CME CREDIT

Prevention and osteoporosis management

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■ **BACKGROUND** Primary osteoporosis affects one in four women over the age of 65 and reflects lifelong processes and trends.

■ **SUMMARY** Skeletal bone constantly repairs the microscopic damage it sustains as a result of the normal activities of living. Women achieve their maximum bone density by the close of adolescence. Hereditary, nutritional, hormonal, and life-style factors affect the process of osteoporosis. Bone densitometry can detect very small deficits long before losses become clinically apparent. Intervention can halt osteoporosis at any point and perhaps increase bone density, but no known therapy can restore the normal bone architecture once it is lost.

■ **KEY POINTS** Women should maintain an adequate intake of calcium throughout their lifetime, especially during adolescence. Bone densitometry at the time of menopause detects preclinical osteoporosis and enables physicians to start therapy to preserve the bone structure.

■ INDEX TERMS: OSTEOPOROSIS; BONE DENSITY; PRIMARY PREVENTION
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THE PROCESS leading up to a broken hip begins decades earlier, perhaps even in adolescence. Clinicians caring for women have the opportunity to prevent osteoporosis throughout the life span. Unfortunately, although loss of bone density can be stopped and sometimes even reversed, once the architecture of the weight-bearing bones is lost, it cannot be replaced. In osteoporosis, a stitch in time saves nine.

BACKGROUND

Primary osteoporosis (ie, osteoporosis without an identifiable cause) affects one in four women over the age of 65 and accounts for about 1.2 million fractures per year. Approximately 15 to 20 million women in the United States are at risk.[1,2] Primary osteoporosis is a multifactorial disease that arises from an interplay among factors such as heredity, peak (or maximal) bone mass achieved during growth, nutrition, exercise, estrogen status, physiologic changes of aging (ie, poor calcium absorption, altered production, and sensitivity to vitamin D), and poorly understood changes in skeletal osteoclastic and osteoblas-

tic activities. Secondary osteoporosis, in contrast, is ascribable to a unique cause such as drugs; endocrine, genetic, or neoplastic diseases; gastrointestinal dysfunction; and idiopathic processes. Very unusual in older women, secondary osteoporosis is often seen in men or, less often, in young women. Therefore, an atypical presentation of osteoporosis should increase one's index of suspicion and prompt one to look for a secondary cause. Osteopenia with or without fractures in individuals of either sex is such a scenario, as are repetitive atraumatic fractures. Likewise, fractures in older postmenopausal patients in the absence of radiologic findings of osteopenia warrant closer scrutiny for secondary causes.

The hallmark of osteoporosis is fractures, because people with asymptomatic low bone mass who do not sustain fractures will probably not see a physician. The process of fracturing is complex, involving low bone mass, trauma, and qualitative changes in the bone.

We are most concerned about trabecular bone because it gives compressive strength to the skeleton. Trabecular bone is honeycombed with microscopic passages; membranes line these inner passages, and the whole area is bathed in fluid and cells from the marrow. In osteoporosis, the trabecular plates are thinner or are broken and are riddled with holes.

Normal daily activities subject the skeleton to microscopic stress cracks ("fatigue damage").[3] The skeleton constantly repairs itself (ie, remodels) in a complex process that is under the influence of a specific functional unit of cells, called the "basic multicellular unit." These cells have unique, specific activities, both temporally and geographically. When an injury occurs, chemical mediators call forth precursor cells that develop into osteoclasts and osteoblasts; these interact with each other in a balanced and measured ("coupled") fashion to repair the injury. Osteoclasts start eating away the damaged area and leave a cleaned-out concavity; they are usually present for 14 days. Subsequently, preosteoblastic cells arise and mature to osteoblasts; ultimately, these mature forms of the cells produce the necessary activity to fill in the hole, and the area returns to the quiescent state in several weeks.[4,5]

