OSTEOPOROSIS
by Agnes Heinz, Ph.D.

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Executive Summary

Osteoporosis is a condition characterized by substantial bone loss. When the extent of bone loss reaches a critical point, fractures may occur as a result of very minor stress. Osteoporosis affects the entire skeleton, but fractures occur most notably in the vertebrae, hips, and wrists. The bones become so weak that normal workloads overcome their capacity. A simple fall can result in a broken hip. Spinal vertebrae can collapse and in extreme cases cause a “dowager’s hump”.

Gradual weakening or thinning out of bones occurs normally with age. The longer we live, the less bone mass we have and the more prone we are to fractures.

Scientists do not know what causes osteoporosis. They do know a lot about factors which can worsen or lessen the extent of bone loss. Osteoporosis is a very complex disease where many different factors influence the rate of bone loss. Advanced age and being a postmenopausal white female are the predominant risk factors. Advanced age and being a postmenopausal white female are the predominant risk factors. Other risk factors include hormonal imbalance, nutrient deficiencies (particularly calcium) and immobility.

The role of dietary calcium in the prevention or treatment of osteoporosis is not clear. Calcium may ameliorate or prevent only bone loss directly related to calcium deficiency, but not bone loss due to other causes. Calcium deficiency, however, is common in women. Most bone loss is influenced by hormonal deficiencies.

Evidence suggests that exercise helps reduce bone loss. However, too much exercise can be counterproductive for women, because it may lower estrogen levels.

At this time, the most effective treatment of osteoporosis is prevention. The stronger the bones are when people are young, the less likely they are to fracture easily later in life. An effective preventive treatment in postmenopausal women is estrogen replacement therapy (ERT). Other treatments, such as calcitonin therapy, may help if estrogen replacement is not advisable for health reasons.

In some persons, osteoporosis cannot be prevented, but steps can be taken to slow bone loss as much as possible.

Once osteoporosis has proceeded to a very advanced stage, involving fractures, it is difficult to treat. Many of the more promising treatments are still experimental. Advanced osteoporosis interferes with a person’s ability to lead a normal life. A simple fall, a wrong movement or even minor stress on the bones can make the difference between an independent or a dependent lifestyle.

As the population ages, the relative percentage and absolute number of elderly will increase, leading to an increase in all diseases associated with aging, including osteoporosis. In 1991, osteoporosis resulted in over 1.5 million fractures, costing over $10 billion in health care. These numbers are expected to increase.

Types of Osteoporosis

Osteoporosis is traditionally divided into primary and secondary osteoporosis. Both types can occur simultaneously in the same person. The cause of primary osteoporosis is not fully understood. Primary osteoporosis is divided into postmenopausal (type I) and senile (type II) osteoporosis. Secondary osteoporosis is less common and defined as bone loss occurring as a result of other diseases, such as Cushing’s syndrome or malignancy.
(Type I) Accelerated or postmenopausal osteoporosis

Bone loss is accelerated in women for five to ten years after menopause due to reduced production of the female sex hormone, estrogen. Ten or more years after menopause, accelerated bone loss slows down and approaches the rate of decline observed in older men (Figure 1). In five to ten percent of postmenopausal women, bone loss is severe and leads to fractures before age 75. Postmenopausal osteoporosis most often results in collapsed vertebrae, which may lead to the dowager’s hump. Other bones, such as wrist bones, are also affected. Type I bone loss occurs in women over six times as frequently as men.

(Type II) Age-related osteoporosis

Age-related osteoporosis occurs in both sexes in women over age 70 and men over age 80.

There is very good evidence that the incidence of fractures increases with the lowering of bone mineral density. Type II bone loss typically results in hip fractures, although fractures occur in other types of bone as well. Elderly men are very susceptible to bone loss, but women get hip fractures about twice as often. It is not clear whether the bone loss is simply an expression of old age which affects some people to a larger extent than others. An underlying disease, a hormonal imbalance or nutrient deficiency may accelerate age-related bone loss.

In general, women have less dense bones than men (usually 30 percent less), and they suffer more bone loss after menopause. This puts women at a disadvantage when age-related bone loss occurs. Women live longer than men, and thus may be more likely to develop fractures. Osteoporosis is rare in young adults and middle-aged men.

Secondary osteoporosis

In some instances, osteoporosis is a side-effect of another health condition. For example, overproduction of cortisone, as in Cushing Syndrome, can lead to osteoporosis. Abnormally low production of sex hormones, as in hypogonadism, castration or “total hysterectomy” can lead to bone loss; certain malignancies, particularly myeloma (a bone marrow cancer), hyperthyroidism and hyperparathyroidism can also result in bone loss. Digestive, kidney, or liver disorders may lead to bone loss. (Table 1)

Osteopenia and Osteomalacia

Osteoporosis is a form of osteopenia. Osteopenia literally means “little bone”. In osteoporosis bone mass is lost. However, the composition of the remaining bone is similar to healthy bone, although not as dense.

