The bone decay of osteoporosis can cripple, but an improved understanding of how the body builds and loses bone is leading to ever better prevention and treatment options

RESTORING AGING BONES

By Clifford J. Rosen

Late last year a new patient, 72-year-old Maxine LaLiberte, limped into my office. She said she had always been very active. She baby-sat frequently for her nine grandchildren and had been looking forward to a long-planned cross-country motor home trip with her husband. But now the excruciating pain between her shoulder blades was curtailing her movements and making her feel old.

I was all too familiar with those symptoms in people my patient's age. Even without examining her, I was reasonably sure that one or more of her vertebrae had fractured as a result of osteoporosis, a disorder characterized by bone loss so severe that fractures occur spontaneously or from even minor bumps.

Osteoporosis afflicts about 10 million Americans, especially women past menopause. Fully half of all postmenopausal women will incur an osteoporosis-related fracture during their lives. Fortunately, the outlook for people with osteoporosis has never been better. Drugs are now available that can restore lost bone and thereby greatly reduce the risk of additional breaks. Furthermore, recent insights into the cellular and molecular bases of osteoporosis have generated exciting ideas for new and even more effective therapies.

Just a decade ago therapeutic options for osteoporosis consisted mainly of calcium supplements, painkillers and, for women past menopause, estrogen replacement therapy—helpful treatments, but imperfect. Estrogen replacement therapy, for instance, increases the risk for heart attack, stroke, breast cancer and

NEW TREATMENTS and preventives for osteoporosis are allowing women—and men—to avoid its worst consequences.

OSTEOPOROTIC SPINE (*left*) shows the bone thinning and collapsed vertebrae characteristic of the disease. In contrast, the vertebrae of a normal spine (*right*) are dense and uniform.

blood clots. Today, in contrast, pharmacies stock several drugs that reduce the likelihood of new fractures by as much as 70 percent in the first year of treatment.

Similarly dramatic improvements have taken place in diagnosis. Not long ago a fracture often was the only tip-off that someone had osteoporosis. But physicians are now using a sophisticated in-office tool called dual-energy x-ray absorptiometry (DEXA) to measure bone mineral density at sites especially susceptible to fracture. DEXA is allowing doctors to diagnose osteoporosis much earlier—in time to initiate drug treatment that can keep bones intact and prevent fractures from occurring. In addition, DEXA can be a useful screening tool to predict the likelihood of future breaks at any site [*see box on opposite page*].

Recent research has also yielded a new appreciation for heredity's role in osteoporosis. The disorder was long considered a "traumatic" condition, in which decades of skeletal wear and tear culminate in fractures and pain. Genetic investigations have now revealed, however, that genes influence bone density and, hence, the risk of fractures. These studies indicate that genetic differences account for up to 70 percent of human variability in bone mass, although such factors as diet and exercise play a part, too. Apparently, many different genes influence propensity. As specific osteoporosis-promoting gene variants are found, they could form the basis for tests to detect susceptibility and could also lead to drugs able to counteract their effects.

Reversing Silent Thievery

THE NEED FOR better preventive and therapeutic options is urgent. Osteoporosis, which literally means "porous bones," is the underlying cause of virtually all broken bones in people older than 65. The vertebrae, hips and wrists are particularly susceptible to osteoporotic fractures. These broken bones can cause chronic, disabling pain and—in the case of the hip—often usher in a series of events that can lead to death: of the 275,000 older Americans who suffer a broken hip every year, 20 percent die within a year of the episode from blood clots, infections or undernutrition. In addition to the 10 million Americans with existing osteoporosis, another 18 million have low bone mass (osteopenia), a condition that does not qualify as osteoporosis but heightens their risk for eventually developing the disorder.

Medicines introduced in the past 10 years are designed to alleviate the suffering of osteoporosis by interfering with a process known as bone remodeling, or turnover. Seemingly inert when viewed from the outside, bone is a living tissue that ceaselessly destroys and rebuilds itself throughout adult life. This remodeling essentially replaces the entire skeleton every 10 years—dissolving, or resorbing, old bone and completely replacing it with new. Remodeling undoubtedly serves some useful functions, such as freeing calcium from bone for use by various tissues and repairing microfractures. But defective remodeling underlies the development of osteoporosis.