The chemical mediators of this process are a matter of scientific investigation. Some are derived from the skeleton itself, including transforming growth factors (analogous to epidermal growth factor), nontransforming growth factors, and cartilage-derived growth factors.[6] Mediators derived from the surrounding marrow cells include monokines and lymphokines.[6] Transforming growth factor beta has a specific effect to stimulate woven bone growth; it may well be used as a treatment in the future.[7]

PATHOPHYSIOLOGY

The destruction that occurs in osteoporosis is an exaggeration of the normal remodeling process. The cells that constitute the basic multicellular units no longer work in a coordinated fashion: where normally there is equal osteoclastic and osteoblastic activity that repairs damage, these processes are no longer equal or chemically coupled. Overactivity of the osteoclastic process produces high-bone-turnover osteoporosis; underactivity of the osteoblastic process produces low-bone-turnover osteoporosis. High turnover is especially important in the first 5 to 10 years after menopause. Low turnover becomes increasingly prominent thereafter.

A number of clinical factors seem to aggravate the overall process. These can generally be grouped into four major areas: heredity, nutrition, hormones, and life-style.

Hereditary factors

Although heredity plays a role in osteoporosis, no identifiable chromosome or gene has been implicated. Some studies reveal that osteoporotic women have relatives whose bone mass is generally lower than it should be for their ages.[8] Other studies indicate that monozygotic twins have highly correlated markers of bone metabolism that include not only chemical evidence of resorption and formation, but also anatomic evidence of similarities in bone density.[9,10] In contrast, dizygotic twins have poor correlations.

Racial differences attest to a hereditary or genetic factor. Black women have little primary osteoporosis; bone turnover is slower in this group and as a result they do not lose bone as fast as do white women.[11]

A recent study may have identified a genetic marker for osteoporosis associated with the gene coding for the vitamin D receptor.[12] This preliminary finding heralds the possibility that alterations in specific genes increase the risk of osteoporosis and may become markers for it.

Nutritional factors

Most nutritional data (which are epidemiologic, not experimental) indicate that people who con-

sume more calcium in childhood have higher bone density as adults.[13] Evidence suggests that dietary abnormalities such as anorexia nervosa negatively influence the mature skeleton.[14] A diet low in calcium but high in phosphorus stimulates secondary hyperparathyroidism and may adversely affect the skeleton.[15]

Whether calcium deficiency causes osteoporosis has been the topic of debate. Data from the National Health and Nutritional Examination Survey (NHANES)[16] years ago showed that men tend to consume more calcium than women do at almost every point in their lives. Women reach their maximal intake of calcium just before they start their teenage years, and thereafter consume less.

Approximately 800 to 1000 mg/day of calcium is necessary to maintain healthy skeletal structure in premenopausal women; up to 1500 mg/day is needed in postmenopausal women.[17] If a person receives less, skeletal deficits can arise over a lifetime because certain hormonal mechanisms remove calcium from the bone when the diet does not provide it. In the pubertal years calcium helps the bone to grow and become maximally calcified. As we get older, dietary calcium is still needed to protect skeletal integrity. Older adults may require more calcium than do younger people because they absorb calcium inefficiently.[18,19]

Recent data suggest that bone mass in young men continues to increase in a linear fashion at least until age 26, whereas in young women, bone growth accelerates at puberty, rises to a maximum, and reaches a plateau before the age of 20.[20] The implications are dramatic: if a woman's bone mass is low at the end of her teenage years, it will remain low for the rest of her life. The other implication is that osteoporosis may be a problem that pediatricians can help to prevent.[21]

In a recent study,[22] the calcium intake of adolescent girls was increased from 80% of the recommended daily allowance to 110% with supplementation with calcium citrate malate. The treated girls experienced significantly greater increases in bone density and mineral content than did girls who received placebo. In theory, such an increase may protect against future osteoporosis.