To diagnose osteoporosis correctly, other bone disorders should be excluded. In osteomalacia, bone tissue is not adequately mineralized, and bone quality is softer than healthy bone. Osteomalacia is primarily due to severe vitamin D deficiency and is an adult form of rickets.
**Table 1: Causes of Secondary Osteoporosis**

<table>
<thead>
<tr>
<th>Cause</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroid therapy and Amenorrhea</td>
<td></td>
</tr>
<tr>
<td>Cushing’s Syndrome</td>
<td>Anorexia Nervosa</td>
</tr>
<tr>
<td>Myeloma</td>
<td>Hyperprolactinemia</td>
</tr>
<tr>
<td>Skeletal metastases</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Gastric surgery</td>
<td>Alcoholism</td>
</tr>
<tr>
<td>Anticonvulsant therapy</td>
<td>Immobilization</td>
</tr>
<tr>
<td>Thyrotoxicosis</td>
<td>Osteogenesis imperfecta</td>
</tr>
<tr>
<td>Male hypogonadism</td>
<td>Homocystinuria</td>
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</tbody>
</table>

**Bone Is an Active Tissue**

Perhaps, because skeletons greatly outlast human life, we get the impression that bones are hard and inert. However, bone is a very active tissue metabolically, and it changes constantly.

The skeleton is soft in the early embryonic state. The fetus starts out with a cartilaginous skeleton, which is gradually replaced by bone. As the embryo grows, mineral salts, deposited into the protein matrix, eventually harden the bones. After birth, bone density increases. By the time an infant is one year old, the skeleton is firm enough to support first attempts at walking. The bones continue to grow in length and mass until adulthood. After longitudinal bone growth is completed, the bones continue to increase in mass and density.

Peak bone density is reached between ages 20 and 35. Thereafter, the process reverses. The bones begin to lose density. At age 40, bones lose less than 0.5 percent of their mass per year. Postmenopausal women can lose up to two to three percent or more bone mass per year. If accelerated loss is not stopped, a susceptible woman can lose 50 percent peak bone mass by the time she reaches 70 or 80 years of age.

**Mechanisms of Bone Formation and Destruction**

Bones are in a continuous state of dissolution and reformation. Two opposing forces occur within the bones to determine their hardness:

1) bone resorption: destruction of old bone tissue,
2) bone formation: production of new bone tissue.

These two forces occur in sequence and are coupled. Old bone is dissolved and new bone is formed so that the size and shape of bone can adapt to the changing shape of the body. Bone resorption initiates the *bone remodeling cycle* and new bone formation concludes the cycle. However, to maintain bone strength, bone formation must keep up with bone resorption. If bone formation lags behind, bone loss is inevitable. This seems to be what happens in osteoporosis.

Bone loss results either from excessive resorption or from inadequate formation.

• During growth bone formation is greater than bone resorption.
• During adulthood bone formation and bone resorption are in balance.
• During aging, bone resorption begins to exceed bone formation.

**High turnover osteoporosis** occurs when the bone remodeling cycle performs at high speed; both excess resorption and excess formation takes place. Bone formation, however, rarely keeps up with excess bone resorption, so a high turnover of bone remodeling often results in rapid bone loss. High turnover osteoporosis occurs primarily in younger people and comprises about ten percent of all osteoporosis cases. **Low turnover osteoporosis** occurs primarily in the elderly where the remodeling cycle has slowed down. Bone resorption is still fairly normal, but formation of new bone is slowed significantly. Postmenopausal women usually have *normal bone turnover*, but bone resorption rates exceed bone formation rates.

**Bone Composition**

Like other tissues, bones are made up of cells. In contrast to soft tissues, however, bone cells lie on the surface of bone, or are enclosed by calcified bone tissue. The enclosed cells, which remain active, are connected to the general circulation through tiny tunnels.

There are three types of bone cells. All play different roles in bone maintenance:

- **Osteoclasts** are responsible for bone resorption and initiation of the bone remodeling cycle.
- **Osteoblasts** are responsible for bone formation and completion of the bone remodeling cycle.
- **Osteocytes** are responsible for maintenance work within bone tissue.

Osteoclasts destroy bone tissue by dissolving minerals. Other cells, macrophages, then digest the protein matrix. Osteoblasts form new bone by secreting protein fibers into the cavities produced by the osteoclasts. Calcium salts harden these protein deposits, a process also controlled by osteoblasts. Osteocytes, former osteoblasts trapped by calcified tissue, perform maintenance work within the bone tissue and control local mineral exchange.

The basic framework of bones is a protein, collagen mesh or matrix. Bone becomes hard because mineral salts are incorporated into the protein mesh. The predominant mineral salt is a calcium phosphate salt, called hydroxyapatite. Magnesium, sodium and potassium salts and small amounts of fluoride and chloride also contribute to the inorganic matter in bone. Bone also contains trace amounts of heavy metals, such as lead and strontium.

Calcium is the major mineral in bone. Bone tissue is constantly dissolved and replaced. Therefore, bone calcium is constantly removed and replaced.