During childhood and adolescence, bone formation proceeds at a faster rate than resorption, causing bone density to increase until young adults attain their peak bone mass at around age 18. Density stays constant throughout young adulthood as bone formation and resorption proceed at the same rate. But around age 40, everyone begins to experience some age-related bone thinning as resorption begins to outpace bone formation. For several reasons, however, the risk of osteoporosis is much greater in women, who account for 80 percent of cases.

The average woman attains a peak bone mass that is generally about 5 percent below that of a man's, so women have a bit less bone density "in the bank" when age-related bone loss begins. In addition, women lose an important bone protector—estrogen—at menopause. As

Overview/*Osteoporosis*

- Bones are constantly being dissolved and remade throughout life. Osteoporosis results when bone-degrading cells, called osteoclasts, are more active than bone-building cells, called osteoblasts.
- Novel treatments for osteoporosis depend on blocking the activity of osteoclasts or killing them.

ILLUSTRATION BY MELISSA SZALKOWSKI, GCa *Photo Researchers, Inc.* (*left spine*), CORBIS (*right spine*) (*preceding pages*); ROBERT M. LEVIN *Boston Medical Center* (*this page*)

a result, bone loss in women can increase sharply for some four to seven years after the shutoff of estrogen at menopause.

Two types of bone cells carry out remodeling—bone-forming osteoblasts and large, bone-resorbing osteoclasts [*see illustration on next page*]. Both cell types come together in three milllion to four million remodeling sites, termed basic multicellular units (BMUs) of bone remodeling, that are scattered throughout the skeleton. Remodeling always occurs in the same sequence: a rapid (two- to three-week) bone resorption phase followed by a slower (two- to three-month) bone formation phase.

Resorption begins when the osteoclasts attach to a microscopic section of bone surface and release substances that degrade the structural parts of bone—calcium, other minerals and the protein collagen. This degrading activity forms an indentation in bone called a resorption pit, after which the osteoclasts disappear, probably as a consequence of programmed cell death (also called apoptosis, or cell suicide). Remodeling's bone formation phase begins when osteoblasts—perhaps attracted by growth factors released during bone resorption—converge on the resorption pit, filling it with new bone by synthesizing and secreting collagen and other bone proteins. Calcium, phosphorus and other minerals then crystallize around the collagen matrix to form hydroxyapatite, the hard, mineralized part of bone that accounts for 90 percent of its mass.

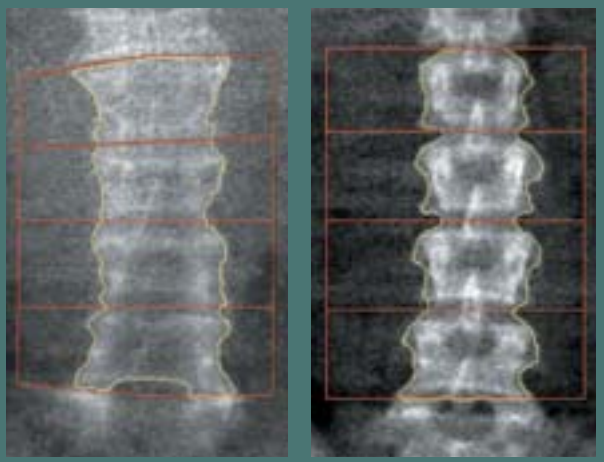
Until late last year, all drugs approved for treating osteoporosis were considered antiresorptives, because they slow resorption more than they promote formation (although in truth, anything that affects one process also affects the other to some degree). Drugs of one antiresorptive class in particular—the bisphosphonates—have transformed osteoporosis treatment over the past decade and are now the first choice for both men and women with osteoporosis. These oral agents slow bone remodeling by attaching readily to the mineral part of bone, where they sit in wait for osteoclasts to bind to the bone's surface. Once that happens, the bisphosphonates diffuse into the osteoclasts and induce those cells to self-destruct.

