Fine-tuning osteoporosis

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What do postmenopausal women and older men have in common? Osteoporosis—a chronic skeletal disorder that weakens the bones and increases the risk of unexpected fractures. The National Osteoporosis Foundation estimates that more than 10 million Americans currently have osteoporosis and another 34 million have osteopenia, or low bone mass. We highlight the importance of osteoporosis prevention and education.

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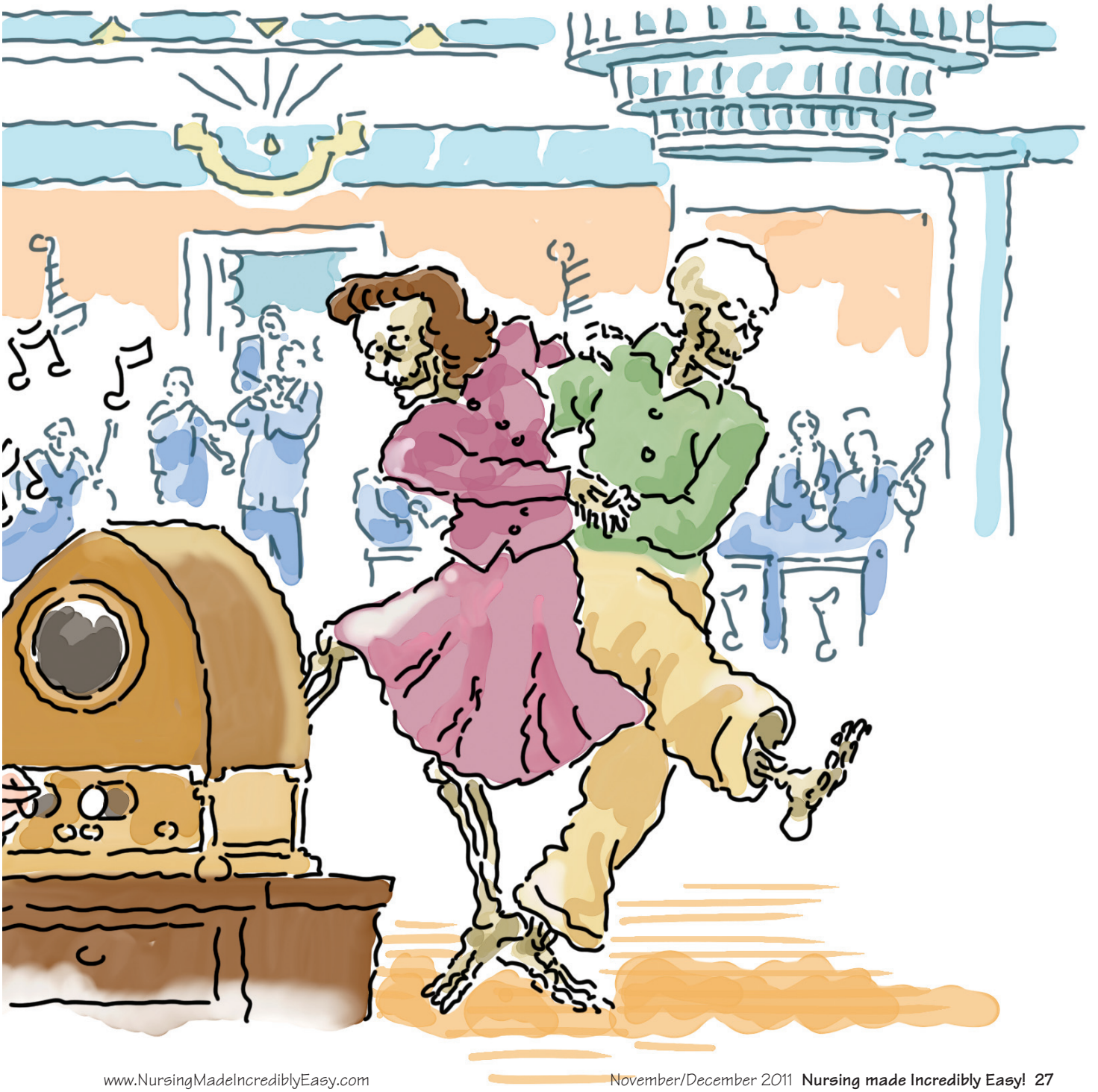
The human skeleton is like the superstructure of a building, its framework supporting and protecting the organs of the body. Bones are functional in design, and their strength encompasses both quality and density. Protective bones, such as the skull and pelvis, are thick, whereas arm and leg bones are long, hollow cylinders that combine lightness with strength. But as we age, we can experience bone loss, or osteoporosis.

With osteoporosis, the simple act of lifting a child, bending down to pick up a newspaper, or even sneezing risks breaking a bone. Known as a fragility fracture, this type of fracture occurs from a standing height or lower. The most common sites for fragility fractures are the spine, wrist, and hip.

outcomes



In this article, we profile osteoporosis, including risk factors, diagnosis, prevention strategies, and pharmacotherapy prescribed in prevention and treatment, as well as the role of education in osteoporosis management.