Our body contains roughly 1,200 grams (about 2.5 pounds) of calcium. Most of the body’s calcium (over 99 percent) is located in the bones. The bones incorporate calcium for hardness while serving as a calcium bank for the rest of the body. Soft tissues require calcium in very small amounts. It is important that these tissues are adequately supplied with calcium by the blood. It is also critical that blood concentrations remain stable at approximately ten milligrams per deciliter. A slight drop or rise in blood calcium concentrations will immediately set off hormonal events that will return blood calcium to normal concentrations.

Bones play an important part in maintaining stable blood calcium concentrations — at the expense of their own calcium stores.

Most calcium in the bone is combined with phosphate. About 80 to 85 percent of body phosphate is located in the skeleton. The ratio of calcium to phosphate in the bone is two to one.
Calcium Stores Determined by Diet and Hormones

Most calcium is excreted via the urine, sweat and feces. This calcium must be replaced by dietary calcium. The intestine can adjust the absorption of dietary calcium to meet the body’s needs.

During growth more calcium is absorbed than in later years. If the amount of dietary calcium intake is low, the intestine compensates (to a degree) by absorbing more calcium. On the other hand, if we consume more calcium than we need, relatively less will be absorbed. This protects the body from absorbing too much. We depend on vitamin D for this adaptive ability.

The absorptive ability of the intestine diminishes with age. This may be a reason why we lose bone. Therefore, older people may need more calcium than younger people to maintain calcium balance. Very young individuals can absorb up to 75 percent of dietary calcium. Healthy adults can absorb between 30 and 40 percent, while older adults may absorb even less.

The blood delivers calcium to bone tissue. In turn, either dietary sources or the bones deliver needed calcium to the blood. The body deals with bone calcium as being more dispensable than blood calcium. In the long run, therefore, low dietary calcium intake can lead to weakening of the bones.

Several hormones influence blood and bone calcium concentrations, thus affecting bone density and stable blood calcium concentrations.

Blood calcium concentrations can be manipulated by:
- increasing or reducing calcium absorption in the intestine,
- increasing or reducing calcium secretion in the kidney,
- depositing or withdrawing calcium into or from bone tissues.

A small decrease in blood calcium concentrations results in increased output of the hormones parathyroid hormone (PTH) and vitamin D (a vitamin which acts as a hormone). Both hormones interact to stimulate bone resorption and calcium absorption in the intestine and to reduce calcium excretion in the kidneys. This results in increased blood concentrations. The two hormones influence each other. For example, adequate blood concentrations of vitamin D depend on the presence of PTH.

When blood calcium concentrations are too high, the hormone calcitonin is released. Calcitonin acts opposite to PTH and vitamin D. It reduces calcium absorption in the intestine, increases calcium deposition in the bone and increases calcium excretion in the kidney. All these events occur just long enough to maintain blood calcium at normal concentrations. Even small reductions in blood calcium concentrations set off bone resorption via PTH. In this way, low dietary calcium can lead to bone loss.

For more information on hormones that affect calcium levels see Appendix 1.

Other Hormones and Biological Substances Influence Bone Density

Other hormones affect bone tissue. How they affect bone density is not understood. It is possible that other hormones modulate the calcium regulating hormones or influence the production of other biological substances that act on bone.

Anabolic steroids such as testosterone, estrogen and progesterone prevent bone loss. A sudden lack of estrogen in women or androgens in men leads to bone loss.

These sex hormones may counterbalance PTH and thus control the extent of bone resorption caused by
this hormone. Some recent evidence suggests that estrogen has a direct effect on bone cells. The role of progesterone in women is less well established but some evidence suggests that it may increase bone density.

Other hormones, such as corticosteroids, can lead to bone loss, if present in excess. For example, Cushing’s Syndrome, where too much cortisone is produced, leads to secondary osteoporosis.

Medications also affect bone strength (Table 2). People receiving cortisone as part of arthritis treatment may be losing bone mass. Cortisone reduces the formation of the protein matrix of the bone and also the absorption of calcium in the intestine. Hyperthyroidism also leads to bone loss. Treatment with excess thyroxine increases the risk for osteoporosis. This is of particular concern for women approaching menopause, who are already in danger of losing bone.

<table>
<thead>
<tr>
<th>Drugs that may worsen bone loss</th>
<th>Drugs that may prevent bone loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>thyroxine</td>
<td>anabolic hormones, such as estrogen</td>
</tr>
<tr>
<td>cortisone</td>
<td>thiazides (calcium sparing diuretic)</td>
</tr>
<tr>
<td>some antibiotics</td>
<td>tamoxifen*: antiestrogen, used to treat breast cancer</td>
</tr>
<tr>
<td>aluminum antacids</td>
<td></td>
</tr>
<tr>
<td>chemotherapeutic drugs</td>
<td></td>
</tr>
<tr>
<td>anticonvulsants</td>
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<tr>
<td>heparin</td>
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* The paradox as to why an estrogen blocker prevents bone loss is not understood.

Recent research suggests that some cells secrete biochemicals that either stimulate bone resorption or enhance bone formation. For example, macrophages (one type of white blood cell) can produce interleukin-1 which stimulates bone resorption. Certain bone cells may produce prostaglandine E-2, which can also induce bone resorption. It is possible that estrogen blocks the activity of some of these biological agents, which may partly explain why estrogen deficiency results in bone loss.

