Chapter 6: Key Messages

- While genetic factors play a significant role in determining bone mass, controllable lifestyle factors such as diet and physical activity can mean the difference between a frail and strong skeleton.
- Calcium has been singled out as a major public health concern today because it is critically important to bone health and the average American consumes levels of calcium that are far below the amount recommended for optimal bone health.
- Vitamin D is important for good bone health because it aids in the absorption and utilization of calcium. There is a high prevalence of vitamin D insufficiency in nursing home residents, hospitalized patients, and adults with hip fractures.
- Physical activity is important for bone health throughout life. It helps to increase or preserve bone mass and to reduce the risk of falling. All types of physical activity can contribute to bone health, albeit in different ways.
- Maintaining a healthy body weight is important for bone health throughout life. Being underweight raises the risk of fracture and bone loss. Weight loss is associated with bone loss as well, although adequate diet and physical activity may reduce this loss.
- Fractures are commonly caused by falls, and thus fall prevention offers another opportunity to protect bones, particularly in those over age 60. Several specific approaches have demonstrated benefits, including muscle strengthening and balance retraining, professional home hazard assessment and modification, and stopping or reducing psychotropic medications.
- Reproductive issues can affect bone health. Pregnancy and lactation generally do not harm the skeleton of healthy adult women. Amenorrhea (cessation of menstrual periods) after the onset of puberty and before menopause is a very serious threat to bone health and needs to be attended to by individuals and their health care providers.
- Several medical conditions and prescription medications can affect bone health through various mechanisms, and health care professionals should treat the presence of such conditions and the use of such medications as a potential red flag that signals the need for further assessment of bone health and other risk factors for bone disease.
- Smoking can reduce bone mass and increase fracture risk and should be avoided for a variety of health reasons. Heavy alcohol use has been associated with reduced bone mass and increased fracture risk.

Chapter 6

DETERMINANTS OF BONE HEALTH

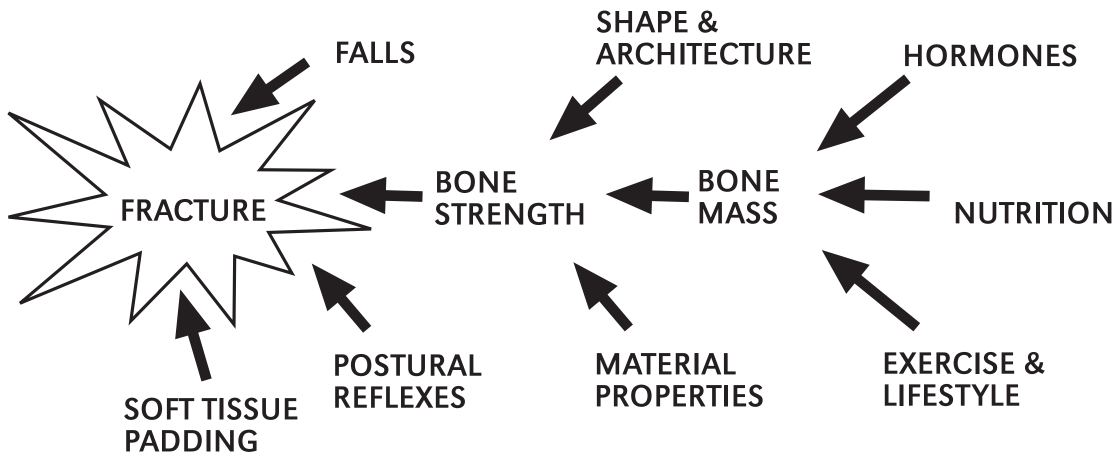
As discussed in Chapter 2, bone is a remarkable tissue with a functional structure (the skeleton) that is strong enough to withstand intense physical activity, adaptive enough to respond to changes in activity, and lightweight enough to allow efficient movement. Bone is resilient because of its intrinsic material characteristics (mass, density, mineral composition, strength) and its dimensions (size, shape, and structure). Throughout life, bone must adapt to the stresses imposed upon it, and its ability to do so depends on both lifestyle and genetic factors. A variety of studies indicate that genetic factors are responsible for determining 50–90 percent of bone mass and other qualitative aspects of bone (Recker and Deng 2002). Heredity not only sets limits on how much bone a person acquires, but also on bone structure, the rate of bone loss, and the skeleton's response to environmental stimuli like nutrients and physical activity. Normal bone mass and strength is controlled by many genetic elements working in concert. The tendency to develop bone diseases like osteoporosis and Paget's disease also appears to be due to genetic factors, although this tendency may also be influenced by environmental factors that are not yet completely understood. Osteogenesis imperfecta (OI), a condition in which bones break easily, often for little or no apparent cause, is clearly determined by the malfunction of specific collagen genes that have been identified. The search for the particular genes that control bone mass and affect the tendency to develop bone diseases is a very active area of research. Finding these elements may lead to new therapeutic strategies and prevention tools for osteoporosis.

While genetic factors play an important role in determining bone mass, it is critical not to underestimate the important role that individuals can play in promoting their own bone health status. In fact, controllable lifestyle factors such as diet and physical activity are responsible for 10–50 percent of bone mass and structure. These influences are illustrated in Figure 6-1.

Controlling these factors can literally mean the difference between a frail and a strong skeleton. This is because even relatively small changes in bone mass can have a significant impact on overall bone health. In fact, it has been estimated that a 10 percent increase in bone mass could reduce fracture risk by as much as 50 percent (Cummings et al. 1993). In other words, paying attention to lifestyle factors such as diet and physical activity throughout life can yield bone health benefits that are equal to or greater than those offered by the most powerful drugs currently used to treat osteoporosis.

While good nutrition and regular physical activity are important to bone health throughout life, the optimal type of nutrition and activity will vary across the life span, as will the impact

Figure 6–1. Factors Influencing Bone Mass Structure



Note: This figure illustrates some of the many factors that can influence the risk of fracture. Genetics, or inherited traits, can play a role in most of these factors but are particularly important in determining peak bone mass.

Source: Heaney 2003.

that each will have on bone. As a result, this chapter will analyze the evidence about the key determinants of bone health. It uses a life span approach, considering the following phases: a) the growth phase that occurs during childhood and adolescence; b) the maintenance phase that occurs during young to middle adulthood; c) the mid-life bone loss phase that typically occurs in adults between age 50–70; and d) the frailty phase that typically occurs in adults over age 70. These phases are general and do not correspond to a specific chronological age in an individual. Additional information on the various kinds of evidence and studies that are cited in this chapter can be found in Appendix B, "How We Know What We Know: The Evidence Behind the Evidence."

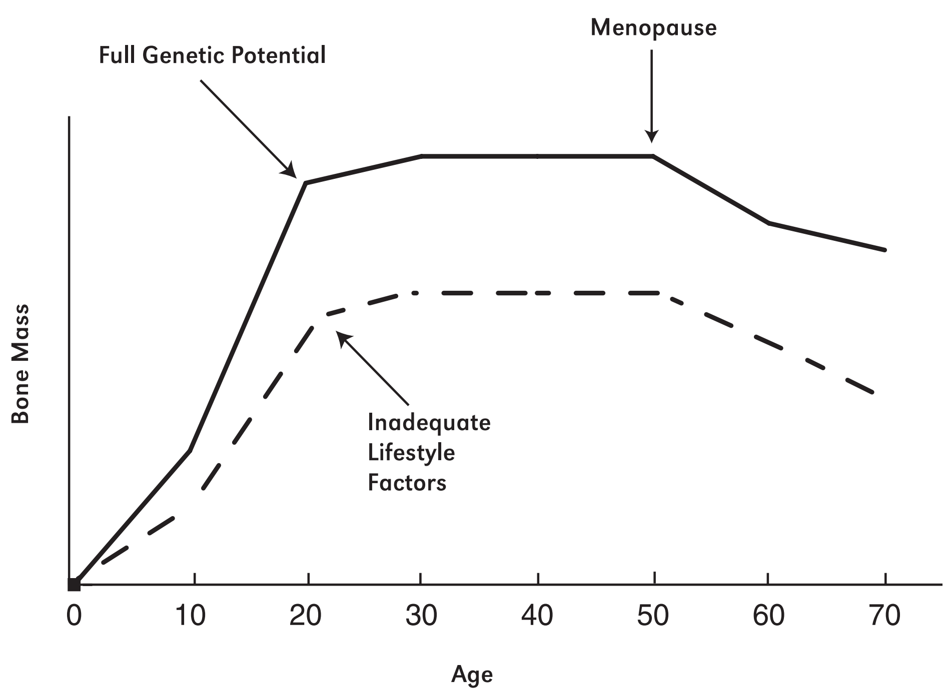
The goal of this chapter is to discuss the evidence related to these controllable factors that affect bone health throughout the different stages of life. Most of the information in this chapter focuses on osteoporosis and fracture; unfortunately, there are no known preventive regimens to address other bone diseases. Early recognition and intervention is the optimal strategy for these other bone diseases at the present time, as described in Chapters 8, 9, and 10.

A Review of the Critical Life Stages of Bone

As discussed in Chapter 2, bone tissue continues to renew itself, or remodel, throughout life by breaking down old bone (bone resorption) and replacing it with new bone (bone formation). Figure 6-2 illustrates how the skeleton changes over the life span. Because lifestyle changes made during the acquisition phase affect the achievement of peak bone mass, these lifestyle changes are critically important to bone health throughout life.

Adolescence is a particularly critical period for bone health because the amount of bone mineral gained during this period typically equals the amount lost throughout the remainder of adult life (Bailey et al. 2000). As illustrated in Figure 6-2, failure to achieve an optimized bone mass at the end of adolescence leaves an individual with much less reserve to withstand the normal losses during later life. Most gains in bone mass during puberty are due to an increase in bone length and size rather than bone density (Katzman et al. 1991). Fracture rates go up during this period of extremely rapid growth, possibly because the bone is temporarily weaker because bone mineralization lags behind growth in bone length (Khosla et al. 2003).

Figure 6–2. Bone Mass Versus Age With Optimal and Suboptimal Bone Acquisition



Source: Based on Heaney et al. 2000.

Review of the Life Stages of Bone, continued

After individuals achieve peak bone mass in late adolescence, bone health is optimized by maintaining as much of this bone mass as possible throughout adulthood. Bone formation and resorption are generally in balance with each other during the young to mid-adult years, so optimally bone mass is maintained at many skeletal sites. There is bone loss at some skeletal sites, such as the hip, before age 50, but it does not normally compromise strength. Bone loss begins or accelerates at midlife for both men and women (Riggs et al. 2002), meaning that the goal during this time of life is to keep bone loss to a minimum and to recognize and avoid both bone-specific and non-specific threats to bone health, such as other illnesses and falls. After age 40–50, bone loss may progress slowly in both sexes, with a period of more rapid loss in women surrounding the menopausal transition. During this period of age–related bone loss, both sexes may lose a total of 25 percent of bone. Bone loss continues in both men and women after age 70 (Riggs et al. 2002).

