

BONE HEALTH AND DISEASE

BONE HEALTH AND DISEASE GOALS AND OBJECTIVES

Course Description

"Bone Health and Disease" is a home study continuing education course for rehabilitation professionals. This course presents current information about bone health and disease including sections on structure, physiology, pathology and etiology, assessment, treatment, rehabilitation, falls and fall prevention, and healthy bone interventions.

Course Rationale

The purpose of this course is to present rehabilitation professionals with current information about bone health and disease. Both therapists and therapy assistants will find this information pertinent and useful when providing care for individuals who have, or are at risk for having, bone disease or trauma.

Course Goals and Objectives

Upon completion of this course, the therapist or assistant will be able to

1. recognize normal bone structure and physiology
2. recognize all of the intrinsic and extrinsic factors that influence bone health
3. identify the signs and symptoms associated with the most common bone disorders
4. understand and discuss all of the risk factors associated with osteoporosis and other common bone disorders
5. identify many of the assessment and diagnostic tools commonly utilized to assess bone health
6. recognize current treatment and rehabilitation concepts relating to osteoporotic fracture management
7. differentiate current treatment concepts specific to other common bone disorders.
8. recognize and list the factors that contribute to falls and fractures in the elderly and apply this knowledge to reduce fall occurrence
9. recognize the morbidity, mortality, and financial impact that bone disease and trauma has on both the individual and society.
10. recognize the actions individuals may take to promote bone health throughout a lifetime.

Course Instructor

Michael Niss, DPT

Target Audience

Physical therapists, physical therapist assistants, occupational therapists, and occupational therapist assistants

Course Educational Level

This course is applicable for introductory learners.

Course Prerequisites

None

Criteria for issuance of Continuing Education Credits

A documented score of 70% or greater on the written post-test.

Continuing Education Credits

Five (5) hours of continuing education credit (5 NBCOT PDUs/5 contact hours)
AOTA - .5 AOTA CEU, Category 1: Domain of OT – Client Factors, Context

Determination of Continuing Education Contact Hours

"Bone Health and Disease" has been established to be a 5 hour continuing education program. This determination is based on an accepted standard for home-based self-study courses of 12 pages of text (12 pt font) per hour. The complete instructional text for this course is 61 pages (excluding Post-Test).

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Overview

The bony skeleton is a remarkable organ that serves both a structural function—providing mobility, support, and protection for the body—and a reservoir function, as the storehouse for essential minerals. It is not a static organ, but is constantly changing to better carry out its functions. The architecture of the skeleton is remarkably adapted to provide adequate strength and mobility so that bones do not break when subjected to substantial impact, even the loads placed on bone during vigorous physical activity. The shape or structure of bone is at least as important as its mass in providing this strength.

The skeleton is also a storehouse for two minerals, calcium and phosphorus, that are essential for the functioning of other body systems, and this storehouse must be called upon in times of need. The maintenance of a constant level of calcium in the blood as well as an adequate supply of calcium and phosphorus in cells is critical for the function of all body organs, but particularly for the nerves and muscle. Therefore, a complex system of regulatory hormones has developed that helps to maintain adequate supplies of these minerals in a variety of situations. These hormones act not only on bone but on other tissues, such as the intestine and the kidney, to regulate the supply of these elements. Thus one reason that bone health is difficult to maintain is that the skeleton is simultaneously serving two different functions that are in competition with each other. First, bone must be responsive to changes in mechanical loading or weight bearing, both of which require strong bones that have ample supplies of calcium and phosphorus. When these elements are in short supply the regulating hormones take them out of the bone to serve vital functions in other systems of the body. Thus the skeleton can be likened to a bank where we can deposit calcium or phosphorus and then withdraw them later in times of need.

Both the amount of bone and its architecture are determined by the mechanical forces that act on the skeleton. Much of this is determined genetically so that each species, including humans, has a skeleton that is adapted to its functions. However, there can be great variation within a species, so that some individuals will have strong bones and others will have weak bones, largely because of differences in their genes. Moreover, bone mass and architecture are further modified throughout life as these functions and the mechanical forces required to fulfill them change. In other words, bones will weaken if they are not subjected to adequate amounts of loading and weight bearing for sufficient periods of time. If they are not (such as in the weightless condition of space travel), rapid bone loss can occur. In other words, as with muscle, it is “use it or lose it” with bone as well. Conversely, the amount and architecture of the bones can be improved by mechanical loading.

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To respond to its dual roles of support and regulation of calcium and phosphorus, as well as to repair any damage to the skeleton, bone is constantly changing. Old bone breaks down and new bone is formed on a continuous basis. In fact, the tissue of the skeleton is replaced many times during life. This requires an exquisitely controlled regulatory system that involves specialized cells that communicate with each other. These cells must respond to many different signals, both internal and external, mechanical and hormonal, and systemic and local. It is not surprising that with so many different tasks to perform and so many different factors regulating how the skeleton grows, adapts, and responds to changing demands, there are many ways that these processes can go astray.

Bone Structure

Bone is a composite material, consisting of crystals of mineral bound to protein. This provides both strength and resilience so that the skeleton can absorb impact without breaking. A structure made only of mineral would be more brittle and break more easily, while a structure made only of protein would be soft and bend too easily. The mineral phase of bone consists of small crystals containing calcium and phosphate, called hydroxyapatite. This mineral is bound in an orderly manner to a matrix that is made up largely of a single protein, collagen. Collagen is made by bone cells and assembled as long thin rods containing three intertwined protein chains, which are then assembled into larger fibers that are strengthened by chemical connections between them. Other proteins in bone can help to strengthen the collagen matrix even further and to regulate its ability to bind mineral. Very small changes in the shape of the bone can act on the cells inside bone (the osteocytes), which produce chemical signals that allow the skeleton to respond to changes in mechanical loading.

To provide the body with a frame that is both light and strong, bones are hollow. The outer dense shell is called cortical bone, which makes up roughly three-quarters of the total skeletal mass. Inside the cortical shell is a fine network of connecting plates and rods called trabecular bone that makes up the remaining 25 percent. Most bones are hollow structures in which the outer cortical bone shell defines the shape of the bone. This cortical shell is essential because it provides strength, sites for firm attachment of the tendons, and muscles and protection without excessive weight. The inner trabecular network has two important functions. It provides a large bone surface for mineral exchange. In addition, trabecular bone helps to maintain skeletal strength and integrity, as it is particularly abundant in the spine and at the ends of the long bones, sites that are under continuous stress from motion and weight-bearing. Fractures are common at these sites when the bone is weakened. The rods and plates of trabecular bone are aligned in a pattern that provides maximal strength without too much bulk, much in the way that architects and engineers design buildings and bridges. The shape and size of both cortical and trabecular bone can

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respond to different kinds of stress produced by physical activity. For example, in most people the cortex of their dominant arm is larger than that of their non-dominant arm. The difference in cortex size is even larger for tennis players and other athletes who routinely use a dominant arm in their sporting activities. Bones do not work in isolation, but rather are part of the musculoskeletal system, providing the “lever” that allows muscles to move. Thus muscle activity is important for the normal function of the bone. When the mechanical force produced by muscle is lost—for example, in patients with muscular dystrophy or paralysis—bone mass and strength are also rapidly lost. It is important to recognize that the bones, joints, and muscles are the key parts of an integrated “musculoskeletal system.” Problems with any one component of this system can affect the other components. Thus, weakness of the muscles can lead to loss of bone and joint damage, while degeneration of the joints leads to changes in the underlying bone, such as the bony spurs or protuberances that occur in osteoarthritis.

Physiology

The process of building the skeleton and continuously reshaping it to respond to internal and external signals is carried out by specialized cells that can be activated to form or break down bone. Both modeling and remodeling involve the cells that form bone called osteoblasts and the cells that break down bone, called osteoclasts. In remodeling there is an important local interaction between osteoblasts and osteoclasts. Since remodeling is the main way that bone changes in adults and abnormalities in remodeling are the primary cause of bone disease, it is critically important to understand this process.

Osteoblasts are derived from precursor cells that can also be stimulated to become muscle, fat or cartilage; however, under the right conditions these cells change (or differentiate) to form new bone, producing the collagen that forms the scaffolding or bone matrix. Calcium and phosphate are added to the matrix to form the hard, yet resilient, tissue that is healthy bone. Osteoblasts lay down bone in orderly layers that add strength to the matrix. Some of the osteoblasts are buried in the matrix as it is being produced and these are now called osteocytes. Others remain as thin cells that cover the surface and are called lining cells. Osteocytes are the most numerous cells in bone and are extensively connected to each other and to the surface of osteoblasts by a network of small thin extensions. This network is critical for the ability of bone to respond to mechanical forces and injury. When the skeleton is subjected to impact there is fluid movement around the osteocytes and the long-cell extensions that provides signals to the bone cells on the surface to alter their activity, either in terms of changes in bone resorption or formation. Failure of the osteoblasts to make a normal matrix occurs in a congenital disorder of the collagen molecule called osteogenesis imperfecta.

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The osteoclasts remove bone by dissolving the mineral and breaking down the matrix in a process that is called bone resorption. The osteoclasts come from the same precursor cells in the bone marrow that produce white blood cells. These precursor cells can also circulate in the blood and be available at different sites in need of bone breakdown. Osteoclasts are formed by fusion of small precursor cells into large, highly active cells with many nuclei. These large cells can fasten onto the bone, seal off an area on the surface, and develop a region of intense activity in which the cell surface is highly irregular, called a ruffled border. This ruffled border contains transport molecules that transfer hydrogen ions from the cells to the bone surface where they can dissolve the mineral. In addition, packets of enzymes are secreted from the ruffled border that can break down the matrix. Excessive bone breakdown by osteoclasts is an important cause of bone fragility not only in osteoporosis, but also in other bone diseases such as hyperparathyroidism, Paget's disease, and fibrous dysplasia.

Removal and replacement of bone in the remodeling cycle occurs in a carefully orchestrated sequence that involves communication between cells of the osteoblast and osteoclast lineages. It is controlled by local and systemic factors that regulate bone remodeling to fulfill both its structural and metabolic functions. The activation of this process involves an interaction between cells of the osteoblastic lineage and the precursors that will become osteoclasts. What stops this process is not known, but the osteoclasts machinery clearly slows down and the osteoclasts die by a process that is called programmed cell death. Thus the amount of bone removed can be controlled by altering the rate of production of new osteoclasts, blocking their activity, or altering their life span. Most current treatments for osteoporosis work by slowing down osteoclastic bone breakdown through use of antiresorptive agents.

Since remodeling serves both the structural and metabolic functions of the skeleton, it can be stimulated both by the hormones that regulate mineral metabolism and by mechanical loads and local damage acting through local factors. Repair of local damage is an important function of remodeling. Over time repeated small stresses on the skeleton can produce areas of defective bone, termed micro-damage. Replacement of that damaged bone by remodeling restores bone strength. Signals for these responses are probably developed by the network of osteocytes and osteoblasts, which, through their multiple connections, can detect changes in the stress placed upon bone and in the health of the small areas of micro-damage. Factors that affect the formation, activity, and life span of osteoclasts and osteoblasts as they develop from precursor cells can affect the remodeling cycle. Drugs have been developed that act in these ways, with the goal of reducing bone loss or increasing bone formation and maintaining skeletal health.

Factors Contributing to Bone Health

Both genes and the environment contribute to bone health. Some elements of bone health are determined largely by genes, and errors in signaling by these genes can result in birth defects. External factors, such as diet and physical activity, are critically important to bone health throughout life and can be modified. As noted above, the mechanical loading of the skeleton is essential for maintenance of normal bone mass and architecture. In addition, the skeleton needs certain nutritional elements to build tissue. Not only does the skeleton require the same nutritional elements as the rest of the body, but it also has a special requirement for large amounts of calcium and phosphorus. While adequate levels of these minerals can be obtained from the mother during pregnancy and nursing, they must come from the diet thereafter.

The growth of the skeleton, its response to mechanical forces, and its role as a mineral storehouse are all dependent on the proper functioning of a number of systemic or circulating hormones produced outside the skeleton that work in concert with local regulatory factors. This complex system of regulatory hormones responds to changes in blood calcium and phosphorus, acting not only on bone but also on other tissues such as the intestine and the kidney. Under normal conditions only part of the dietary calcium is absorbed and some calcium is secreted into the intestinal tract so that the net amount of calcium entering the body normally is only a small proportion of dietary calcium. In healthy young adults there is calcium balance, where the amount taken in is equal to the amount excreted. The bones are constantly remodeling, but breakdown and formation are equal. The kidney filters the blood, including a large amount of calcium, but most of this is taken back into the body by the kidney cells. When calcium and/or phosphorus are in short supply, the regulating hormones take them out of the bone to serve vital functions in other systems of the body. Too many withdrawals can weaken the bone. The regulatory hormones also play critical roles in determining how much bone is formed at different phases of skeletal growth and how well bone strength and mass is maintained throughout life. For example, sex hormones and the growth hormone system described below are increased during puberty, a time of rapidly increased skeletal growth.