Some local (produced in the vicinity of the bone) growth factors such as somatomedin C or insulin-like growth factor (IGF) increase bone density. The presence and activity of these local factors are regulated by hormones. For example, human growth hormone stimulates the production of local growth factors. Insulin also promotes bone growth by stimulating osteoblast activity. However, lack of insulin has not been shown to play a significant role in osteoporosis.

Tumor cells may also produce biological substances that activate osteoclasts, which leads to bone loss.
Osteoporosis Risk Factors and Their Possible Mechanisms

Several risk factors for osteoporosis are known. Risk factors are not necessarily causes of a disease, but represent conditions in which the disease is more frequently observed, and therefore may increase a person’s likelihood of getting the disease. However, there are many people with osteoporosis who do not have any of the known risk factors. The best known risk factors for osteoporosis are listed in Table 3.

Table 3: Risk Factors for Osteoporosis

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian or Asian heritage</td>
<td>Inactivity</td>
</tr>
<tr>
<td>Premature menopause or</td>
<td>Inactivity</td>
</tr>
<tr>
<td>prolonged ammenorrhea</td>
<td>Nulliparity</td>
</tr>
<tr>
<td>Positive family history</td>
<td>Causes of secondary osteoporosis</td>
</tr>
<tr>
<td>Short stature, low body weight</td>
<td>Smoking</td>
</tr>
<tr>
<td>Low calcium intake or absorption</td>
<td>High alcohol consumption</td>
</tr>
</tbody>
</table>

Age

Osteoporosis effects mostly older individuals.

For unknown reasons, osteoclasts gradually begin to outperform osteoblasts. Thus, more bone is lost than rebuilt. In the elderly, osteoblasts are probably not as efficiently produced as in younger people. Bone turnover has either slowed down or come to a standstill.

Hormone balance changes with age. Women produce much less estrogen after menopause. Men gradually produce less androgens with age.

PTH concentrations are often slightly increased, probably to compensate for low vitamin D or low calcium concentrations, common in older people. The elderly are usually less efficient in synthesizing vitamin D. The kidney may become less efficient in converting vitamin D into its active form or the intestine may be less responsive to vitamin D. These disturbances can result in a vicious cycle: less functional vitamin D results in less calcium uptake. This leads to low blood calcium, which in turn causes PTH to be released, which causes bone resorption.

These processes may be a natural part of aging, but they may also be accelerated by other mechanisms. As people age, they often tend to change their lifestyle. Many become less mobile and eat less varied diets, which may ultimately lead to weakened bones.

Estrogen deficiency

Postmenopausal women tend to be in negative calcium balance. The main reason for this is estrogen deficiency. Calcium requirements appear to rise with decreasing estrogen concentrations. Thus, postmenopausal women may need more than the usual amounts of calcium.

Sex hormone deficiency increases bone resorption. Natural menopause or premature loss of ovarian function causes a sudden reduction of estrogen resulting in significant loss of both cortical (the predominant
constituent of the long bones or the arms and legs) and cancellous bone (very porous, spongy bone which pre-
dominates in the vertebrae, ribs, hips, wrists and the interior of long bones), especially cancellous bone located
in the spine. Bone loss is substantially accelerated for five to ten years after menopause. Thereafter, the rate of
bone loss returns to that observed in normal aging. Estrogen replacement therapy can significantly slow down
this accelerated bone loss if started early enough.

Postmenopausal women may also have slightly reduced PTH blood concentrations, which also lead to
less production of active vitamin D. Less vitamin D results in less calcium absorption in the intestine.

How estrogen prevents bone resorption is not yet understood. One theory suggests that it counteracts
the activity of PTH (the hormone responsible for bone resorption). Without estrogen, the bones are more sensi-
tive to PTH and more bone will be destroyed in spite of lower concentrations of PTH. This leads to calcium
loss in the urine. Estrogen may also interfere with the formation of local bone destroying factors.

Even before menopause, women gradually produce less estrogen and progesterone. Thus, bone can also
be lost before menopause. Female athletes who exercise to the point where menstruation ceases (amenorrhea),
as a result of less estrogen, also increase their risk for osteoporosis.

More recent evidence suggests that other disturbances in the menstrual cycle (shortened luteal phase,
cycles in which ovulation does not occur, or excess production of the hormone prolactin) can lead to bone loss
even in relatively young women, often as severe as that observed in older women. The culprit is assumed to be
progesterone deficiency. If such findings are confirmed, significant bone loss may occur in healthy menstruat-
ing women well before menopause.

Diet

The extent to which diet influences bone loss is not known. However, an inadequate diet can lead to
nutrient deficiencies. Insufficient calcium intake throughout life can contribute to osteoporosis.

An intake of excess dietary protein may increase urinary calcium secretion by causing urine to be
acidic. However, dietary phosphate reduces calcium excretion. Thus, foods high in protein and phosphate such
as meat, fish and dairy products result in little or no increase in calcium excretion. Insufficient dietary protein
is also detrimental because some protein is needed for calcium absorption. Protein is also necessary for bone
production.