These later stages in bone life are depicted in Figure 6-3, which shows three women with increasingly severe bowing of the spine (kyphosis) due to osteoporotic fractures of the spine. But fractures are not a natural consequence of aging. Rather, they can be avoided, to some extent, by focusing on controllable factors such as diet and physical activity.

Figure 6-3. The Progression of Osteoporosis

Note: Three women demonstrate increasingly severe bowing of the spine (kyphosis) due to osteoporotic fractures of the spine.

Source: Higgs and AAOS 2001.

Nutrition's Impact on Bone Health: A Review of the Evidence

Nutrition and Bone Health: What the Evidence Tells Us

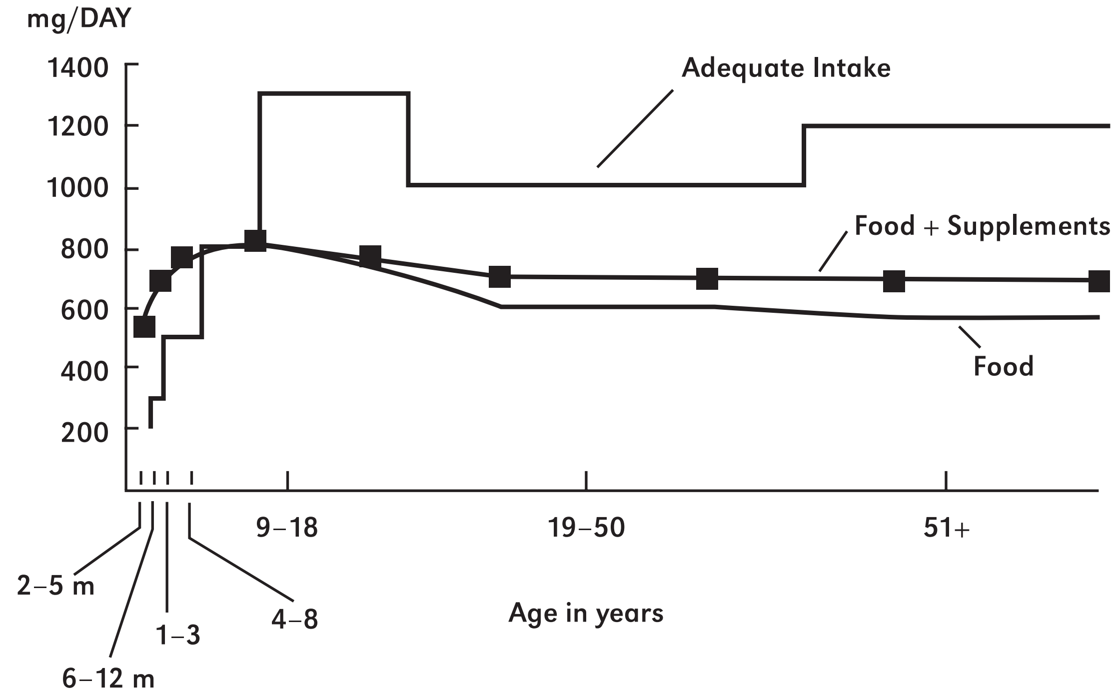
- Research suggests that a well-balanced diet is important for bone health throughout life. Depending on age, it may help increase or preserve bone mass.
- Much of the research to date has focused on calcium and vitamin D. Calcium and vitamin D play crucial roles in bone health, although other nutrients are also important.
- The Institute of Medicine recommends a steady increase in calcium intake as children age, beginning with 210 mg per day in infants and rising to 1,300 mg per day in those age 9–18. Recommended levels drop to 1,000 mg per day in those age 19–50, and then increase to 1,200 mg per day for those over age 50. The same age-dependent recommendations for calcium apply to pregnant or nursing women. Recommended levels of vitamin D intake are 200 IU per day for those under age 50, 400 IU per day for those 50–70, and 600 IU per day for those over age 70.

The evidence suggests that the composition of the diet can play an important role in building and maintaining bone mass throughout life, primarily by providing bone-building nutrients and by influencing absorption and retention of these nutrients. In addition, diet provides calories (energy input), which together with physical activity (energy output), determines body weight. Maintenance of an adequate body weight can help promote optimal bone health, as discussed later in this chapter.

Background: Why Focus on Vitamin D and Calcium?

As discussed later in this chapter, consuming adequate levels of calcium and vitamin D throughout life are critically important to an individual's bone health. The Institute of Medicine conducted a major review of bone-related nutrients in 1997 (IOM 1997) and developed a set of evidence-based recommendations for calcium and vitamin D intake. The goal of this effort was to determine the level of nutrient intake for normal, healthy individuals that would prevent the development of a chronic condition associated with that nutrient. While many nutrients play a role in bone health, calcium has been singled out as a major public health concern today not only because it is a critical nutrient for bone but also because of national surveys that suggest that the average calcium intake of individuals is far below the levels recommended for optimal bone health (Figure 6-4). One reason for these low levels of calcium intake relates to current lifestyle and food preferences, which have resulted in reduced intake of dairy products and other naturally calcium-rich foods. For some individuals lactose intolerance may play a role in not consuming adequate levels of calcium. Lactose intolerance is a condition in which individuals cannot metabolize lactose, the main sugar found in milk and other calcium-rich dairy products. An estimated 30–50 million Americans (about 25 percent of the U.S. population) are affected by lactose intolerance, although to varying degrees. While least common among Whites (it affects about 15 percent of White adults), lactose

Figure 6–4. Median Calcium Intakes of Females, 1988-1994, Compared to Adequate Intake Recommendations



Source: Looker 2003.

intolerance is widespread among other ethnic groups. Among the adult population, an estimated 70 percent of African-Americans, 74 percent of Native Americans, 53 percent of Mexican-Americans, and 90 percent of Asian-Americans are affected (Jackson and Savaiano 2001, National Women's Health Information Center 2001).

Lactose intolerance has been shown to be associated not only with low milk intake, but also with low bone mass and increased risk of fracture (Obermayer-Pietsch et al. 2004). Thus, these individuals may experience a detrimental effect on their bone health if they avoid consuming dairy products and do not replace them with other good sources of calcium. Strategies to cope with lactose intolerance are described in more detail in Chapter 7.

While for most individuals the problem is too little calcium, it is important to remember that too much calcium does not have any additive benefit, and can have negative effects in some individuals. For this reason, the Institute of Medicine set a tolerable upper limit for calcium of 2,500 mg per day.

Vitamin D is important for good bone health because it aids in the absorption and utilization of calcium. The main source of vitamin D is sunlight, and most people throughout the world get their supply of vitamin D by the conversion of precursors in the skin to active vitamin D, a process caused by exposure to sunlight. Several factors can limit the production of vitamin D by the skin, including where one lives (those who live in northern latitudes during the winter months do not get adequate exposure to sunlight (Webb et al. 1988)), how much body surface is covered by clothing or sunscreen, the degree of skin pigmentation (darker skin takes longer to make active vitamin D), and age (older individuals are less efficient in making vitamin D). Strategies for overcoming some of these limitations are discussed in Chapter 7.

Due to concerns that individuals do not get enough vitamin D through sunlight, recommendations for intake are set at a level to be adequate for individuals having no sun exposure. The most accurate way to tell if an individual or population group is getting enough vitamin D is by measuring levels of serum 25-hydroxy vitamin D. These levels have been measured in various populations, and they indicate a high prevalence of vitamin D insufficiency in nursing home residents, hospitalized patients, and adults with hip fractures (Webb et al.1990, LeBoff et al. 1999, Thomas et al. 1998). Vitamin D levels commonly deteriorate in older adults, and thus the requirement for vitamin D increases with age. But inadequate vitamin D levels can be a problem at any age. Exclusively breast-fed infants, particularly non-Whites or infants with decreased sunlight exposure, are at greatest risk. As a result, the American Academy of Pediatrics (Gartner and Greer 2003) recommends supplementing breast-fed infants with vitamin D, since breast milk may be a poor source of vitamin D. Infant formulas are fortified with appropriate levels of the vitamin.

Finally, as with calcium, too much vitamin D can be harmful to the skeleton as well. Vitamin D is a fat-soluble vitamin, so it can be stored in the body. Excess vitamin D can be toxic, leading to hypercalcemia, kidney failure, and calcification of soft tissue (IOM 1997). As a result, the Institute of Medicine has established a tolerable upper limit for dietary vitamin D intake of 2,000 IU per day. Physicians will often use much higher levels, however, to correct deficiencies.

Absorption of Calcium

To reach the skeleton, calcium eaten in the diet must first be absorbed into the body. In fact, much of the calcium consumed in the diet does not make its way to the skeleton; studies indicate that in adults only about 30 percent of calcium intake is actually absorbed by the body (IOM 1997). Moreover, some calcium is excreted from the body into the intestine so that the actual net absorption is even lower (Heaney and Abrams 2004).

Several factors can affect the body's ability to absorb dietary calcium, including vitamin D and estrogen. Deficiencies in either can reduce calcium absorption. The problem of reduced calcium absorption is more acute in older persons, who absorb less dietary calcium because their intestines are no longer as responsive to the action of 1,25-dihydroxy vitamin D (Heaney et al. 1989). Poor absorption of calcium can be overcome by increasing overall calcium intake and maintaining adequate levels of vitamin D.

The Evidence Supporting the Effect of Calcium and Vitamin D on Bone

Individuals who consume adequate amounts of calcium and vitamin D throughout life should enjoy better overall bone health for two reasons. First, they are more likely to achieve optimal skeletal mass early in life, and second, they are less likely to lose bone later in life. The net result should be higher bone mass and fewer fractures. Selected evidence to support the relationship between these nutrients and bone health during different stages of life is summarized below.

The Growth Stage (Children and Adolescents)

The role of calcium and other minerals in achieving peak bone mass begins before birth. Premature infants tend to have lower bone mineral content later in life, although this may in part be due to their tendency to be light and short for their age (Fewtrell et al. 1999, Bowden et al. 1999). Low birth weight is also associated with low bone mass later in life (Yarbrough et al. 2000, Antoniades et al. 2003). As discussed in Chapter 10, providing premature and low birth-weight infants with supplemental calcium, phosphorus, and protein may help them to "catch up."

Many observational studies make it clear that the role of calcium in achieving optimal peak bone mass continues into childhood and adolescence (Heaney et al. 2000). Perhaps the most often cited study is that of Matkovic et al., who compared two regions of Croatia with different intakes of calcium (Matkovic et al. 1979). Although the high-calcium region had lower fracture rates, the populations differed in other variables such as exercise that could partially explain the different fracture rates. This study spurred further research into the role of childhood and lifetime calcium consumption on the risk of osteoporosis and fracture.