Hormonal factors

Hormones affect both osteoclastic and osteoblastic functions. In young women, estrogen levels, which increase during puberty, are the major force promoting bone formation. Further, loss of estrogen at the time of menopause or after oophorectomy leads to increased bone loss. Lindsay[23] examined bone mass in women who had undergone surgical menopause, gave them estrogen for 8 years, and found that their mineral mass tended to be fairly constant.[23] Once the estrogen was stopped, however, deficiency ensued. These findings were confirmed by others.[24–26]

Declining levels of estrogen are associated with an increase in local cytokines, especially interleukin 6, which stimulate osteoclastic cell production and activity.[27] These abnormalities resolve when estrogen is provided.[27,28]

Life-style factors

Lack of stress on bone eventually causes it to weaken, as the muscle pulling on the bone is the inciting factor for strengthening and repairing it. Inadequate physical activity during the developmental years leads to less than maximal calcification. Consequently, such an individual's skeletal mass at midlife would be lower than it should be. Sustained lack of activity in adulthood promotes further deficiency. Immobilization in a body cast causes osteoporosis, as does weightlessness during space flights of 3 weeks or longer, although these are extreme examples.

Premenopausal women face a dilemma in regard to exercise, however. One might think that if a woman is highly active throughout her life she could continue to increase the strength and density of her bone. This is true until puberty, but thereafter the mathematical relationship between intensity of exercise and bone mineral density is a bell-shaped curve: bone density increases with increasing exercise up to a point, and then declines.

Athletically induced amenorrhea is the reason.[29,30] Increased activity suppresses the menstrual cycle, leading to estrogen deficiency, increased osteoclastic activity, and high-turnover bone disease. Unfortunately, we do not know how to prescribe the optimum amount of exercise to preserve bone mass. In postmenopausal women, physical activity will preserve skeletal mass but will not restore it.

Abuse of alcohol[31–33] and tobacco[34–37] is also known to negatively affect the adult skeleton. Alcohol is a skeletal toxin, inhibiting osteoblastic activity in experimental settings. Similarly, tobacco abuse is a risk factor for osteoporosis. Smoking decreases estrogen levels in women who use estrogen compounds. A recent study of cigarette smoking in

monozygotic twins showed that a twin who smoked had a 5% to 10% lower bone density than her sibling.[38]

DIAGNOSING OSTEOPOROSIS

By the time the symptoms of osteoporosis are evident (ie, fractures, loss of height, back pain, and spinal deformities), the disease has been rampant for 10 years or more. Early asymptomatic osteoporosis is silent. Typical roentgenograms of the spine or hip are insensitive to bone loss of less than 20% or 30%. Only bone densitometry can detect changes below this threshold.

Bone densitometry

Dual-energy x-ray absorptiometry (DEXA) is the preferred method for determining bone density. The older technique—dual-photon absorptiometry (DPA)—is still used but clearly is obsolescent. DEXA is less expensive, since it does not require a costly isotope for its energy source. Moreover, it has greater precision and resolution and requires shorter scanning times (about 5 to 10 minutes per site). Radiation exposure is only 1 to 5 mSv per scan, compared with 950 to 2700 mSv for a spinal roentgenogram.

Present guidelines call for using bone densitometry to (1) determine if a woman who lacks estrogen has low bone mass and needs estrogen supplementation; (2) evaluate radiographic findings of vertebral deformities or low bone mineral content; (3) determine if a patient is susceptible to steroid-induced bone loss; and (4) assist in determining whether hyperparathyroid patients need surgery.[39]

Many postmenopausal women do not want to take estrogen because they fear perceived side effects such as uterine or breast cancer and continued menstrual flow. Counseling often fails to alleviate these concerns. However, known low bone density warrants a more serious consideration of hormonal therapy. Women with hip or spine density one standard deviation or more below that expected for premenopausal women (35 to 40 years) are at greater risk for a fracture.

Often, radiographic suspicion of osteopenia is corroborated by evidence from bone mineral density measurements. Mild vertebral deformities (ie, wedging) need not be related to osteoporosis. Such changes may be secondary to past accidents or could be normal variants. However, combined with a low bone mineral density, they are more significant.[39]

Not all patients who use glucocorticoids become osteopenic and develop osteoporotic fractures. Identifying such patients early is mandatory. Bone density measurements can help the physician decide whether to reduce the steroid dosage, institute antiosteoporotic therapy, or both—and can help monitor the efficacy of this therapy.

