Osteoporosis

It is common knowledge that calcium and vitamin D work together to help prevent osteoporosis. But what about the many other essential minerals and nutrients needed for bone health? And which kind of calcium is really the best? Many people are surprised to learn it is probably not the kind they are taking on a regular basis.

The human skeleton is the single largest organ system in the body. Composed of a complex mix of organic proteins and inorganic mineral crystals, bones are much more than just structural supports. They are the body's only reservoir of minerals such as calcium and phosphorus, which are critical for virtually every other organ system. The bones are also highly sensitive to hormonal changes. During puberty, when hormone levels surge in both boys and girls, bones are stimulated to grow rapidly as teenagers become full-sized adults. Thus, it is not really surprising that in later years, as hormone levels decline, the bones become vulnerable.

Maintaining healthy bones goes far beyond calcium and vitamin D, although these are vital. A healthy bone matrix also relies on vitamins and minerals that are rarely mentioned in the context of osteoporosis, including zinc, boron, copper, magnesium, vitamin K, silicon, folic acid, and others. This information is vital to the 10 million people, including 2 million men, who are known to suffer from osteoporosis in the United States.

CAUSES OF OSTEOPOROSIS: BONE REMODELING

Osteoporosis is defined as a reduction of bone mass, or bone density, which causes the bones to become brittle and fragile. People afflicted with osteoporosis are at increased risk of a range of fractures, including fractures of the hip, spine, and wrist. Fractures associated with osteoporosis are debilitating and costly (Melton LJ 2003; Woolf AD et al 2003). Mortality rates one year after hip and spine fractures have been reported to be as high as 30 percent (Rossell PA et al 2003; Kanis JA et al 2004). Many studies report high rates of institutionalization, loss of function, and death after hip and spine fractures.

Bone is living tissue comprising both organic protein matrix (30 percent) and various minerals (70 percent). Throughout life, cells known as osteoblasts construct bone matrix and fill it with calcium. At the same time, cells called osteoclasts work just as busily to tear down and resorb the bone. This fine balance is regulated by many factors, including systemic hormones and cytokines. Bone mass reaches its peak by the middle of the third decade of life and plateaus for about 10 years. During this time bone turnover is constant, meaning bone formation approximately equals bone resorption.

As our bodies age, this fine balance is lost. As the relative hormone levels shift in midlife—more drastically in women than in men—the osteoclasts gain the upper hand, and bone mass begins dwindling. Some bone is already being lost by the time women reach menopause, but the rate of loss can increase as much as tenfold during the first six years after menopause. This is the essence of primary osteoporosis, or osteoporosis that occurs as a natural part of aging.

From midlife onward, bone health is threatened by overactive osteoclasts. To add to the problem, the osteoblasts may become less active from age 60 onward, causing type II osteoporosis. Whereas trabecular (spongy looking) bone in the vertebrae and elsewhere was formerly at risk from excess osteoclast activity, now the cortical (dense) bone of the hip, shin, pelvis, and other sites becomes more prone to fracturing because osteoblasts do not make enough of it.

Osteoporosis can also be caused by medications, especially glucocorticoids and corticosteroids, testosterone-deprivation therapy in prostate cancer patients, and any condition that impairs calcium metabolism, including kidney disease, organ transplants, smoking, and others.

Recent research suggests that advanced glycation end products, or AGEs, are implicated in bone loss. AGEs are formed when proteins interact with glucose molecules to form damaged structures in the body. One study examined the proteins in osteoporotic bones to determine if there was damage by AGEs. More AGEs present resulted in fewer bone-building osteoblasts (Hein G et al 2006).

NUTRITIONAL THERAPIES: CALCIUM AND BEYOND

Calcium and vitamin D are the cornerstone of osteoporosis prevention, yet they are not the whole story. Other minerals and nutrients that are vital to a healthy bone matrix include magnesium, potassium, vitamin C, vitamin K, vitamin B12, and others, including zinc, manganese, boron, copper, and silicon (Nieves JW 2005; Hirota T et al 2005).

Calcium. Many studies have shown that calcium can reduce bone loss and suppress bone turnover. Calcium intake is a foundation of osteoporosis prevention (Kasper DL et al 2005). Calcium requires the presence of vitamin D for maximum absorption.