Large-scale, randomized clinical trials have shown unequivocally that the most potent bisphosphonates—alendronate (Fosamax) and risedronate (Actonel)—not only prevent further bone loss but can also increase bone density in most patients by 5 to 10 percent over three years. That bone buildup may seem modest, but it is enough to reduce the risk of spine, hip and wrist fractures by as much as 50 percent at three years, with more significant fracture reduction evident in the first year of therapy. The bisphosphonates need to be taken just once a week and seem exceptionally safe: aside from heartburn, side effects are rare. These drugs have been in use for only a decade, however, so their long-term safety beyond 10 years remains to be demonstrated.

Seeking New Drug Targets

MOTIVATED IN PART by a desire for more effective osteoporosis drugs, scientists are now intensively studying how bone remodeling is regulated so that those controls can be manipulated to en-

TO SCREEN OR NOT TO SCREEN?



SPINAL SCANS made with dual-energy x-ray absorptiometry (DEXA) are used to diagnose osteoporosis. Bone in the lumbar (lower) spine of someone with osteoporosis (*left*) is much less dense than that in the spine of a healthy individual (*right*). The vertebrae have also begun to collapse, shifting the spine out of alignment (*indicated by red lines*).

SHOULD OLDER WOMEN be screened to see if they are at risk for osteoporotic fractures? Ever since tools for measuring bone mineral density became available to doctors, this question has elicited intense controversy.

Studies show that density measurements—of the hip or spine, for example—can reliably predict a person's risk for a fracture at that site. The "gold standard" for measuring bone mineral density is a technology called dual-energy x-ray absorptiometry (DEXA), which uses x-rays but involves very little radiation exposure. DEXA diagnoses osteoporosis when it finds that the measure of density is much lower than the average for healthy young women at the spine, hip or wrist (2.5 or more standard deviations from the mean).

DEXA not only tells a woman whether she has osteoporosis; it can predict her risk for fracture at that site over the next several years—potentially useful knowledge, because new drugs can rebuild bone density and prevent fractures before they occur. Yet critics of screening note that mineral density is just one of many factors (including exercise, nutrition, genetics and bone quality) that influence a woman's fracture risk. In addition, critics say, women worried about low scores might be scared into taking drugs, such as estrogen, that might produce dangerous side effects.

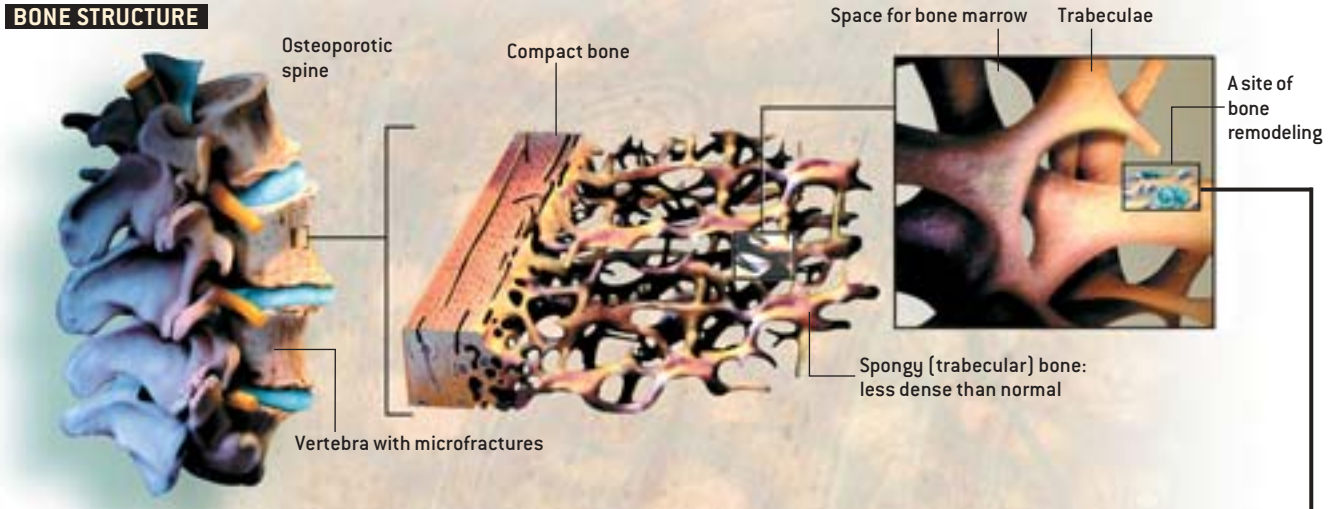
Last September the U.S. Preventive Services Task Force came down firmly on the side of screening, recommending for the first time that all women aged 65 and older have their bone density measured at least once to assess their risk of fracture. In support of its recommendation, the task force emphasized that the risk for osteoporosis "increases steadily and substantially with age." Compared with women aged 50 to 54, the task force wrote, the odds of having osteoporosis are 5.9 times higher in women aged 65 to 69 and 14.3-fold higher in women aged 75 to 79. —*C.J.R.*