Genes, hormones, local factors, and lifestyle all play a role in determining one's peak bone mass, a level that is typically achieved by the time an individual reaches his or her late teens or early 20s. The stronger the bones are at this time, the better able they are to deal with any withdrawals of calcium and phosphorus that are needed and with any other changes to bone that occur with aging.

Hormones

Calcium-Regulating Hormones

Three calcium-regulating hormones play an important role in producing healthy bone: 1) parathyroid hormone or PTH, which maintains the level of calcium and stimulates both resorption and formation of bone; 2) calcitriol, the hormone derived from vitamin D, which stimulates the intestines to absorb enough calcium and phosphorus and also affects bone directly; and 3) calcitonin, which inhibits bone breakdown and may protect against excessively high levels of calcium in the blood.

Parathyroid Hormone or PTH - Produced by four small glands adjacent to the thyroid gland. These glands precisely control the level of calcium in the blood. They are sensitive to small changes in calcium concentration so that when calcium concentration decreases even slightly the secretion of PTH increases. PTH acts on the kidney to conserve calcium and to stimulate calcitriol production, which increases intestinal absorption of calcium. PTH also acts on the bone to increase movement of calcium from bone to blood. Excessive production of PTH, usually due to a small tumor of the parathyroid glands, is called hyperparathyroidism and can lead to bone loss. PTH stimulates bone formation as well as resorption.

In recent years a second hormone related to PTH was identified called parathyroid hormone-related protein (PTHrP). This hormone normally regulates cartilage and bone development in the fetus, but it can be over-produced by individuals who have certain types of cancer. PTHrP then acts like PTH, causing excessive bone breakdown and abnormally high blood calcium levels, called hypercalcemia of malignancy (Stewart 2002).

Calcitriol - hormone produced from vitamin D (Norman, Okamura et al. 2002). Calcitriol, also called 1,25 dihydroxy vitamin D, is formed from vitamin D by enzymes in the liver and kidney. Calcitriol acts on many different tissues, but its most important action is to increase intestinal absorption of calcium and phosphorus, thus supplying minerals for the skeleton. Many people need vitamin D in their diet because they do not derive adequate levels from exposure to the sun. This need occurred as people began to live indoors, wear clothes, and move further north. In northern latitudes the sun's rays are filtered in the winter and thus are not strong enough to make sufficient vitamin D in the skin. Vitamin D deficiency leads to a disease of defective mineralization, called rickets in children and osteomalacia in adults. These conditions can result in bone pain, bowing and deformities of the legs, and fractures. Treatment with vitamin D can restore calcium supplies and reduce bone loss.

Calcitonin - calcium-regulating hormone produced by cells of the thyroid gland, although by different cells than those that produce thyroid hormones (Sexton,

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Findlay et al. 1999). Calcitonin can block bone breakdown by inactivating osteoclasts, but this effect may be relatively transient in adult humans. Calcitonin may be more important for maintaining bone development and normal blood calcium levels in early life. Excesses or deficiencies of calcitonin in adults do not cause problems in maintaining blood calcium concentration or the strength of the bone. However, calcitonin can be used as a drug for treating bone disease.

Sex Hormones

Along with calcium-regulating hormones, sex hormones are also extremely important in regulating the growth of the skeleton and maintaining the mass and strength of bone. The female hormone estrogen and the male hormone testosterone both have effects on bone in men and women (Falahati-Nini, Riggs et al. 2000). The estrogen produced in children and early in puberty can increase bone growth. The high concentration that occurs at the end of puberty has a special effect—that is, to stop further growth in height by closing the cartilage plates at the ends of long bone that previously had allowed the bones to grow in length.

Estrogen - acts on both osteoclasts and osteoblasts to inhibit bone breakdown at all stages in life. Estrogen may also stimulate bone formation. The marked decrease in estrogen at menopause is associated with rapid bone loss. Hormone therapy was widely used to prevent this, but this practice is now controversial because of the risks of increased breast cancer, strokes, blood clots, and cardiovascular disease with hormone therapy.

Testosterone - important for skeletal growth both because of its direct effects on bone and its ability to stimulate muscle growth, which puts greater stress on the bone and thus increases bone formation. Testosterone is also a source of estrogen in the body; it is converted into estrogen in fat cells. This estrogen is important for the bones of men as well as women. In fact, older men have higher levels of circulating estrogen than do postmenopausal women.

Other Important Hormones

Growth hormone from the pituitary gland is also an important regulator of skeletal growth. It acts by stimulating the production of another hormone called insulin-like growth factor-1 (IGF-1), which is produced in large amounts in the liver and released into circulation. IGF-1 is also produced locally in other tissues, particularly in bone, also under the control of growth hormone. Growth hormone is essential for growth and it accelerates skeletal growth at puberty. Decreased production of growth hormone and IGF-1 with age may be responsible for the inability of older individuals to form bone rapidly or to replace bone lost by resorption (Yakar and Rosen 2003). The growth hormone/IGF-1 system stimulates both the bone-resorbing and bone-forming cells, but the dominant effect is on bone formation, thus resulting in an increase in bone mass.

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Thyroid hormones increase the energy production of all body cells, including bone cells. They increase the rates of both bone formation and resorption. Deficiency of thyroid hormone can impair growth in children, while excessive amounts of thyroid hormone can cause too much bone breakdown and weaken the skeleton (Vestergaard and Mosekilde 2002). The pituitary hormone that controls the thyroid gland, thyrotropin or TSH, may also have direct effects on bone (Abe et al. 2003).

Cortisol, the major hormone of the adrenal gland, is a critical regulator of metabolism and is important to the body's ability to respond to stress and injury. It has complex effects on the skeleton (Canalis and Delany 2002). Small amounts are necessary for normal bone development, but large amounts block bone growth. Synthetic forms of cortisol, called glucocorticoids, are used to treat many diseases such as asthma and arthritis. They can cause bone loss due both to decreased bone formation and to increased bone breakdown, both of which lead to a high risk of fracture (Kanis et al. 2004).

There are other circulating hormones that affect the skeleton as well. Insulin is important for bone growth, and the response to other factors that stimulate bone growth is impaired in individuals with insulin deficiency (Lu et al. 2003, Suzuki et al. 2003). A recently discovered hormone from fat cells, leptin, has also been shown to have effects on bone (Elefteriou et al. 2004, Cornish et al. 2002).

Reproductive Factors and Bone Health

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.

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Studies indicate that neither extended lactation nor multiple pregnancies are associated with subsequent osteoporosis (Paton et al. 2003). 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).

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. 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 contain variable amounts of the hormones estrogen and progesterone. 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. There may be a 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. (Melton et al. 2003).

Medications and Bone Health

Medications that can affect skeletal health include the following:

Corticosteroids

Corticosteroids are the most common cause of secondary osteoporosis. They have powerful effects on bone. For example, doses of prednisone 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. Even very small doses may increase risk of spine fractures (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).

Thyroid Hormone

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. 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. 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

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

Antiseizure or anticonvulsant medications, particularly diphenylhydantoin, phenobarbital, carbamazepine, and sodium valproate, can cause bone loss (Ensrud et al. 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.

Weight and 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 (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.

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).

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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. 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).

Older women who experience weight loss in later years have also been found to have a twofold 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).

Smoking, Alcohol, and Environmental Threats to Bone Health

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). 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 (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. All of these factors can lead to lower bone density and higher risk of fracture (Baron et al. 2001).

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 (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. Alcohol inhibits bone remodeling, possibly by affecting vitamin D or by reducing bone formation. 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 (Hoidrup et al. 1999).

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

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and a latent effect on other organ systems through release from bone long after the initial exposure. 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.

Bone Disease

Maintaining a strong and healthy skeleton is a complicated process that requires having the right amount of bone with the right structure and composition in the right place. There are many things that can go wrong along the way.

Genetic abnormalities can produce weak, thin bones, or bones that are too dense. The disease osteogenesis imperfecta is caused by abnormalities in the collagen molecule that make the matrix weak and can lead to multiple fractures. In another congenital disorder, osteopetrosis, the bones are too dense because of failure of osteoclast formation or function. This failure of the remodeling process results in persistence of trabecular bone in the marrow space so that the marrow cavity may not be large enough to form red and white blood cells normally. These dense bones cannot remodel well in response to mechanical forces or micro damage and hence may be weaker and subject to fracture even though bone mass is increased. There are also other abnormalities of the genes that affect the size and shape of the skeleton and can cause deformities or abnormal growth.

Nutritional deficiencies, particularly of vitamin D, calcium, and phosphorus, can result in the formation of weak, poorly mineralized bone. In children, vitamin D deficiency produces rickets in which there is not only a marked weakness of bone and fractures but also bowing of the long bones and a characteristic deformity due to overgrowth of cartilage at the ends of the bones. In adults, vitamin D deficiency leads to a softening of the bone (a condition known as osteomalacia) that can also lead to fractures and deformities.

Many hormonal disorders can also affect the skeleton. Overactive parathyroid glands or hyperparathyroidism can cause excessive bone breakdown and increase the risk of fractures. In severe cases, large holes or cystic lesions appear in the bone, which makes them particularly fragile. A deficiency of the growth hormone/IGF-1 system can inhibit growth, leading to short stature. Loss of gonadal function or hypogonadism in children and young adults can cause severe osteoporosis due to loss of the effects of testosterone and estrogen. In

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addition, too much cortisol production by the adrenal gland can occur in Cushing's syndrome.

Use of glucocorticoids as medication is a common cause of bone disease. Excess glucocorticoids will stop bone growth in children and cause marked thinning of the bone in adults, often leading to fracture.

Many bone disorders are local, affecting only a small region of the skeleton. Inflammation can lead to bone loss, probably through the production of local resorbing factors by the inflammatory white cells. This process can occur around the affected joints in patients with arthritis. Bacterial infections, such as severe gum inflammation or periodontal disease, can produce loss of the bones around the teeth, and osteomyelitis can produce a loss of bone at the site of infection. This type of bone loss is due to the direct damaging effect of bacterial products as well as the production of resorbing factors by white cells. Paget's disease is a multifaceted condition in which the first change is the formation of large, highly active, and unregulated osteoclasts that produce abnormal bone resorption. The precise cause of Paget's disease is not known, but it appears to be the consequence of both genetic factors and environmental factors, possibly a viral infection. The osteoblasts try to repair this damage by increasing bone formation. However, the normal bone architecture has been disrupted, leading to weak bones and the potential for fractures and deformities (even though the bones may appear dense on an x-ray). One reason for this is that the new bone formed is disorderly, "woven" bone, which does not have the proper alignment of mineral crystals and collagen matrix. In addition, the new bone may not be in the right place to provide strength.

Osteoporosis

Osteoporosis is a disease characterized by low bone mass and deterioration of bone structure that causes bone fragility and increases the risk of fracture. For practical purposes, the World Health Organization has defined osteoporosis as a bone mineral density (BMD) value more than 2.5 standard deviations below the mean for normal young White women. Osteoporosis is a common disease affecting millions of Americans. Individuals with osteoporosis are at high risk of suffering one or more fractures, injuries that can often be physically debilitating and potentially lead to a downward spiral in physical and mental health. Generalized osteoporosis is the most common form of the disease, affecting most of the skeleton. Osteoporosis can also occur in localized parts of the skeleton as a result of injury or conditions that reduce muscle forces on the bone, such as limb paralysis. There are a variety of different types of osteoporosis. The most common form of osteoporosis is known as "primary osteoporosis"—that is, osteoporosis that is not caused by some other specific disorder. Bone loss

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caused by specific diseases or medications is referred to as “secondary osteoporosis.”

Primary (Age-Related) Osteoporosis

Age-related osteoporosis is by far the most common form of the disease. There are many different causes of the ailment, but the bone loss that leads to the disease typically begins relatively early in life, at a time when corrective action could potentially slow down its course. While it occurs in both sexes, the disease is two to three times more common in women. This is partly due to the fact that women have two phases of age-related bone loss—a rapid phase that begins at menopause and lasts 4–8 years, followed by a slower continuous phase that lasts throughout the rest of life (Riggs et al. 2002). By contrast, men go through only the slow, continuous phase. As a result, women typically lose more bone than do men. The rapid phase of bone loss alone in women results in losses of 5–10 percent of cortical bone and 20–30 percent of trabecular bone. The slow phase of bone loss results in losses of 20–25 percent of cortical and trabecular bone in both men and women, but over a longer period of time.

Although other factors such as genetics and nutrition contribute, both the rapid phase of bone loss in postmenopausal women and the slow phase of bone loss in aging women and men appear to be largely the result of estrogen deficiency. For women, the rapid phase of bone loss is initiated by a dramatic decline in estrogen production by the ovaries at menopause. The loss of estrogen action on estrogen receptors in bone results in large increases in bone resorption, combined with reduced bone formation. The end result is thinning of the cortical outer shell of bone and damage to the trabecular bone structure.

By contrast, the slower phase of bone loss is thought to be caused by a combination of factors including age-related impairment of bone formation, decreased calcium and vitamin D intake, decreased physical activity, and the loss of estrogen's positive effects on calcium balance in the intestine and kidney as well as its effects on bone. This leads to further impairment of absorption of calcium by the intestine and reduced ability of the kidney to conserve calcium. If the amount of calcium absorbed from the diet is insufficient to make up for the obligatory calcium losses in the stool and urine, serum calcium begins to fall. Parathyroid hormone levels will then increase, removing calcium from bone to make up for the loss. The net result of this process is an increase in bone resorption. It is important to realize that these mineral losses need not be great to result in osteoporosis. A negative balance of only 50–100 mg of calcium per day (far less than the 300 mg of calcium in a single glass of milk) over a long period of time is sufficient to produce the disease.