Several randomized clinical trials have examined the effect of calcium supplements or calcium-rich foods in children and adolescents (Lee et al. 1994, Lee et al. 1995, Lloyd et al. 1993, Nowson et al. 1997, Bonjour et al. 2001, Johnston et al. 1994, Dibba et al. 2000, Cadogan et al. 1997, Merrilees et al. 2000, Chan et al. 1995). These studies have been combined and summarized in a meta-analysis (Wosje and Specker 2000), which concluded that higher calcium intake increases bone mineral density (BMD) in children and adolescents in certain circumstances. Increases in BMD were more likely in cortical bone sites and among populations with low baseline calcium intakes, and in most studies the increase did not persist beyond the calcium supplementation period. A few studies have examined the impact of higher calcium intake over time. Results from most of these studies suggest that the intake must be maintained for the positive effects on bone to persist (Bonjour et al. 2001, Slemenda et al. 1997, Lee et al. 1996).

Adequate levels of calcium intake may also be important in maximizing the positive effect of physical activity on bone during the growth period. Two recent studies found that physical activity was more beneficial to bone health in infants or young children consuming higher amounts of calcium (Specker et al 1999, Specker and Binkley 2003).

There have been no randomized clinical trials to measure the impact of vitamin D supplements alone on bone health in children and adolescents. However, vitamin D deficiency is known to cause inadequate mineralization of the growing skeleton, leading to rickets (Goldring et al. 1995). In addition, one small observational study found higher bone density in prepubertal girls who took vitamin D supplements during infancy (Zamora 1999).

The Maintenance Stage (Adults)

Eating adequate amounts of nutrients continues to be important during the young adult years when bone formation and bone resorption are balanced. Unfortunately, most studies of diet and supplement use and bone health have focused on either younger or older individuals.

A meta-analysis of calcium and bone density in premenopausal women indicated that calcium had a positive effect on BMD in this group, as the supplemented groups lost less bone per year (Welten et al. 1995). However, only one of the four intervention studies in this meta-analysis used a double-blinded, placebo-controlled design. In addition, these studies focused on premenopausal women between the age of 30 and 55, not on younger adult women. There have not been many studies of vitamin D in young adults. One study did find that even young men may experience low vitamin D levels in the winter, and that these low levels were associated with lower BMD (Valimaki et al. 2004). More information is needed about the role of calcium, vitamin D, and other nutrients in maintaining bone in this age group of women and in men.

The Early Bone Loss and Frailty Stages (Older Adults)

Most randomized clinical trials examining the effect of calcium and vitamin D on bone health have focused on postmenopausal women and the elderly, so the role of these nutrients in promoting bone health is more clearly established for this age group. In fact, a carefully conducted meta-analysis of randomized clinical trials on the effects of calcium supplementation for the prevention of postmenopausal osteoporosis was recently published (Shea et al. 2002). The investigators performed a thorough search to identify all trials (including unpublished ones) examining the effect of calcium (with minimal vitamin D) on bone density and fractures in postmenopausal women since 1966. Of the 66 trials that were identified and screened, 15 met the inclusion criteria. After analyzing these trials, the investigators concluded that calcium supplements reduced bone loss by approximately 2 percent after two or more years of use. More importantly, their results suggested that calcium supplements led to a significant (roughly 23 percent) reduction in the risk of spine fractures.

Just as with children, moreover, it appears that there may be a positive interaction between the effects of physical activity and calcium on bone health in older adults. (This relationship is discussed further in the section on physical activity.) Calcium may also help enhance the effect of drugs that reduce bone loss, such as estrogen and bisphosphonates (e.g., drugs that restrict the action of cells that resorb bone) (Heaney 2001).

A carefully conducted meta-analysis of randomized trials on the effect of vitamin D on bone density and fracture risk has also been recently conducted (Papadimitropoulos et al. 2002). All trials, including unpublished studies, conducted since 1966 were evaluated, with 25 meeting the criteria for inclusion. While the results from the different trials tended to vary somewhat, the authors concluded that vitamin D supplements reduced the risk of spine fractures by approximately 37 percent. This decline in fracture risk may be due in part to vitamin D's ability to reduce the risk of falls. Vitamin D may reduce falls by acting directly on muscle. There are vitamin D receptors in human muscle that may play a role in increasing muscle strength and thereby enhancing stability (Bischoff et al. 2001). While elderly individuals who are vitamin D deficient face an increased risk of falls (Flicker et al. 2004), studies have shown that vitamin D supplementation in these individuals may negate this effect (Bischoff et al. 2003, Latham et al. 2003, Dukas et al. 2004). It is important to note that the design of many of the randomized, controlled trials examining the effect of vitamin D supplements on bone loss or fracture incidence also called for participants to use a calcium supplement. Thus, it is not possible to isolate the benefits of calcium and/or vitamin D alone in these studies. While a few studies have simultaneously evaluated the effects of the two nutrients separately, the results are mixed. For example, one study found that calcium prevented hip bone loss in most elderly men and women, but vitamin D only modestly lowered bone loss (Peacock et al. 2000). In a different study, annual vitamin D injections did not prevent hip fractures (Heikenheimo et al. 1992). However, in a third randomized, controlled trial, 400 IUs of vitamin D per day prevented hip bone loss over 2 years in elderly women (Ooms et al. 1995). In a recent study, vitamin D supplementation was found to have more beneficial effects when used in combination with calcium supplementation in women who had suffered a hip fracture (Harwood et al. 2004). Thus, the question of the role of vitamin D alone in promoting bone health remains unresolved. Vitamin D can probably be most effective in populations with an underlying deficiency and in those individuals for whom other components of bone health, such as adequate levels of calcium and physical activity, are optimized.

It may not be realistic, however, to try to dissect the individual contributions of calcium, vitamin D, and physical activity on bone health, since they all need to be optimized. As a result, some studies have looked at the impact of combinations of the three on bone health. The most promising study of a combination of calcium and vitamin D on bone fractures was conducted in France in the early 1990s (Chapuy et al. 1992). Over 3,000 elderly women received supplements with calcium and vitamin D or placebo pills. Hip fractures were reduced by 43 percent among the women treated with vitamin D and calcium compared to those who received placebo. This is the only large trial to date to show a reduction in hip fractures due to supplements. The women in the study were quite elderly (average age 83) and vitamin D deficient, so it is possible that correcting the deficiency led to the dramatic drop in fractures. In a smaller study of elderly individuals in New England, Dawson-Hughes and colleagues showed that supplementation with calcium and vitamin D moderately reduced bone loss and the incidence of non-spine fractures (Dawson-Hughes et al. 1997). Tests of calcium and vitamin D supplementation to prevent hip fractures are currently being conducted in a large population of healthy postmenopausal women in the Women's Health Initiative; these results should be available in late 2005 (Jackson et al. 2003).

Other Nutrients With a Role in Bone Health

Bone health requires more than just attention to calcium and vitamin D. In fact, data suggest that many other nutrients can affect bone in positive or negative ways. (For more information, see Table 7-5, which lists some of the other nutrients that can affect bone.) The roles of many of these nutrients with respect to bone health have not been as well established as for calcium and vitamin D. Since the vast majority of individuals consume an appropriate amount of these nutrients (i.e., not too much or too little), they have not become a target for special attention.

Nevertheless, the Institute of Medicine recently considered other bone-related nutrients, including phosphorus, magnesium, and fluoride (IOM 1997). Phosphates make up more than half the mass of bone mineral. About 85 percent of the body's phosphorus and 60 percent of the body's magnesium are found in the skeleton. Both phosphorus deficiency and excess have been considered as having adverse effects on bone health (Heaney 2004), but both can be avoided with a healthy diet. Magnesium may enhance bone quality by influencing growth of crystals of hydroxyapatite, the mineral compound found in bone. Fluoride is known to reduce cavities in teeth, a hard tissue that is similar to bone, but its role in maintaining skeletal health is less clear (IOM 1997). Other nutrients/dietary components that appear to play a positive role in bone health include vitamin K, vitamin C, copper, manganese, zinc, and iron. These micronutrients are essential to the function of enzymes and local regulators and therefore are important to forming the optimal bone matrix.

Potassium also appears to play an important role in bone health. Diets abundant in potassium-rich fruits and vegetables may reduce the need for calcium to be mobilized from the skeleton. Epidemiologic and short-term intervention studies suggest higher intakes of alkaline potassium salts reduce urine calcium excretion and markers of bone resorption and have been associated with increased bone density (Barzel 1995, Sellmeyer et al. 2002, New et al. 2000, New et al. 2004, Tucket et al. 1999, Sebastian et al. 1994).

It is important to remember that some dietary components may negatively affect calcium balance. While their effects tend to be small, these include caffeine, protein, and excess phosphorus intake (i.e., more than 3-4 grams per day) (Fitzpatrick and Heaney 2003; Kerstetter et al. 2003). Sodium also affects calcium balance by increasing its excretion, and high-salt diets are fairly common in the United States. But unlike with these other nutrients, the effects of sodium on calcium balance are more pronounced. Results of two studies in adult women suggest that each additional gram of sodium eaten per day increases bone loss by 1 percent per year, unless the extra calcium lost in the urine is replaced by more calcium in the diet (Devine et al. 1995, Shortet al. 1988). The negative effects of sodium and these other dietary components can be countered by consuming an adequate amount of calcium in the diet. Diets high in sodium are associated with hypertension. Therefore, lowering intake of sodium in concert with meeting calcium requirements is prudent (USDA 2000). Finally, although protein causes some loss of calcium from the body, only very high protein diets that are not compensated for by extra calcium are a concern (Dawson-Hughes 2003). In fact, higher protein intakes may be associated with higher levels of IGF-1, a marker of bone formation, and lower levels of urinary n-telopeptide crosslinks, a marker of bone breakdown (Dawson-Hughes et al. 2004). Far more serious is the low protein intake of many older persons (Rizzoli and Bonjour 2004). Inadequate protein intake negatively affects bone health in the elderly (Kerstetter et al. 2003) and may diminish the ability to repair and recover from fractures (Schurch et al. 1998). Nutritional supplementation has been recommended as a means of boosting protein intake in elderly individuals recovering from a hip fracture (Schurch et al. 1998), although the evidence to support this approach is limited (Avenell and Handoll 2004). Finally, excess dietary vitamin A (as retinol) may also negatively affect bone health by increasing bone resorption (Sheven and Hamilton 1990).

Since many nutrients in addition to calcium and vitamin D play a role in bone health, it is important to consume a well-balanced diet containing a variety of food, rather than just focusing on one or two bone-related nutrients. This approach can have positive effects on other aspects of health as well. For example, the DASH diet (Dietary Approach to Stop Hypertension), which encourages fruit and vegetable intake in addition to more calcium and less sodium intake, has been linked to lower bone turnover and better cardiovascular status (Lin et al. 2003). In a recent study of young girls a high intake of fruits and vegetables was associated with increased bone mineral content (Tylavsky et al. 2004). Fruit and vegetables also provide vitamins, minerals, and fiber, and should be encouraged for overall good nutrition. As alluded to above, abundant potassium intake via increased fruit and vegetable intake may be particularly beneficial for skeletal health. Specific suggestions for selecting a well-balanced diet are provided in Chapter 7.