Our aging bones

Everyone experiences a natural decrease in bone density as they age, which usually begins between ages 30 and 35. Bone formation outpaces resorption until peak bone mass is reached. After that time, bone reabsorption slowly begins to exceed bone formation (see *Bone formation and reabsorption*). Bones are heaviest and strongest around age 35, at which point they make up about 10% of a person's body weight. In individuals with osteoporosis, normal bone loss is accompanied by an activated loss of calcium absorption by the gut and kidney.

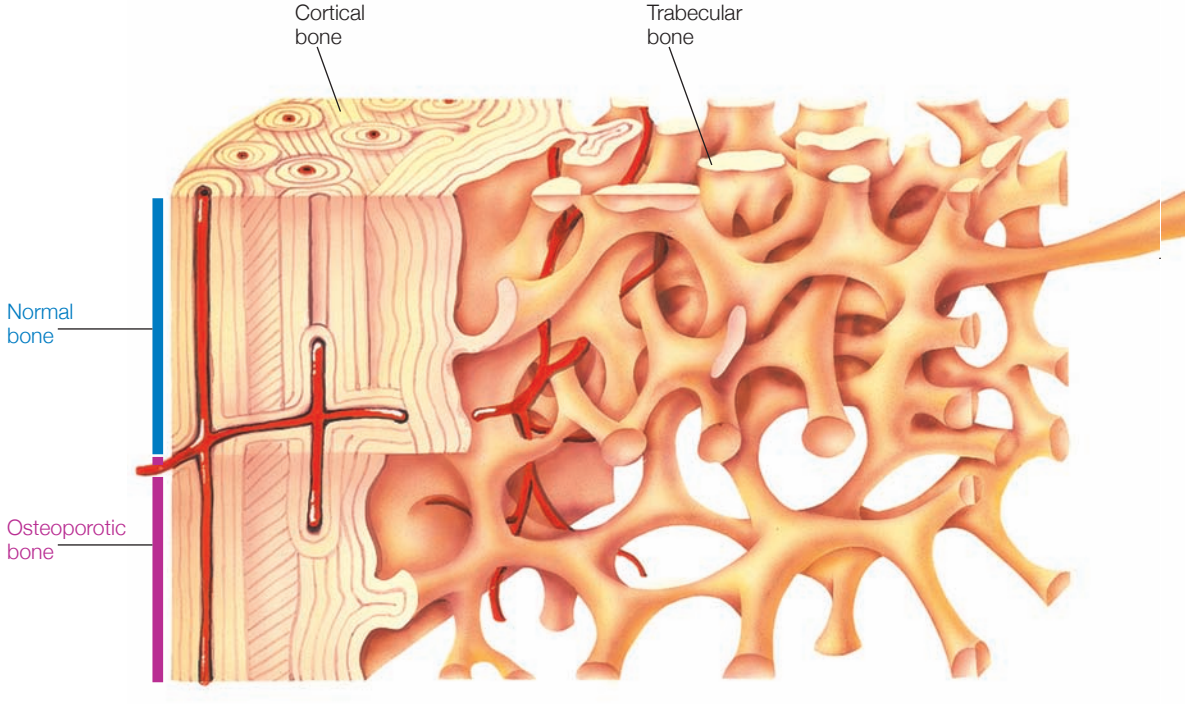
Cortical bone is lost continuously and evenly by both sexes. However, after menopause, women lose this tissue twice as fast as men. Trabecular bone is destroyed quickly; by age 80, women with osteoporosis have lost more than half of their trabecular bone tissue (see *What happens in osteoporosis?*). Mainly composed of trabecular bone, the vertebrae can become compressed. The vertebrae of the upper spine often collapse more frequently in the front and become wedge shaped, bending the upper spine forward and causing the back to hunch over.

The collapse of multiple vertebrae over time leads to shrinkage of the entire spinal column.

Bone formation and reabsorption

The organic portion of bone, called osteoid, acts as the matrix or framework for the mineral portion. Bone cells, called osteoblasts, produce the osteoid matrix. The mineral portion, which consists of calcium and other minerals, hardens the osteoid matrix.

Large bone cells, called osteoblasts, reshape mature bones by resorbing the mineral and organic components. However, in osteoporosis, osteoblasts continue to produce bone, but resorption by osteoclasts exceeds bone formation.