FAYE LIQUE *Maine Center for Osteoporosis Research and Education*

OSTEOPOROSIS AND TARGETS FOR THERAPY

THE BODY CONTINUOUSLY renews, or remodels, the bones throughout life using two types of cells: osteoclasts, which destroy old bone, and osteoblasts, which make new bone. Osteoporosis results when the normal balance between the activity of osteoclasts and osteoblasts becomes disrupted, tipping the scales in favor of bone destruction. Various drugs are now on the market or under development (*gold boxes*) to treat osteoporosis by decreasing the action of osteoclasts or boosting that of osteoblasts.

BONE STRUCTURE

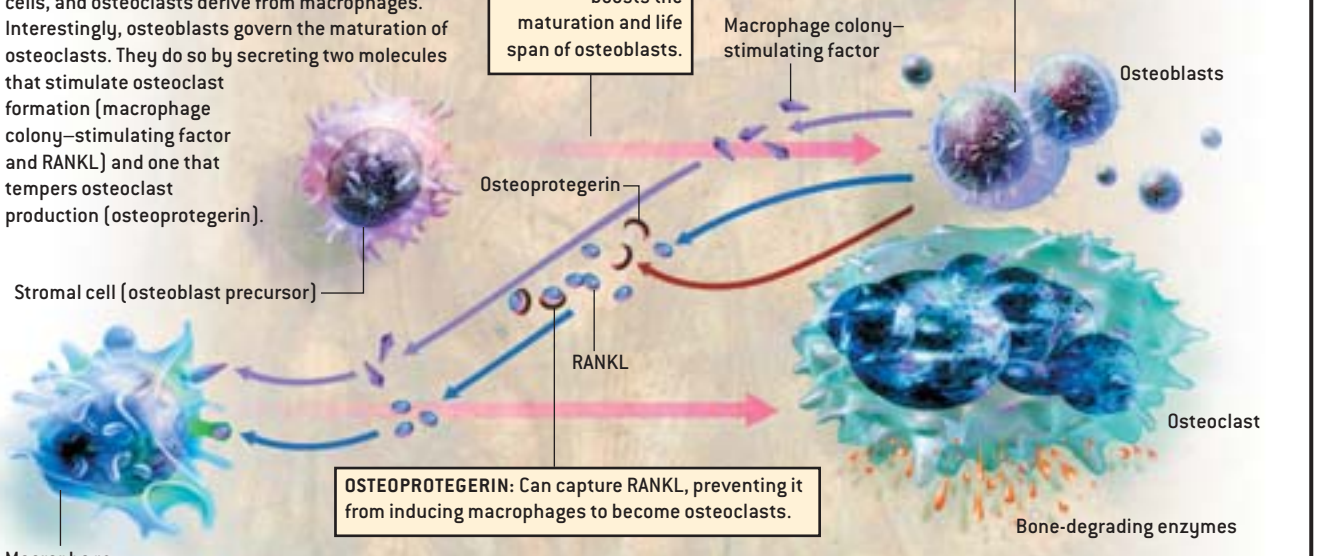


OSTEOCLAST AND OSTEOBLAST FORMATION

OSTEOBLASTS arise from precursors called stromal cells, and osteoclasts derive from macrophages. Interestingly, osteoblasts govern the maturation of osteoclasts. They do so by secreting two molecules that stimulate osteoclast formation (macrophage colony–stimulating factor and RANKL) and one that tempers osteoclast production (osteoprotegerin).