For aging men, sex steroid deficiency also appears to be a major factor in age-related osteoporosis. Although testosterone is the major sex steroid in men,

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some of it is converted by the aromatase enzyme into estrogen. In men, however, the deficiency is mainly due to an increase in sex hormone binding globulin, a substance that holds both testosterone and estrogen in a form that is not available for use by the body. Between 30–50 percent of elderly men are deficient in biologically active sex steroids (Khosla et al. 1998). In fact, except for the lack of the early postmenopausal phase, the process of bone loss in older men is similar to that for older women. As with women, the loss of sex steroid activity in men has an effect on calcium absorption and conservation, leading to progressive secondary increases in parathyroid hormone levels. As in older women, the resulting imbalance between bone resorption and formation results in slow bone loss that continues over life. Since testosterone may stimulate bone formation more than estrogen does, however, decreased bone formation plays a relatively greater role in the bone loss experienced by elderly men.

Idiopathic Primary Osteoporosis

There are several different forms of idiopathic osteoporosis that can affect both children and adolescents, although these conditions are quite rare (Norman 2003). Juvenile osteoporosis affects previously healthy children between the ages of 8 and 14. Over a period of several years, bone growth is impaired. The condition may be relatively mild, causing only one or two collapsed vertebrae, or it may be severe, affecting virtually the entire spine. The disease almost always goes into remission (spontaneously) around the time of puberty with a resumption of normal bone growth at that time. Patients with mild or moderate forms of the disease may be left with a curvature of the spine (kyphosis) and short stature, but those with a more severe form of the disease may be incapacitated for life.

Primary osteoporosis is quite rare in young adults. In this age-group, the disease is usually caused by some other condition or factor, such as anorexia nervosa or glucocorticoid use (Khosla et al. 1994). When idiopathic forms of primary osteoporosis do occur in young adults, they appear in men as often as they do in women (this is in contrast to age-related primary osteoporosis, which occurs more often in women). The characteristics of the disease can vary broadly and may involve more than one disorder. Some young adults with idiopathic primary osteoporosis may have a primary defect in the regulation of bone cell function, resulting in depressed bone formation, increased bone resorption, or both. Others with a mild form of the disease may simply have failed to achieve an adequate amount of skeletal mass during growth. In some patients, the disease runs a mild course, even without treatment, and the clinical manifestations are limited to asymptomatic spinal compression fractures. More typically, however, multiple spine fractures occur over a 5–10 year period leading to a height loss of up to 6 inches.

Secondary Osteoporosis

Young adults and even older individuals who get osteoporosis often do so as a byproduct of another condition or medication use. In fact, there are a wide variety of diseases along with certain medications and toxic agents that can cause or contribute to the development of osteoporosis (Stein and Shane 2003).

Individuals who get the disease due to these “outside” causes are said to have “secondary” osteoporosis. They typically experience greater levels of bone loss than would be expected for a normal individual of the same age, gender, and race. Secondary causes of the disease are common in many premenopausal women and men with osteoporosis; in fact, by some estimates the majority of men with osteoporosis exhibit secondary causes of the disease (Orwoll 1998). In addition, up to a third of postmenopausal women with osteoporosis also have other conditions that may contribute to their bone loss (Tannenbaum et al. 2002).

Several genetic diseases have been linked to secondary osteoporosis. Idiopathic hyper-calciuria and cystic fibrosis are the most common. Patients with cystic fibrosis have markedly decreased bone density and increased fracture rates (Ott and Aitken 1998) due to a variety of factors, including calcium and vitamin D malabsorption, reduced sex steroid production and delayed puberty, and increased inflammatory cytokines. Some patients with idiopathic hypercalciuria have a renal defect in the ability of the kidney to conserve calcium. This condition may be aggravated if they are advised to lower their dietary calcium intake to prevent kidney stones.

Estrogen or testosterone deficiency during adolescence (due to Turner's, Kallman's, or Klinefelter's syndrome, anorexia nervosa, athletic amenorrhea, cancer, or any chronic illness that interferes with the onset of puberty) leads to low peak bone mass. Estrogen deficiency that develops after peak bone mass is achieved but before normal menopause (due to premature ovarian failure for example) is associated with rapid bone loss. Low sex steroid levels may also be responsible for reduced bone density in patients with androgen insensitivity or acromegaly. By contrast, excess thyroid hormone (thyrotoxicosis), may be associated with substantial bone loss (Ross 1994). Likewise, excess production of glucocorticoids caused by tumors of the pituitary or adrenal glands (Cushing's syndrome) can lead to rapidly progressive and severe osteoporosis, as can treatment with glucocorticoids.

Primary hyperparathyroidism is a relatively common condition in older individuals, especially postmenopausal women, that is caused by excessive secretion of parathyroid hormone. Most often, the cause is a benign tumor (adenoma) in one or more parathyroid glands.

Diseases that reduce intestinal absorption of calcium and phosphorus, or impair the availability of vitamin D, can also cause bone disease. Moderate

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malabsorption results in osteoporosis, but severe malabsorption may cause osteomalacia. Celiac disease, due to inflammation of the small intestine by ingestion of gluten, is an important and commonly overlooked cause of secondary osteoporosis (Bianchi and Bianchi 2002). Likewise, osteoporosis and fractures have been found in patients following surgery to remove part of the stomach (gastrectomy), especially in women. Bone loss is seen after gastric bypass surgery even in morbidly obese women who do not have low bone mass initially (Coates et al. 2004). Increased osteoporosis and fractures are also seen in patients with Crohn's disease and ulcerative colitis (Bernstein et al. 2000). Glucocorticoids, commonly used to treat both disorders, probably contribute to the bone loss. Similarly, diseases that impair liver function (primary biliary cirrhosis, chronic active hepatitis, cirrhosis due to hepatitis B and C, and alcoholic cirrhosis) may result in disturbances in vitamin D metabolism and may also cause bone loss by other mechanisms. Primary biliary cirrhosis is associated with particularly severe osteoporosis. Human immunodeficiency virus (HIV) infected patients also have a higher prevalence of osteopenia or osteoporosis (Brown et al. 2004). This may involve multiple endocrine, nutritional, and metabolic factors and may also be affected by the antiviral therapy that HIV patients receive (Thomas and Doherty 2003).

Autoimmune and allergic disorders are associated with bone loss and increased fracture risk. This is due not only to the effect of immobilization and the damage to bone by the products of inflammation from the disorders themselves, but also from the glucocorticoids that are used to treat these conditions (Lien et al. 2003, Orstavik et al. 2004). Rheumatic diseases like lupus and rheumatoid arthritis have both been associated with lower bone mass and an increased risk of fractures.

Many neurologic disorders are associated with impaired bone health and an increased risk of fracture (Lloyd, Spector et al. 2000). This may be due in part to the effects of these disorders on mobility and balance or to the effects of drugs used in treating these disorders on bone and mineral metabolism. Unfortunately, however, health care providers often fail to assess the bone health of patients who have these disorders or to provide appropriate preventive and therapeutic measures. For example, patients with stroke, spinal cord injury, or neurologic disorders show rapid bone loss in the affected areas (Altintas et al. 2003). There are many disabling conditions that can lead to bone loss, and thus it is important to pay attention to bone health in patients with developmental disabilities, such as cerebral palsy, as well as diseases affecting nerve and muscle, such as poliomyelitis and multiple sclerosis. Children and adolescents with these disorders are unlikely to achieve optimal peak bone mass, due both to an increase in bone resorption and a decrease in bone formation. In some cases very rapid bone loss can produce a large enough increase in blood calcium levels to produce symptoms (Go 2001). Fractures are common in these

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individuals not only because of bone loss, but also because of muscular weakness and neurologic impairment that increases the likelihood of falls. Epilepsy is another neurologic disorder that increases the risk of bone disease, primarily because of the adverse effects of anti-epileptic drugs. Many of the drugs used in epilepsy can impair vitamin D metabolism, probably by acting on the liver enzyme which converts vitamin D to 25 hydroxy vitamin D (Sheth 2002). In addition, there may be a direct effect of these agents on bone cells. Due to the negative bone-health effects of drugs, most epilepsy patients are at risk of developing osteoporosis. In those who have low vitamin D intakes, intestinal malabsorption, or low sun exposure, the additional effect of anti-epileptic drugs can lead to osteomalacia.

Psychiatric disorders can also have a negative impact on bone health. While anorexia nervosa is the psychiatric disorder that is most regularly associated with osteoporosis, major depression, a much more common disorder, is also associated with low bone mass and an increased risk of fracture (Hirsch et al. 2001). Many studies show lower BMD in depressed patients (Michelson et al. 1996). In addition, one large study found an increased incidence of falls and fractures among depressed women, even though there was no difference between their BMD and that of non-depressed women included in the study (Whooley, Kip et al. 1999). One factor that may cause bone loss in severely depressed individuals is increased production of cortisol, the adrenal stress hormone. Whatever the cause of low BMD and increased fracture risk, measurement of BMD is appropriate in both men and women with major depression. While the response of individuals with major depression to calcium, vitamin D, or antiresorptive therapy has not been specifically documented, it would seem reasonable to provide these preventive measures to patients at high risk.

Medication Induced Osteoporosis

Osteoporosis can also be a side effect of particular medical therapies

Glucocorticoid-Induced Osteoporosis (GIO). GIO is by far the most common form of osteoporosis produced by drug treatment. Glucocorticoids, which are used to treat a wide variety of inflammatory conditions (e.g., rheumatoid arthritis, asthma, emphysema, chronic lung disease), can cause profound reductions in bone formation and may, to a lesser extent, increase bone resorption (Saag 2002), leading to loss of trabecular bone at the spine and hip, especially in postmenopausal women and older men. The most rapid bone loss occurs early in the course of treatment, and even small doses (equivalent to 2.5–7.5 mg prednisone per day) are associated with an increase in fractures (van Staa et al. 2002). The risk of fractures increases rapidly in patients treated with glucocorticoids, even before much bone has been lost. This rapid increase in fracture risk is attributed to damage to the bone cells, which results in less

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healthy bone tissue. To avoid this problem, health care providers are urged to use the lowest possible dose of glucocorticoids for as short a time as possible.

Other Medications That Can Cause Osteoporosis. Cyclosporine A and tacrolimus are widely used in conjunction with glucocorticoids to prevent rejection after organ transplantation, and high doses of these drugs are associated with a particularly severe form of osteoporosis. Bone disease has also been reported with several frequently prescribed anticonvulsants, including diphenylhydantoin, phenobarbital, sodium valproate, and carbamazepine (Stein and Shane 2003). Patients who are most at risk of developing this type of bone disease include those on long-term therapy, high medication doses, multiple anticonvulsants, and/or simultaneous therapy with medications that raise liver enzyme levels. Low vitamin D intake, restricted sun exposure, and the presence of other chronic illnesses increase the risk, particularly among elderly and institutionalized individuals. In contrast, high intakes of vitamin A (retinal) may increase fracture risk (Michaelsson et al 2003). In addition, gonadotropin-releasing hormone (GnRH) agonists, which are used to treat endometriosis in women and prostate cancer in men, reduce both estrogen and testosterone levels, which may cause significant bone loss and fragility fractures (Smith 2003).

Rickets and Osteomalacia

Rickets (which affects children) and osteomalacia (which affects adults) are relatively uncommon diseases in the United States, since they can generally be prevented by ensuring adequate levels of vitamin D. These diseases can have devastating consequences to those who get them.

A number of childhood diseases cause rickets, a condition that results from a delay in depositing calcium phosphate mineral in growing bones, thus leading to skeletal deformities, especially bowed legs. In adults, the equivalent disease is called osteomalacia. Since longitudinal growth has stopped in adults, deficient bone mineralization does not cause skeletal deformity but can lead to fractures, particularly of weight-bearing bones such as the pelvis, hip, and feet. Even when there is no fracture, many patients with rickets and osteomalacia suffer from bone pain and can experience severe muscle weakness.

Rickets and osteomalacia are typically caused by any of a variety of environmental abnormalities. While rare, the disorder can also be inherited as a result of mutations in the gene producing the enzyme that converts 25-hydroxy vitamin D to the active form, 1,25-dihydroxy vitamin D, or in the gene responsible for the vitamin D receptor. Osteomalacia can also be caused by disorders that cause marked loss of phosphorus from the body. This can concur as a congenital disorder or can be acquired in patients who have tumors that produce a protein that affects phosphorus transport in the kidney.

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Since vitamin D is formed in the skin by sunlight, the most common cause is reduced sun exposure. This is particularly important in northern latitudes where the winter sun does not have the power to form vitamin D in the skin. Thus the disease is often seen in individuals living at northern latitudes, particularly immigrants who have pigmented skin that decreases the formation of vitamin D or who habitually cover themselves. This problem can also occur in children who are confined indoors and in individuals who are house-bound (e.g., due to chronic ill health or frailty). Patients with diseases of the gastrointestinal tract, such as gastrectomy, malabsorption syndromes, and small bowel resection, are also at higher risk, since these conditions reduce vitamin D absorption from the diet.