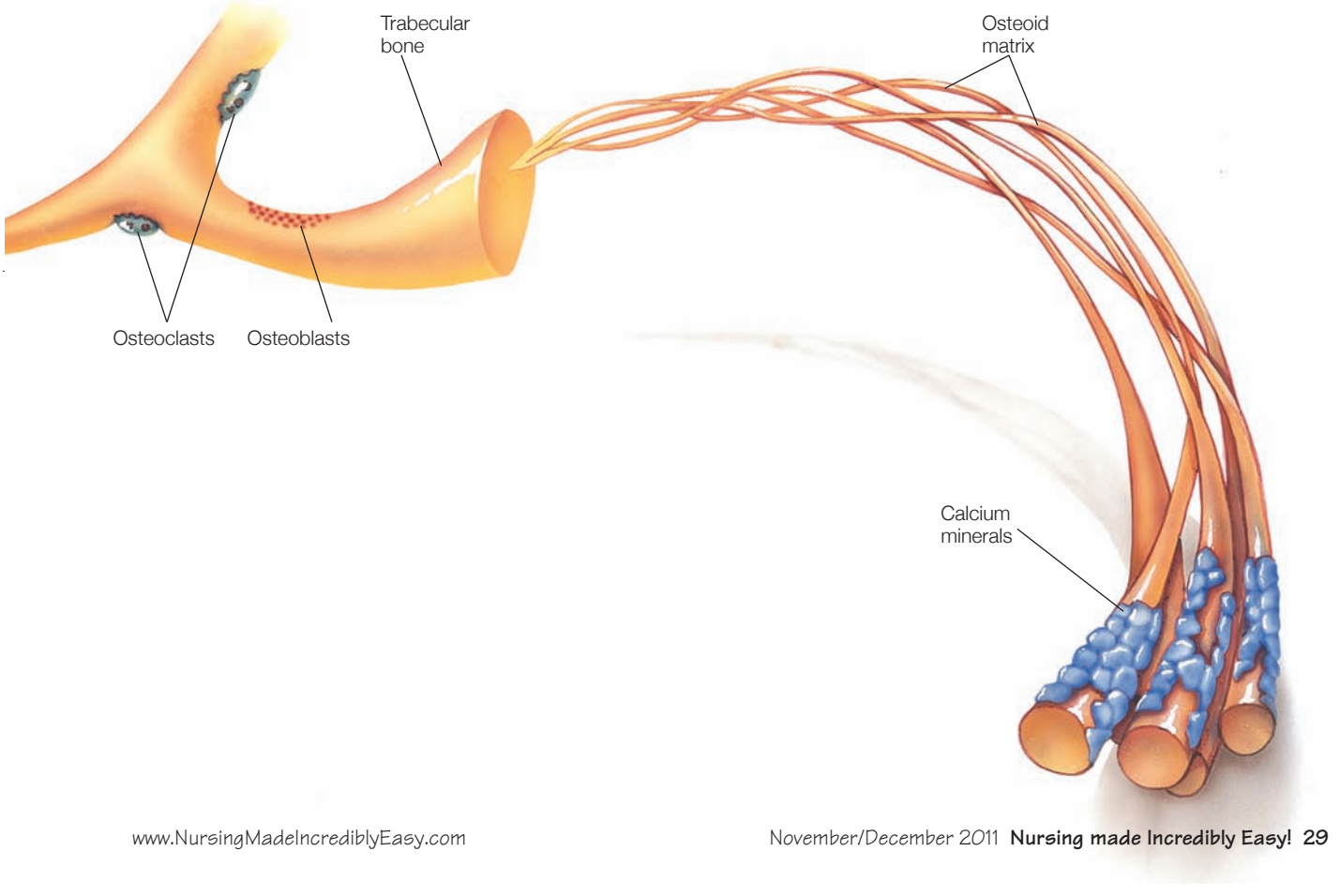


As the spine shortens, it bends forward, shortening the chest and causing the lower ribs to rest on the bones of the pelvis. This may lead to difficulty breathing, shortness of breath, and lung infections. The abdomen also compresses and bulges, which can cause digestive problems. Over one-third of women with collapsed vertebrae develop a curvature of the lower spine, which causes pain and stiffness that may affect their ability to perform activities of daily living.

The most serious and debilitating osteoporotic fracture is of the hip. Hip fractures are expensive and can be deadly, especially in the elderly population. The fractured bone itself isn't as dangerous as the long period of inactivity required for healing, with the ever-present potential for complications such as pneumonia, pulmonary embolism, decubitus ulcers, urinary tract infections, depression, and malnutrition. Many fractures result in a death that could have been avoided by a reduction in bone loss.

Who's at risk?

Osteoporosis is most commonly seen in postmenopausal women and older men. In the premenopausal period, normal estrogen levels regulate osteoclast activity. However, during the postmenopausal years, decreased estrogen levels can lead to an increase in osteoclast activity, resulting in bone loss. One in two women and one in five men older than age 65 will sustain bone fractures caused by osteoporosis.



The most predominant risk factor for osteoporosis is low bone mass, which by itself predicts fracture risk. Given the potentially devastating effects of osteoporosis, educating patients about the prevention of bone loss, screening early, and working with patients to develop effective management plans for osteoporosis or osteopenia are critical.