Patients with asymptomatic hyperparathyroidism constitute a dilemma about when and if surgical intervention is needed. Bone densitometry can indicate if such a patient is losing bone mass and therefore requires surgery.

Other findings

Primary osteoporosis is biochemically and hematologically silent. Any abnormalities found on testing suggest a secondary cause, ie, a hormonal abnormality, intestinal dysfunction, or neoplasm.

Most radiographic findings of osteoporosis appear only after skeletal losses of 20% to 30%. These signs include "washing out" of the density of the bone, differences in the trabecular patterns of the bones of the spine, compression deformities, and end-plate deformities of the vertebral bodies, producing concave or "codfish" vertebrae.

The patient's history may reveal risk factors for primary or secondary osteoporosis. Examination may reveal a skeletal deformity diagnostic of osteoporosis, osteoarthritis, or anatomical malalignment. Routine blood tests (automated multichannel serum analysis and complete blood profiles) should be normal. A 24-hour urinary calcium measurement is useful because a low level suggests either inadequate intake or poor absorption. Increased levels of serum parathyroid hormone in the presence of low or normal serum calcium concentrations often indicate a secondary hyperparathyroid state caused by poor calcium intake or poor absorption. These increased levels of hormone may be a risk for femoral bone loss. Calcium and vitamin D supplements can reverse these hormonal changes.

Several new markers of bone metabolism are under investigation. One is osteocalcin, a marker of bone formation; the other, a marker for bone loss, may replace older assays for urinary hydroxyproline, ie, urinary pyridinoline or its related serum component, carboxy-terminal telopeptide of collagen.[40–42] Neither of these new tests clearly confirms the diagnosis of osteoporosis: the overlap between patients with and without osteoporosis is too great. These

markers may, however, help identify patients with rapid bone loss and assess their response to therapy.

Any biochemical abnormality found should be further investigated. The importance of this is illustrated by the following case.

A 70-year-old woman had been without complaint until she injured her back while playing golf several weeks previously. Analgesics provided no relief. She noted some anorexia and weight loss for several months. Her medical history was significant for overuse of tobacco and alcohol. She was not using any prescribed drugs. The roentgenogram showed osteoporosis and a vertebral compression fracture at the second lumbar vertebra. On physical examination, she had a normal pulse and blood pressure. She was emaciated, unkempt, and in significant pain. The laboratory data were as follows: serum calcium 8.6 mg/dL, phosphorus 3.0 mg/dL, alkaline phosphatase 100 U/L, total protein 6.0 g/dL, albumin 3.0 g/dL, hemoglobin 10 g/dL, hematocrit 39%, sedimentation rate 100 mm/hour, aspartate aminotransferase 25 U/L, and lactate dehydrogenase 200 U/L.[43]

The abnormalities made us suspect primary osteoporosis. A subsequent study revealed a lymphoma causing the compression fracture in her back.

TREATMENT STRATEGIES

The goals of pharmacologic treatment are to stabilize the skeleton that already exists and, ideally, to stimulate bone growth. Calcium and vitamin D are stabilizing entities, fluoride stimulates bone growth somewhat, and the hormones estrogen, progesterone, parathyroid hormone, and calcitonin and the bisphosphonates may do both. However, no known treatment can restore the architecture of damaged bone. Exercise theoretically has a place in the overall scope of prevention and treatment of osteoporosis.