Although calcium is readily available in dairy products and other dietary sources, many Americans are calcium deficient. There are a few possible explanations for calcium deficiencies:

- Decreased vitamin D availability, possibly due to kidney or liver problems or insufficient exposure to sunshine (ultraviolet radiation)
- Decreased gastrointestinal tract absorption due to stomach or intestinal problems
- Increased loss of calcium from the kidneys
- Increased loss of calcium from the colon and bowels
- Low dietary calcium intake
- Medications that inhibit calcium absorption

There are many forms of calcium on the market, including the common calcium carbonate, calcium gluconate, and calcium citrate. Of these, calcium citrate is the most easily absorbed and a good way to receive supplemental calcium.

It may also turn out that not only is supplementation vital to preventing and treating osteoporosis but that the timing of the supplementation is important. For example, in a study of healthy volunteers, two doses of 500 mg calcium and 400 IU vitamin D taken six hours apart produced a more prolonged decrease in serum parathyroid hormone levels (low levels of which indicate adequate calcium levels) than a single dose with the same total amounts of calcium and vitamin D.

Magnesium. Magnesium plays essential roles in bone formation and helps with calcium absorption. Studies have found that magnesium deficiency is associated with osteoporosis and bone fragility (Sasaki S 2006; Saito N et al 2005) and that adequate magnesium intake is associated with increased bone mineral density among white men and women (Ryder KM et al 2005).

Unfortunately, many people have magnesium deficiency, which may be caused by alcohol abuse or malabsorption (Takami S et al 2005). Dietary magnesium deficiency in North Americans often occurs because people do not consume enough dark green, leafy vegetables, which are rich in magnesium. If not provided in the diet, magnesium should be taken as a supplement.

Recommendations for postmenopausal women to increase calcium intake can lead to an unfavorable calcium-to-magnesium ratio unless magnesium intake is increased accordingly; the optimum ratio of calcium to magnesium is believed to be 2:1, though extra magnesium may be needed to protect against atherosclerosis.

Phosphorus. Phosphorus regulates bone formation, inhibits bone resorption, and also affects the regulation of calcium metabolism. Although there are few studies on the direct effect of phosphorus on bone mineral density, it is important to maintain a proper phosphorus-to-calcium intake because of the effect phosphorus has on calcium metabolism (Kawaura A et al 2005). One researcher recommended a daily intake of 1000 mg calcium, with three-quarters as much (750 mg) phosphorus, as this intake was associated with higher bone mineral density among young women (Kawaura A et al 2005). It is also a good idea to reduce the consumption of soft drinks since they are high in phosphorus and can unfavorably alter the calcium/phosphorus balance.

Other minerals and trace elements. Few people are aware of the importance of balanced intake of minerals and trace elements, including copper, zinc (Yamada S et al 2004), silicon, and boron. Recent research suggests that it is important to ensure adequate intake of these minerals (Miggiano GA et al 2005).

Copper plays an essential role in bone metabolism and turnover. It modulates the differentiation and proliferation of osteoblast precursors, namely the mesenchymal stem cells (Rodriguez JP et al 2002). Women taking copper supplementation have shown improved bone density, while copper deficiency can produce osteoporosis in animal models of the disease (Klevay LM et al 2002).

Boron assists with calcium absorption and bone formation. It maximizes the body's utilization of calcium, vitamin D, and magnesium and has shown antiosteoporotic activity (Burnham BS 2005). It is especially effective in the presence of deficiencies in vitamin D, magnesium, and potassium (Schaafsma A et al 2001).

The role of zinc in osteoporosis is less well understood, but it is increasingly apparent that zinc deficiency is a risk factor for osteoporosis. It has been theorized that zinc deficiency may lead to the increase of natural anticoagulants in the blood (Atik OS et al 2006). In alcoholics, zinc has also been shown to limit the damaging effects of alcohol on bone (Gonzalez-Reimers E et al 2005).

Silicon is also important to bone health. A study of both men and women in the large Framingham Heart Study found that silicon intake was positively related to increases in bone mineral density in the hip and spine (Jugdaosingh R et al 2004).