There is also a second form of rickets and osteomalacia that is caused by phosphate deficiency. This condition can be inherited (this is known as X-linked hypophosphatemic rickets), but it is more commonly the result of other factors. Individuals with diseases affecting the kidney's ability to retain phosphate rapidly are at risk of this condition, as are those with diseases of the renal tubule that affect the site of phosphate reabsorption. While most foods are rich in phosphate, phosphate deficiency may also result from consumption of very large amounts of antacids containing aluminum hydroxide, which prevents the absorption of dietary phosphate. Finally, rickets due to phosphate deficiency may occur in individuals with acquired or inherited defects in acid secretion by the kidney tubule and those who take certain drugs that interfere with phosphate absorption or the bone mineralization process.

There are also patients who develop tumors that secrete a factor that causes loss of phosphate from the body. This condition is called tumor-induced or oncogenic osteomalacia.

Renal Osteodystrophy

Patients with chronic renal disease are not only at risk of developing rickets and osteomalacia, but they are also at risk of a complex bone disease known as renal osteodystrophy. This condition is characterized by a stimulation of bone metabolism caused by an increase in parathyroid hormone and by a delay in bone mineralization that is caused by decreased kidney production of 1,25-dihydroxyvitamin D. In addition, some patients show a failure of bone formation, called adynamic bone disease. By the time the patient progresses to end-stage renal failure, clinical manifestations of the disease appear, including bone cysts that result from stimulation of osteoclasts by the excess parathyroid hormone. While dialysis can significantly extend the life-expectancy of patients with chronic renal failure, it does nothing to prevent further progression of the osteodystrophy. In fact, the managing of the patient through dialysis may lead to further bone abnormalities that become superimposed on the underlying osteodystrophy, thus

increasing the risk of fractures. While a renal transplant may reverse many features of renal osteodystrophy, the use of antirejection medication in transplant patients may cause bone loss and fractures.

Paget's Disease of Bone

Paget's disease of bone is a progressive, often crippling disorder of bone remodeling that commonly involves the spine, pelvis, legs, or skull. If diagnosed early, its impact can be minimized. Individuals with this condition experience an increase in bone loss at the affected site due to excess numbers of overactive osteoclasts. While bone formation increases to compensate for the loss, the rapid production of new bone leads to a disorganized structure. The resulting bone is expanded in size and associated with increased formation of blood vessels and connective tissue in the bone marrow. Such bone becomes more susceptible to deformity or fracture. Depending on the location, the condition may produce no clinical signs or symptoms, or it may be associated with bone pain, deformity, fracture, or osteoarthritis of the joints adjacent to the abnormal bone. Paget's disease of bone can also cause a variety of neurological complications as a result of compression of nerve tissue by pagetic bone.

Although Paget's disease is the second most common bone disease after osteoporosis, many questions remain regarding its pathogenesis. There is a strong familial predisposition for Paget's disease, but no single genetic abnormality has been identified that can explain all cases. Paget's disease can be transmitted across generations in an affected family; 15–40 percent of patients have a relative with the disorder (Morales-Piga et al. 1995). Studies in the United States (Siris et al. 1991) suggest that a close relative of a pagetic patient is seven times more likely to develop Paget's disease than is someone who does not have an affected relative. However, environmental factors are likely play a role in the majority of cases. For example, some studies have suggested that Paget's disease may result from a "slow virus" infection with measles (Friedrichs et al. 2002).

Developmental Skeletal Disorders

A large number of genetic and developmental disorders affect the skeleton. Among the more common and more important of these is a group of inherited disorders referred to as osteogenesis imperfecta or OI. Patients with this condition have bones that break easily. There are a number of forms of OI that result from different types of genetic defects or mutations. These defects interfere with the body's production of type I collagen, the underlying protein structure of bone. Most, but not all, forms of OI are inherited. The disease manifests through a variety of clinical signs and symptoms, ranging from severe manifestations that are incompatible with life to a relatively asymptomatic disease. However, most OI

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patients have low bone mass (osteopenia) and as a result suffer from recurrent fractures and resulting skeletal deformities. There are four main types of OI, which vary according to the severity and duration of the symptoms.

The most common form (Type I) is also the mildest version; and patients may have relatively few fractures. The second mildest form of the disease (which is called Type IV, because it was the fourth type of OI to be discovered) results in mild to moderate bone deformity, and sometimes in dental problems and hearing loss. These patients also sometimes have a blue, purple, or gray discoloration in the whites of their eyes, a condition known as blue sclera. A more severe form of the disease (Type III) results in relatively frequent fractures, and often in short stature, hearing loss, and dental problems. Finally, patients with the most severe form of the disease (Type II) typically suffer numerous fractures and severe bone deformity, generally leading to early death.

OI is not the only group of developmental skeletal disorders. An even larger group of rare diseases (sclerosing bone disorders) causes an increase in bone mass (Whyte 2003). One of these, osteopetrosis (marble bone disease), is more or less the opposite of osteoporosis. Instead of overactive osteoclasts, osteopetrosis results from a variety of genetic defects that impair the ability of osteoclasts to resorb bone. This interferes with the normal development of the skeleton and leads to excessive bone accumulation. Although such bone is very dense, it is also brittle and thus fractures often result. In addition, by compressing various nerves, the excess bone in patients with osteopetrosis may cause neurological symptoms, such as deafness or blindness. These patients may also suffer anemia, as blood-forming cells in the bone marrow are “crowded out” by the excess bone. Similar symptoms can result from over-activity of these bone cells, as in fibrous dysplasia where bone-forming cells produce too much connective tissue.

Bone Tumors

Some other skeletal disorders are not inherited but rather develop only later in life. One of the most common of these acquired skeletal disorders is a tumor of the bone. Bone tumors can originate in the bone (these are known as primary tumors) or, much more commonly, result from the seeding of bone by tumors outside of the skeleton (these are known as metastatic tumors, since they have spread from elsewhere). Both types of tumors can destroy bone, although some metastatic tumors can actually increase bone formation. Primary bone tumors can be either benign (noncancerous) or malignant (cancerous).

The most common benign bone tumor is osteochondroma, while the most common malignant ones are osteosarcoma and Ewing's sarcoma. Metastatic tumors are often the result of breast or prostate cancer that has spread to the

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bone. These may destroy bone (osteolytic lesion) or cause new bone formation (osteoblastic lesion). Breast cancer metastases are usually osteolytic, while most prostate cancer metastases are osteoblastic, though they still destroy bone structure. Many tumor cells produce parathyroid hormone related peptide, which increases bone resorption (Bryden et al. 2002). This process of tumor-induced bone resorption leads to the release of growth factors stored in bone, which in turn increases tumor growth still further.

Bone destruction also occurs in the vast majority (over 80 percent) of patients with another type of cancer, multiple myeloma, which is a malignancy of the plasma cells that produce antibodies. The myeloma cells secrete cytokines, substances that may stimulate osteoclasts and inhibit osteoblasts (Tian et al. 2003). The bone destruction can cause severe bone pain, pathologic fractures, spinal cord compression, and life-threatening increases in blood calcium levels (Callander and Roodman 2001). A benign form of overproduction of antibodies, called monoclonal gammopathy, may also be associated with increased fracture risk.

Bone-resorbing cytokines are also produced in acute and chronic leukemia, Burkitt's lymphoma, and non-Hodgkin's lymphoma; patients with these chronic lymphoproliferative disorders often have associated osteoporosis. Both osteoporosis and osteosclerosis (thickening of trabecular bone) have been reported in association with systemic mastocytosis, a condition of abnormal mast cell proliferation. In addition, there are other infiltrative processes that affect bone, including infections and marrow fibrosis (myelofibrosis).

Assessing Bone Health

The first step for health care providers in assessing individuals is to identify the relatively small number of younger individuals (out of the majority of individuals who do not have bone disease) who require further evaluation. This initial assessment ensures that more extensive (and expensive) testing is reserved for those who likely need it. This multi-pronged process is described below.

Identify Potential Risk Factors

Although there is a great deal more that needs to be discovered about which risk factors are most important for deciding to measure bone mineral density (BMD) in younger men and women (i.e., those for whom BMD is not recommended because of age alone), enough information already exists to dramatically improve diagnosis, prevention, and treatment of bone disease. That information needs to be applied more broadly by health care professionals.

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All individuals, young and old, should be assessed to determine how many (if any) of these risk factors they have, and then those with a sufficient degree of risk need to undergo further evaluation (often a BMD test) to determine the appropriate next course of action (e.g., changes to lifestyle, pharmacologic treatment). If these steps are taken, much can be done to decrease the burden of bone disease in the population, and much illness and suffering can be avoided. This risk factor analysis is also critical in ensuring the efficient use of health care resources, helping to identify those at-risk individuals in need of BMD testing and potentially treatments without the need for expensive, universal screening. Finally, it is important to remember that bone health can be compromised at any age, and thus the risks for poor bone health should be evaluated in individuals of all ages. Assessment of calcium and vitamin D intake, physical activity, and adverse behaviors such as smoking should be part of health care for all.

Indicators of Compromised Bone Health

There are a number of indicators that might signal potential problems with an individual's bone health at different ages. These "red flags" apply to both men and women.

One of the most important indicators is a previous fragility-related fracture, as such a fracture is one of the strongest indicators that an individual may have osteoporosis or some other metabolic bone disease (Haentjens et al. 2003). Any individual with a history of fractures related to only mild or moderate trauma (e.g., a fall from standing height or less) should be assessed further for the potential for bone disease.

Another important indicator relates to family history of the disease, since there is a component of heredity not only in osteoporosis, but also in Paget's disease and hyperparathyroidism as well as congenital disorders such as osteogenesis imperfecta. Health care professionals should be alert to looking for other family members who have bone disease.

Low body weight is another important "red flag" signaling the potential for osteoporosis; low body weight is associated with lower BMD and greater bone loss, even in premenopausal women. Moreover, weight loss of more than 1 percent per year in the elderly is associated with more rapid bone loss and increased risk of fracture (Ensrud et al. 2003).

There are other potential indicators as well. While bone disease is rare in children, the possibility of congenital disorders should be considered when children fracture, particularly with little trauma. In adolescents, health care professionals should consider abnormalities of sex hormone function, particularly at puberty, to be a potential risk factor, along with late onset of sexual

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development or loss of sexual function with cessation of menstrual periods. This is often related to marked weight reduction, in anorexia nervosa, or to intense physical activity, in the athletic amenorrhea syndrome. Individuals of all ages with calcium and vitamin D deficiency or prolonged immobilization and paralysis should also be carefully evaluated, as should those who have other diseases that increase the risk of bone loss and fractures, including gastrointestinal and kidney disorders and arthritis.

Those patients being treated with drugs that affect bone metabolism (e.g., glucocorticoids) should also be considered as potentially being at risk. Finally, patients already diagnosed with osteoporosis should be screened for secondary, treatable causes of the disease, especially in men or premenopausal women who suffer fragility fractures. Diseases linked to secondary osteoporosis are relatively uncommon in the population, but they can have a devastating effect on the bone health of the patients with these conditions and consequently may require specific treatment.

Risk Assessment Tools

Population-wide BMD testing is not a cost-effective or practical method for assessing the risk of bone disease. While BMD testing has been recommended for some populations (women over age 65), BMD tests are not routinely used for other individuals, the vast majority of whom do not have and are not at risk for bone disease. Widespread BMD testing makes little economic or medical sense. Rather, the evidence supports the assessment of other risk factors first, in order to identify a subset of at-risk individuals who are most likely to benefit from the test (e.g., younger women with multiple risk factors and both men and women who have had fragility fractures or who have diseases that can greatly increase fracture risk).

There is great interest in developing a screening tool or “clinical prediction rule” based on risk factors that can easily be assessed clinically (e.g., height and weight) or by patient report (e.g., personal or family history of fracture). The goal of a risk factor assessment tool is to produce a more individualized approach to diagnosis and treatment for all age, gender, and ethnic groups. Ideally, nurses and other nonphysician health care professionals should be able to administer the tool (e.g., by having a patient fill out a short questionnaire) and interpret the results, thus allowing someone other than the busy physician to play a lead role in identifying at-risk individuals.

A number of risk-factor assessment tools are in various stages of development.

The National Osteoporosis Foundation (NOF) checklist, for example, may be suitable for individual self-assessment. Individuals can use this checklist and discuss any concerns about their bone health at their next medical encounter.

The Osteoporosis Risk Assessment Instrument (ORAI) calculates scores based on age, weight, and current estrogen use; it has a sensitivity of 93 percent—i.e., it identifies 93 percent of the people with low BMD—and specificity of 39 percent—i.e., 61 percent of the people identified do not have low BMD (Cadarette et al. 2004).

The Simple Calculated Osteoporosis Risk Estimation (SCORE) considers six risk factors—age, race, weight, estrogen use, rheumatoid arthritis, and personal fracture history—and has a sensitivity of 91 percent and specificity of 40 percent (Lydick et al. 1998), results that are quite similar to the ORAI tool.