Physical Activity

Physical Activity, Body Weight, and Bone Health: What the Evidence Tells Us

- Physical activity is important for bone health throughout life.
  - ~ Depending on age, it may help increase or preserve bone mass.
  - ~ It may also help reduce the risk of falling.
- All types of physical activity can contribute to bone health.
  - ~ Activities that are weight bearing or involve impact are most useful for increasing or maintaining bone mass.
  - ~ Some activities that are not weight bearing or are low impact may help improve balance and coordination and maintain muscle mass, which can help prevent falls.
  - ~ Specific recommendations are given in Chapter 7.

Physical activity of all kinds has overall benefits to health and weight maintenance. Regular physical activity lowers risk factors for cardiovascular disease, colon cancer, and type 2 diabetes, and helps to control blood pressure (USDA 2000). Physical activity plays an important role in skeletal health because, as discussed in Chapter 2, bone mass is responsive to the mechanical loads placed on the skeleton.

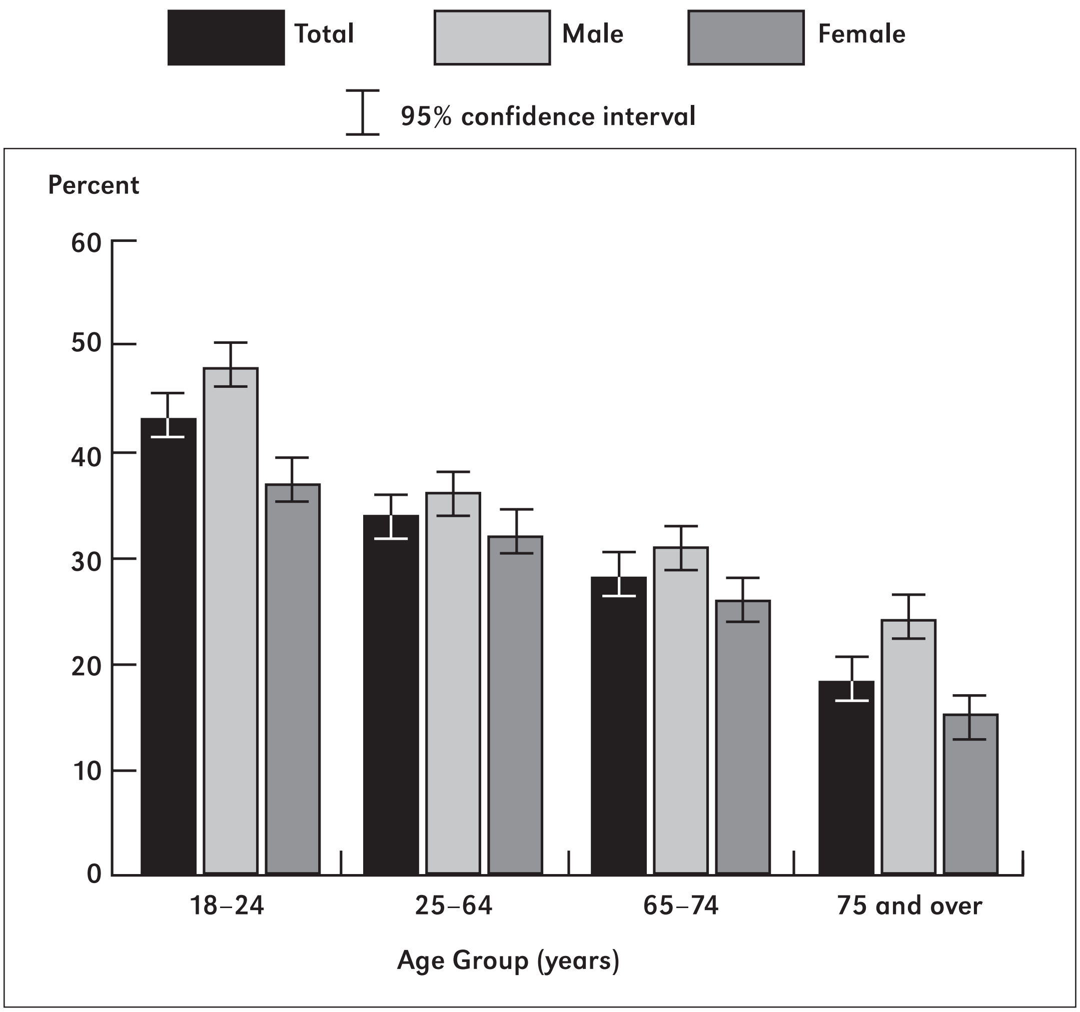
Background: Why Focus on Physical Activity?

As discussed in Chapter 2, the body constantly monitors the strain on bones caused by muscle action, and any substantial increase in these forces signals the need to build more bone. Conversely, reductions in biomechanical forces from lower activity levels or loss of muscle mass (sarcopenia) signals less need for bone, which leads to the elimination of bone. The latter process may be worsened by estrogen deficiency, which appears to reduce the sensing of biomechanical strains by bone cells (Riggs et al. 2002).

Physical activity has been identified as one of the Leading Health Indicators in the *Healthy People 2010* health objectives for the Nation during the next decade. It is one of the most important controllable lifestyle changes to help prevent (or reduce the risk of) a number of chronic conditions, including heart disease, diabetes, and some cancers. It also helps with weight control and the lessening of symptoms related to arthritis (USDHHS 19996).

Many adult Americans do not engage regularly in leisure-time physical activity. As shown in Figure 6-5, the participation by both men and women declines with age, with women being consistently less active than men (Schiller et al. 2004). The same problem exists for children. Many children become far less active as they pass through adolescence. Only half of those age 12–21 exercise vigorously on a regular basis and 25 percent report no exercise at all (Gordon-Larsen et al. 1999). Children may find

Figure 6–5. Percent of Adults Aged 18 Years and Over Who Engaged in Regular Leisure Time Physical Activity, by Age Group and Sex: United States, January–September 2003



Note: This measure reflects the definition used for the physical activity leading health indicator in Healthy People 2010. Regular leisure-time physical activity is defined as engaging in light-moderate leisure-time physical activity for greater than or equal to 30 minutes at a frequency greater than or equal to five times per week, or engaging in vigorous leisure-time physical activity for greater than or equal to 20 minutes at a frequency greater than or equal to three times per week. The analyses excluded 697 persons (3.0%) with unknown physical activity participation. For both sexes combined, the percent of adults who engaged in regular leisure-time physical activity decreased with age. For all age groups, women were less likely than men to engage in regular leisure-time physical activity.

Source: Ni et al. 2004.

it difficult to get daily physical activity in schools. While most schools have requirements for physical activity of some kind, only 8 percent of elementary schools, 6.4 percent of middle/junior high school, and 5.8 percent of senior high schools provide physical education on a daily basis (SHPPS 2001). At the other extreme, some girls and young women, especially those training for elite athletic competition, exercise too much, eat too little, and as a result develop delayed puberty or amenorrhea (cessation of menstrual periods). These girls are at risk for low bone mass and fractures (Warren 1999). One of the national health objectives for 2010 is to increase to 30 percent the proportion of adults who perform, more than 2 days per week, physical activities that enhance and maintain muscular strength and endurance (USDHHS 2000). Only 12 percent of people age 65–74 and 10 percent of those over age 75 meet that objective, underscoring the need for programs that encourage older adults to incorporate strength training and regular physical activity into their lives (Kruger et al. 2004).

To encourage increased levels of physical activity among all age groups, "Physical Activity and Health: A Report of the Surgeon General" recommends a "minimum of 30 minutes of physical activity of moderate intensity (such as brisk walking) on most, if not all, days of the week" (USDHHS 1996). Children and adolescents should aim for at least 60 minutes of physical activity per day (USDA 2000). In addition to helping achieve healthy weight and avoid chronic diseases like heart disease and diabetes, this type of physical activity can benefit skeletal health by building muscle mass and promoting balance and coordination, which may help individuals avoid falls and/or minimize the impact if a fall does occur. But the skeleton responds preferentially to strength training and short bouts of high-load impact activity (such as skipping or jumping), both of which improve bone mass and strength, as discussed below. In light of this, "Physical Activity and Health: A Report of the Surgeon General" also recommended that adults supplement their cardiorespiratory endurance activity with strength-developing exercise at least two times per week (USDHHS 1996). Chapter 7 will address some specific ways to incorporate strength and loading activities into an overall habit of physical activity.

Physical Activity and Bone Health: A Review of the Evidence

This section will discuss the evidence of the impact of exercise and physical activity on fractures and on bone mass and other bone qualities.

Impact of Physical Activity on Fractures

Although no randomized intervention trials have addressed the issue, data from longitudinal observational studies have shown a link between physical activity and reduced fracture risk. In these studies, subjects are asked about their physical activity habits and then followed for some period of time to determine if they fracture. As suggested earlier, this study design cannot prove that physical activity causes a reduction in risk, since there is an inherent bias in the study—i.e., that healthy people are able to be more active. A number of risk factors for osteoporosis and fracture (e.g., health, diet, body size) may be unequally distributed between those who choose to be physically active and those who do not. Nevertheless, recent reviews of the epidemiologic evidence suggests that physical activity is associated with reduction in the risk of hip fracture in both men and women and that there is a "dose-response" effect, i.e., risk goes down as physical activity level goes up (Gregg et al. 2000, Karlsson 2002). In a large

Challenges in Studying the Impact of Physical Activity on Bone Health

One of the biggest challenges to researchers in determining the effect of physical activity on bone is to have an accurate and measurable outcome. Fracture would be the best outcome to study, but there are no large studies that have determined the effect of physical activity on the risk of fracture using a randomized clinical trial design. Most physical activity studies have had small sample sizes and have used BMD, as measured by dual-energy x-ray absorptiometry (DXA), as the outcome. As described in Chapter 8, DXA measurements of bone-mineral content (measured in grams) and areal bone-mineral density (g/cm^2 [grams per centimeter squared]) do not directly measure bone size or reflect bone geometry, and thus they can significantly underestimate the effect of physical activity on overall bone strength (Jarvinen et al. 1999). Thus, while a convenient measure, BMD may not be sensitive to the multiple effects of physical activity on the musculoskeletal system.

study of older women (Gregg et al. 1998), higher levels of leisure time physical activity and household chores were associated with an overall 36 percent reduction in hip fractures. The effect varied with the level of the activity, with very active women having greater reductions in risk compared with inactive women. However, even walking, the most common leisure time physical activity for women, can have a positive effect on bone health. For example, the Nurses Health Study concluded that walking at least 4 hours per week was associated with a 41 percent lower risk of hip fracture compared with walking less than an hour per week, even among women who did no other exercise (Feskanich et al. 2002). Several other longitudinal observational studies have confirmed a similar reduction in hip fracture risk in men who exercise regularly compared to inactive men (Paganini-Hill et al. 1991, Kujala et al. 2000).

Impact on Bone Mass, BMD, and Other Bone Qualities

Randomized intervention trials that focused on the effects of physical activity on bone mass (either bone mineral density or bone mineral content) have identified some important points about physical activity and skeletal health.