VITAMINS TO SUPPORT HEALTHY BONES

Vitamin D. Vitamin D, a hormone-like substance, promotes the absorption of calcium. Vitamin D is made by the skin after exposure to sunlight or ultraviolet radiation, and vitamin D deficiency is widespread throughout the United States. People with light skin synthesize vitamin D in their skin easier than dark-skinned people. In the winter when people spend more time indoors and have less exposure to sunlight, their vitamin D levels plummet. Of special concern, vitamin D deficiency is a very important winter-time risk for people with dark-skin, who must have more exposure to sunlight than light-skinned people in order to generate similar amounts of vitamin D. Some people must avoid exposure to sunlight for various reasons, such as incompatibility of sunlight with certain medications. Recent studies have suggested that the recommended US RDA for vitamin D (600 IU daily) is actually too low and that people would benefit from 800 to 1000 IU and more daily (Nieves JW 2005).

Vitamin C and vitamin E. Vitamin C, also known as ascorbic acid, is essential for the formation of collagen and the stimulation of proteins derived from osteoclasts (Schaafsma A et al 2001). Studies show that vitamin C contributes to increased bone mineral density by improving markers of bone turnover (Hall SL et al 1998; Katsuyama H et al 2005) and that increased antioxidant intake, especially vitamin E, is associated with reduced risk of hip fracture, especially among smokers. It is also necessary for the synthesis of steroid hormones and neurotransmitters, which are vital to bone formation. In addition, this vitamin makes iron more available. Vitamin C is a powerful antioxidant and helps protect the body from cytokines that are produced during bone breakdown. Studies demonstrate a significant decrease in antioxidant defenses in older women (Maggio D et al 2003).

Bioflavonoids. Bioflavonoids include rutin, quercetin, hesperidin, and eriodictyol. They are found in onions, peppers, garlic, black currants, blueberries, red berries, buckwheat, and green tea. These nutrients have been shown to stimulate bone morphogenetic proteins, which are known to increase bone formation (Mundy GR 2006).

Vitamin B12. Recent evidence has implicated elevated homocysteine as a possible risk factor for osteoporosis, especially in women (Gjesdal CG et al 2006; Herrmann M et al 2005). Vitamin B12, together with folic acid and vitamin B6, can help lower homocysteine. Before the evidence connecting elevated homocysteine to osteoporosis emerged, vitamin B12 had already been identified as a possible strategy to reduce the risk of osteoporotic fracture, primarily because vitamin B12 deficiency has been associated with decreased bone-mineral density in the hip (Stone KL et al 2004). Vitamin B12 and folate have been shown to reduce the risk of hip fracture in elderly Japanese people who have suffered stroke (Uebelhart B et al 2006).

Vitamin K. Vitamin K facilitates the activity of calcium in bone building. Vitamin K is necessary for the activation of osteocalcin, a protein found in relatively high amounts in the bone, which allows calcium to bind to bone matrix. Osteocalcin that is not appropriately synthesized with vitamin K may lead to low bone mineral density and an increased risk of osteoporosis (Schaafsma A et al 2001; Okano T 2005).

Diets with more vegetables and less meat are higher in vitamin K. One study examined the relationship between vitamin K intake and hip fracture. Using 10 years of data on 72,000 participants in the Nurses' Health Study, researchers found that study participants who received the most vitamin K were about a third less likely to get a hip fracture. Those who ate lettuce every day slashed their risk of hip fracture in half compared to those who ate it less than once a day (lettuce is a source of vitamin K) (Feskanich D et al 1999). The effect of taking vitamin K was greater than the effect of taking synthetic estrogen, which did not protect the participants' bone density in this study, nor did vitamin D. In fact, women who took a lot of vitamin D but had low intakes of vitamin K had a doubled risk of hip fracture. Although vitamin D increases the amount of bone-friendly osteocalcin, only vitamin K can make it work properly.

Vitamin K shows remarkable results against bone loss in postmenopausal women. A study of 1 mg vitamin K daily for two weeks demonstrated it increased the bone-building protein gamma-carboxyglutamic acid in women (Knapen MH et al 1989). Another study showed that vitamin K slowed calcium loss by one-third in people who have a tendency to lose it (Knapen MH et al 1993). Drugs containing vitamins K1 and K2 are being used to treat osteoporosis (Hodges SJ et al 1991). The dosage used in Japan is 45 mg daily (Shiraki M et al 2000).