Excess caffeine intake is associated with reduced calcium absorption or excess excretion. Moderate
caffeine consumption is not considered to endanger calcium balance in women who consume sufficient calci-
um. Similarly, excess sodium may reduce absorption of calcium to some degree.

Adequate calcium intake is necessary to achieve peak bone mass, and lifelong calcium deficiency is a
recognized risk factor for osteoporosis. Adequate dietary calcium prevents the body from drawing upon the
calcium reserves in the bones. Older people may need more calcium to stay in calcium balance. However, sex
hormones appear to play a more important role in maintaining a positive calcium balance than dietary calcium.

Bone density at different ages was measured in two Yugoslavian populations each including women
before and after menopause. One population consumed large amounts of dairy products while the other did
not. As shown in Fig 2., the women with higher milk consumption had greater bone density during most of
their life. The advantage, however, disappeared with increasing age. There was not much difference in bone
density 30 years after the beginning of menopause. This study suggests that although dietary calcium is impor-
tant, it is not sufficient in itself in preventing osteoporosis.

Middle-aged women appear to consume less calcium than most other people. The average American woman consumes less than the recommended dietary allowance of 800 mg of calcium per day (1200 mg for adolescents and pregnant women).

Older people, particularly those in extended care facilities, may not be receiving sufficient vitamin D through sunlight or through their diet. While severe vitamin D deficiency leads to osteomalacia, mild vitamin D deficiency may contribute to osteoporosis. When blood calcium concentrations are low due to mild deficiency of vitamin D, PTH is released to raise blood calcium concentrations. Mild vitamin D deficiency may lead to a modest rise in PTH, which results in increasing in bone resorption.

Phosphate supplies in our food are usually more than sufficient. There is some concern that we are consuming too much phosphate in our food. However, high dietary phosphate intake appears to help build bones rather than the reverse. People who consume high levels of aluminum antacids may be prone to phosphate deficiency, and thus to osteomalacia, which can contribute to osteoporosis.

Malabsorption syndromes can also lead to insufficient calcium uptake. Deficiencies of other micronutrients such as vitamins A, C, and K and minerals, copper, boron, zinc, manganese, fluoride and magnesium may also negatively affect bone density. Their role in osteoporosis is currently being investigated.

Alcoholism
Excess intake of alcohol may compromise bone density, either from the effect of alcohol on the liver, where vitamin D is activated or from the poor dietary practices of many alcoholics. Alcohol may also interfere with calcium absorption. Excess alcohol may be toxic to bone cells. Osteoporosis in young and middle-aged men is often a result of alcoholism.

Cigarette smoking
Cigarette smoking is associated with enhanced osteoporosis, although how smoking affects bone is not understood. While smoking does reduce estrogen concentrations, smoking has also been shown as a risk factor in men, who would not be affected by reduced estrogen levels. Smokers tend to weigh less than non-smokers, which may contribute to bone loss.

Low body weight
Reduced body weight is a risk factor for osteoporosis. Thin and petite women are more susceptible than obese women.

Weight increases the load on bones and thus increases bone density. Anorexics have reduced body weight and are also at higher risk. Anorexics may also be at risk because they are nutritionally deficient, often to the point of becoming amenorrheic. Obese women are less prone to osteoporosis, possibly because their bones carry more weight or possibly because their fat cells convert the steroid hormone androgen into estrogen.

Lack of weight-bearing exercise
Osteoporosis is more common in developed nations than in developing nations. This may be due to the
fact that less physical activity is necessary for survival. Immobilized limbs in casts lose bone, as do invalids and people who spend much time in bed. Astronauts lose bone mass during their travel into gravity-free space.

Exercise increases the load on the skeleton and promotes greater bone density. Exercise may also affect hormone concentrations that favor bone strength. Similar to muscle tissue, disuse of bone tissue can lead to bone loss. Preliminary studies have shown that physical activity may reduce bone loss, even in post-menopausal women. The type of exercise is important. Weight-bearing exercise such as tennis is more effective than swimming. Apparently, antigravity muscles must be involved to maximize the benefits of exercise. A high muscle to bodyweight ratio is also associated with increased bone density. Muscles may have a direct effect on bone or may simply reflect frequent physical activity. Exercise is most effective if calcium intake is adequate.

There is compelling evidence that exercise during growth and development optimizes bone density and delays bone loss later in life.

**Genetic predisposition**

Osteoporosis occurs to varying degrees in different races, presumably because of different peak bone mass. Blacks usually have denser bones (by approximately ten percent) than whites and Asians. Peak bone mass may be genetically determined. However, the genetic basis for osteoporosis is poorly understood. Nevertheless, family history of osteoporosis is considered a risk factor. Certain rare types of osteopenia are clearly inheritable, such as osteogenesis imperfecta, where the bone matrix is defective.

**Risk factors not related to bone density**

Low bone mass is not the only contributor to risk for fractures. The general mental and physiological state of the individual is also important since neurological and cardiovascular disorders can increase the likelihood of accidents and resulting fractures. Similarly, certain medications, such as antihistamines and tranquilizers, reduce coordination and alertness.