The Osteoporosis Self-Assessment Tool (OST) uses only two risk factors—age and weight—and also has similar sensitivity (92 percent) and higher specificity (46 percent) (Richy et al. 2004).

Efforts have also begun to expand clinical risk assessment tools beyond the question of who should get a BMD test. Tools are being developed to assess not just the risk of low BMD, but also the risk for fractures (which is ultimately what we are trying to prevent). Individuals identified as having a high risk of fracture can be targeted for early intervention. A recently developed tool allows for a more global assessment of risk factors. The risk factors used to develop this tool were derived from the large “Study of Osteoporotic Fractures” (Cummings et al. 1995). This study identified numerous risk factors for hip fracture in elderly White women that are independent of BMD or personal fracture history. These risk factors relate to genetic influences on bone size (e.g., maternal fracture history) and bone turnover, lifestyle issues (e.g., exercise), height loss, weight changes, and other factors. These risk factors have been proven to be important in identifying fracture risk.

One of the most important needs going forward with respect to risk assessment tools is to incorporate the risk of falling into the system, since so many fragility-related fractures occur as a direct result of a fall. Risk factors for falling include visual or cognitive impairment, use of specific medications, and gait and balance disorders. Poor vision is a particularly important risk factor for the elderly (even those with glasses), since many elderly individuals do not have their eyes and glasses checked regularly.

Those individuals who are identified as being both at risk of bone disease and at high risk of a fall might become candidates for further intervention, including exercise programs to improve strength and balance, modifications to the home

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environment, changes in medications that might make one prone to fall, and use of hip protectors to “cushion the blow” from a fall.

Measuring Bone Mineral Density (BMD)

BMD testing remains the “gold standard” test for those at risk of osteoporosis. The reason for this is relatively straightforward—in the laboratory, bone strength is strongly related to BMD. More importantly, BMD remains a strong independent predictor of fracture risk. In fact, there is a clear relationship between BMD and fracture risk in older women. For each standard deviation decrease in BMD (in the spine, a one-standard deviation drop represents a loss of 10–12 percent of BMD), the risk of fracture increases by 1.5–2.5 times. The relationship between BMD and fracture is stronger than the relationship between cholesterol and heart attack, and as strong as the relationship between blood pressure and stroke (Marshall et al. 1996). BMD measurement can be used to assess fracture risk and to establish the diagnosis and severity of osteoporosis. BMD testing can be used to assess changes over time (monitoring) in treated and untreated individuals. It is important to note that while standard x-rays are used to diagnose fractures, they are not useful for measuring bone mass. It is estimated that one must lose 30 percent of BMD for bone loss to be noted on x-ray; furthermore, an improperly performed x-ray in a normal person may have the appearance of bone loss.

Recommendations for Screening

The U.S. Preventive Services Task Force (USPSTF) recommends bone density screening for all women age 65 and older and for younger postmenopausal women age 60–64 who are at high risk (body weight less than 70 kilograms, no current use of estrogen) (U.S. Preventive Services Task Force 2002). Risk factors that should also be considered include smoking, weight loss, family history, decreased physical activity, alcohol or caffeine use, or low calcium and vitamin D intake.

BMD testing is also recommended for men who present with fractures or are receiving treatment with a GNRH agonist for prostate cancer, as well as for all individuals who have primary hyperparathyroidism or are on long-term glucocorticoid treatment.

BMD testing should also be performed on any individual who has other potential risk factors for osteoporosis, especially anyone who has had a low-trauma fracture or who exhibit another clinical indication of osteoporosis (e.g., x-ray evidence of low bone mass), as well as those who have diseases or conditions known to cause increased bone loss (e.g., hyperthyroidism [increased activity of the thyroid gland in the neck], hyperparathyroidism [increased activity of the parathyroid gland in the neck], rheumatoid arthritis, certain diseases of the

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stomach or intestines, long-term menstrual irregularities, cessation of menstrual bleeding) and those who are using a medication that may cause increased bone loss (e.g., glucocorticoids, excessive doses of thyroid hormone, certain blood thinners, certain drugs that treat seizures, drugs that block sex hormone production) (Leib et al. 2004).

Methods for Measuring BMD

The most widely accepted method for measuring BMD is dual x-ray absorptiometry (DXA). DXA is very safe, as it involves levels of radiation that are lower than that derived from daily background radiation from the sky when taking a trans-Atlantic airplane flight, and much lower than those from undergoing an x-ray of the back. DXA measures BMD in the spine and hip, sites that are likely to fracture in patients who have osteoporosis. These central skeletal sites are also most appropriate for monitoring the effectiveness of therapy, as they are more likely than peripheral sites to show an increase in BMD in response to treatment. DXA is precise and permits monitoring of patients over time. DXA also can be used to measure bone density in the forearm and whole body.

Several other techniques are available for bone mass measurement and are described briefly below (Grampp et al. 1997). While these methods do assess bone density and may provide an indication of fracture risk, it is important to note that the WHO recommendations and other guidelines for using BMD and interpreting BMD results for diagnosis are based on DXA measurements of the hip or spine. In the future, these alternative tests may be further refined and others may be developed, thus improving the ability to identify individuals at risk of osteoporosis.

Peripheral DXA (pDXA) uses scaled-down DXA instrumentation to measure peripheral sites such as the forearm, heel, or finger. These tests can help to identify at-risk individuals who are most likely to benefit from further BMD testing. Using the test for this purpose is tricky, requiring the setting of a proper threshold for determining who needs further evaluation. A too-low threshold could prove ineffective in screening, with the result being that many healthy individuals undergo further (expensive) evaluation. A too-high threshold could result in at-risk individuals being “screened out” and thus failing to receive further evaluation that could have resulted in timely diagnosis and treatment of bone disease. At present there is no scoring system for peripheral DXA that has been found to be preferable to using risk factor analysis as a means of determining who should and should not undergo DXA of the spine and hip.

Peripheral quantitative computed tomography (pQCT) uses specialized equipment to measure cortical bone (the outer, more solid shell of bone) and cancellous bone (the inner, honeycomb-like bone) in the forearm. This technique is used primarily for research.

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Quantitative computed tomography (QCT) uses standard computed tomography equipment, usually with a phantom that must be scanned with the patient. It provides a true volumetric measurement of cancellous bone density in the spine. Although it involves greater radiation exposure, it may be used as an alternative to spine and hip DXA measurements.

Quantitative ultrasound (QUS) uses sound waves to assess bone mass and thus does not use radiation. It can be used to measure bone in a variety of peripheral sites, such as the heel, tibia (leg), radius (wrist), and finger. Ultrasound devices measure the speed of sound (SOS), as well as specific changes in sound waves (i.e., broadband attenuation or BUA) as the sound waves pass through bone. Most devices use a formula to calculate a bone density equivalent or “T-score equivalent.”

Radiogrammetry uses measurements derived from standard x-rays of the hand to determine an index that compares cortical thickness with the total bone width in the mid-shaft of at least two metacarpal (palm) bones.

Radiographic absorptiometry (RA), also called photodensitometry, uses a standard x-ray of the hand to measure density in the middle bones of the second, third, and fourth fingers. Specialized equipment is used to scan the film at high resolution, and special software is used to calculate bone volume and bone density. The cortical thickness of the bones also can be measured.

Single x-ray absorptiometry (SXA) is used to measure peripheral sites such as the heel and forearm. The body part being measured is immersed in a water bath or water equivalent device. The SXA picture is similar to that obtained with DXA technology.

Incorporating these techniques for bone assessment into future clinical trials and observational studies will help in better understanding their appropriate use as a means of predicting the risk of bone disease and fracture.

Using and Interpreting BMD Measurements

An individual’s BMD can be compared to the mean value in a reference population, such as young healthy adults. The difference between an individual’s BMD and the mean BMD for the reference population can be expressed in standard deviation (SD) units; a score of 0 indicates BMD equal to the mean; a score of +1 indicates one standard deviation above the mean, and a score of -1 is one standard deviation below. When an individual’s BMD is compared to the mean BMD score in a young healthy population, this standard deviation measurement is referred to as a T-score. The T-score is calculated using the following formula:

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T-Score = Patient's BMD – Young Normal Mean

In 1994, a working group of the World Health Organization developed a classification system for osteoporosis based on BMD using the known gradient of the risk of fracture in the population as a whole. They sought to define osteoporosis using BMD so that the proportion of individuals identified as having osteoporosis by this method would be related to the lifetime risk of fracture in the population. Four general diagnostic categories were proposed for assessments done with DXA (Kanis 1994, Kanis 2002b):

Normal: Hip BMD that is no more than 1 standard deviation below the young adult female reference mean (T-score greater than -1).

Low bone mass (osteopenia): Hip BMD that is between 1–2.5 standard deviations below the young adult female mean (T-score less than -1 and greater than -2.5).

Osteoporosis: Hip BMD that is 2.5 standard deviations or more below the young adult female mean (T-score less than -2.5).

Severe osteoporosis (established osteoporosis): Hip BMD that is 2.5 standard deviations or more below the young adult mean in the presence of one or more fragility fractures.

In the young healthy population, about 15 percent of the women have a T-score of less than -1 and thus have low bone mass or osteopenia, while about 0.5 percent of women fall into the osteoporotic range, with a T-score of -2.5 or less. The proportion of women affected by osteoporosis increases with age as average bone density declines and risk of fracture increases.

Not everyone with low BMD has osteoporosis; osteomalacia and other bone disorders should also be considered. In addition, as noted previously, low bone density is not the only risk factor for fracture; other factors include age, risk of falling, risk of injury, previous low-trauma fracture, family history of osteoporosis, etc.

Biochemical Markers

One major thrust relates to efforts to identify “markers” that reflect the rates at which bone breaks down and builds up. Tests are now available that look for specific blood and urine markers that reflect the rate of each of these processes for the whole skeleton. While BMD measurements provide valuable information on fracture risk, they contribute no insight into the rate of bone turnover in a given patient. To the extent that the imbalance in the rate of bone resorption and formation may predict the rate of bone loss or enhance the ability to predict the

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risk of fracture, biochemical markers of bone turnover have the potential to complement the information provided by BMD measurements.

Resorption Markers.

Resorption markers are primarily based on measurement of collagen breakdown products that are released into the circulation as bone is resorbed. In recent years rapid and relatively inexpensive tests capable of measuring these breakdown products have been developed, representing a major advance in this area. Most commonly used are the tests for urine and, more recently, blood (serum) (Looker et al. 2000) These markers measure cross-linked (connected) fragments of type I collagen that are released as bone collagen is broken down. While initially a sophisticated technique was required to measure these molecules, there are now a number of relatively easy to perform tests that can measure them in the blood and urine.

Formation Markers.

Since bone resorption and formation are coupled processes, blood-based bone formation markers are also useful in assessing bone turnover. Osteocalcin and bone specific alkaline phosphatase (BSAP) can serve as such markers, as they are proteins that are made during the process of bone formation. In addition, since a major product of osteoblasts is type I collagen, tests have also been developed that can measure fragments of the collagen precursor chain that are removed and released into the circulation during the processing of the collagen precursor molecule in bone.

Treatment of Osteoporotic Fractures

For all osteoporotic fractures, the consistent goal is for patients to regain their pre-fracture level of function. All patients with low-trauma fractures should be evaluated for other bone diseases (see below) and secondary causes of bone loss. They should also be evaluated with respect to the need for additional preventive measures (calcium, vitamin D, exercise, fall prevention) and for drug therapy.

Hip Fractures

Surgery is the most common treatment for individuals who suffer a hip fracture. Virtually all intertrochanteric fractures and most femoral neck fractures are surgically stabilized with the use of internal metal devices. A large percentage of displaced femoral neck fractures are treated with partial or total replacement of the hip because of the significant risk of healing complications.

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Proper management of hip fracture patients begins before surgery, at the time of admission. Evaluation and management of pre-existing medical conditions is necessary before proceeding to surgery. When possible, management of pre-existing conditions and surgical repair within 24–48 hours of admission has been shown to decrease the incidence of post-surgery complications and the possibility of death within a year of surgery by more than 40 percent (Zuckerman et al. 1995). The vast majority of hip fracture patients should be encouraged to become mobile by the first or second post-operative day. Mobility can help to avoid the medical problems associated with prolonged bed rest, such as muscle atrophy, blood clots in the legs or lungs, pressure sores, skin breakdown, and overall deconditioning.

The use of antibiotics for the first 24–48 hours after surgery is also advisable, as this practice has been shown to be effective in decreasing post-surgery infections. Use of techniques to thin the blood after surgery has also been shown to be effective in decreasing the incidence of blood clots, particularly in patients who are slow to mobilize (Todd et al. 1995). Adequate pre- and post-surgery pain control is also important, not only for patient comfort, but also to promote active participation in rehabilitation.

Since hip fractures generally occur in elderly patients with other, associated medical and psychosocial problems, the health care team should include professionals from many disciplines, including the orthopaedic surgeon, medical specialists (geriatricians, physiatrists, primary care physicians, and medical subspecialists as necessary), nurses, physical and occupational therapists, nutritionists, and social workers.