THE BEST TEST FOR OSTEOPOROSIS

Around perimenopause, which begins near age 40 in women, many physicians begin talking to their female patients about risk factors for osteoporosis and regular screening to detect the disease. Osteoporosis is an insidious condition because it usually has no symptoms until the bones become so thin and brittle that they cannot withstand the pressures exerted on them, and they break.

Two tests are used to measure bone mineral density. The dual energy X-ray absorptiometry (DEXA) test is most commonly used because there are more DEXA testing devices in doctors' offices than the more advanced quantitative computed tomography (QCT) equipment. However, studies suggest that the QCT test is much more sensitive.

In one clinical study, osteoporosis was present in 63 percent of men at the time of diagnosis of prostate cancer, prior to any therapy. In this landmark paper, the investigators evaluated DEXA bone mineral density testing and compared it to QCT bone mineral density testing in the same patients. A significantly greater percentage of men were found to have osteoporosis by the QCT

methodology than by means of the DEXA approach. DEXA bone mineral density evaluation detected osteoporosis in only 5 percent of men, whereas with QCT technology, 63 percent of men were diagnosed with osteoporosis. Using QCT technology, bone density abnormalities (osteopenia and osteoporosis) were found in 95 percent of men, compared to 34 percent of men evaluated with DEXA (Smith MR et al 2001).

Although QCT testing exposes patients to more radiation than DEXA does, the amount of radiation associated with QCT for determining bone density is roughly equivalent to that of a dental series and is approximately 50 percent that of a mammogram (depending on the technique used). Most important, QCT generates far less radiation exposure—orders of magnitude is less than a contrast-enhanced abdominal CT scan.

The results of bone density testing are given in T-scores. These scores are developed by comparing the person being tested to a young adult of the same gender between 25 and 45 years of age. A T-score of -2.5 or lower indicates high fracture risk, or a 60 percent chance of fracturing a hip. For every decrease of 1 in T-score, there is a twofold increase in risk of fracture. Individuals with a T-score of -1.1 to -2.5 are diagnosed with osteopenia, or mild bone loss.

Results are also given as Z scores, which measures individual results against people of the same age, gender, and race.

In addition to measuring bone density directly, physicians might recommend a number of tests to measure calcium levels, such as the level of calcium in the urine, as well as the levels of various hormones such as parathyroid hormone and calcitonin. Lab tests can also indicate absorption problems in the gut. The effectiveness of therapy may be monitored by tests that measure bone formation and bone turnover.

CONVENTIONAL TREATMENT OF OSTEOPOROSIS

In many cases, the first exposure someone with osteoporosis has to treatment is emergency medical treatment to repair a fractured bone. Hip fractures almost always require surgery, ranging from pins and plates to support of the hip to total hip replacements. For painful spinal fractures, painkillers may be recommended, along with anti-inflammatory medications. Other fractures, such as wrist or ankle fractures, are often treated with supportive care.

In addition, exercise is highly recommended. Weight-bearing exercise has been shown to reduce the rate of bone loss among postmenopausal women, although it does not seem to increase bone mass (Kasper DL et al 2005). Also, exercise promotes healthy joints, ligaments, and muscles, which make falling less likely.

If pharmacological treatment is necessary, a number of agents or drugs may be prescribed, including the following:

Hormone replacement therapy. Estrogen replacement therapy has long been prescribed to increase bone mineral density. Many studies have proved that estrogen replacement therapy can improve markers of bone turnover and reduce the risk of fracture (Prior JC 1990; Prior JC et al 1994; Zarcone R et al 1997; Castelo-Branco C 1998).

The benefits of estrogen replacement therapy, however, have to be weighed against recent evidence linking conventional estrogen replacement therapy to increased risk of breast cancer, stroke, heart attack, and blood clots. One study reported that women had a 20 percent to 70 percent increase in their risk of breast cancer while using estrogen alone or estrogen and a synthetic progestin. This study also showed that the carcinogenic risk of estrogen-progestin replacement therapy was more pronounced when it was used for 10 years or longer (Colditz GA et al 2000).