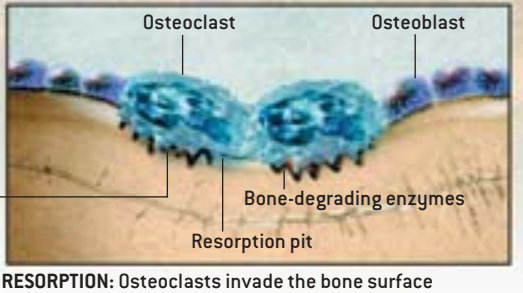
PARATHYROID HORMONE: Given intermittently, boosts the maturation and life span of osteoblasts.

ESTROGEN (AND RELATIVES): Estrogen, SERMs and ANGELs prompt osteoblasts to make more osteoprotegerin. They also prolong the life of osteoblasts and kill osteoclasts.



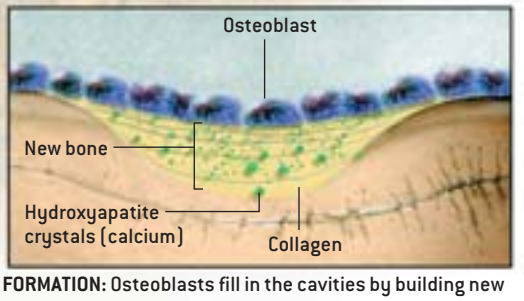
OSTEOPROTEGERIN: Can capture RANKL, preventing it from inducing macrophages to become osteoclasts.

BONE REMODELING



BISPHOSPHONATES: Induce osteoclasts to self-destruct.

RESORPTION: Osteoclasts invade the bone surface and secrete bone-dissolving enzymes, which carve out cavities (resorption pits) to release calcium.



FORMATION: Osteoblasts fill in the cavities by building new bone. Osteoporosis occurs when osteoclasts carve too deeply or when osteoblasts fail to fill enough new bone.

KEITH KASNOT

courage bone formation. In the past two years they have made progress in teasing out the features that regulate osteoclastogenesis—the birth and maturation of osteoclasts, the bone-dissolving cells.

Osteoblasts and osteoclasts both arise through the differentiation of predecessor cells in bone marrow (which also houses the body's blood-producing cells). So-called stromal cells mature into osteoblasts, and macrophages (a type of white blood cell) differentiate into osteoclasts. Recently biologists have learned that stromal cells and their offspring, the osteoblasts, govern the production of the bone-degrading osteoclasts; they do so by secreting three different signaling molecules—two that promote osteoclast development and one that suppresses it.

Early on, for instance, osteoblasts secrete a signaling molecule called macrophage colony–stimulating factor that binds to a receptor on macrophages, inducing them to multiply. A second chemical, RANKL, secreted by osteoblasts, binds to a different receptor on macrophages, inducing the cells to differentiate into osteoclasts. The third osteoblast product, however, osteoprotegerin, can block osteoclast formation by acting as a decoy receptor—latching onto RANKL and preventing it from coming into contact with its intended receptor on macrophages.

In theory, anything that interferes with osteoclast formation—and thus with bone resorption—should enhance bone density. Research involving one intervention based on the new molecular understanding—delivery of osteoprotegerin—is ongoing. In human trials, injections of the molecule have slowed the rate of bone resorption by at least 60 percent. Biologists have also identified nearly a dozen other chemical signals involved in coordinating bone formation and resorption—among them estrogen, parathyroid hormone and insulinlike growth factor-1. Study of these substances has suggested additional strategies for preventing and treating osteoporosis.

Circulating estrogen exerts its differing influences in the body by teaming up with estrogen receptors present in various tissues, including the uterus, breast, colon, muscle and bone. Doctors have known for 50 years that estrogen helps to preserve bone density, but the molecular mechanisms have long been a mystery. It is now clear that one of estrogen's functions is to interfere with the creation of osteoclasts.