Spine Fractures

Spine fractures usually occur in the middle or lower section of the back as a result of minor strain, such as lifting a grocery bag. Some patients develop fractures without any identifiable trauma. Spine fractures due to osteoporosis result in the progressive collapse of bones in these areas, which typically cause increasing levels of spinal deformity and pain. However, about 67% of spine fractures go undiagnosed because there is little or no pain, or the pain is attributed to one of the many other causes of back pain (Johnell et al. 2002). Similarly, other signs of a spine fracture, including deformities and height loss, are often accepted as a normal part of aging and thus not investigated further.

It is not unusual for patients to have prolonged pain and disability following spine fractures. Treatment of spine fractures typically focuses on pain control and progressive increases in levels of mobilization. Back braces are of limited benefit. More recently, procedures have been developed to treat patients who have prolonged pain. Vertebroplasty is a technique in which acrylic cement (or

orthopedic cement mixture) is injected into the spine bone for the purpose of stabilizing the fracture (Evans et al. 2003). Kyphoplasty involves using a balloon to re-expand the collapsed bone and then filling the cavity with bone cement. This procedure has the potential to stabilize the fracture, prevent further collapse, and restore some degree of height to the bone (Lieberman et al. 2001). Both vertebroplasty and kyphoplasty have been shown to provide effective pain relief and stabilization of the fracture. Although complications from these procedures have been infrequent, they can be significant if the bone cement leaks out into the blood stream or into the spinal canal, causing nerve damage. Unfortunately, the potential benefit of these two procedures has not yet been accurately assessed in RPCTs, where they might be compared to each other and to nonsurgical management.

Wrist Fractures

Wrist fractures commonly occur as a result of osteoporosis. They include fractures of the radius and/or ulna, as well as of the small bones of the wrist. The term Colles' fractures refers to fractures of the end of the radius, which has a large amount of trabecular bone. Wrist fractures are usually treated by either surgical repositioning and casting or placement of an external fixation device to prevent further fracture. Depending on the type of fracture, one of the following will be used to immobilize the wrist until an x-ray shows evidence of healing (usually in 4–8 weeks): a brace or splint, cast, external fixation, internal fixation, or combined external and internal fixation. Although most patients return to an adequate level of functioning, many do experience some loss of range of motion of the wrist.

Rehabilitation of Osteoporotic Fractures

Hip Fractures

As noted previously, hip fracture patients typically undergo surgery to reposition the hip through internal fixation or to replace the hip through joint replacement. Immediately following either type of surgery, in-hospital rehabilitation focuses on training the patient to safely move in bed, to get out of bed, and to begin walking with partial weight-bearing on the surgical side using either a walker or crutches.

Since the inpatient hospital stay typically is limited to 2–3 days after surgery, most patients require additional rehabilitation. Transfer to a rehabilitation facility is common, with length of stay in this setting ranging from several days to several weeks. Following discharge to home, rehabilitation is continued through in-home therapy with a physical therapist or visits to an outpatient facility. This phase of

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the rehabilitation focuses on general conditioning, strengthening of muscle, and walking longer distances on different terrains and with less assistance. The degree to which a patient progresses from relying on the support of assistive devices during walking to more complete weight-bearing on the fractured limb will depend on the type of surgery and implanted metal as well as the physical condition of the patient. The “typical” patient progresses from a walker to a four-footed cane to a single-point cane to no assistive device for walking. However, 85 percent of patients still use an assistive device for walking 6 months after the fracture (Marotolli et al. 1992).

Nutrition has been shown to be important during recovery from hip fracture. Supplementation with calcium, vitamin D, and protein (20 grams per day) have been reported to improve hospital and rehabilitation courses and to increase BMD a year after the fracture (Schurch et al. 1998).

Six months after hospital discharge, an evaluation should be performed to determine the patient’s functional status and to set goals for the future. Many patients require further therapy to reach these goals, whereas others may have reached their potential.

Spine Fractures

As noted above, only about one-third of spine fractures come to clinical attention, but those that do usually are painful. Therefore, pain control is a high priority after the initial spine fractures and after multiple fractures, when chronic pain often becomes a problem. Bedrest should be partial (resting in bed interspersed with 30- to 60-minute periods of erect sitting, standing, and walking) and limited to 4 days or less. Individuals should be taught to position themselves (e.g., while sitting, standing, or lying down) and to move (e.g., when lifting, dressing, doing housework) while maintaining good posture, which reduces loads on the fracture and minimizes pain. To minimize pain and decrease risk of a new spine fracture, family members should be taught to assist patients in performing tasks without increasing the loads on the patient’s spine.

Walking should be encouraged even in frail individuals. A gradual progression starting at only 2–3 minutes and working up to twenty or more minutes can be achieved by adding a minute or two to walking sessions each week. Short-term use of a back brace is recommended when trunk weakness prevents a patient from maintaining an upright posture. Weaning from the device, as muscle strength and endurance improve, will maximize recovery. However, in some patients with chronic pain and deformity, continued use of a flexible support device that helps maintain back strength and posture may be helpful in reducing pain and improving function (Pfeifer et al. 2004). If walking is limited due to pain, use of a rolling walker with four wheels and hand brakes may help the patient

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stay active during recovery, thus preventing loss of muscle strength and bone mass. This type of walker allows the use of the arms to keep the trunk erect, thereby shifting the weight of the upper body away from the newly fractured bone. Individuals with a new spine fracture should avoid use of a standard walker, since each time the walker is lifted the loads on the vertebral bodies are increased.

Exercising in a way that safely challenges balance is also important for rehabilitation of spinal fracture patients, although this exercise must be accompanied by an assessment of the risk of falling and the addressing of modifiable risk factors for falling, such as vision problems, medications that cause dizziness, and hazards in the home. Active range of motion exercises should be continued during recovery, but resistance/strengthening exercises should not be initiated or resumed until the fracture has healed (in approximately 8 to 12 weeks). Since the risk of another spine fracture is high in patients who have had fractures, patients should be instructed to avoid exercises and activities that put high loads on the bones of the spine, such as flexing or rotating the spine (sit ups, toe touches). Exercises and activities done with good spine alignment and low to moderate amounts of weight should be gradually increased, with the goals of regaining muscle strength and promoting maintenance of bone mass. Abdominal strengthening (by tightening the muscles in the abdomen or belly without moving the back) is safe and important to reducing loads on the low back. Spinal extension exercise within a moderate range is safe and can improve hyperkyphosis and may help prevent new spine fractures (Sinaki et al. 2002).

Wrist Fractures

Rehabilitation of the wrist after the cast, brace, or surgical metal is removed requires about 3 months, but reaching maximum levels of recovery can take up to 24 months, and some problems may persist for years. During healing of a wrist fracture, all of the following are important: arm elevation; early mobilization of the hand, elbow, and shoulder; and control of swelling. Progressive exercises typically include active and passive range of motion and resistance and grip strengthening, such as squeezing a ball. A small number of patients suffer from sympathetic dystrophy after a wrist fracture, resulting in swelling, weakness, and chronic pain in the wrist.

Treatment of Other Bone Diseases

There are specific, effective (and often curative) treatments for a number of bone diseases other than osteoporosis, including hyper-parathyroidism, rickets, and osteomalacia. There is also treatment available for some congenital bone

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disorders and for bone disease associated with kidney failure. Early recognition and treatment of all of these conditions is the key to avoiding crippling deformities and fractures.

Primary Hyperparathyroidism

Primary hyperparathyroidism is caused by an excessive release of PTH from one or more of the parathyroid glands. Surgical removal of the parathyroid adenoma (benign tumor) or of three-and-a-half glands (if all four glands are enlarged) often cures the disease. Patients who are clearly symptomatic with bone disease or kidney stones should be advised to have surgery. There is considerable controversy concerning the need for intervention in patients who have no clear signs or symptoms of the disease. Treatment guidelines for non-symptomatic patients relate to the degree of hypercalcemia (greater than 1 mg/dL serum calcium above the upper limits of normal), hypercalciuria (greater than 400 mg per day urine calcium), and age (under age 50).

Currently, there are no FDA-approved medications for primary hyperparathyroidism. However, medical therapy may be available in the future. Specifically, calcimimetic (calcium-mimicking) agents, which can inhibit parathyroid hormone secretion, offer a direct approach to the medical therapy of primary hyperparathyroidism. Antiresorptive therapy can be used in patients with primary hyperparathyroidism and low bone mass who refuse surgery or for whom surgery is contraindicated.

Renal Osteodystrophy

Treatment of renal osteodystrophy depends on the type of abnormality in the bone and on the stage of the renal disease. An important aspect of prevention of renal osteodystrophy is the early implementation of dietary phosphate and protein restriction, oral 1,25-dihydroxy vitamin D (calcitriol) treatment, and adequate oral intake of calcium and vitamin D.

Paget's Disease of Bone

The primary therapy involves use of bisphosphonates, which decrease bone resorption and slow bone turnover (Lyles et al. 2001). Alendronate, risedronate, tiludronate, and etidronate are bisphosphonates that are approved for the treatment of Paget's disease. Calcitonin (as an under-the-skin injection or nasal spray) has also been used to treat Paget's disease, but is less effective than bisphosphonates (Deal 2004). PTH should not be given to patients with Paget's disease.

Bone Cancer

There are some treatments available to treat bone metastases caused by cancers. Bisphosphonates, which are potent inhibitors of bone resorption, significantly reduce skeletal morbidity in patients with advanced breast cancer and can reduce metastasis to bone by human breast cancer cells in an experimental model. Pamidronate, a second generation bisphosphonate, has recently been approved by the FDA for treatment of breast cancer osteolysis. Zoledronic acid, a third-generation bisphosphonate, has also been approved for treatment of cancer patients. Another inhibitor of bone resorption, the protein osteoprotegerin, has also been shown to be effective in reducing bone metastases in animal models of breast and prostate cancer and in reducing bone pain in patients (Cancer Supplement 2003). Although bisphosphonates significantly reduce skeletal morbidity associated with solid tumor metastases to bone, most studies indicate no improvement in survival.

Osteogenesis Imperfecta

Treatment of patients is mainly oriented at preventing and treating fractures in these patients. It involves a team of health professionals that typically includes orthopedists, rehabilitation physicians, and physical therapists. Encouraging results have been reported with bisphosphonate therapy (Glorieux et al. 1998).

Falls and Fall Prevention

Background

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. 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,

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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.

Risk Factors for Falls

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. 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.

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

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of either set of factors. 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. 2001). 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.

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.

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. 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 2003). The optimal duration or intensity of these approaches has not been defined.

Reducing Falls

Guidelines issued by the American Geriatrics Society, British Geriatrics Society, and American Academy of Orthopedic Surgeons panel on falls prevention include the following recommendations for older persons:

- Providers should ask their older patients at least once a year about falls.
- Those who have fallen one or more times should have their balance and ability to walk evaluated.
- Those who need medical attention after a fall or who have fallen several times in the past year should have a fall evaluation. This evaluation should

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include taking a history related to the circumstances of the fall and performing an examination of vision, balance, walking, muscle strength, heart function, and blood pressure. A specialist, such as a geriatrician, may be needed for this evaluation.

- Health care providers should consider prescribing a program of physical activity and balance training, with an emphasis on those activities that may help reduce risk of falling.
- Physicians should review all patient medications (including over-the-counter ones) at least once per year.
- Vision should be checked annually.
- Homes should be evaluated for possible hazards that could cause a fall, such as loose rugs, poor lighting, electrical cords, or lack of handrails in the tub/shower.

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. 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).

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 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.

Impact of Bone Diseases

Mortality

While the chance of dying varies by fracture type, the vast majority of individuals suffering from osteoporosis and osteoporotic-related fractures do not die directly as a result of their disease. As noted previously, hip fractures are among the

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most devastating type of fracture; it has been estimated that approximately 20 percent of all patients die within a year (Leibson et al. 2002). The oldest hip fracture patients are most likely to die, and survival rates are lower for men (both White and Black) than for women, although Black women are more likely to die from a hip fracture than are White women. These differences may be due in part to the older age at which men and Black women are likely to suffer a hip fracture as well as to differences in their medical care. It is important to note, however, that the typical hip fracture patient is about 80 years old, and thus their risk of death from any cause is not trivial. Thus, it is more accurate to say that a hip fracture decreases the chance of survival in the first year by about 12–20 percent in this already at-risk population. Another way to look at this statistic is that 9 out of every 100 women with a hip fracture will die as a result of the fracture (Magaziner et al. 1997). The increased risk of death is especially high (10 times more than the expected death rate) in the first few weeks following a hip fracture. While the excess risk of death due to hip fractures diminishes with time, there may still be some additional risk for a number of years. For example, roughly 5 percent of hip fracture patients experience a severe medical complication, causing an increase in their risk of death (Lawrence et al. 2002). In addition, as noted previously, most hip fracture patients have other serious medical problems. Even so, with any given amount of preexisting comorbidity, the occurrence of a hip fracture substantially increases the likelihood of dying (Poór et al. 1995).

Other types of fractures are less likely to result in death. For example, patients suffering a wrist fracture are no more likely to die than anyone else (Melton 2003). Other limb fractures have been linked to an increased risk of death (Browner et al. 1996), although only a few of these deaths are related directly to the fracture.

