith W, Hayes CW, Khurana JS, Biller BMK, Neer RM, Klibanski A. Age and bone mass in premenopausal women. J Bone Mineral Res. 1989;4:533–538.
7. Buchanan JR, Myers C, Lloyd T, Leuenberger P, Demers LM. Determinants of peak trabecular bone density in women: The role of androgens, estrogen, and exercise. J Bone Mineral Res. 1988;3:673–680.
8. Buchanan JR, Hospodar P, Myers C, Leuenberger P, Demers LM. Effect of excess endogenous androgens on bone density in young women. J Clin Endocrinol Metab. 1988;67:937–
9. Lanyon LE. Strain-related bone modeling and remodeling. Top Geriatr Rehabil. 1989;4:13–24.
10. Margulies JY, Simkin A, Leichter I, Bivas A, Steinberg R, Giladi M, Stein M, Kashtan H, Milgrom C. Effect of intense physical activity on the bone-mineral content in the lower limbs of young adults. J Bone Joint Surg. 1986;68A:1090–1092.
11. Davee AM, Rosen C, Adler RA. Exercise patterns and trabecular bone density in college women. J Bone Mineral Res. 1990;5:245–250.
12. Drinkwater BL, Nilson K, Ott S, Chesnut CH. Bone mineral density after resumption of menses in amenorrheic athletes. JAMA. 1986;256:380–382.
13. Lindberg JS, Fears WB, Hunt MM, Powell MR, Boll D, Wade CE. Exercise-induced amenorrhea and bone density. Ann Intern Med. 1984;101:647–648.
14. Marcus R, Cann C, Madvig P, Minkoff J, Goddard M, Bayer M, Martin M, Gaudiani L, Haskell W, Genant H. Menstrual function and bone mass in elite women distance runners. Ann Intern Med. 1985;102:158–163.
15. Jones KP, Ravnikar VA, Tulchinsky D, Schiff I. Comparison of bone density in amenorrheic women due to athletics, weight loss, and premature menopause. Obstetrics Gynecol. 1985;66:5–7.
16. Frost HM. Vital biomechanics: proposed general concepts for skeletal adaptations to mechanical usage. Calcif Tissue Int. 1988;42:145–156.
17. Dhuper S, Warren MP, Brooks-Gunn J, Fox R. Effects of hormonal status on bone density in adolescent girls. J Clin Endocrinol Metab. 1990;71:1083–88.