More specifically, estrogen binds to osteoblasts in bone and induces them to increase their output of osteoprotegerin and to suppress their RANKL production—a combination of signals that suppresses osteoclast formation, keeping bone loss in check. The reduction of estrogen that accompanies menopause thus contributes to bone loss largely by removing an important brake on osteoclast formation and activity. In addition, estrogen appears to prolong the lives of osteoblasts while simultaneously promoting the suicide of osteoclasts. So the decline of estrogen at menopause hits women with a triple whammy: shorter-lived osteoblasts must contend with more osteoclasts that have longer life spans.

Until last year, physicians routinely urged their female patients to take hormone replacement therapy (usually estrogen combined with progestin, a form of progesterone) at menopause, not only to protect against osteoporosis but to ward off other age-related health problems for which estrogen was considered useful, including heart disease and dementia. The health benefits of hormone replacement therapy were thought to outweigh any possible dangers.

So women and their doctors were stunned last July when medical authorities overseeing the federally sponsored Women's Health Initiative determined that hormone replacement therapy caused small increases in breast cancer, heart attack, stroke and blood clots and that the risks of the therapy outweighed its modest benefits, which included small decreases in the risks for hip fractures and colon cancer. Three months later, after reviewing results from this and similar studies, the influential U.S. Preventive Services Task Force recommended against the use of combined estrogen and progestin therapy for preventing cardiovascular disease and other chronic conditions, such as osteoporosis in postmenopausal women. For now, the best estrogen alternatives for bone health are the bisphosphonates. In a meta-analysis that our group recently completed, combining data from many studies, the bisphosphonates proved slightly better than estrogen therapy at increasing bone mineral density and preventing fractures.

Drugs known as selective estrogen receptor modulators (SERMs) may also be useful for the long-term treatment of women fearful about breast cancer. SERMs act like estrogen in some tissues (bone, for example) while at the same time blocking estrogen's effects in other tissues, such as the breast. So far the only SERM approved for the treatment and prevention of osteoporosis is raloxifene (Evista), but others are being tested. Raloxifene is not as effective as estrogen in increasing bone mineral density and preventing fractures, and it can cause hot flashes; however, studies involving women being treated for osteoporosis have found that raloxifene reduced their risk for breast cancer.

Controlling the Controllers

BUT AN EVEN BETTER ANSWER may be on the way. In a few years, scientists may begin human testing of synthetic estrogens that offer all of estrogen's bone benefits and none of the risks—and help men as well as women. Work on those agents began in response to a radical hypothesis proposed a few years ago by Stavros C. Manolagas of the University of Arkansas for Medical Sciences.

Manolagas proposed that estrogen exerts its effects on cells in two separate ways. One is the well-established mechanism by which estrogen influences *all* its target tissues in females, reproductive

THE AUTHOR

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BLAME IT ON EVOLUTION

MILLIONS OF YEARS AGO our ancestors emerged from the sea and evolved into land mammals that confronted a serious problem: how to satisfy their calcium needs, now that absorbing calcium from seawater was no longer an option.

Humans and other mammals evolved an ingenious solution to the calcium challenge, relying on our own skeletons—where 99 percent of bodily calcium resides—as calcium "banks." In a process known as calcium homeostasis, the mineral is deposited into or withdrawn from the skeleton so that blood levels are kept within the narrow range essential for nerve conduction, blood clotting, muscle contraction and other vital physiological functions. Unfortunately, this process is at the root of osteoporosis, because it calls for sacrificing the skeleton if that is what it takes to maintain adequate blood calcium levels.

The regulatory system at the heart of calcium homeostasis features parathyroid hormone (PTH), vitamin D and ingested calcium. When the parathyroid gland (located near the thyroid gland in the neck) senses a dip in circulating calcium levels, it secretes PTH—a hormone that works in several ways to boost blood calcium levels. PTH powerfully influences osteoporosis by inducing bone-degrading cells (osteoclasts) to dissolve bone and release calcium into the blood. The hormone also stimulates the kidneys to return calcium to the blood instead of excreting it and induces the small intestine to absorb calcium more efficiently from food—a feat that PTH accomplishes indirectly, by increasing the body's production of vitamin D.