Perhaps more disturbing are the results of the large Women's Health Initiative study. This study found that conventional hormone replacement therapy, with either estrogen alone or estrogen and synthetic progestin, was associated with an increased risk of stroke (Bushnell CD 2006). Additionally, in the first one to two years of therapy, women experience an increased risk of coronary heart disease, stroke, deep vein thrombosis, or pulmonary embolism. Moreover, the risk of fracture does not decline until the fifth year of treatment (LaCroix AZ 2005). These findings had a dramatic effect on the number of women taking conventional hormone replacement therapy: some studies report that as many as 80 percent discontinued their treatment after the results were made public (Bestul MB et al 2004).

It is important to understand, however, that the results from the Women's Health Initiative detailed the risk of taking strong synthetic estrogens that are derived from horses' urine. They were not looking at bio-identical hormone therapy using estrogens that are specially formulated to match a woman's natural estrogen levels. Ultimately, the evidence that estrogen replacement therapy can protect bone loss is strong and must be balanced against the increased risk on an individual basis. Women who are at increased risk of breast cancer and cardiovascular disease may want to avoid estrogen replacement therapy, while women who are experiencing significant menopausal symptoms or are at high risk of osteoporosis may consider various natural estrogen options now available. For a more thorough discussion of the benefits and methods of bio-identical hormone replacement, see the chapter Female Hormone Restoration.

Bisphosphonates. Bisphosphonates are prescription drugs that interfere with osteoclast function and reduce the number of osteoclasts. The net result is an increase in bone mineral density and a reduced risk of fractures (Greenspan SL et al 2000; Fleisch HA 1997). They are also used to reduce the risk of fracture among people with glucocorticoid-induced osteoporosis (Kasper DL et al 2005). This class of drugs includes alendronate (Fosamax®), risedronate (Actonel®), pamidronate (Aredia®), etidronate, zolendronate (Zometa®), and ibandronate.

While studies have shown that bisphosphonates are effective at reducing bone turnover and increasing bone mass, these drugs have side effects. The most commonly reported side effects of oral bisphosphonates are gastrointestinal complications, such as esophagitis, gastritis, and diarrhea (Aki S et al 2003). They can also cause serious eye problems (Fraunfelder FW et al 2003), including acute glaucoma (Fraunfelder FW et al 2004).

More recently, bisphosphonates have been linked to osteonecrosis (death of the bone) in the jaw. In one study of women being treated with alendronate, pamidronate, or zolendronate, researchers reviewed records from a referral center. They identified 23 patients with osteonecrosis of the jaw who did not also have metastatic bone disease in that area. Of those 23, 100 percent had been treated within the previous 12 months with bisphosphonates (Farrugia MC et al 2006). Treatment for this condition includes stopping bisphosphonate treatment, as well as possible debridement and even radical surgery (Farrugia MC et al 2006).

Selective estrogen receptor modulators. These drugs selectively bind to estrogen receptors in osteoclasts, thereby decreasing bone turnover in postmenopausal women. Raloxifene (Evista®) was the first member of this family of drugs, which have been shown to have a positive effect on a woman's bone density (Fontana A et al 2001). Raloxifene is related to tamoxifen (Nolvadex®), which has been used to treat breast cancer for many years and is also approved for use in osteoporosis.

Studies have found significant increases in bone density with raloxifene and other drugs of this type. They are not without risk and should not be taken by people with liver disease, nor will they help with postmenopausal hot flashes.

An Exciting New Osteoporosis Drug

Taking antiosteoporosis drugs, such as bisphosphonates, for the long term is difficult for most people because of persistent side effects. Finally, however, a newer drug called Protelos® (strontium ranelate) promises to become a tolerable, easier therapy for osteoporosis.

Protelos® is the first dual-action osteoporosis drug on the market. It works by both increasing new bone formation and decreasing bone resorption, thus rebalancing bone turnover in favor of bone creation and strengthening the bones (Ortolani S et al 2006).

Two large, multinational studies have been conducted on the safety and effectiveness of Protelos® at 2 g daily. The Spinal Osteoporosis Therapeutic Intervention trial found that Protelos® reduced the risk of a new vertebral fracture by 41 percent after three years, compared with placebo. The Treatment of Peripheral Osteoporosis study found a 16 percent reduction in the risk of nonvertebral fractures in all patients and a 36 percent reduction in hip fractures among high-risk patients (Burlet N et al 2006).

In both studies, Protelos® was well tolerated with a lower side-effect profile than existing osteoporosis drugs (Adami S 2006).