Inherited bone diseases have been found to increase the risk of death; in fact, in some cases these diseases are so severe that they are incompatible with life. Likewise, survival is much reduced among patients with bone cancer and multiple myeloma (Praemer et al. 1999). It is unclear whether or not patients with primary hyperparathyroidism face an increased risk of death, although survival does appear to be worse for the most severely affected patients, including those with the highest blood calcium levels and those with other serious diseases (Vestergaard et al. 2003).

Morbidity

Bone diseases dramatically affect the functional status of those who get them. Many individuals who suffer fractures as a result of osteoporosis suffer significant pain, height loss, and may lose the ability to dress themselves, stand up, and walk. These patients are also at risk of acute complications such as pressure sores, pneumonia, and urinary tract infections. Nearly one in five ends up in a

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nursing home. Different types of osteoporotic fractures have a different impact on the patients who suffer them. Wrist fractures commonly occur in women in their mid-50s and usually have only a short-term impact, whereas spine fractures typically occur at a later age and may give rise to permanent morbidity. By contrast, hip fractures occur later in life (around age 80 on average) and usually result in permanent disability (Kanis and Johnell 1999).

Two-thirds of hip fracture patients do not return to the level of function they enjoyed before the fracture (OTA 1994), particularly those who become depressed (Magaziner et al. 2003). Many lose their ability to walk. In fact, only 40–79 percent of patients regain their previous ambulatory function a year after the fracture, and less than half return to their prefracture status with respect to the activities of daily living (Greendale and Barrett-Connor 2001). For example, data from the Established Populations for Epidemiologic Studies of the Elderly (EPESE) project show that 86 percent of patients could dress by themselves before the fracture, but only 49 percent afterwards. Similarly, 90 percent could move from chair to standing before the fracture and only 32 percent after. Comparable figures for walking across the room are 75 percent and 15 percent (Marottoli et al. 1992). Indeed, hip fracture patients are as likely to have impaired ambulation and other functional deficits as are those who suffer a stroke (Lieberman et al. 1999). Hip fractures cause an “extra” 10 percent of women to become functionally dependent (i.e., 10 percent more women become dependent than would have in the absence of the fractures), and 19 percent of women who suffer hip fractures require long-term nursing home care (Chrischilles et al. 1991).

Other types of fractures, while somewhat less devastating than hip fracture, nevertheless take a toll on those who suffer them. For example, while spine fractures rarely cause institutionalization, their adverse influence on most activities of daily living is almost as great as that seen for hip fractures (Greendale et al. 1995).

Wrist fractures seldom cause long-term disability, but they nonetheless are painful, requiring repositioning of the bones to their normal position and stabilization in a cast for 4–6 weeks. Recent studies suggest that wrist fractures may cause a number of short-term problems, including persistent pain, loss of function, nerve impairments (such as carpal tunnel syndrome), bone deformities, and arthritis (Greendale and Barrett-Connor 2001). In fact, nearly half of all patients report only fair or poor functional outcomes 6 months following a wrist fracture. Women and the elderly are the most likely to report such outcomes. There is no question that the overall impact of wrist fractures on a patient’s functional status is much less than that of a hip fracture. In fact, less than 1 percent of wrist fracture patients become completely dependent as a result of the fracture (Chrischilles et al. 1991). These fractures may be as disabling as hip

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fractures with respect to some specific activities of daily living such as meal preparation.

Financial Impact

Bone diseases are expensive, in terms of direct health care expenditures and indirect expenditures as well as lost productivity/workdays for patients and caregivers. While the figures cited below are large, it is important to remember that they represent today's costs. Given health care inflation and the projections for significant increases in the number of fractures, it is not unreasonable to assume that the direct and indirect costs of bone disease will more than double or triple in the coming decades (Burge et al. 2003).

Direct Costs

Studies show that annual direct care expenditures for osteoporotic fractures range from \$12.2–\$17.9 billion per year in 2002 dollars (Tosteson 1999). While women account for the majority of these costs, White men also incur substantial overall costs for osteoporotic fracture care (representing 18 percent of the total costs of osteoporosis, or \$3.2 billion). In addition, non-White women and men of all ages account for \$1 billion annually in total direct care expenditures on osteoporotic fractures (Ray et al. 1997).

Although large, expenditures related to osteoporosis represent just 7 percent of total health care costs among women age 45 and older (Hoerger et al. 1999). This is more than double the amount spent for gynecological cancers but only a fraction of the cost of cardiovascular disease. However, osteoporosis accounts for nearly 14 percent of all nursing home days, due to the late age at which expenses are incurred for osteoporosis relative to other diseases (Hoerger et al. 1999).

Hospital care accounts for more than half of the total direct costs, with nursing home care also responsible for a large portion of the total. As noted, hip fractures are the most devastating complication of osteoporosis, and therefore it is no surprise that they account for the largest proportion (63 percent or \$11.3 billion) of medical care costs. This is because hip fractures are very expensive to treat, with per-fracture costs estimated to range from \$30,100–\$43,400 in 2002 dollars (Tosteson 1999). The costs of caring for hip fractures are not limited to this initial treatment, however, as those suffering hip fractures require follow-up care as a direct result of their injury. A recent study estimated that hospital and outpatient care (excluding nursing home care) due to a hip fracture adds \$14,600 to direct medical expenditures in the year following the fracture (Gabriel et al. 2002). The overall lifetime cost attributable to a hip fracture could exceed \$81,000 (Braithwaite et al. 2003).

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Although hip fractures account for the majority of costs, more than \$6.5 billion is spent annually to treat those suffering from other types of osteoporotic fractures (Ray et al. 1997).

The direct costs of osteoporotic fractures are typically borne by society, primarily through Medicare and Medicaid. Among women over age 45, the government pays for most of the costs of osteoporotic fractures: Medicaid covers almost a fourth of the expense and Medicare pays nearly half (Hoerger et al. 1999). This is to be expected since nearly three-quarters of all hip, spine, and distal forearm fractures occur among patients 65 years and over.

Indirect Costs

In addition to imposing direct medical costs on society, osteoporosis also results in indirect costs, primarily related to reduced productivity due to disability and premature death. Indirect costs are inherently difficult to measure, and much more needs to be done in this area. One method judges lost productivity on the basis of reduced earnings. For bone diseases, which affect a large number of retired persons, indirect costs are underestimated by this approach. Nonetheless, assuming that people are worth what they earn, one study estimates that the cost of premature death and of restricted activity resulting from fractures accounts for 26 percent of total fracture costs and 12 percent of hip fracture costs (Praemer et al. 1999). A recent study from California found that the indirect cost to society (based only on lost earnings from premature deaths) accounted for 17 percent of the total cost related to osteoporosis (Max et al. 2002).

Healthy Bones Lifestyle

Physical Activity

The foundation of a good physical activity regimen involves at least 30 minutes (adults) or 60 minutes (children) of moderate physical activity every day. This regimen can and should involve a variety of activities. Some can be routine activities like walking or gardening. Others may occur more infrequently and differ from day to day and week to week, such as dancing, aerobic classes, biking, swimming, tennis, golf, or hiking. However, it is clear from the evidence that physical activity to specifically benefit bone health should involve loading (stressing) the skeleton. As a result, weight-bearing activities such as walking should be included in an optimal physical activity regimen to benefit the musculoskeletal system. Moreover, the evidence suggests that the most beneficial physical activity regimens for bone health include strength-training or resistance-training activities. These activities place levels of loading on bone that are beyond those seen in everyday activities; examples include jumping for the

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lower limbs and weight lifting or resistance training for the lower and upper skeleton. Finally, while a focus on activities that build or maintain bone strength is appropriate and necessary, many older individuals will remain at high risk of fracture. For these individuals, balance training can provide the added benefit of helping to prevent potentially injurious falls.

The evidence does not lead to a specific set of exercises or practices but rather a set of principles that can be applied and varied according to the age and current physical condition of an individual. Many of these principles have been reviewed by expert panels of the American College of Sports Medicine (ACSM) (Kraemer et al. 2002) and they lead to the following suggestions for the frequency, intensity, length, and type of physical activity regimens to benefit bone health for individuals of all ages:

- Since continued physical activity provides a positive stimulus for bone, muscle, and other aspects of health, a lifelong commitment to physical activity and exercise is critical.
- Ending a physical activity regimen will result in bone mass returning to the level that existed before the activity began. Since repetitive programs of physical activity may be discontinued due to lack of motivation or interest, variety and creativity are important if physical activity is to be continued over the long term.
- Physical activity will only affect bone at the skeletal sites that are stressed (or loaded) by the activity. In other words, physical activity programs do not necessarily benefit the whole skeleton, although any type of activity provides more benefit to bone than does no activity at all.
- For bone gain to occur, the stimulus must be greater than that which the bone usually experiences. Static loads applied continuously (such as standing) do not promote increased bone mass.
- Complete lack of activity, such as periods of immobility, causes bone loss. When it is not possible to avoid immobility (e.g., bed rest during sickness), even brief daily weight-bearing movements can help to reduce bone loss.
- General physical activity every day and some weight-bearing, strength-building, and balance-enhancing activities 2 or more times a week are generally effective for promoting bone health for most persons.
- Any activity that imparts impact (such as jumping or skipping) may increase bone mass more than will low- and moderate-intensity, endurance-type activities, such as brisk walking. However, endurance activities may still play an important role in skeletal health by increasing muscle mass and strength, balance, and coordination, and they may also help prevent falls in the elderly. Endurance activity is also very important for other aspects of health, such as helping to prevent obesity, diabetes, or cardiovascular disease.
- Load-bearing physical activities such as jumping need not be engaged in for long periods of time to provide benefits to skeletal health. In fact, 5–10 minutes daily may suffice. Most adults should begin with weight-bearing

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exercise and gradually add some skipping and jumping activity. Longer periods (30–45 minutes) may be needed for weight training or walking/jogging. Those who have been inactive should work up to this amount of time gradually using a progressive program, e.g., start with shorter times and easier activities (light weights or walking) and then increase time or intensity slowly (by no more than 10 percent each week) in order to avoid injury.

- Physical activities that include a variety of loading patterns (such as strength training or aerobic classes) may promote increased bone mass more than do activities that involve normal or regular loading patterns (such as running).

These fundamental principles can be used to develop age-specific regimens, as outlined in the sections that follow.

Physical Activity for Children and Adolescents

For children over age 8 and adolescents, a bone-healthy program of physical activity could include the following:

- At least 60 minutes of moderate intensity, continuous activity on most days, preferably daily. This level of activity can help achieve a healthy body weight and lower the risk of other diseases such as cardiovascular disease and diabetes (IOM 2002).
- Inclusion of weight-bearing and short, intense impact activities such as basketball, gymnastics, and jumping as part of this regular activity program.
- Performance of weight-bearing activities that increase muscle strength, such as running, hopping, or skipping. The best activities work all muscle groups. Examples include gymnastics, basketball, volleyball, bicycling, and soccer. Swimming, while highly beneficial to many aspects of health, is not a weight-bearing activity and thus does not contribute to increased bone mass.

Physical Activity for Adults

Adults should strive to get at least 30 minutes of physical activity on most days, preferably daily (IOM 2002). As part of that regular physical activity program, the following can help enhance bone health:

- For those individuals who can tolerate impact activities, a simple, 10-minute program of physical activity that incorporates 50 3-inch (8-centimeter) jumps per day.
- A progressive program of weight training that uses all muscle groups, with the amount of weight lifted increased gradually over time.
- A jogging or stair-climbing program for those who cannot tolerate higher impact physical activity.
- Active recreational activities such as tennis, hiking, or basketball.

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In addition, it is advisable for adults to try to find ways to add extra weight-bearing exercise into everyday activities. For example, consider parking farther away in the parking lot or taking the stairs instead of the elevator.

It is also recommended that weight-bearing exercises and strength and balance training be added as a part of regular physical activity (Seguin and Nelson 2003). Lifestyle activities such as walking, gardening, and raking leaves can also be a valuable part of regular physical activity (USDHHS 1996).

It is important to begin any physical activity program slowly and to consider previous activity levels. Those who have been inactive should begin with 5–10 minutes of activity per day and a pre-exercise evaluation by a physician may be advised. Those who are more fit can increase physical activity levels to 20–30 minutes of moderate activity at a higher heart rate (60–85 percent of maximum heart rate). Generally, it is advisable to increase activity levels by no more than 10 percent each week to avoid injury. For example, those who begin with 15 minutes per day can progress to 17 minutes the second week, and so on.

Physical Activity for Older Adults

Most elderly individuals should strongly consider engaging in regular physical activity. Physical activity is the only single therapy that can simultaneously improve muscle mass, muscle strength, balance, and bone strength. As a result, it may decrease the risk of fractures, in part by reducing the risk of falling. In fact, fall-risk reduction may be the biggest benefit of physical activity for the elderly.