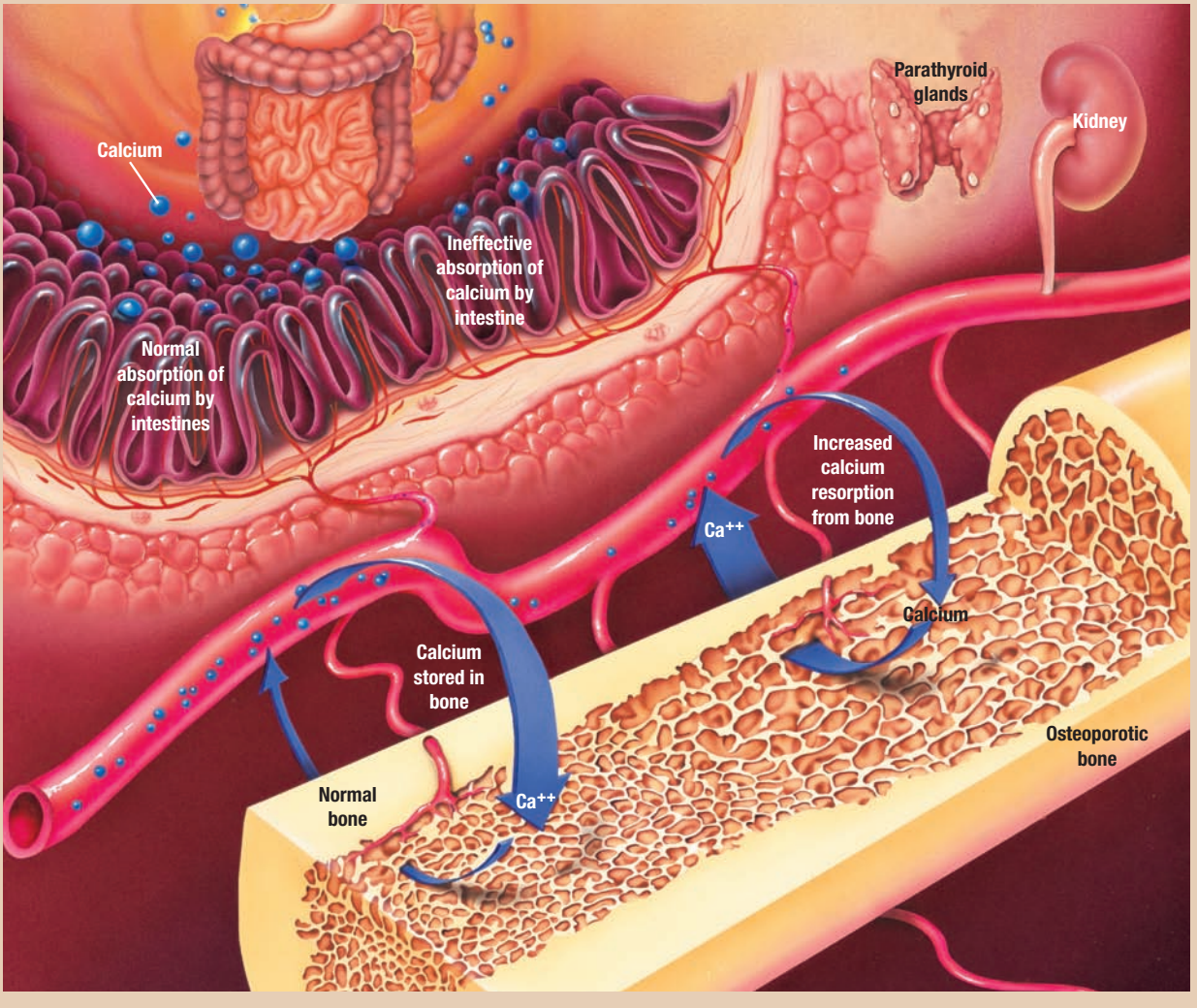
In addition to low bone mass, major risk factors include:

- aging
- history of fractures in a first-degree relative

What happens in osteoporosis?

In normal bone, the rates of bone formation and resorption are constant; replacement follows resorption immediately, and the amount of bone replaced equals the amount of bone resorbed. Blood absorbs calcium (Ca++) from the digestive system and deposits it in the bones.

Osteoporosis develops when the remodeling cycle is interrupted and new bone formation falls behind resorption (see *Bone remodeling* on the opposite page). When bone is resorbed faster than it forms, the bone becomes less dense. Men have about 30% greater bone mass than women, which may explain why osteoporosis occurs most often in women and develops later in men.



• small, slender body type
• Caucasian or Asian ethnicity
• female sex.

There are other factors believed to play a role in affecting bone strength. It's worth evaluating each of these potential risk factors as part of a comprehensive assessment:

• low calcium intake
• vitamin D deficiency
• high sodium and caffeine intake
• immobility
• alcohol intake of at least three or more drinks per day
• smoking, both active and passive
• glucocorticoid therapy for 3 months or longer
• premature estrogen deficiency
• low testosterone levels; for men with hypogonadism, testosterone has been linked to improvement in bone quality and quantity.

Osteoporosis also has a number of secondary causes, such as rheumatic and autoimmune diseases, hypogonadal states, liver diseases, endocrine disorders, and gastrointestinal disorders. Celiac disease, which compromises absorption of nutrients from the gut, is highly prevalent in patients with osteoporosis and is often missed because it's commonly asymptomatic.

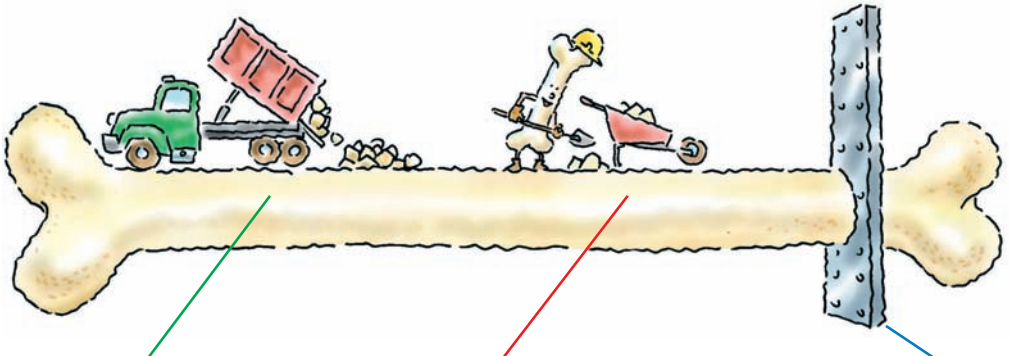
X-ray specs

In osteoporosis, two factors are important: the amount of tissue inside the bone itself and the quality and health of the tissue. A thorough personal and family history, a physical exam, and lab values are required to assess patients older than age 50 who might be at risk for osteoporosis.