- First, these studies show that bone mass is improved, but only at the skeletal sites that received the impact. In other words, lifting weights with arms will not improve bone density of the hips.
- Second, the effects of physical activity on bone health will vary by age, and thus younger individuals should be studied separately from older individuals.
- Third, the effect of physical activity on bone does not persist if the activity level is stopped or reduced (an exception may be the effect of physical activity on bone that occurs during childhood and adolescence). Thus, as with intake of dietary calcium, physical activity levels need to be maintained for optimal bone health to be achieved.
- Fourth, the effect of physical activity on bone appears to be greater in those who are less active than in those who are already active, e.g., bone gains will be greater in a sedentary person who becomes physically active than in an active person who increases his or her level of physical activity.

More specific evidence supporting these points is presented on the following pages.

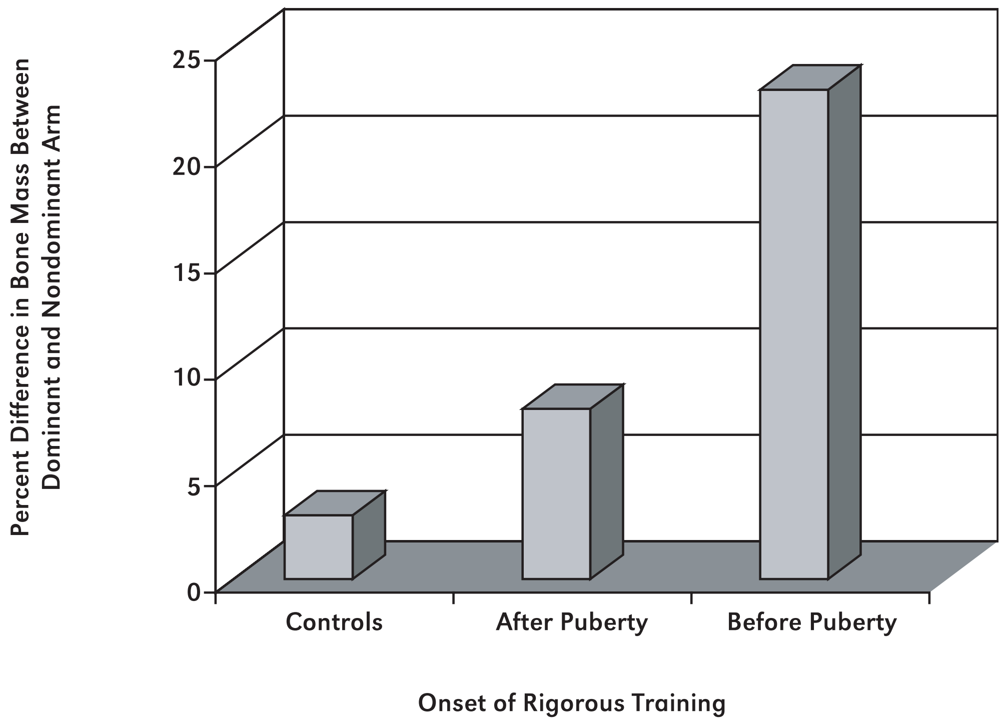
Children and Adolescents. As noted earlier, physical activity appears to increase the positive effects of calcium. A randomized trial of physical activity with or without supplemental calcium in young children (3–5 years old) indicated that calcium intake can modify the bones' response to physical activity (Specker and Binkley 2003). In this study, bone mineral density was not the most sensitive indicator of physical activity effects on bone; rather it was primarily the shape and size of bone that was being affected. The combination of both increased activity and 1,000 mg of supplemental calcium increased the width of the cortical bone and the entire diameter of the bone in the leg more than did exercise alone. Both of these changes suggest greater bone strength, and they are particularly important if they represent permanent differences. The study results also suggest that high calcium is necessary to realize the full potential benefits of physical activity on the bone of children. A different study of tennis players found that loading exercises before puberty increased bone size and bone's resistance to bending (Bass et al. 2002).

The pubertal phase of adolescence is a particularly valuable time to improve bone mass via physical activity. As noted previously, the period of puberty represents a 2- to 3-year window when, on average, 25–30 percent of total body adult bone mass is gained (Bailey et al. 2000). During this period, bone may be especially responsive to activity-induced loading (MacKelvie et al. 2002). Hormone levels may also influence the amount of bone gained during this period. In a trial with prepubertal and early pubertal girls, greater gains in bone mass with physical activity were seen in the girls in early puberty, possibly because of their increasing estrogen levels (MacKelvie et al. 2001).

A study conducted in Finland provided even more evidence of the benefits of physical activity during puberty. This study compared the bone mineral content of the playing arm of adult woman tennis and squash players with their non-dominant arm. In other words, each woman in the study served as her own control (Kannus et al. 1995). Most people have about a 3–5 percent difference in their dominant and non-dominant arm, which reflects greater use of the dominant arm in everyday life. In the racquet players, the difference in bone content between the two arms was much greater (12–16 percent), due to their training regimen. But the difference was twofold greater when the comparison was restricted to women who began training before puberty versus those who took up the sport later (Figure 6-6). This observation underscores the importance of the timing of physical activity and supports the concept that there is a "window of opportunity" during childhood and adolescence for building bone (Khan et al. 2000).

Exercise-intervention studies in girls (Morris et al. 1997) suggest that relatively short periods of appropriate exercise can stimulate bone gain at trabecular bone sites (hip and spine). Jumping activities appear to be particularly effective, and the greatest gains occur in early or mid-puberty (MacKelvie et al. 2003). High-intensity jumping improves both hip and lumbar spine bone mass and increases bone area in pre-pubertal children (Fuchs et al. 2001). Moreover, the bone mass gains at the hip that accrue from high-impact jumping are retained for at least a short period of time (an equivalent period of detraining) (Fuchs and Snow 2002). Thus, jumping from a moderate height (roughly 20 inches is a safe, effective, and simple method of improving bone mass and size in children, and these activities could easily be incorporated into physical education classes) (Figure 6-7). What is not clear, however, is whether or not early gains in bone mass and geometry confer a long-lasting reduction in

Figure 6–6. Bone Mass Differences in the Playing Arms of Women Racquet Players



Note: Most people (controls) have a small difference in bone mass between their dominant and nondominant arm due to greater daily, though not strenuous, use of the arm. In competitive racquet sport players (tennis or squash), the differences in the two arms are exaggerated. Moreover, if the player began rigorous training before puberty the differences can be greater than 20%. This indicates the powerful influence of physical activity during the adolescent period.

Source: Kannus et al. 1995.

fracture rate. Although some evidence supports a lasting beneficial effect of early sports training and exercise on bone (Kontulainen et al. 2001, Bass et al. 1998), this area remains controversial and it may be that stopping exercise or reducing its intensity over time may lessen its benefit in old age (Seeman 2001). For example, Karlsson et al. (2000) found little residual protection in soccer players who had been retired for more than 20 years. So the benefits of physical activity in reducing fracture risk, even if started in youth when bone is most malleable, may be attenuated if an individual becomes sedentary later in life.

Adults. Because adulthood is a time of bone conservation—not bone building—the primary impact of physical activity is to maintain bone mass

Figure 6–7. High-Intensity Jumping Improves Hip and Lumbar Spine Bone Mass and Size in Pre-Pubertal Children

Note: Jumping from a moderate height of approximately 20 inches is safe and effective in increasing bone mass and size in children, with the greatest gains occurring in early or mid-puberty.

Source: Fuchs et al. 2001. Reproduced from J Bone Miner Res 2001: Jan; 16(1): 148–56 with permission of the American Society for Bone and Mineral Research.

during this stage. While it is not possible to assign a specific age range to this period of bone maintenance, it would optimally last from the end of puberty until age- or menopause-related bone loss begins. Very little research has focused on the impact of physical activity on bone mass in this age range. However, several reviews and meta-analyses have included pre-menopausal women (Wolff et al. 1999, Wallace and Cumming 2000, Kelley et al 2001) and they have generally found a modest but consistent positive effect (approximately 1 percent) from exercise on BMD; a similar effect was found in postmenopausal women. The effect is more clear at the spine than the hip, and no optimal types of exercise could be discerned from these analyses.

The Cochrane Collaboration has reviewed the trials of exercise for preventing or treating osteoporosis in postmenopausal women specifically (Bonaiuti et al, 2002). These analyses indicated that aerobic, weight-bearing, and resistance exercises were all effective in increasing BMD at the spine, while walking (as an exercise intervention) was effective in increasing BMD at both the hip and spine.

As alluded to earlier, there is a synergistic effect between physical activity and calcium intake. A meta-analysis of 17 randomized and nonrandomized intervention trials in peri- and postmenopausal women suggests that physical activity is more beneficial in increasing BMD in individuals with high calcium intakes (1,000 mg per day) than in those with lower calcium intakes (Specker 1996). Not all of the studies, however, reported on the calcium intake of participants.

In postmenopausal women, physical activity programs also serve the all-important role of maintaining bone mass. Maintaining bone at a time when bone loss typically increases provides important benefits for the skeleton. Although results may vary, studies suggest that high-impact loading such as jumping, strength-training exercises, or a combination of these can slightly increase or conserve spine bone mass in healthy postmenopausal women and also has a positive effect at the hip (Bassey and Ramsdale 1994, Kohrt et al 1995, Going et al 2003).

One of the few studies to date that included men over age 60 showed significant increases in bone mass among exercisers after 4–8 months (Blumenthal et al 1991). These results are consistent with those found for adult women. In addition, one meta-analysis found that site-specific exercise may help to improve and maintain BMD in men over age 30 (Kelley et al, 2000).

Older Adults (Frailty). Regular physical activity is particularly important for frail older persons, because it delays the onset of functional limitations and loss of independence that are common in this population, especially those over age 75 (Singh 2002). Thus, the substantial reduction in physical activity that is typically seen in individuals as they get older (which was documented earlier in this chapter) represents another important threat to bone health. Maintaining, or preferably increasing, customary physical activity can mitigate some of the musculoskeletal problems of aging and can also provide many other health benefits. Although physical activity must be maintained to preserve bone mass in this age group, the biomechanical strains from enhanced physical activity may promote increases in bone size that can help preserve bone strength even in the face of bone loss (Kaptoge et al. 2003). This protective expansion of bone area is more pronounced in men, possibly because of their higher testosterone levels.

One of the biggest bone-related problems facing the frail elderly relates to the loss of muscle strength and function (Doherty 2003). Sarcopenia is the involuntary loss of skeletal muscle mass and function that occurs as people age. On average, 5 percent of muscle mass is lost per decade after age 30 and this loss may accelerate after age 65. This muscle loss results in impaired functional performance and increased risk for falls. It is unclear whether the age-related decrease in muscle size and strength is related to the age-related decrease in BMD, or whether both contribute to increased fracture risk independently.