Exercise

Much is written about the salutary effect of weight-bearing exercise on osteoporosis. For the clinician, however, this advice begs the questions of what kind of exercise, how much, and how often. Clearly, complete lack of exercise (ie, immobility) is harmful, as evidenced by the deleterious effect of paralysis on the skeleton. Although exercise in general may be good, contradictions in study results are rampant.[44]

Walking and swimming may be helpful or not. Site-specific exercise increases regional bone density rather than systemic density.[45] Weight training with or without estrogen replacement seems to consistently increase bone density.[46,47] However, the positive gains are lost if exercise is discontinued. Of interest also is the observation that aerobic training may attenuate spinal bone loss in women during the first 6 years after menopause. This program used treadmill exercise three times per week at 70% to 80% of the maximal heart rate.[48]

Calcium

The role of calcium as a prophylactic agent needs careful evaluation. Adequate dietary calcium is essential throughout a woman's life; however, calcium is insufficient to prevent bone loss due to deficiencies of estrogen, as in menopause, because calcium does not regulate osteoclastic activity as well as estrogen or other compounds, which act as antiresorbing agents. Ten years or more after menopause, calcium again becomes effective in controlling bone loss due to aging.

Most postmenopausal women need to consume between 1.0 and 1.5 mg/day of elemental calcium, depending on their absorptive ability. An estimated 25% of normal postmenopausal women may not achieve calcium balance even at these or higher levels of intake. Calcium supplementation is popular because some women find nutritional sources of calcium such as dairy products unpalatable or have lactose intolerance. Calcium carbonate may be poorly absorbed in the elderly because of unsuspected achlorhydria. Calcium citrate may be advantageous because it is better absorbed.

The efficacy of calcium absorption is assessed in clinical practice by measuring 24-hour urinary calcium excretion. Radioisotopic techniques — the "gold standard" — are reserved for research applications. A person who absorbs calcium effectively should excrete more than 100 mg/24 hours. We see many people whose values are much lower, in the range of 5 to 10 mg/24 hours. Such individuals either cannot absorb calcium effectively or have inadequate intake.

Patients whose 24-hour urinary calcium excretion is less than 100 mg/24 hours should be questioned about their calcium intake. If it is low, they should increase the dietary intake to 1000 to 1500 mg per day. If they cannot tolerate the usual dairy nutrients that supply most dietary calcium, they need a calcium supplement.

Older patients may require supplemental vitamin D to increase calcium absorption because the intestinal tract's ability to respond to endogenous concentrations of vitamin D tends to decline with age. Other people may not be able to manufacture their own vitamin D. Calcium and vitamin D supplementation may benefit elderly patients: in one study, patients 69 to 106 years of age who took vitamin D3 (800 units) and 1.2 g of elemental calcium (aqueous suspension tricalcium phosphate) had higher hip density and fewer hip fractures.[48]

Estrogen

The only drugs officially sanctioned by the Food and Drug Administration for osteoporosis are estrogen and calcitonin: estrogen to prevent postmenopausal osteoporosis, and calcitonin to treat it. Lindsay[49] measured bone mineral density in women for up to 15 years after menopause and found that estrogen essentially preserved mineral density at the same level from the time the drug was initiated. This implies that estrogen therapy should be initiated sooner rather than later to protect the existing bone. Hormone replacement therapy may not confer any greater advantage in skeletal health if started 10 or more years after menopause than does calcium or the other therapies listed below. However, one can still consider using hormone therapy for other reasons such as to maintain the health of the urogenital tract or to reduce cardiovascular risk.

The dosage of conjugated equine estrogen is 0.625 mg per day given alone or cyclically with progestin or progesterone. Equivalent dosages of oral estradiol (1 mg daily) or transdermal estradiol (0.05 or 0.10 mg twice weekly) are also used. Patients with a uterus should also take a progestin for 12 to 14 days each month, usually medroxyprogesterone 2.5 to 5.0 mg daily. The combined therapy prevents endometrial cancer. Generally, progesterone is not used in patients without a uterus.

Calcitonin

Only injectable calcitonin is available in the United States, but an intranasal spray is used in other countries; this form would probably improve compliance. The dosage is 50 to 100 units of injectable calcitonin daily.

Calcitonin has been identified by the Food and Drug Administration as a useful agent in treating established osteoporosis. More than 10 years ago, Gruber and coworkers[50] treated osteoporosis with injectable calcitonin, calcium, and vitamin D, and followed up their patients for approximately 26 months. Compared with the group that received only calcium and vitamin D, the treated group tended to have a mild increase in mineral mass. However, there were wide variations in response, suggesting that calcitonin stabilized the bone mass but did not increase it as much as we would like it to increase. One of the more disturbing findings was that bone density initially increased but then declined. Studies are in progress to determine whether calcitonin will reduce the rate of fractures, a more clinically relevant endpoint than an increase in bone density.