PHYTOESTROGENS: A SAFER ESTROGEN?

Considering the health risks associated with conventional HRT, many women are reluctant to consider estrogen replacement therapy. Fortunately, phytoestrogens from soy, including genistein and daidzin, provide a possible alternative. We now know that genistein and daidzin bind loosely with estrogen receptors and that diets high in soy may protect against estrogen-induced cancers. Soy may also have an impact on bone health.

A six-month study to investigate bone density and bone mineral content in response to soy therapy was conducted. In this study, women received daily either phytoestrogens derived from soy protein or milk-derived protein (which contained no phytoestrogens). The results showed significant increases in bone density and bone mineral content for the lumbar spine in the women receiving the phytoestrogens derived from soy protein diets. Increases in other skeletal areas also were noted in the women on the soy diets. Researchers concluded that soy isoflavones show real potential for maintaining bone health (Potter SM et al 1998).

Another study found that soy foods reduced the risk of fracture in postmenopausal women, particularly among women who just finished menopause (Zhang X et al 2005). In this study, Chinese officials studied soy consumption among approximately 24,400 postmenopausal women and discovered that women with the highest soy intake were less like to suffer from fractures.

Ipriflavone. Ipriflavone, a synthetic isoflavone, has attracted attention and research, especially in Europe, where it is now used as a drug in treating osteoporosis. It has been shown to inhibit bone resorption and enhance bone formation in men and women. A double-blind, placebo-controlled study of ipriflavone in 255 postmenopausal women found that forearm bone mineral density remained constant for two years in the treatment group while diminishing significantly in the placebo group. Markers of bone turnover were higher in the placebo group than in the treated group. Not all studies show a bone protecting effect for ipriflavone.

BALANCING HORMONES FOR HEALTHY BONES

Progesterone. Although not proven by conventional standards, alternative doctors have long recommended the use of natural progesterone creams to promote osteoblasts and protect against osteoporosis. Osteoblasts require the hormone progesterone to maintain youthful bone-forming capability during and after menopause. Studies have shown that progesterone stimulates proliferation of osteoblasts (Liang M et al 2004).

California-based Dr. James Lee demonstrated increased bone density in women using progesterone cream. Since natural progesterone cannot be patented, there is little economic incentive to conduct the kind of extensive clinical trials that have been done with progestin drugs approved by the Food and Drug Administration. However, Dr. Lee studied the clinical outcomes for years and found them positive.

Parathyroid hormone and calcitonin. Parathyroid hormone (PTH) is produced by the tiny parathyroid glands, located behind the thyroid gland. PTH is partially responsible for maintaining adequate calcium levels in the blood. If calcium levels in the blood are too low, PTH stimulates calcium and phosphate resorption from the bones to ensure adequate blood calcium levels for normal body functions. PTH also causes the kidneys to decrease urinary calcium excretion.

In contrast, calcitonin, a hormone produced by the thyroid gland, stimulates calcium absorption by bones when blood calcium levels are excessive. Low levels of estrogen cause increased resorption of calcium from bones by increased sensitivity of bones to parathyroid hormone. When elevated, PTH is a good predictor of hip-bone mineral density.

Both PTH and calcitonin are sometimes prescribed to treat women with osteoporosis. Calcitonin has been shown to increase bone mass in women who are more than 5 years past menopause, while PTH is approved to treat both men and women at high risk of fracture. While side effects of PTH are generally mild, it is limited because of its mode of delivery: it is injected daily for up to two years (Kasper DL et al 2005).

Testosterone and osteoporosis in men. While osteoporosis in women tends to attract the most attention, the fact is that about 20 percent of people with osteoporosis are men, who usually suffer from the symptoms of osteoporosis about a decade later than women. Like women, men undergo a rapid loss of hormones as they age. This period is sometimes referred to as andropause and described as a period when levels of testosterone and other hormones decline. Not surprisingly, this is the same period when osteoporosis becomes a significant health concern for men.

Testosterone promotes bone formation, and many studies have shown that normal levels of testosterone are associated with higher bone mineral density and that decreased testosterone levels contribute to the development of osteoporosis (Orozco P et al 2000; Zofkova I et al 2000; Gurlek A et al 2001; Cetin A et al 2001). Low levels of free testosterone are a reliable predictor of low bone mineral density in the lumbar spine and associated with low mineral density in the hip bone (Center JR et al 1999).