**Diagnosis**

Symptoms seldom announce the presence of osteoporosis before the first fractures occur. By this time bone loss has already reached a significant stage. The earliest symptom is pain, typically back pain following a vertebral fracture.

Some fractures may be so minute that they are not noticed immediately. However, they can add up and lead to bone weakening. More severe fractures may cause intense pain.

It is difficult to detect osteoporosis in its early stages. Bone mass measurement techniques have not yet reached a stage where they can be applied for mass screening, although they are rapidly increasing in sophistication. Currently available tests submit the patient to low-level radiation, are time-consuming and can be costly. These procedures measure the current density of the bones, but one measurement is usually not sufficient to accurately determine whether the patient is losing bone rapidly. The measurements need to be performed at intervals of one to three years to determine a trend in changing bone mass. At present, these techniques may be useful in supporting the diagnosis in persons considered to be at high risk, to follow the success of treatment
In patients and to test new experimental treatment in clinical studies. The most available bone mass techniques are:

**Single beam (photon) absorptiometry (SPA):** measures mostly the compact cortical bone mass. It is fairly inexpensive and uses low radiation doses.

**Dual Beam (photon) absorptiometry (DPA):** measures both cortical and cancellous bone mass and total bone mass. It uses slightly more radiation than SPA.

**CT (computed tomography) scan:** measures primarily cancellous bone, i.e., cross sections of vertebrae. It is expensive and uses high radiation doses.

**Digital radiography:** measures the bone density of fingers using low-level radiation.

Peak cancellous bone mass is reached at an earlier age than peak cortical bone mass. Cancellous bone is also the first to be resorbed when our bones gradually dissolve with age, particularly after menopause. In age-related osteoporosis, both cancellous and cortical bone are lost.

Risk factor analysis may help determine who should receive preventive care. For example, women are considered at higher risk if they have other risk factors as well, such as low body weight and/or a positive family history. They should consider preventive treatment. However, the reliability of such risk factors for predicting risk in women approaching menopause was recently questioned.

**Certain metabolites** may be detected in the urine that give some indication of a high rate of bone resorption (calcium and hydroxyproline) or of a high rate of bone formation (alkaline phosphatase). These methods do not shed light on actual bone density, but they may be helpful in assessing the rate of bone loss. This is important because a person who has high bone density but also high resorption rates could be at the same risk as a person with very low bone density and low resorption rates. Blood calcium and phosphate concentrations are usually normal in osteoporotic individuals. This helps to distinguish osteoporosis from other bone loss diseases, in which these values do change.

**Prevention and Treatment**

**General**

Everyone can make adjustments in their lifestyle to prevent fractures, such as learning proper lifting and bending techniques. For example, lifting a heavy object is better done by bending the knees than by stooping. Improving vision and using appropriate footwear can prevent accidents. Much can be done during the formative years to fulfill the genetic potential to achieve maximum peak bone mass, such as exercise and adequate nutrition.

Once peak bone mass is reached, steps can be taken to slow down the age-related decline in bone mass. There is much evidence that adequate nutrition and exercise, even after age 35, contribute to slowing bone loss.

Severe osteoporosis appears to be preventable, but difficult to treat and to cure. No treatment delivers consistent results, and some of the more promising types of treatment are still being tested. Efforts are usually directed toward rehabilitation and decreasing pain from fractures. As soon as pain subsides, the patient must
resume regular movement and, if possible, exercise.

The goal of treatment is to maintain current bone mass as much as possible and to prevent further loss. Treatment usually centers around the type of bone loss.

**Estrogen replacement therapy**

Women approaching or going through menopause, who are predisposed to developing osteoporosis, may want to consider, in consultation with their physician, estrogen replacement therapy (ERT).

ERT has proven beneficial in reducing the incidence and severity of osteoporosis. However, it is a known risk factor for endometrial cancer and could worsen existing breast cancer. But the risk for endometrial cancer and possibly breast cancer from ERT may be mitigated by cyclic administration and by combination with progestin.

Although still controversial, many studies have suggested that ERT may have substantial benefits in reducing cardiovascular morbidity and mortality by nearly 50 percent in postmenopausal women. Because cardiovascular disease is the leading cause of death in women, these benefits could, in fact, be very substantial and could compliment the benefits of ERT of reducing osteoporosis. Overall, the risks and benefits of ERT to women must be based on their individual medical history.

Depending on dose and schedule, ERT can cause continuation of the menstrual cycle, to which many women object. Continuous estrogen with transdermal patches may reduce this side effect. Women who have breast cancer are advised against taking ERT. Women who are at particular risk for developing breast cancer are advised to combine the treatment with yearly mammograms. Other side effects of ERT, nausea and headaches, are probably due to oral ingestion. Transdermal forms are likely to result in fewer side effects.

Estrogen has little benefit if treatment is started too late after menopause. Estrogen is able to delay bone loss, but not to reverse damage already done.