The mechanisms that underlie sarcopenia are just beginning to be understood. As people age, their ability to synthesize certain proteins decreases in comparison to their ability to break down protein. This leads to loss of type II, or fast-twitch, muscle fibers. Several other age-related changes are also thought to contribute to sarcopenia, including declines in: a) enzyme activity in the muscle cell mitochondria; b) hormones important in muscle turnover, such as testosterone and growth hormone; and c) muscle blood flow and nerve function (Greenlund and Nair 2003). Sarcopenia occurs in all individuals to some degree as they age, but it can be accelerated by a variety of factors, including chronic illness, inactivity, and poor nutrition, especially inadequate protein and caloric intake. Although physical activity cannot completely reverse the effects of aging, it can increase mitochondrial enzyme activity. Muscle-strengthening exercises and activities appear to improve strength and performance even in frail nursing home residents (Morris et al.1999). Thus it appears that physical activity and muscle strengthening may be useful for treating or preventing sarcopenia.

The response of elderly individuals' muscles to physical activity may have greater significance to bone health than does the response of BMD. Muscle strengthening reduces the risk of fractures by improving balance, mobility, and speed of movement, each of which helps to prevent or reduce the severity of falls. In fact, muscle strength seems highly adaptable to physical activity in the elderly, with increases of over 100 percent being reported in men in their 80s and 90s who exercise (Fiatarone et al. 1990). This increase is far greater than the corresponding increase in muscle volume and BMD. A training program for 21 men over 60 resulted in a 39 percent increase in upper body and a 38 percent increase in lower body strength, as well as a 3 percent increase in femoral neck BMD (Ryan et al. 1994). Generally, strength, flexibility, balance, and reaction time—the factors most amenable to modification—can be addressed in exercise intervention programs to prevent falls in the elderly (Lord et al. 2002). Several large studies have reported that exercise leads to 10 percent fewer falls, while balance training leads to 17 percent fewer falls (Province et al. 1995). In a series of key studies, lower limb strength and balance exercises reduced the rate of falls among women age 80 and older (Robertson et al. 2002).

Weight

Weight: What the Evidence Tells Us

- Very low body weight in children and adolescents may limit peak bone mass.
- Low body weight increases the risk of hip fracture in older women.
- Weight loss of 10 percent or more in older women also increases the risk of hip fracture.

Maintaining a healthy body weight is one of the goals of *Healthy People 2010* (USDHHS 2000). Although overweight and obesity are the focus of most health campaigns that focus on weight, low body weight can be a problem for bone health. A higher body weight may influence BMD through a variety of mechanisms, including higher mechanical loading, more muscle mass, higher levels of sex hormones and their precursors, and lower bone turnover (Nelson et al. 2002). Body weight may also be related to the level of fat padding, which can provide a cushion during a fall on the hip.

Body weight and pubertal development are the most consistent predictors of bone mass in adolescents (Bachrach 2001, Heaney et al. 2000). Fear of fat and obsession with thinness among pre-teen and teenage girls frequently translates into diets that fail to meet their caloric, calcium, and protein needs. Young women who repeatedly diet to lose weight also have lower bone density, even if they are not underweight (Van Loan and Keim 2000).

Both low body weight and weight loss have been associated with reductions in bone mass and increases in fracture risk in epidemiologic studies. In a follow-up to the first NHANES, women who were relatively thin in middle age (age 50-64) and had lost at least 10 percent of their body weight had the highest risk of hip fracture (Langlois et al. 2001). Although body weight is very strongly associated with BMD (Reid 2002), the relationship of body weight to bone mass is confounded by the fact that smaller people tend to have smaller bones and lower bone mass. Nevertheless, they can have a perfectly adequate skeleton.

Low body weight and weight loss are a particular problem for the elderly, as they may signal a variety of medical problems. Older women who are thin have a higher risk of hip fracture (Farmer et al. 1989, Kiel et al. 1987). Although "thin" has been defined variably in different studies and may be open to clinical interpretation, a large prospective study of older women found a roughly twofold increased risk of hip fracture in women who were below 127 pounds (Ensrud et al. 1997). This study also found no protective effect from increasing weight in these thin women. The increased risk was entirely attributable to hip bone density, which has led to the suggestion that low body weight be used as a surrogate for increased fracture risk when bone density measurements are unavailable. As discussed in Chapters 8 and 10, weight is used in some assessment instruments as an aid in deciding whether BMD testing is necessary.

Older women who experience weight loss in later years have also been found to have a two-fold greater risk of subsequent hip fracture, irrespective of current weight or intention to lose weight. These findings indicate that even voluntary weight loss in overweight elderly women increases hip fracture risk (Ensrud et al. 2003).

Whether being overweight reduces fracture risk is less clear. Some older studies have reported a lower risk of fracture in overweight women (Farmer et al. 1989), but a more recent study reported that women of average weight had a risk of hip fracture that was similar to that of heavier women (Ensrud et al. 1997). Of course, being overweight raises the risk of many other health problems, including heart disease and diabetes. The epidemic of overweight and obesity in the United States is well documented (Flegal et al. 2002). As a result, public health efforts should continue to focus on weight reduction in overweight or obese individuals and maintenance of body weight in normal weight individuals, especially at older ages. For overweight individuals, achieving weight loss while maintaining skeletal integrity is the goal. The key may be to increase physical activity in addition to restricting caloric intake. For example, Salamone (1999) found that women who lost weight did lose more bone than weight-stable women, but this bone loss was lessened among those who increased their physical activity. Consuming adequate calcium during weight loss may also help prevent bone loss, at least in postmenopausal women (Ricci et al. 1998). If these results are confirmed in other studies, weight loss recommendations should include physical activity, preferably weight bearing, and adequate calcium to help protect the skeleton.

Finally, the relationship between weight and weight loss, bone density, and fracture risk in men has not been thoroughly addressed.

Falls and Fall Prevention

Falls and Bone Health: What the Evidence Tells Us

- Falls contribute to most fractures.
- There are a number of identifiable risk factors for falls in the elderly.
- Interventions targeted at multiple risk factors can reduce the number of falls and possible the number of fractures as well.

Background: Why Focus on Falls?

Falls contribute to fractures, and thus fall prevention offers another opportunity to protect the bones throughout life, particularly in those over age 60. While low bone mass may put an individual at high risk of fracture, it is often a fall that precipitates the injury. Falls are one of the most common problems that threaten the independence of older individuals. About 10–15 percent of falls in the elderly result in fracture (Nevitt et al. 1991), and some may result in death. The risk of falling increases with age and varies according to living status. One study found that between 30–40 percent of those over age 65 who live in the community fall each year (Tinetti et al. 1988). The rate of falls is even greater in long-term care settings, as the general health of these individuals is more fragile (Thapa et al. 1996). An elderly individual's level of social integration—that is, the degree to which he or she has developed and maintained networks of family members and friends, also has an impact on falls. Those with stronger networks have a lower risk of falling (Faulkner 2003). A history of falling is also an important predictor of future falls, as almost 60 percent of those who fell during the previous year will fall again (Nevitt et al. 1991).

Falls in older individuals are rarely due to a single cause. They usually result when a threat to the normal mechanisms that maintain posture occurs in someone who already has problems with balance, mobility, sensory changes and lower extremity weakness, and/or blood pressure or circulation. The new threat may involve an acute illness (e.g., infection, fever, dehydration, arrhythmia), or an environmental stress (e.g., taking a new drug or walking on an unsafe surface). Since they may already have several health problems as a result of aging or chronic disease, many elderly people cannot compensate for the additional burden posed by the new threat.

Some Facts About the Prevalence of Falls

- One third of people over age 65 fall each year, with half of those falls being recurrent (i.e., the individual has fallen before).
- One in 10 falls results in a serious injury, such as a hip fracture. In fact, 90 percent of hip fractures result from falls.
- Falls account for 10 percent of visits to emergency room visits and 6 percent of urgent hospitalizations in the elderly.
- The risk of falling varies tremendously depending upon an individual's risk factors. An elderly person with no risk factors has only a 10 percent chance of falling each year, compared to an 80 percent likelihood of falling for a person with four or more risk factors.

(Tinetti 2003)

Risk Factors for Falls

- Age
- Arthritis
- Depression
- Fall in blood pressure upon standing (i.e., orthostasis)
- Poor cognition
- Poor vision, gait, or balance
- Need for home health care
- Use of four or more medications

(Tinetti 2003)

Falls and Fall Prevention: A Review of the Evidence

Many well-designed studies of risk factors for falls have been published over the several decades (Tinetti et al. 1988, Nevitt et al. 1991). These studies show that the more risk factors an individual has, the more likely he or she is to fall (Tinetti et al. 1988, Nevitt et al. 1991). As noted previously, one of the most important risk factors for falls is a previous history of falls. Other risk factors included age, being female, Alzheimer's disease or other types of cognitive impairment, weakness in the legs and feet, balance problems, use of drugs for depression and psychosis, and arthritis. Being hospitalized also increased risk of falling among those who already had other risk factors. Age-related declines in vision, balance and coordination, inner ear function, muscle amount and responsiveness, blood pressure regulation, and problems with staying hydrated also can lead to falls. Finally, those requiring bi- or tri-focal glasses are also at increased risk of falls and hip fractures (Lord et al. 2002, Felson et al. 1989).

Medication use is one of the most modifiable risk factors for falls. Drugs that affect the central nervous system (CNS) frequently have been linked to risk of falling. Examples of these drugs include neuroleptic drugs (used to treat psychotic behavior), benzodiazepines (used to treat anxiety), and tricyclic or serotonin reuptake inhibitors (used to treat depression) (Ensrud et al. 2002). Drugs to control blood pressure may also increase the risk of falling (Mukai and Lipsitz 2002). In addition to these specific drug classes, recent changes in the dose of a medication and the total number of prescriptions appear to be associated with an increased risk of falling (Cumming et al. 1991). Attention by physicians to the potential effects of medications on falls in the elderly may lead to some modification of therapy (e.g., changes in dose or timing of use) and/or to enhanced fall prevention activities.

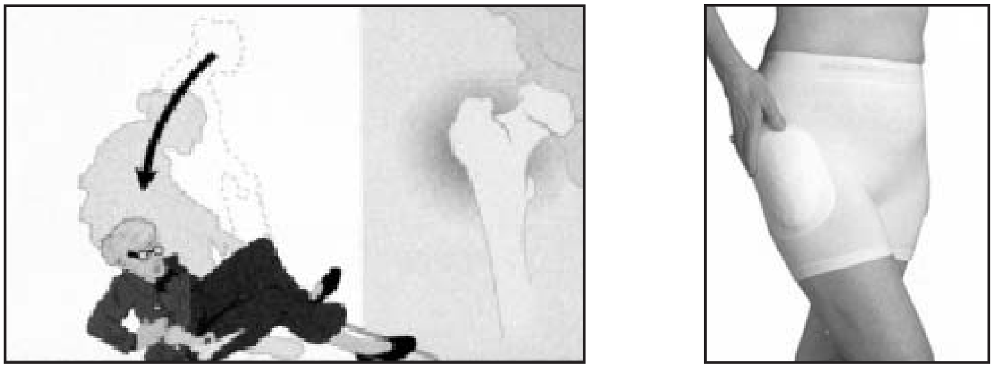
Environmental factors, such as poor lighting or loose rugs, may also increase the risk of falling. Most well-designed studies on methods to prevent falls combine efforts to improve the individual's health-related risks with efforts to remove environmental hazards, making it difficult to separate out the unique contribution of either set of factors (Tinetti et al. 1994). One study, for example, investigated the usefulness of having an experienced occupational therapist visit the home to assess and help modify potential environmental hazards (Cumming et al. 1999). The visits reduced the risk of falling by 36 percent in high-risk patients (e.g., those who fell one or more times in the previous year). However, the therapist's visit may have also prompted behavior changes in these patients that lowered their falling risk.