Dehydroepiandrosterone. Dehydroepiandrosterone (DHEA) is a steroid hormone produced by the adrenal glands. DHEA plays many important roles in the body, including that of a precursor of testosterone and estrogen. DHEA has been shown to stimulate osteoblast activity to help prevent bone loss. Osteoblasts may convert DHEA to estrone through a reaction regulated by vitamin D3 (Takayanagi R et al 2002). DHEA levels decrease with aging, and this decrease is associated with many degenerative changes, as well as with decreased bone mineral density (Legrain S et al 2003; Buvat J 2003).

A study assessed the effects of 100 mg oral DHEA daily on a group of elderly men over a six-month period. Results indicated no adverse effects and increased bone mineral density (Sun Y et al 2002). The recommended dose for most women is about 25 to 50 mg daily.

Melatonin. Melatonin is a hormone produced by the pineal gland. It is abundant in bone marrow, where the bone cell precursors are located. It also decreases with age. Recent studies indicate that melatonin may help in the prevention of bone loss in several ways (Cardinali DP et al 2003; Ostrowska Z et al 2001; Pandi-Perumal SR et al 2003):

- Signaling the production of bone matrix proteins
- Suppressing circadian levels of certain factors related to bone metabolism
- Inhibiting osteoclast formation and bone resorption through antioxidant and free radical scavenger properties
- Promoting osteoblast proteins and procollagen type I c-peptide
- Promoting circadian growth hormone secretion

AMINO ACIDS TO PREVENT BONE LOSS

Proteins are constructed of various amino acids, each with a very specific function. Most amino acids are produced in the liver, and 20 percent must be obtained through diet. The amino acids not produced by the body are known as essential amino acids. L-arginine and L-lysine are essential amino acids necessary for protein synthesis; production of collagen; calcium absorption; production of hormones, enzymes, and antibodies; and tissue repair.

Several studies document the effects of essential amino acids on bone growth and metabolism, and there is sufficient support that essential amino acid supplementation contributes to bone formation and may be useful for preventing or treating osteoporosis (Conconi MT et al 2001). One animal study found that supplementation with L-arginine prevented the inhibition of bone growth and resorption of bone induced by glucocorticoids (Pennisi P et al 2005). Another study demonstrated that both L-arginine and L-lysine stimulated osteoblast cells to reproduce and activate (Torricelli P et al 2003).

LIFE EXTENSION FOUNDATION RECOMMENDATIONS

The benefits of a healthy diet and exercise for people with osteoporosis are widely accepted. However, most conventional medical

sources touch upon only calcium and vitamin D when it comes to nutrients that help reduce the risk of osteoporosis. In reality, researchers are discovering that bone health and remodeling are complex processes that are influenced by many hormones and nutrients.

One of the most well known approaches to osteoporosis among women is the use of hormone replacement therapy to help slow bone loss. In light of the recent findings of the Women's Health Study, in which hormone replacement therapy was associated with increased risk of breast cancer, stroke, and heart disease, many women discontinued conventional hormone therapy, which relied on strong estrogens derived from the urine of pregnant mares. However, the beneficial effects of estrogen—providing it is the right kind of estrogen—on fracture risk were not called into question. Life Extension recommends that postmenopausal women, who comprise about 80 percent of osteoporosis patients, have their hormone levels tested and, if necessary, begin a program of hormone replacement therapy with bio-identical hormones that are specially formulated to mimic the natural levels of estrogen. Phytoestrogens from soy have also been shown to protect women against fractures. Among men, testosterone therapy is linked to stronger bones. For more information on bio-identical hormone replacement therapy, call 1-800-544-4440.