**Calcitonin therapy**

Calcitonin may be an alternative to estrogen. Like estrogen and calcium, calcitonin reduces bone resorption. Calcitonin is also useful when bone loss is more rapid, as in younger people. However, the effect of calcitonin is rarely long-lasting. The reason for this lies in the physiological role of this hormone, which is to reduce blood calcium. To do this, it increases calcium deposition in the bones, reduces calcium absorption (caused by calcitonin) and increases calcium excretion. For bone strength, the first effect is desirable, but the other two are not. Low blood calcium concentrations, due to excess excretion and low absorption, will stimulate secretion of PTH. PTH will then override the inhibitory effect of calcitonin on bone resorption and render it ineffective. For this reason, calcitonin is most effective if used intermittently, possibly in conjunction with other medication. Calcitonin is expensive and must be injected because it can not be absorbed intact orally. This is inconvenient and time consuming. A nasal spray is currently being examined as an alternative route of administration.

**Calcium balance and supplementation**

Dietary or supplemental calcium cannot substitute for ERT. However, it appears to enhance ERT treatment. Low dietary intakes of calcium should be avoided at all stages of life. Evidence supporting calcium
nutriture or supplementation for the prevention of osteoporosis, beyond that needed to prevent a deficiency, is inconsistent.

Calcium plays an important role in achieving peak bone mass, which is an important preventive factor. Younger people need more calcium, because their bones are still growing. Pregnant and lactating women also require more calcium (Table 4).

Even though adequate calcium should help reduce bone loss, calcium supplementation has only been shown to have small beneficial effect on bone density in older people. Calcium appears to increase cortical bone density without affecting cancellous bone density.

Older people do not absorb calcium as well as and may excrete calcium more easily than younger people. Therefore, many health care professionals recommend large amounts of calcium (1,000 - 1,500 mg and higher) to postmenopausal women, because it might help and probably will not harm. The argument is often made that rather than run the risk of suffering calcium deficiency through an improper diet or because of milk intolerance, supplementing may be of value. Even a small decrease in blood calcium concentration can stimulate PTH release affecting bone resorption. Calcium supplementation in the recommended amounts (see above) is not harmful. It may help people who do not tolerate milk. However, too much calcium may lead to overly alkaline urine, which may increase susceptibility to kidney stones or urinary tract infection.

Many other factors, particularly calcium regulating hormones, seem to play a major role in osteoporosis. This may explain why the studies using calcium are inconsistent.

Some forms of calcium are better absorbed than others. The calcium in animal products, such as milk products, is fairly well absorbed. Much of the calcium from plant sources is less well absorbed since the calcium is often present as compounds (calcium phytate, calcium oxalate, etc.) that do not easily dissolve in our intestine.

When taking supplements, it is important to use those that are most likely to dissolve in the stomach. Most commonly used calcium salts, such as calcium carbonate, calcium citrate, calcium gluconate and calcium lactate are all well absorbed. Calcium citrate is better absorbed in people who have low stomach acid (achlorhydria), a condition frequently observed in older women and men. Many foods are now supplemented with calcium.

It is too early to tell whether longterm calcium supplementation prevents further bone loss in those with established osteoporosis. Calcium deficiency should certainly be avoided.
Table 4: Calcium content of common foods
(RDA for adults is 800mg. For adolescents or pregnant women, it is 1200mg.)

<table>
<thead>
<tr>
<th>Food</th>
<th>Serving Size</th>
<th>Calcium (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>milk (skim, whole, etc.)</td>
<td>8 oz</td>
<td>300</td>
</tr>
<tr>
<td>yogurt, whole milk</td>
<td>8 oz</td>
<td>275</td>
</tr>
<tr>
<td>yogurt, skim with nonfat milk solids</td>
<td>8 oz</td>
<td>452</td>
</tr>
<tr>
<td>American cheese</td>
<td>1 oz</td>
<td>195</td>
</tr>
<tr>
<td>Sardines, canned with bones</td>
<td>3.5 oz</td>
<td>449</td>
</tr>
<tr>
<td>Orange</td>
<td>1 medium</td>
<td>65</td>
</tr>
<tr>
<td>Almonds or hazelnuts</td>
<td>12-15</td>
<td>38</td>
</tr>
<tr>
<td>Bean curd (tofu)</td>
<td>3.5 oz</td>
<td>128</td>
</tr>
<tr>
<td>Beans, red kidney</td>
<td>0.5 cup</td>
<td>110</td>
</tr>
<tr>
<td>Broccoli, cooked</td>
<td>2/3 cup</td>
<td>88</td>
</tr>
</tbody>
</table>

Source: U.S. Dept. of Agriculture, Human Nutrition Information Service

Vitamin D
Adequate vitamin D consumption is important. However, there is no evidence that intake of vitamin D beyond the recommended daily allowance of 400 I.U. increases calcium deposition in the bones. In fact, too much vitamin D can increase calcium excretion and calcification of the soft tissues. Only people with certain metabolic disorders are candidates for prescriptions of vitamin D in excess of recommended amounts.

Exercise
Athletes usually have higher peak bone density than sedentary persons, particularly in cancellous bone. While exercise cannot replace ERT in postmenopausal women, it is certainly better than inactivity. Exercising to the extent that menstruation ceases can promote bone loss. The type of exercise is important. Tennis and walking are more effective than swimming. Exercise is more useful if calcium intake is adequate.