A different study examined the role of hazard reduction more directly. In that study, people age 70 and older were randomly assigned either to a group that received a home hazard assessment, information on hazard reduction, and installation of safety devices, or to a control group that did not receive these things (Stevens et al. 2001a and b). A research nurse visited the homes of people in both groups once. At the end of the study, there were fewer hazards in the homes of the group that received the information and safety devices than in the control group, but the number of falls did not differ between the two groups (Stevens et al. 2001a and b).

Fall prevention in the hospital and nursing home settings are also important. In hospital settings, bed rails do not appear to change the total number of falls, although they can decrease the number of serious falls (Hanger et al. 1999).

Several studies to identify effective ways to reduce falling risk have been conducted over the past decade. The approaches studied include programs to improve strength or balance, educational programs, optimization of medications, and environmental modifications.

Figure 6–8. Rationale for the Use of Hip Protectors to Prevent Fractures



Note: Falls to the side are associated with the majority of hip fractures. Energy absorption in soft tissue may account for up to 75% of the energy in a fall. Hip protector systems can be designed to be energy absorbing or energy shunting. The protective effect of this intervention is immediate, as opposed to the typical 1-2 years required for pharmacologic therapies.

Source: Kiel 2002.

Some approaches have targeted a single risk factor, while others have focused on modifying several factors simultaneously. The latter have been more successful, since falls are generally caused by more than one risk factor (Gillespie et al. 2001). Specific approaches that have demonstrated benefit included: a) muscle strengthening and balance retraining; b) professional home hazard assessment and modification; and c) stopping or reducing psychotropic medication (Tinetti et al. 1994, Tinetti 2003). The optimal duration or intensity of these approaches has not been defined. As noted earlier in this chapter, vitamin D deficiency is associated with an increased risk of falls and hence the use of vitamin D supplementation to reduce falls may be promising (Bischoff et al. 2003, Bischoff-Ferrari et al. 2004, Dukas 2004).

Finally, a complementary approach to reducing fractures due to falls is to attempt to minimize the impact of those falls that do occur through use of a hip protector or hip pad that helps to “cushion the blow” from a fall, as shown in Figure 6-8. A recently updated systematic review of the efficacy of hip protectors concluded that hip protectors reduce the risk of hip fracture for elderly individuals who live in nursing homes and residential care facilities, as well as those in supported living at home; the generalization of the results beyond this high risk population is unknown (Parker 2003). One of the larger studies (Kannus 2000) included in this systematic review found that 41 patients would need to be offered treatment with a hip protector to prevent one hip fracture over the course of one year, a finding that suggests that hip protectors may be a reasonable and cost-effective option for patients at high risk of falls.

While hip protectors appear to be effective when used, the biggest problem may relate to getting people to wear them. A recent randomized controlled trial among women over age 70 living in the community found that hip protectors offered no significant reduction in the risk of hip fracture (Birks et al. 2004). But compliance rates were quite low (roughly 30 percent). This study, the Kannus study described above, and others have documented low rates of compliance (i.e., those who have hip protectors do not wear them), suggesting the need to develop more acceptable, easy-to-use devices that can protect fragile bones by absorbing some of the energy of falls. The policies of nursing homes and other residential care facilities might also influence usage rates. While hip protectors may be relatively inexpensive, the decision to use them for residents of these facilities may be influenced by the cost and how much staff time is required in helping residents to put them on and take them off. But a recent economic analysis of ambulatory nursing facility residents demonstrated that hip protectors save money and are economically attractive over a wide range of cost and utility assumptions (Colon-Emeric 2003).

The Bottom Line on Fall Prevention

The approaches summarized above have modestly reduced the frequency and/or impact of falling. When combined with strategies to improve underlying bone strength, they can likely decrease fracture risk. In fact, based on a review of the evidence, the USPSTF recommends counseling elderly patients on specific measures to prevent falls. The USPSTF also recommends that more intensive individualized multi-factorial interventions be implemented for high-risk elderly patients in settings where adequate resources to deliver such services are available (USPSTF 1996).

Reproductive Factors

Reproductive Factors and Bone Health: What the Evidence Tells Us

- Pregnancy and lactation generally do not harm the skeleton of healthy adult women.
- Amenorrhea (cessation of menstrual periods) is linked to low bone mass.
- Bilateral oophorectomy (removal of both ovaries) is linked to increased bone loss and fracture risk.
- The effects of oral contraceptives on bone health may differ depending on type, and have not been clearly established.

Reproductive hormones play a central role in BMD levels among both women and men, but these hormones have been most widely evaluated in young to middle-aged women, particularly with respect to pregnancy, lactation, and contraception.

Pregnancy and Lactation

Several changes occur during pregnancy and lactation that can affect bone mass, including changes in reproductive hormones and in hormones that affect calcium metabolism. Since fetal and infant bone growth during pregnancy and lactation depends on calcium transfer from the mother, the possibility that pregnancy and lactation affect risk for osteoporosis later in life has been investigated. Intestinal calcium absorption increases during pregnancy to meet much of the fetal calcium needs, but maternal bone loss may occur in the last months of pregnancy (Reed et al. 2003). The mother's skeleton also loses bone during breastfeeding, but this loss is largely restored during weaning, as ovulation and menses is re-established. This bone loss and its subsequent restoration appear to be independent of lifestyle behaviors, including dietary calcium intake and physical activity patterns (Kalkwarf and Specker 2002).

Epidemiologic studies indicate that neither extended lactation nor multiple pregnancies are associated with subsequent osteoporosis, whether measured by BMD levels (Karlsson et al. 2001, Paton et al. 2003) or by assessment of fracture risk. In fact, the risk of hip fracture in women has been found to decrease by 5–10 percent with each additional child, and there is no apparent association between the duration of lactation and fracture risk (Michaelsson et al. 2001). Thus, in general, pregnancy and lactation in healthy adult women do not appear to cause lasting harm to the skeleton. For example, in one recent study, women with more than 10 pregnancies and extended lactation had BMD levels similar to those in women who have not been pregnant (Henderson et al. 2000). Having more children also does not appear to increase fracture risk (Cumming and Klineberg 1993). For pregnant teens who have not yet reached peak bone mass, the 30 g of calcium required for the fetal skeleton competes with the demands of calcium for the teen's mineral accrual. Whether peak bone mass is compromised in women who experience teen pregnancies remains controversial (Lloyd et al. 2002).

Menstrual Cycling

Regular menstrual cycles are the outward vital sign of a normally functioning reproductive system in the premenopausal female. The impact on bone health of irregular cycles or subtle hormonal changes during the menstrual cycle has not been clearly established. However, amenorrhea, or the cessation of menstrual periods, should be viewed with concern, and its cause should be investigated. Primary amenorrhea may be due to a variety of endocrine abnormalities, but the cessation of regular cycling can also be due to an imbalance of energy intake (nutrition) and energy expenditure (exercise). Anorexia nervosa is the most serious cause of secondary amenorrhea and the most difficult to treat. The onset of anorexia nervosa frequently occurs during adolescence when maximal bone mineral accrual takes place, thereby making adolescent girls with anorexia nervosa at high risk for reduced peak bone mass (Soyka et al. 2002).

Female athletes may also experience amenorrhea, especially those participating in sports where leanness is an advantage and very strenuous training is the norm (e.g., cross country running, ballet). While some athletes experience amenorrhea due to disordered eating patterns, others experience it because of chronically inadequate caloric intake that does not compensate for the energy expended. Complications associated with amenorrhea include compromised bone density, failure to attain peak bone mass in adolescence, and increased risk of stress fractures. The most effective treatment is to decrease the intensity of the exercise and increase the nutritional intake (Warren 2003). Adolescent and young adult women who experience amenorrhea lasting for more than 3 months (regardless of the cause) should consult their health care provider.

Contraceptive Practices

Oral contraceptives were first marketed in the United States in 1960, gaining immediate and widespread use. It is estimated that 80 percent of American women born since 1945 have used birth control pills at some point in their lives. About 45 percent of the estimated 24 million women who report using reversible methods of birth control use oral contraceptives (Piccinino et al. 1998). Use is highest in women under age 30, who are also completing bone mass accrual.

Oral contraceptives contain variable amounts of the hormones estrogen and progesterone. Given the known impact of these hormones on bone, it is natural to ask what effect oral contraceptives have on bone mass and density. The factors that determine the effect of an oral contraceptive on bone health are the dose of estrogen and the age of the woman. The formulations of oral contraceptives have changed dramatically over the years, with older types having higher estrogen levels than do newer ones. These different formulations have a different overall impact on total estrogen exposure and ultimately on fracture risk. Both the short- and long-term effects of oral contraceptives on bone health are unclear at this time (Reed et al. 2003). There may be may relatively little impact on bone health from oral contraceptives in women who have already achieved peak bone mass, but low-dose oral contraceptives could potentially compromise the acquisition of bone in younger women (Cromer 2003).

Hysterectomy and Oophorectomy

Roughly 600,000 hysterectomies are performed annually in the United States, and 55 percent of women undergoing this procedure also have both ovaries removed (Keshavarz et al. 2002). Removing the ovaries (oophorectomy) affects calcium metabolism, fracture risk, and bone mineral content because it results in estrogen deficiency.

Bilateral oophorectomy in postmenopausal women results in a 54 percent increase in fractures of the hip, spine, and wrist, and a 35 percent increase in fractures at other sites. The increase in fracture risk among women who underwent bilateral oophorectomy after natural menopause is consistent with the hypothesis that androgens produced by the postmenopausal ovary may be important for endogenous estrogen production that protects against fractures (Melton et al. 2003).

Medical Conditions and Drugs

Medical Conditions and Drugs: What the Evidence Tells Us

- Several medical conditions and prescription medications can affect bone health through various mechanisms. A detailed list of conditions and medications is shown in Chapter 3 and further described below.