Some 90 percent of the average person's vitamin D is synthesized in the skin using energy from the sun's ultraviolet rays (we also get some vitamin D from foods such as fatty fish and vitamin D–fortified dairy products). In an ongoing chemical reaction that progresses from the skin to the liver to the kidney, PTH helps to transform vitamin D3 (the vitamin D precursor made when ultraviolet rays strike the skin's epidermis) into vitamin D's most active form. Vitamin D acts directly on the small intestine, boosting its absorption of calcium from food so that more of the mineral is available for physiological functions and for building bones.

A falloff in vitamin D curtails the amount of calcium absorbed from food and causes blood calcium levels to decline, prompting the parathyroid gland to secrete more PTH to raise levels of active vitamin D. People with consistently low levels of the vitamin tend to have chronic elevations in serum PTH, a condition known as secondary hyperparathyroidism. The elevated PTH level manages to maintain vitamin D and calcium at close to normal levels but also accelerates the bone resorption that leads to osteoporosis in many people.

Recent surveys have found that low serum vitamin D levels are surprisingly common, especially among people living in northern latitudes, where sun exposure is limited. In studies involving older women, vitamin D supplements have been found effective in returning vitamin levels to normal and in preventing bone loss. I recommend that women older than 65 living in northern latitudes take 400 International Units (IU) of vitamin D daily, plus an additional 400 IU during the winter months, when bone densities tend to fall and fracture rates rise.

Ingesting sufficient quantities of calcium (1,000 to 1,500 milligrams per day) is equally important. Studies indicate that the best time for an adequate calcium intake is not later in life but during childhood and adolescence, when peak bone mass is being built. The same holds true for exercise, which is often recommended for keeping older bones healthy. When combined with adequate calcium intake, exercise—particularly jogging and other forms of weight-bearing exercise—helps to slow bone loss and may even increase bone density in older people. But studies involving young athletes strongly suggest that regular exercise—like calcium intake—exerts its major bone-building effect during youth. The higher the bone mass one attains as a young adult, the lower one's risk for developing osteoporosis later in life. —*C.J.R.*

GETTY IMAGES (*glass of milk*); JONELLE WEAVER *Getty Images (cheese)*; FRANÇOISE SAUZE *Photo Researchers, Inc. (calcium pills)*; INC. JANEART *Getty Images (woman walking)*

BONE-BUILDING ESSENTIALS include foods rich in calcium and vitamin D—such as fortified milk and cheese—or vitamin and mineral supplements. Weight-bearing exercise also keeps bones strong and healthy.

and nonreproductive alike: After estrogen crosses a cell's outer membrane and cytoplasm, it enters the nucleus and binds to its receptor. This estrogen/receptor duo (along with other nuclear proteins known as co-activators) directly interacts with specific sequences of DNA to induce certain genes to give rise to specific proteins needed for cellular activities.

But this "genotropic" pathway (so named because of estrogen's direct contact with genes) could not explain all of estrogen's numerous effects on cells. So Manolagas hypothesized that estrogen also acts through a different mechanism that influences bone and other nonreproductive tissues in both males and females and has no effect on reproductive tissues.

In this scenario, estrogen still binds to receptors in cells, but then the hormone and its receptor induce cellular changes by acting on kinases, enzymes that reside outside the nucleus, in the cytoplasm. (In the case of bone tissue, these kinases exist in the cytoplasm of osteoblasts and osteoclasts.) The activated kinases then migrate to the nucleus, where they help to regulate the expression of genes.

Manolagas and his colleagues synthesized an estrogenlike hormone, dubbed estren, designed to act exclusively through the nongenotropic pathway. Last October in *Science,* Manolagas and his team reported on mouse studies comparing estren with estrogen. Estren was even more effective than estrogen in rebuilding bone in female mice whose ovaries had been removed to simulate menopause. Just as important, estren did not increase the weight of mice uteri, confirming the drug's lack of effect on reproductive tissue. Similar results were observed in male mice: estren proved just as good as testosterone in rebuilding lost bone in mice whose testes had been removed, and, unlike testosterone, it had no effect on the weight of seminal vesicles in male mice.