Exercise is useful even if osteoporosis is well established. In addition to helping prevent further bone loss, it strengthens musculature and promotes agility and coordination. Falls are then less likely to be severe. Unfortunately, fractures are often associated with severe pain. This can lead to a vicious cycle: pain discourages exercise, lack of exercise worsens bone loss. The type of exercise needs to be carefully selected in people with advanced osteoporosis, because exercise that is too intense, such as tennis can overly stress already weak bones. Walking is a good choice.

Treatments still under investigation
Parathyroid Hormone: Even though this hormone stimulates bone resorption, it also activates vitamin D, and in this way increases intestinal calcium uptake. Also, by stimulating bone resorption, PTH initiates the bone remodeling cycle. Bone growth cannot occur without some preceding bone resorption. PTH treatment is useful in treating low turnover osteoporosis. However, because prolonged and high PTH treatment will cause
too much bone to be resorbed, it must be used intermittently at low doses. Currently under investigation, combination therapy combines PTH and activated vitamin D. PTH is given to activate the bone remodeling cycle, and vitamin D is given to supply calcium by making sure that dietary calcium is well absorbed.

**Fluoride:** It is still not clear whether treatment with sodium fluoride (NaF) is beneficial. It increases cancellous bone mass dramatically when combined with adequate calcium and vitamin D. Theoretically, it may be useful in preventing vertebral crushing. However, it was not shown to reduce spinal fractures and it may actually increase fractures of the hip. Fluoride supplementation, in amounts above those in fluoridated water, contributes to higher bone density, but possibly of a lesser quality. It is currently not recommended as treatment and is still under investigation.

**Thiazides** (diuretic): In some people or in some conditions, excess calcium is lost in the urine. Calcium-sparing diuretics are given to prevent this loss. Whether thiazide therapy has a role in osteoporosis has not been determined.

**Activated vitamin D** (calcitriol): This already activated form of vitamin D is rarely used, because, as does excess vitamin D in general, it can result in increased urinary excretion of calcium and increased calcification of the soft tissues without increasing bone calcium.

**Coherence Therapy:** Several drugs, hormones and calcium affect the bone at different stages of the remodeling cycle. Coherence therapy uses these drugs and hormones intermittently to activate remodeling, minimize the resorption phase and maximize formation phase.

For example, as described above, PTH stimulates resorption, and thus starts the remodeling cycle. Once this is accomplished, PTH is withdrawn and drugs which suppress resorption, such as diphosphonates (etidronate), are given. Then these drugs are removed and bone formation is allowed to proceed undisturbed, making sure that enough calcium is present. After a while this sequential intermittent treatment is repeated.

Coherence therapy is also called ADFR therapy. The letters stand for the different steps of the therapy: A is for activate, D is for depress, F for free (the period where bone formation proceeds undisturbed) and R for repeat.

**Other:** Certain synthetic androgens have been tested. However, they tend to cause undesirable masculinization and may also increase the risk for heart disease. Drugs that inhibit enzymes involved in bone resorption or that stimulate production of bone growth factors are being investigated.

### Appendix 1: The three major calcium regulators

1) Parathyroid Hormone (PTH) is secreted by the parathyroid glands, which are located on the thyroid gland, in response to low blood calcium concentrations. Its job is to increase blood calcium concentrations. To do this, PTH stimulates bone resorption, reduces calcium excretion in the kidneys, and increases vitamin D conversion in the kidneys, which facilitates greater calcium absorption in the intestine. Too little PTH, by causing low blood calcium concentrations, leads to tetany. Too much PTH leads to weak bones and high blood calcium concentrations. Low blood calcium can lead to secondary hyperparathyroidism.

2) Vitamin D (cholicalciferol) is absorbed from food or through ultraviolet light conversion in the skin. Vitamin D from either source must be converted into active form by the liver and by the kidney. The activated
vitamin D then travels to the intestinal cells. There it effects the cell membranes in such a way that more calcium is absorbed into the body. Vitamin D is technically a hormone. If we get sufficient sunlight, we can make enough vitamin D in our body. However, conditions may be less than ideal, so that we often depend on food to receive the required amount. Severe vitamin D deficiency leads to osteomalacia, inadequate bone mineralization. Mild vitamin D deficiency can lead to secondary hyperparathyroidism, which can contribute to osteoporosis. Excess supplementary vitamin D (over 45µg/day) leads to calcification of soft tissues as well as to loss of calcium from bone. Vitamin D keeps blood calcium levels adequate, either by increasing intestinal absorption or by increasing bone resorption.

3) Calcitonin is a hormone secreted by a section of the thyroid gland in response to high blood calcium concentrations. It reduces blood calcium concentrations by increasing calcium secretion in the kidney, inhibiting calcium absorption, inhibiting bone resorption (osteoclasts) and increasing calcium deposition into bone tissues.

Further Reading


Mundy, G.R., Osteopenia, *Disease-a-Month*, 33/10, 1987, pp. 537.