Lab tests include:

• ***calcium*** (9 to 11 mg/dL)—usually normal in osteoporosis, but may be elevated with other bone diseases
• ***serum 25-hydroxy vitamin D*** (29 to 32 ng/mL)—measures peak calcium absorption efficiency; deficiencies can lead to decreased calcium absorption
• ***thyroid tests*** (T4 [4.5 to 11.5 mcg/dL] and TSH [0.35 to 5.5 µIU/mL])—used to rule out thyroid disease; hypothyroidism is linked to increased bone reabsorption

Bone remodeling



1 Osteoblasts deposit new bone.

2 Osteoclasts increase long-bone diameter. They also promote longitudinal bone growth by reabsorbing previously deposited bone.

3 Growth continues until the epiphyseal plates ossify during adolescence. (The epiphyseal plates are cartilage that separates the *diaphysis*, or shaft of a bone, from the *epiphysis*, or end of a bone.)

• ***parathyroid hormone (PTH)*** (11 to 54 pg/mL)—used to check for hyperparathyroidism; PTH regulates calcium reabsorption and phosphorous excretion
• ***testosterone*** (0.3 to 1.0 mcg/dL)—deficiencies in testosterone have been linked to osteoporosis in men
• ***alkaline phosphatase*** (42 to 136 units/L)—increased levels may be indicative of a problem with the bones.

Ordinary X-rays can show fractures typical of osteoporosis, but they aren't helpful in determining the amount of bone mass. A person would have to lose as much as 40% of bone calcium before it would become evident on an X-ray. Therefore, techniques have been developed to measure bone mass loss. Such testing is helpful both in determining the degree of damage and in monitoring treatment responses.

Dual X-ray absorptiometry (DXA) measurement of bone mineral density is the gold standard for diagnosing osteoporosis. At the present time, the clinical diagnosis of osteoporosis is made by the result of this test, along with other conclusive clinical evidence.

Osteoporosis is defined as bone mineral density at least 2.5 standard deviations below the gender-specific young adult mean. The T-score compares the patient's bone density to that of a young adult of the same sex. A negative score indicates bone loss. A T-score of -1 to –2.5 shows low bone mineral density. A T-score of -2.5 or greater is diagnostic of osteoporosis. The higher the negative number result on the test, the greater the risk of fracture.

The Z-score compares bone density to that of other people of the same age, sex, and ethnic group. A negative Z-score means a patient's bones are thinner and weaker than those of similar individuals; a positive number means his or her bones are stronger. However, the Z-score may not be very useful in older adults because some bone loss is normal as we age. A patient could have a positive Z-score and still be at risk for fractures.

did you know?

Because the primary source for vitamin D is sunlight, a person needs 5 to 30 minutes of sun exposure to the skin of the face, arms, back, or legs two times per week. The amount of exposure depends on the time of the year. People living on the northern border of the United States may need to consume additional vitamin D from foods during the winter. Hazy, cloudy days will also interfere with sun exposure and may warrant additional dietary vitamin D intake. With a sunscreen protection of 8, vitamin D production is cut by 98%.

After being absorbed, vitamin D is chemically converted in the liver and kidneys into an active form. The end substance stimulates calcium absorption in the intestine. During menopause, the kidney loses some of its ability to convert vitamin D into its active form.

In early 2011, the U.S. Preventive Services Task Force updated its recommendations to advocate DXA screening for all women age 65 and older, and additionally for women younger than age 65 whose clinical risk factors place them at a fracture risk similar to a 65-year-old woman. Men age 70 and older, as well as men ages 50 to 70 with clinical risks, should also be screened.

Other diagnostic tests include quantitative ultrasound (QUS) and quantitative computerized tomography (QCT). ***QUS*** is used to test at the heel because it contains trabecular bone like the lumber spine. DXA measures bone density, whereas QUS measures bone quality (the structure, elasticity, and strength of bones). QUS is portable, less costly than DXA, and has a lower amount of radiation exposure involved. ***QCT*** provides knowledge about bone mass density (cortical and/or trabecular) and bone geometry (volume and cross-sectional areas). Unlike DXA, QCT reports volumetric mineral density in mg/cm^3 rather than bone mineral density as a Z-score.