Many individuals have medical conditions or take medications that can affect bone health. Chapter 3 contains two tables with a reasonably complete list of these drugs and diseases. This section will discuss the more common prescription drugs and medical conditions that affect bone health. These medical situations, which are known as secondary causes of osteoporosis (Schneider and Shane 2001), should act as a "red flag" to individuals and health care professionals about bone health. A person who has one of these conditions or takes one of these drugs should speak to his or her health care provider about safeguarding bone health. Children who must take one or more of these prescription drugs or who have one of these medical conditions may not accumulate as much bone as they should during adolescence and thus may enter adulthood with abnormally low BMD. Adults who develop one of these diseases or begin taking one or more of these prescription drugs may experience even larger or more rapid bone loss than they would normally have during menopause and aging. In most cases, therefore, measurement of bone density will be necessary to determine whether there has been excessive bone loss.

Medications that can affect skeletal health include the following:

Corticosteroids are a class of drugs that reduce inflammation and suppress the body's immune response. They are called by a number of different names, including cortisone, glucocorticoids, prednisone, prednisolone, steroids, and ACTH. Corticosteroids may be inhaled, taken by mouth, given through the veins, or rubbed on the skin. They are used most commonly to treat lung diseases (emphysema, asthma, cystic fibrosis, sarcoidosis), diseases of the joints (lupus, rheumatoid arthritis, polymyalgia rheumatica), gastrointestinal tract diseases (ulcerative colitis, Crohn's disease), kidney diseases (glomerulonephritis), and certain skin diseases (psoriasis, eczema). Corticosteroids are the most common cause of secondary osteoporosis. They have powerful effects on bone (Saag 2002). For example, doses of prednisone (a corticosteroid) above 7.5 mg per day have been shown to completely shut off formation of new bone, while the loss of older bone continues at a faster rate than normal. As a result, bone is lost very rapidly, particularly during the first year or so after beginning corticosteroids. As shown in Figure 3-4 in Chapter 3, even very small doses may increase risk of spine fractures (van Staa et al. 2000, Kanis et al. 2004a). The risk of fracture increases rapidly after the start of oral corticosteroid therapy (within 3 to 6 months) and decreases after stopping therapy. This increase in risk is independent of underlying disease, age, and gender (van Staa et al. 2002).

Elevated thyroid hormone is associated with secondary osteoporosis (Ross 1994). High levels of thyroid hormone can be the consequence of endogenous conditions such as Grave's disease or thyrotoxicosis (an overly active thyroid gland that produces too much of this hormone). However, prolonged, elevated levels are much more likely to be the result of prescribing thyroid hormone as a drug to treat an underactive or enlarged thyroid gland or to control growth of nodules in the thyroid gland. Too much thyroid hormone, no matter what the source, increases both the breakdown of old bone and the formation of new bone to take its place. However, more bone is lost than is formed. People with abnormally high levels of thyroid hormone are at increased risk for fracture, and the fractures often occur at younger ages. Postmenopausal women are probably at greater risk than premenopausal women or men, but all patients with a history of an overactive thyroid gland or those who must take thyroid hormone for any reason should have bone density testing. The lowest possible dose of thyroid hormone that corrects the medical problem being addressed should be used, since the effects on bone are related to the dose.

Gonadotrophin-releasing hormone agonists are drugs that lower the blood levels of male and female sex hormones (testosterone, estrogen). They may be referred to as GnRH agonists or hormone deprivation therapy. In men, these drugs are used to treat prostate cancer. In premenopausal women, they may be used to treat endometriosis or as a form of contraception. Hormone deprivation therapy causes levels of bone loss that are similar to that seen in women after menopause. Both men and premenopausal women undergoing this therapy have lower-than-expected BMD, while fracture rates are higher in men with prostate cancer who have undergone this treatment (Smith 2003).

Antiseizure or anticonvulsant medications, particularly diphenylhydantoin, phenobarbital, carbamazepine, and sodium valproate, can cause bone loss (Schneider and Shane 2001, Ensrud et al. 2004). The effect on bone health differs depending on the specific drug prescribed, and the mechanisms by which the drug affects bone are not fully understood. Effects on vitamin D metabolism and on bone or the parathyroid glands have been implicated (Fitzpatrick 2004). Individuals who take these drugs are more likely to have bone disease if they: a) have been on the drugs for years; b) require high doses and/or more than one anticonvulsant; c) avoid dairy products and do not take multivitamins and thus have low dietary intake of vitamin D; d) have chronic illnesses; and e) are institutionalized and thus get little sunlight. However, all patients taking these drugs should be evaluated for osteoporosis and vitamin D deficiency.

Medical conditions or events that should prompt a discussion of bone health fall into three major categories:

1. Warning signs that osteoporosis may already be present include any fracture that occurs during adulthood, loss of height, and the development of osteoporosis in another family member, such as a parent, sibling, or child.
2. The development of any disorder that increases the risk of falling is an important risk factor to consider. For example, an individual who has had a stroke that affects the ability to walk or causes difficulty with balance might be expected to fall more often and thus be at increased risk of fracture. Other diseases that fall into this category include Parkinson's disease, spinal cord injuries, any disorder that causes muscle weakness, and the onset of frailty in the elderly. Similarly, it is important for individuals who are beginning to take medications that increase the risk of falling (tranquilizers, sleeping pills, diuretics, and certain blood pressure pills) to discuss this risk with their health care providers.
3. Many medical conditions can result in low bone mass. The most common are genetic diseases (cystic fibrosis, muscular dystrophy), diseases that lower estrogen levels before menopause (eating disorders, excessive physical activity, ovarian failure of any cause), endocrine disorders (diabetes, hyperparathyroidism, Cushing's syndrome), gastrointestinal diseases (celiac disease, intestinal malabsorption, primary biliary cirrhosis, Crohn's disease), blood disorders (hereditary anemias, multiple myeloma, leukemia), rheumatoid arthritis, lupus, and depression. Anyone with these conditions should consult with a physician about bone health and potential preventive measures.

Smoking, Alcohol, and Environmental Threats to Bone Health

Smoking, Alcohol, and Environmental Threats: What the Evidence Tells Us

- Smoking is associated with reduced bone mass and increased fracture risk.
- Alcohol may have both harmful and beneficial effects on bone.
  - ~ Heavy alcohol consumption is associated with reduced bone mass and increased fracture risk
  - ~ Moderate alcohol use has been associated with higher bone density in some studies.
- Lead is among the most significant environmental threats to bone health in the United States.

Smoking

Smoking may harm the skeleton both directly and indirectly (USDHHS 2004). The nicotine and cadmium found in cigarettes can have a direct toxic effect on bone cells (Riebel et al. 1995, Fang et al. 1991). Smoking may also harm bone indirectly by lowering the amount of calcium absorbed from the intestine, altering the body's handling of vitamin D and various hormones needed for bone health, or lowering body weight (Michnovicz et al. 1986, Baron et al. 1995, Krall and Dawson-Hughes 1999, Brot et al. 1999). Smokers may also be less physically active. Smoking influences estrogen metabolism and the risk for multiple estrogen-sensitive outcomes. Smokers are likely to require higher doses of hormone therapy to achieve clinical effects on bone density that are comparable to those observed in nonsmokers (Tansavatdi et al. 2004). All of these factors can lead to lower bone density and higher risk of fracture (Cummings et al. 1995, Baron et al. 2001).

Several studies have linked smoking to higher fracture risk. A meta-analysis of data from postmenopausal women (Law and Hackshaw 1997) demonstrates that smoking increases the risk of hip fracture. More recent data on the association between smoking and fractures at other skeletal sites, while more limited, also support a relationship between smoking and fracture risk (Honkanen et al. 1998, Jacqmin et al. 1998). A recent meta-analysis, using data from 10 different observational studies from around the world, found that smoking was associated with an increased risk of hip and other fractures in both men and women (Kanis et al. 2004b). Although the lower BMD and BMI of smokers were found to contribute to the increased risk of fracture, these factors did not completely explain the increased risk. After adjustment for BMD, BMI, and age, the risk of hip fracture was 55 percent higher in smokers than in non-smokers. In addition to current smoking, a history of smoking was also associated with a higher risk of fracture, although the risk for former smokers was not as high as for current smokers.

Alcohol

Alcoholism is known to have negative effects on bone (Scharpira 1990), but moderate alcohol use in women has been associated with higher bone density in some studies (Felson et al. 1995, Sampson 2002). This apparent beneficial effect of moderate alcohol intake may be seen in women and not men because of the effect of alcohol on adrenal androgens or estrogen (Wild et al. 1987). Alcohol inhibits bone remodeling, possibly by affecting vitamin D or by reducing bone formation (Laitinen et al. 1991). It may also increase calcium and magnesium losses from the body. Although some studies suggest moderate alcohol intake increases bone density, it does not seem to lower fracture risk (Cummings et al. 1995, Hoidrup et al. 1999), and high alcohol intake may increase likelihood of fracture (Grisso et al. 1994). It is conceivable that the higher fracture risk is caused by an increased risk of falling or other types of trauma.

Environmental Threats to Bone

While a number of heavy metals can be detrimental to bone health, lead is among the most significant environmental threats to bone health in the United States Lead may accumulate in bone due to environmental or dietary exposures. Periods of high remodeling (pregnancy, lactation, postmenopausal period) are particularly critical since lead can have both a direct effect on bone and a latent effect on other organ systems through release from bone long after the initial exposure (Silbergeld and Flaws 2002, Gulson et al. 2003). High calcium intake may actually blunt the effect of stored lead release from bone in pregnant women (Hernandez-Avila et al. 2003). One potential dietary source of lead is calcium supplements. Certain preparations of calcium (e.g., bone meal and dolomite) can have significant contamination with lead and other heavy metals. However, most commercial calcium preparations are tested to ensure that they do not contain significant contamination of heavy metals (Optimal 1994).

Key Questions for Future Research

Much remains to be learned about the genetic and environmental factors that affect bone health, and, as discussed in Chapter 7, the behavior changes that are necessary to promote bone health throughout life. Some of the most important research questions for Chapters 6 and 7 are listed below:

- What are the genetic factors involved in regulating bone mass acquisition, bone loss, and the response of bone to environmental factors such as nutrients and loading?
- What are the optimal physical activity programs to maximize peak bone mass in children and adolescence and to minimize bone loss in adults?
- What is the potential for changes in the acid/base balance in blood and extracellular fluid—either through dietary manipulation or potassium supplementation—to influence bone and muscle health? Over a long period of time, a more acidic balance may create an environment in which the breakdown of existing bone is favored over the formation of new bone.
- What are the optimal muscle loading regimens to prevent sarcopenia and bone loss in the frail elderly?
- What can be done to imitate the effects of exercise (i.e., "exercise mimetics") in individuals who are paralyzed, chronically immobile, traveling in space, or otherwise not capable of engaging in loading activities that benefit bone health?
- What mechanisms and interventions can preserve bone mass during weight loss?
- What is the relationship between weight and weight loss, bone density, and fracture risk in men?
- What are the best ways to promote the adoption of bone-healthy practices by individuals?
- What are the best comprehensive fall prevention programs that can be easily adopted by communities and individuals?
- What impact do different oral and injectable contraceptives have on bone health? How does this impact vary by age?
- What interventions optimize bone health in children and adolescents who need to take glucocorticoids or other drugs that can be harmful to bone?

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