Calcitonin is much more expensive than estrogen, and 10% to 20% of patients experience side effects, notably nausea, flushing, dysgeusia, diuresis, and diarrhea.[51] Nausea is the most common complaint. Most side effects disappear with continued use. In some cases, reducing the dose temporarily and then titrating it back up will minimize side effects. In my experience, most people who develop intestinal problems with calcitonin have a preexisting intestinal disease.

Calcitonin has an analgesic effect quite distinct from that of typical narcotic agents. It has no central nervous system side effects, and in some patients it provides better pain control than do narcotic drugs.

Parathyroid hormone

Experimentally, small amounts of parathyroid hormone stimulate bone growth, but too much hormone destroys the bone. Finding the proper dosage therefore poses a dilemma, but studies are in progress. Unfortunately, parathyroid hormone is very expensive.[52]

Fluoride

Fluoride is the only mineral known to stimulate osteoblastic formation and new bone growth. Unfortunately, the new bone may not be quite normal, and consequently over time fluoride may actually cause and contribute to bone fragility. A little bit of fluoride is good, but too much is probably bad. Fluorosis, common in certain countries of the Far East, is a major cause of osteoporotic fractures.

A study by Riggs and colleagues[53] illustrates the problem. In this study, fluoride treatment increased the mineral density of the trochanter, the femoral neck, and the lumbar areas. However, there was a

modest decrease in the density of the forearm. Most sobering and troublesome, fluoride did not decrease the incidence of vertebral fractures, despite the increases in density. In fact, there were more fractures after the use of fluoride. Unfortunately, the study design was troublesome because the dosages of fluoride were higher than usual. Most clinicians would prescribe 35 to 50 mg/day of sodium fluoride, but a large number of the people in this study used 75 mg or more. This implies that there is a small safety margin between the dosage providing benefit and the dosage producing a toxic effect. A follow-up study by these original investigators indicates that lower doses may be beneficial.[54]

TABLE
PREVENTING OR TREATING PRIMARY OSTEOPOROSIS THROUGHOUT THE LIFE SPAN

Group	Process	Recommendations
Adolescents	Increased estrogen production promotes maximal bone growth	Promote adequate calcium intake through diet and supplementation Promote active life-style and avoidance of tobacco and alcohol
Young adults	*Bone mass stable*	*Nutritional counseling, especially* in pregnant or nursing women Moderate exercise Therapy to stop smoking and alcohol abuse, if needed
Menopausal women	Falling estrogen levels may produce high bone turnover, especially in spine and distal forearm	Baseline densitometry in women at risk Estrogen replacement therapy Progestin replacement (in patients with a uterus) Etidronate or calcitonin (in women who cannot tolerate estrogen) Good nutrition and exercise Calcium supplementation
Elderly	Low-turnover disease causes loss of trabecular and cortical bone Fractures of hip, pelvis, and long bones are common Serum parathyroid hormone levels rise, calcium absorption is poor, and vitamin D production is inadequate	*In women at risk:* Sodium fluoride Etidronate or calcitonin Calcium and vitamin D supplementation Fall-proof the living quarters Good nutrition Exercise

In any event, commercially made sodium fluoride preparations are not available in this country, although they are in Europe and Canada. The only fluoride preparations available here are those sold in health food stores or made by pharmacists.