The following supplements and nutrients have been shown to reduce the risk of fractures:

- **DHEA**—suggested starting dose of 15 to 75 milligrams (mg) daily, followed by blood testing in three to six weeks to make sure that optimal levels of this hormone are maintained
- **Calcium**—1200 mg (dicalcium malate and calcium bisglycinate) daily
- **Vitamin D3**—800 international units (IU) daily
- **Magnesium**—340 mg daily
- **Zinc**—2 mg daily
- **Manganese**—1 mg daily
- **Silicon**—5 mg daily
- **Boron**—3 mg daily
- **Melatonin**—1 to 3 mg daily at bedtime
- **Vitamin C**—1 to 3 grams (g) daily
- **Vitamin E**—400 IU daily (with 200 mg gamma tocopherol)
- **Vitamin B12** with folic acid—300 to 1200 micrograms (mcg) B12 and 800 to 3200 mcg folic acid daily
- **Vitamin K**—10 mg daily
- **Whey protein**—up to 50 g daily (contains the essential amino acids L-arginine and L-lysine)
- **Soy isoflavones** (genistein, daidzein, glycitein)—55 to 120 mg daily

PRODUCT AVAILABILITY

All the nutrients and supplements discussed in this section are available through the Life Extension Foundation Buyers Club, Inc. For ordering information, call anytime toll-free 1-800-544-4440, or visit us online at www.LifeExtension.com.

The blood tests discussed in this section are available through Life Extension National Diagnostics, Inc. For ordering information, call anytime toll-free 1-800-208-3444, or visit us online at www.LifeExtension.com.

Osteoporosis Safety Caveats

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

Calcium

- Do not take calcium if you have hypercalcemia.
- Do not take calcium if you form calcium-containing kidney stones.
- Ingesting calcium without food can increase the risk of kidney stones in women and possibly men.
- Calcium can cause gastrointestinal symptoms such as constipation, bloating, gas, and flatulence.
- Large doses of calcium carbonate (12 grams or more daily or 5 grams or more of elemental calcium daily) can cause milk-alkali syndrome, nephrocalcinosis, or renal insufficiency.

Magnesium

- Do not take magnesium if you have kidney failure or myasthenia gravis.

Melatonin

- Do not take melatonin if you are depressed.
- Do not take high doses of melatonin if you are trying to conceive. High doses of melatonin have been shown to inhibit ovulation.
- Melatonin can cause morning grogginess, a feeling of having a hangover or a “heavy head,” or gastrointestinal symptoms such as nausea and diarrhea.

Silicon

- High doses of silicon may cause siliceous renal calculi.

Soy

- Do not take soy if you have an estrogen receptor-positive tumor.
- Soy has been associated with hypothyroidism.

Vitamin B12 (cyanocobalamin)

- Do not take cyanocobalamin if you have Leber's optic atrophy.

Vitamin C

- Do not take vitamin C if you have a history of kidney stones or of kidney insufficiency (defined as having a serum creatine level greater than 2 milligrams per deciliter and/or a creatinine clearance less than 30 milliliters per minute.
- Consult your doctor before taking large amounts of vitamin C if you have hemochromatosis, thalassemia, sideroblastic anemia, sickle cell anemia, or erythrocyte glucose-6-phosphate dehydrogenase (G6PD) deficiency. You can experience iron overload if you have one of these conditions and use large amounts of vitamin C.

Vitamin D

- Do not take vitamin D if you have hypercalcemia.
- Consult your doctor before taking vitamin D if you are taking digoxin or any cardiac glycoside.
- Only take large doses of vitamin D (2000 international units or 50 micrograms or more daily) if prescribed by your doctor.
- See your doctor frequently if you take vitamin D and thiazides or if you take large doses of vitamin D. You may develop hypercalcemia.
- Chronic large doses (95 micrograms or 3800 international units or more daily) of vitamin D can cause hypercalcemia.

Vitamin E

- Consult your doctor before taking vitamin E if you take warfarin (Coumadin).
- Consult your doctor before taking high doses of vitamin E if you have a vitamin K deficiency or a history of liver failure.
- Consult your doctor before taking vitamin E if you have a history of any bleeding disorder such as peptic ulcers, hemorrhagic stroke, or hemophilia.
- Discontinue using vitamin E 1 month before any surgical procedure.

Vitamin K

- Do not take vitamin K if you are taking warfarin sodium unless, the vitamin K is specifically prescribed by your physician.

Zinc

- High doses of zinc (above 30 milligrams daily) can cause adverse reactions.
- Zinc can cause a metallic taste, headache, drowsiness, and gastrointestinal symptoms such as nausea and diarrhea.
- High doses of zinc can lead to copper deficiency and hypochromic microcytic anemia secondary to zinc-induced copper deficiency.
- High doses of zinc may suppress the immune system.

For more information see the Safety Appendix