The findings indicate that estren could become the first of a new class of osteoporosis drugs that Manolagas has named ANGELS (activators of nongenomic estrogenlike signaling). These agents might work even better than estrogen in building bone without causing estrogen's unwanted effects on reproductive tissue, such as uterine and breast cancer.

In the Driver's Seat

MUCH AS ESTROGEN defends against bone loss by limiting osteoclast development, parathyroid hormone (PTH) can be considered the engine that "drives" osteoporosis, because it promotes the action of osteoclasts. PTH triggers osteoclast formation indirectly, by binding to osteoblasts and prompting them to increase RANKL output and decrease osteoprotegerin production—precisely opposite to the way estrogen regulates RANKL and osteoprotegerin to block osteoclast formation and preserve bone. Paradoxically, however, the notoriously "resorptive" PTH was recently approved as the first bone-building agent, as opposed to the antiresorptives, and some data suggest that it could be the best of all osteoporosis treatments.

Although the body's own PTH promotes bone loss when elevated over long periods, intermittent injections turn out to elicit quite a different response. The first inkling that PTH could build bone emerged in 1928, when researchers noted that PTH injections increased bone density in dogs. But the finding was ignored until the 1970s, when researchers at Massachusetts General Hospital and at the University of Cambridge began independently experimenting with delivering natural, and later recombinant, PTH. Over the past 25 years, experiments in humans have shown that intermittently administered PTH has an amazing ability to increase bone density (especially in the vertebrae), enhance the structural integrity of bone, and prevent fractures in both men and postmenopausal women. Typically, daily PTH injections result in bone-density increases of 8 to 10 percent after one year, with the risk of fracture reduced by an impressive 60 percent. Injectable PTH, under the brand name Forteo, was approved in late 2002 by the U.S. Food and Drug Administration for the treatment and prevention of osteoporosis in both men and women.

Why does the body's own PTH cause bone thinning, whereas PTH "pulses" have a bone-building effect? The intermittent doses seem to direct osteoblast precursors to mature into osteoblasts while simultaneously preventing established osteoblasts from dying, resulting in much greater numbers of bone-forming osteoblasts that function for longer periods. One particular molecule activated by intermittent PTH treatment is insulinlike growth factor-1 (IGF-1), which stimulates stromal cells to differentiate into bone-forming osteoblasts. It also circulates in high concentrations in the blood. Healthy adults have wide differences in their serum IGF-1 levels—and these can have important implications for bone density. For example, an evaluation of women in the Framingham Heart Study found that women in the highest quartile for serum IGF-1 had the highest bone density in the spine, hip and wrist.

Although diet has some influence over IGF-1 (malnutrition can cause steep declines), levels of IGF-1 are largely genetically determined. Over the past decade my laboratory in Bar Harbor, Me., has studied the genetic regulation of IGF-1 using two strains of mice that exhibit major differences in bone mineral density. Our research has shown that 60 percent or more of IGF-1 is genetically determined—a significant finding, because emerging evidence suggests that the "high normal" IGF-1 levels that protect against osteoporosis also correlate with an increased risk for breast cancer, prostate cancer and, perhaps, colon cancer. In the future, measuring IGF-1 levels in people may serve as a useful risk predictor, with high levels indicating a low risk for osteoporosis but an elevated risk for certain types of cancer.

In the end, the DEXA scan of Maxine's spine confirmed my suspicions. She had suffered a recent fracture of her eighth thoracic (T8) vertebra, near her shoulder blades, and her vertebral bone mineral density was more than 2.5 standard deviations below that of a 35-year-old woman. Either finding alone was sufficient for a diagnosis of osteoporosis, yet her prognosis was good. I told her that the back pain would diminish over the next several weeks. And I prescribed a bisphosphonate drug that would restore 5 to 10 percent of her bone density and reduce by 70 percent the likelihood that she would experience a fracture within the next year. The news cheered her. With more grandchildren on the way, her baby-sitting responsibilities were about to increase. SA

MORE TO EXPLORE

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