The side effects of fluoride are essentially intestinal, but rheumatologic complaints can arise. In our experience, dyspepsia is so common that when people say they take fluoride but do not have any side effects, I suspect they are not taking it. A delayed-release sodium fluoride preparation under study in the United States is a promising new drug.[55]

Bisphosphonates

Although not approved by the Food and Drug Administration to treat osteoporosis, etidronate is widely used for this purpose. The bisphosphonates were developed as water softeners, and etidronate was serendipitously found to abate calcification in a child with myositis ossificans progressiva. Etidronate is now approved to treat Paget's disease of the bone, hypercalcemia, and ectopic calcification; it and related compounds are being used experimentally to treat osteoporosis.[56] Bisphosphonates increase bone mass and decrease the incidence of fractures to a greater or lesser degree, depending on the population under study. People at high risk of fractures have a greater response than people at low risk.[57] The bisphosphonates are relatively inexpensive on a yearly basis, and their side effects are minimal. When etidronate is used to treat osteoporosis, the dosage is different from when it is used to treat Paget's disease: 400 mg daily for 2 weeks every 3 months. An empty stomach is important for adequate absorption. Patients must be seen in follow-up—all too often, they may use the drug incorrectly. Repeated bone densitometry every 1 or 2 years will show increases in most patients.

Thiazide diuretics

Patients who have been treated with thiazide diuretics for hypertension have lower hip-fracture

rates.[58] Short-term use of thiazides produces little or no benefit.[59,60] Thiazide diuretics will probably never be primary treatment for established disease because benefit may not be evident for years.

OSTEOPOROSIS THROUGHOUT THE LIFE SPAN

Because primary osteoporosis reflects lifelong trends, an understanding of the processes taking place at different times throughout the life span helps in selecting appropriate interventions to prevent and treat it (*Table*).

Maximal bone deposition occurs in adolescence, and it would appear reasonable to promote adequate calcium intake, and perhaps give calcium supplements, during this period. Of course, an extremely long-term study would be required to prove that this is beneficial. Likewise, during the young adult years, hygienic measures should be encouraged such as a diet adequate in calcium, a reasonably active lifestyle, avoidance of tobacco, and moderation in alcohol intake.

Problems begin to become evident within 5 to 10 years after menopause, when falling estrogen levels produce high-bone-turnover osteoporosis. Bone turnover is rapid in the trabecular compartment of the spine and distal forearm, and a preponderance of fractures takes place in these regions. The process is sensitive to estrogen and other antiosteoclastic agents. Neither calcium nor physical activity is adequate to completely control loss, but an adequate intake of calcium is necessary, even when estrogen, calcitonin, or etidronate is given.

I believe that every woman at significant risk should undergo baseline bone densitometry studies at the time of menopause. This would identify women whose bone density is lower than it should be and permit them to begin treatment before their osteoporosis becomes clinically apparent.[61] Although we cannot restore a patient's bone, we can preserve it at its present level, and this testing would permit us to preserve it at a higher level.

A low-turnover process occurs in men and women over age 70. Trabecular and cortical bone are lost. Fractures of the hip, pelvis, and long bones are common. Serum parathyroid hormone levels rise, calcium absorption is poor, and production of vitamin D is inadequate. Supplementation with calcium and vitamin D may be important considerations.[48]

Theoretically, the appropriate treatment for low-turnover osteoporosis is stimulation of bone growth. Unfortunately, no currently available treatment can repair the skeleton once the disease is rampant. If the trabecular network is not intact, adding mass to it will probably be ineffective. If the network is of better quality and is intact, adding mass to it may prevent deterioration. Most therapies employed add between 3% and 7% to bone mass as represented by early changes in bone density.

The ideal drug to stimulate bone growth has yet to be found. It must be without major side effects, relatively inexpensive, and highly effective in stimulating the repair of the destroyed bone network.

SUMMARY

Preserving the skeleton is of primary concern in adults. Once maximal bone mass has been achieved at the end of puberty, very little bone is added to the overall mass. Most subsequent skeletal activity is a remodeling or repairing process that attempts to conserve the amount of bone present. Hence, prevention must be considered in everyone. Once the disease destroys the skeletal architecture, no drug restores the depleted framework to normal. All therapies slow bone turnover and prevent further deterioration. Some bone mass is added by almost any technique evaluated, but this serves only to strengthen preexisting architecture, not to regrow what is missing.

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