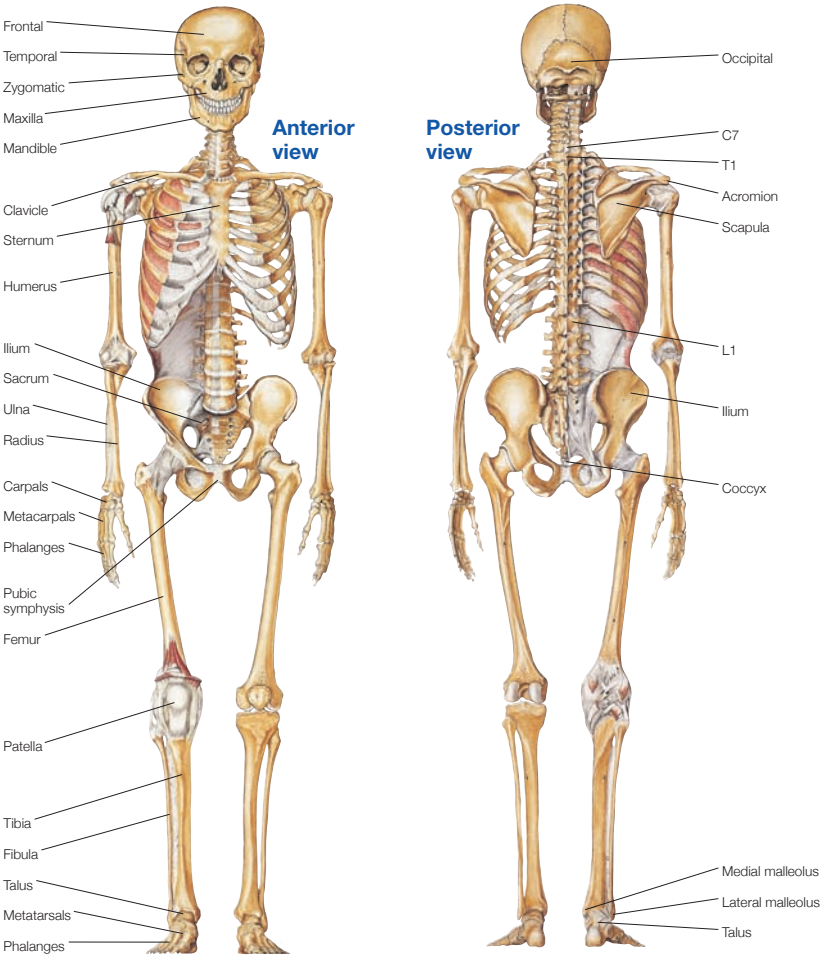
It has been recognized that some difficulty exists in accurately measuring bone mass and quality. The World Health Organization developed the Fracture Risk Assessment Tool (FRAX) to assess the 10-year probability of hip or major osteoporosis fractures in postmenopausal women and men ages 40 to 90 not treated for osteoporosis. It's important to remember that the algorithm is applicable only for patients who remain untreated. And the FRAX questionnaire isn't without its limitations. It lists 12 risk factors for osteoporosis and requires a numeric value or "yes" or "no" response as appropriate. Incorrect entries may lead to wrong conclusions that may affect treatment decisions. Current recommendations for treatment are a fracture risk of 20% or greater or a hip fracture risk of 3% or greater.

Building better bones

The best treatment for osteoporosis is prevention. After a fracture has occurred because of osteoporosis, it's too late to implement the most effective treatment strategies. Although some improvement in bone mass and quality has been demonstrated with aggressive treatment, the primary focus must be on stopping or slowing any further bone loss. Osteoporosis prevention and treatment includes calcium, vitamin D, and weight-bearing exercise, along with prevention of falls.

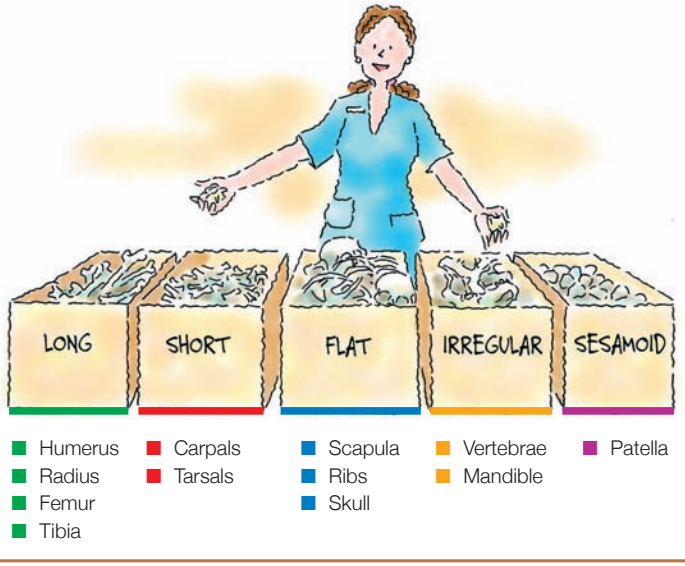
Bone serves as an effective reservoir of essential minerals for the rest of the body, supplying calcium when tissues need it and acting as a dam when the tissues are getting too much (see *Picturing the skeletal system*). If calcium concentration in

Picturing the skeletal system



Bone classification

Bone are typically classified by shape.



the blood begins to fall, the bones release more calcium to make up for the deficit. If the calcium concentration gets too high, the bones extract the excess. This is a state of dynamic equilibrium in which calcium is always moving in one direction or another to maintain a constant level in nonskeletal tissue. Although 99% of all calcium is in the bones, the remaining 1% is spread throughout the body and is crucial to the proper functioning of all organs and the smooth performance of all body systems.