The following guidelines should be used to maximize the potential fall prevention benefits of physical activity in the elderly:

- Physical activity needs to be of sufficient intensity to improve muscle strength, since poor muscle strength is a known risk factor for falls. Strength or resistance training is best for building muscle, but even aerobic endurance activity can yield some improvements in muscle strength.
- Improving balance can be an important component of any physical activity program designed to decrease falls. This program may include balance training exercises or a movement activity such as Tai Chi. Any activity that requires weight bearing and challenges the postural system can improve balance and potentially help reduce falls.
- Physical activity must be performed on average 3 times per week for 30–45 minutes per session for at least three months for strength and balance benefits to be realized, and it must be continued if benefits are to be maintained.
- Those who suffer a fall that requires a visit to a health care provider or an emergency room should ask for a fall risk assessment that includes a program of physical activity. Physical activity is most effective if delivered as a part of a comprehensive fall prevention program.

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Nutrition

Since many nutrients are important for bone health, it is important to eat a well-balanced diet containing a variety of foods. Following the Dietary Guidelines for Americans (USDA 2000) can help, although attention should be paid to serving sizes. These guidelines urge individuals to eat 6–11 servings of grain foods, 3–5 servings of vegetables, 2–4 servings of fruits, 2–3 servings of dairy or other calcium-rich foods, and 2–3 servings of meat or beans each day.

Calcium

The Food and Nutrition Board (FNB) of the Institute of Medicine updated recommended intakes for several nutrients important to the skeleton in 1997, including calcium (IOM 1997). Recommended amounts of calcium differ by age. These recommendations are meant for healthy people. Those with osteoporosis or other chronic conditions may need more calcium, but unfortunately the calcium requirements for individuals with this disease have not yet been clearly identified (Heaney and Weaver 2003). The highest amount (1,300 mg per day) is recommended for children and adolescents ages 9–18, a period when bones are growing rapidly. Pregnant or lactating women are advised to consume an age-appropriate amount of calcium.

Americans obtain most of their calcium from dairy products. In fact, approximately three 8-ounce glasses of milk each day, combined with the calcium from the rest of a normal diet, is enough to meet the recommended daily requirements for most adults. Lowfat or nonfat versions of dairy products are good choices because they have the full amount of calcium, but help to avoid eating too much fat. Foods that have been fortified with calcium are also good sources of the nutrient. There are many foods that serve as good sources of calcium, including fortified cereal, nonfat milk, and calcium-fortified orange juice from frozen concentrate (Keller et al. 2002). Vegetables also contain calcium, but the amount of calcium absorbed from these sources varies; some, like broccoli and kale, contain calcium that is well absorbed, while others, such as spinach, do not (Weaver et al. 1999). It would be impractical for most people to eat enough vegetables or other low-calcium foods to meet recommended levels if these were the only sources of calcium in the diet.

Many individuals, especially non-Whites, suffer from lactose intolerance. These individuals may avoid dairy products, which can result in a low calcium intake unless other good sources of calcium are consumed. Those with lactose intolerance may develop the capability to digest lactose if they slowly build up milk intake over a period of days or weeks so that they develop an intestinal flora capable of digesting milk's lactose (Suarez et al. 1997). Many lactose-intolerant individuals can tolerate up to one cup of milk twice a day if it is consumed with food (McBean and Miller 1998). In addition, some other calcium-rich dairy products such as cheese and yogurt are usually well tolerated by lactose-intolerant people. Finally, there are a number of calcium-rich foods that do not

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contain lactose, including lactose-free milk, fortified soy beverage, and fortified juice and cereal.

The Institute of Medicine recommends that nutrients be obtained from food when possible because they provide a package of nutrients that are good for other tissues besides bones. However, fortified foods and supplements can assist those individuals who do not consume an adequate amount of dairy products or other naturally calcium-rich foods to meet recommended levels of calcium intake. Those who take supplements or consume fortified foods should note that: a) all major forms of calcium (e.g., carbonate, citrate) are absorbed well when taken with meals; b) calcium from supplements or fortified foods is best taken in several small doses (no more than 500–600 mg at one time) (Heaney 1975) throughout the day for better absorption; and c) supplements may differ in their absorbability due to manufacturing practices (IOM 1997). One need not choose the most expensive products on the market, as the cost of supplements of comparable quality can vary fivefold (Heaney et al. 2001). In a recent evaluation of calcium sources, calcium carbonate supplements were found to be the least expensive supplemental source of calcium. Since virtually all calcium sources—food or supplement—reduce the absorption of iron, calcium and iron supplements should be taken at different times.

Vitamin D

Most individuals need 200 IU of Vitamin D per day, although these recommendations are raised to 400 IU per day in those age 50–70, and to 600 IU per day in those over age 70. There are two sources of vitamin D: sunlight and dietary intake.

Vitamin D can be made in the skin by being exposed to sunlight. For some individuals, particularly children and others who get enough exposure during warmer months, the sun can provide adequate levels of vitamin D throughout the entire year. For many, however, it is not practical to get adequate levels of vitamin D from exposure to sunshine. These individuals should instead look to boost their vitamin D levels through diet. This is especially true for elderly individuals who have higher vitamin D needs and who may have difficulty getting outside everyday. People with dark skin and those who live in areas with heavy air pollution may also find it more practical to obtain most or all of their vitamin D from diet, since they need longer periods of sun exposure to get adequate levels of vitamin D. One cup of fortified milk contains 100 IU vitamin D, half of the recommended intake for individuals under age 50. Since vitamin D-fortified milk is not used when making cheese, ice cream, or most yogurts, many other dairy foods are not good sources of vitamin D. Other good dietary sources of vitamin D include fatty fish and vitamin D-fortified orange juice. The best way to know whether a dairy food contains vitamin D is to check the nutrition label.

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Vitamin D is also available in dietary supplements. While few supplements contain vitamin D alone, many calcium supplements also contain vitamin D. Multivitamin supplements contain up to 400 IU of vitamin D. The amount of vitamin D in a single dose of many calcium and multivitamin supplements may not be sufficient to meet the recommended levels, especially for people over age 70 who need 600 IU per day. To make sure that the recommended amount of vitamin D is consumed, check the nutrition label on the supplement for the amount of vitamin D per dose, and, if necessary, supplement vitamin D intake through other sources. However, because vitamin D can have negative effects if taken in very high doses, it is also important to avoid consuming more vitamin D than the tolerable upper level of 2,000 IU per day. Larger doses can initially be given to patients who are deficient as a means of replenishing the stores of vitamin D in the body.

Protein

Adequate dietary protein is important for bone health. In short-term studies, low protein intakes have been shown to result in decreased calcium absorption, while protein supplementation after hip fracture has been shown to speed healing and decrease mortality. However, increasing protein intake also increases urine calcium excretion. The long-term effect of both high and low protein diets on skeletal health has yet to be determined. Following the current dietary guidelines for servings of protein-containing foods such as meat, poultry, beans, and dairy products does not present any problems for calcium and bone health. These guidelines can be achieved by consuming 2–3 servings of meat or beans and 2–3 servings of milk and cheese per day. Higher intakes may be necessary in individuals with a history of low protein intake and those who are recovering from fracture in order to bring protein levels back to normal (as long as they also are getting sufficient levels of calcium intake). Important sources of protein include low-fat dairy products, which also provide calcium, phosphorus, and other important nutrients. Most vegetables provide fiber and minerals in addition to small amounts of protein, while soy protein sources such as tempeh, soybeans, and full-fat tofu provide isoflavones (plant compounds with estrogenic effects), which have been shown to increase bone density in some short-term clinical trials (long-term studies are ongoing). Nutritional supplements containing protein are available for those who cannot get enough protein from diet.

Other Nutrients Important to Bone

The Institute of Medicine recently provided recommended intakes for other bone-related nutrients, including phosphorus and magnesium (IOM 1997). Most Americans consume adequate quantities of phosphorus through their regular intake of meats, cereals, milk, and processed foods. While some beverages such as soft drinks also contain phosphorus, they are not a preferred source of phosphorus because they may displace calcium-rich beverages like milk (Whiting et al. 2001).

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Magnesium intakes may be suboptimal in those who do not eat enough green leafy vegetables, whole grains, nuts, and dairy products. Fortunately, most diets contain adequate levels of other bone-related micronutrients, such as vitamins K and C, copper, manganese, zinc, and iron, to promote bone health.

Some dietary components may potentially have negative effects on bone health, especially if calcium intakes are not adequate. For example, high levels of sodium or caffeine intake can increase calcium excretion in the urine. The effects of these factors can be overcome by increasing the amount of calcium in the diet (Fitzpatrick and Heaney 2003). Studies have linked excessive amounts of phosphorus to altered calcium metabolism, but it appears that the typical level of phosphorus consumed by most individuals in the United States should not negatively affect bone health (IOM 1997). Excessive amounts of preformed vitamin A (e.g., retinol) can also have negative effects on bone, so individuals should not consume more than the recommended dietary allowance for this vitamin (IOM 2000). The vitamin A precursor (beta carotene) found in many fruits and vegetables does not have negative effects on bone, however.

Conclusion

Significant strides have been made in understanding bone health and bone disease over the past few decades. Much is known about how to keep bones healthy throughout life and how to prevent and treat bone disease and fractures in those whose bone health deteriorates. Yet too few people—individuals and health professionals alike—make use of this information. As a result, too many people have or are at risk of getting bone disease. The time has come to address this problem, to “get the word out” about the importance of bone health and the serious consequences and significant costs of bone disease and fractures.

Resources

American Academy of Orthopaedic Surgeons (AAOS) <http://www.aaos.org>
American Academy of Pediatrics (AAP) http://aappolicy.aappublications.org/policy_statement/index.dtl#C
American Council on Exercise <http://www.acefitness.org>
American College of Sports Medicine <http://www.acsm.org>
American Dietetic Association (ADA) <http://www.eatright.org>
American Society for Bone and Mineral Research (ASBMR) <http://www.asbmr.org>
ASBMR Bone Curriculum Web Site <http://depts.washington.edu/bonebio/ASBMRRed/ASBMRRed.html>
Bone Builders <http://www.bonebuilders.org/>

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Foundation for Osteoporosis Research and Education (FORE) <http://www.fore.org/>
Growing Stronger: Strength Training for Older Adults <http://nutrition.tufts.edu/research/growingstronger>
International Bone and Mineral Society (IBMS) <http://www.ibmsonline.org/>
International Osteoporosis Foundation (IOF) <http://www.osteofound.org/>
International Society for Clinical Densitometry (ISCD) <http://www.iscd.org/visitors/osteoflash/index.cfm>
National Dairy Council (NDC) <http://www.nationaldairycouncil.org>
National Osteoporosis Foundation (NOF) <http://www.nof.org>
National Strength and Conditioning Association <http://www.nasca-lift.org>
Osteoporosis and Bone Physiology, University of Washington <http://courses.washington.edu/bonephys>
Osteoporosis Education, University of Washington <http://www.osteoeed.org/faq/index.html#male>
Osteogenesis Imperfecta Foundation (OIF) <http://www.oif.org>
The Paget Foundation (TPF) <http://www.paget.org>
Shape-Up America! <http://www.shapeup.org>
U.S. Bone and Joint Decade <http://www.usbjd.org>

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BONE HEALTH AND DISEASE

BONE HEALTH AND DISEASE

POST-TEST

1. Twenty five percent of skeletal mass is made of a fine network of connecting plates and rods known as _____.
 - A. cortical bone
 - B. trabecular bone
 - C. collagen
 - D. hydroxyapatite
2. Which of the following is NOT a calcium regulating hormone?
 - A. Parathyroid hormone
 - B. Calcitrol
 - C. Calcitonin
 - D. Cortisol
3. What is the most common cause of secondary osteoporosis?
 - A. Corticosteroids
 - B. Hyperthyroidism
 - C. Amenorrhea
 - D. Anticonvulsant medications
4. What percentage of trabecular bone is lost by women during the rapid phase of age related osteoporosis?
 - A. 5-10%
 - B. 10-20%
 - C. 20-30%
 - D. 30-50%
5. Which of the following is TRUE concerning Paget's Disease?
 - A. It most commonly involves the small bones of the hands and wrists.
 - B. It is the third most common bone disease.
 - C. There is an increased formation of blood vessels in the skeletal cortex.
 - D. There is a strong familial predisposition for the disease
6. The most severe form of Osteogenesis Imperfecta is:
 - A. Type I
 - B. Type II
 - C. Type III
 - D. Type IV

BONE HEALTH AND DISEASE

7. What is the most widely accepted method of measuring bone mineral density?
 - A. Dual x-ray absorptiometry
 - B. Peripheral quantitative computed tomography
 - C. Quantitative ultrasound
 - D. Radiographic absorptiometry

8. Approximately, what percentage of osteoporotic spine fractures goes undiagnosed?
 - A. 25%
 - B. 33%
 - C. 50%
 - D. 67%

9. Which of the following is FALSE regarding falls and fall prevention in the elderly?
 - A. Cognitive impairment is a risk factor for falls.
 - B. Anti-depressant drugs increase the risk of falls.
 - C. Using bed rails in hospitals decreases the number of falls
 - D. Wearing hip protectors reduces the risk of hip fracture for elderly individuals who live in nursing homes.

10. Approximately, what percentage of people die within 1 year after fracturing their hip?
 - A. 10%
 - B. 15%
 - C. 20%
 - D. 25%