Food and dietary supplements are the body's only outside sources of calcium, and enough must be consumed and absorbed to maintain normal blood levels. However, most people consume well below the U.S. dietary reference intake of 800 to 1,500 mg/day. This deficiency is particularly dangerous in growing children, adolescents, and individuals over age 45. When the blood level of calcium is low, the intestine will absorb more and the kidneys will eliminate less. If this doesn't provide an adequate amount, the skeletal storehouse will be called on to supply more of the needed mineral. This often leads to women entering menopause far below their genetic potential, making their age and sex-related bone loss devastating.

Three hormones play an important role in this complicated biologic process: PTH; calcitonin, a peptide hormone; and vitamin D. As the blood calcium level falls, PTH is excreted by the parathyroid gland to speed up bone breakdown. Calcitonin is a hormone produced by the thyroid gland, and it acts to conserve calcium in the bones by blocking the effects of PTH. Vitamin D is produced in skin tissue during exposure to the sun's UVB rays.

The National Institutes of Health (NIH) Consensus Panel on Osteoporosis recommends a calcium intake for adults of up to 1,500 mg/day. Children aren't to be excluded; children ages 4 to 8 should take in 800 mg/day, while adolescents ages 9 to 18 should consume 1,300 mg/day. The most common calcium supplementation product and the least expensive is elemental calcium carbonate. It has been suggested that calcium supplements be taken with juice or foods that provide acid to aid in dissolution. When purchasing calcium supplements, it's imperative that patients read the label and ensure that the elemental calcium content is adequate (see *A closer look at calcium supplements*).

Daily supplementation with 800 to 1,000 international units of vitamin D_3 is also suggested. A combination of vitamin D_3 and calcium supplementation has been shown to reduce fracture rates and risk of falls, but vitamin D_3 alone doesn't appear to be as effective.

Dietary tips to help your patients maintain healthy bones include:

- Eat plenty of foods high in absorbable calcium and vitamin D, such as broccoli,

Major risk factors for osteoporosis

cheat sheet

Risk factor	Associated characteristics
Low bone mass	By itself, predicts fracture risk.
Aging	The longer an individual lives, the greater the chance of developing osteoporosis. Sluggish intestines, inactivity, and increased tearing down of bone tissue play a major role.
History of fractures in first-degree relatives	Potential bone mass is genetically determined.
Small, slender body type	Individuals with a small, thin frame tend to have less bone mass to begin with, which means there's less bone to work with.
Ethnicity	Individuals of African ethnicity have thicker bones and average 10% more bone mass than Caucasians or Asians.
Sex	Women have smaller, thinner bones, with a peak bone mass that's 30% less than men. Women tend to give up bone more rapidly than men, and this is accelerated after menopause.

chestnuts, most dark green leafy vegetables, flounder, and salmon.

• Eat cottage cheese, sliced cheese, and dairy products for good sources of calcium.

• Within reason, include eggs in the diet because they contain sulfur, which is needed for healthy bones.

• Avoid red meats and foods high in fat because they bind calcium in the intestine.

• To avoid competition for absorption of calcium, avoid phosphorus-containing products, such as soft drinks, high-protein animal products, and alcohol.

A sufficient protein intake has been shown to improve the clinical outcomes of hip fractures. Very low protein intake has been associated with a decrease in bone formation and overall bone strength. Fruits and vegetables, which in turn counter the effect of acid produced by animal protein and fats, have a positive effect when three to nine servings a day are consumed.

Exercise, and its relationship to bone health, has taken on an increased importance. A key factor related to the benefit of exercise is its importance in the prevention of peak bone loss in later life. The NIH recommends 3 to 4 hours weekly of weight-bearing and resistance exercises, such as walking along with the use of handheld weights. Additionally, it's believed that exercise can help promote good posture, balance, strength, movement, flexibility, and healthy outcomes.

Other lifestyle factors to consider include:

• Alcohol intake has been linked to osteoporosis. Although it isn't known how much is too much, it's an accepted fact that alcohol has a negative effect on the liver, which helps convert vitamin D to its active form.

• Cigarette smoking has been shown to decrease estrogen levels, with a subsequent earlier onset of menopause. Nicotine constricts the blood vessels, which may impair bone nourishment and general bone health. Smokers lose bone at a greater rate, and smoking is associated with a 40% to 50% increase in hip fracture risk.

A closer look at calcium supplements

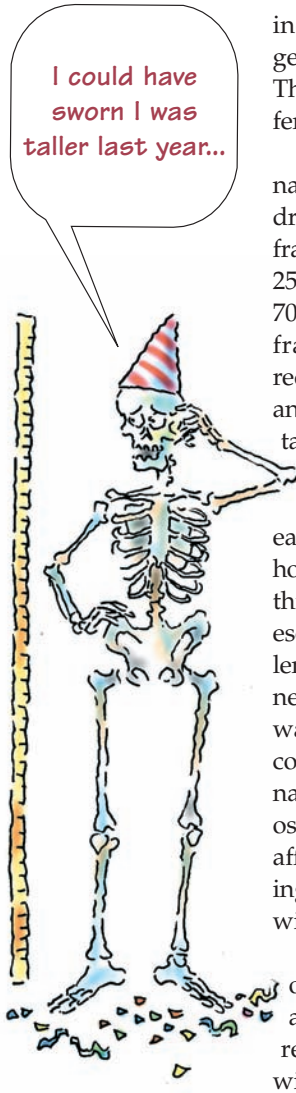
Calcium supplements	Implications
Calcium citrate	• Best absorbed in an acidic environment • Can be taken any time of the day (even on an empty stomach) • People with acid reflux may not be able to tolerate citrate • Due to the fact that citrate provides less elemental calcium, a larger amount needs to be taken
Calcium carbonate	• Commonly available in over-the-counter medications • Best taken after meals
Dolomite, bone meal, or oyster shell	• These calcium pills may contain heavy metal or lead and are, therefore, best avoided
Calcium gluconate, calcium lactate	• Because low amounts of elemental calcium are available, a larger amount needs to be taken

• Caffeine from soft drinks, tea, coffee, and many other food products is believed to lead to a waste of calcium, making less available to be absorbed by the bones.

• Medications, such as glucocorticoids, diuretics, antacids, tetracyclines, and some anticonvulsants, may interfere with calcium absorption. Long-term use of glucocorticoids is the most frequent cause of drug-induced osteoporosis. A risk versus benefit analysis needs to be made for patients using glucocorticoids who are at risk for osteoporosis.

What's new in pharmacologic management?

Pharmacotherapy regimens for osteoporosis prevention and treatment are individually designed. When to begin, as well as how long therapy should continue, is based on whether the patient is experiencing osteopenia or osteoporosis, in conjunction with the patient's history and clinical picture. The overall goal is to reduce fractures and increase bone mineral density as much as possible. Antiresorptive agents



include biphosphonates, calcitonin, estrogen therapy, and other hormone therapy. These medications slow bone loss by interfering with the activity of osteoclasts.

Oral biphosphonates include alendronate, risedronate, ibandronate, and zoledronic acid. With oral bisphosphonate use, fracture reduction rates have ranged from a 25% reduction in nonvertebral fractures to a 70% reduction in vertebral fractures. Hip fracture rates have been reported as reduced by 41%. Approved for both men and women, these medications must be taken first thing in the morning on an empty stomach with 8 oz of plain water. The patient must remain upright and not eat or drink anything for 30 minutes to 1 hour after taking the pill. When adhering to this regimen, patients experience less esophageal erosion. Because of the challenge posed by oral biphosphonates, a newer monthly administration protocol was developed with the goal of improved compliance. Recently, the use of biphosphonates has been linked to a development of osteonecrosis of the jaw. A rare condition, affecting 0.001% to 0.002% of patients taking these agents, it's more often associated with high doses of I.V. biphosphonates.

Calcitonin is approved for postmenopausal osteoporosis treatment and is often used as an off-label analgesic agent for the reduction of bone pain that's associated with vertebral compression fractures. An oral agent, calcitonin is also available as a nasal spray. With the use of calcitonin, the risk of vertebral fractures is believed to be reduced by about 30% to 35%. This medication is well-tolerated.

Estrogen and ***estrogen-progesterone combination products*** have long been known to significantly increase bone mineral density. Because of the identified increased occurrence of coronary heart disease, embolic events, stroke, and breast cancer, this treatment modality is now reserved for women with moderate-to-severe menopause-related symptoms, and isn't recommended for health promotion alone.

Raloxifene, a selective estrogen receptor modulator that acts on the estrogen receptors throughout the body, is effective in reducing the risk of vertebral fractures by 30% to 50% and increasing bone mineral density by 2.1% to 2.4% at the hip and 2.6% to 2.7% at the spine. This medication has dual FDA indications for osteoporosis and breast cancer prevention, making it an ideal selection for women with osteoporosis who are at high risk for breast cancer.

Teriparatide is the only parathyroid medication currently approved by the FDA for osteoporosis treatment. This medication is believed to be highly effective in building bones and reducing fracture. There's a reported 65% reduction in vertebral fracture rates and a 53% reduction in nonvertebral fracture rates. However, teriparatide isn't generally used as a frontline therapy. This could be related to its high cost; the occasional nausea, vomiting, and headache associated with it; and the need to educate patients to self-inject.

Denosumab, a recently approved monoclonal antibody, is administered to women with postmenopausal osteoporosis at high risk for fracture. It helps to decrease bone resorption and strengthen bones. It's given as an injection, once every 6 months. A 68% reduction in vertebral fracture rates has been noted.

A team approach to education

As our population continues to age, osteoporosis will have an even more profound impact on the health of Americans, and the economic consequences are enormous. Lifestyle and personal risk factors must be evaluated. Practitioners must look at ways to prevent the disease from starting and what can be done to diminish the devastation after it has occurred. Many of our patients who are prescribed medication for osteoporosis will stop taking it at the end of the first year, a rate often similar to

patients who stop taking BP and cholesterol medications.

If a patient takes the prescribed medication and then stops, bone density continues to decline with no overt evidence until a fracture occurs. Therefore, consistent patient education using a team approach for maintaining and building bone strength, early identification of bone loss, and prevention of falls is key for preventing fractures and their consequences. Remember, prevention begins with knowledge. Knowledge, participation, and commitment will help keep your patients' bones strong throughout their lives. ■

Learn more about it

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