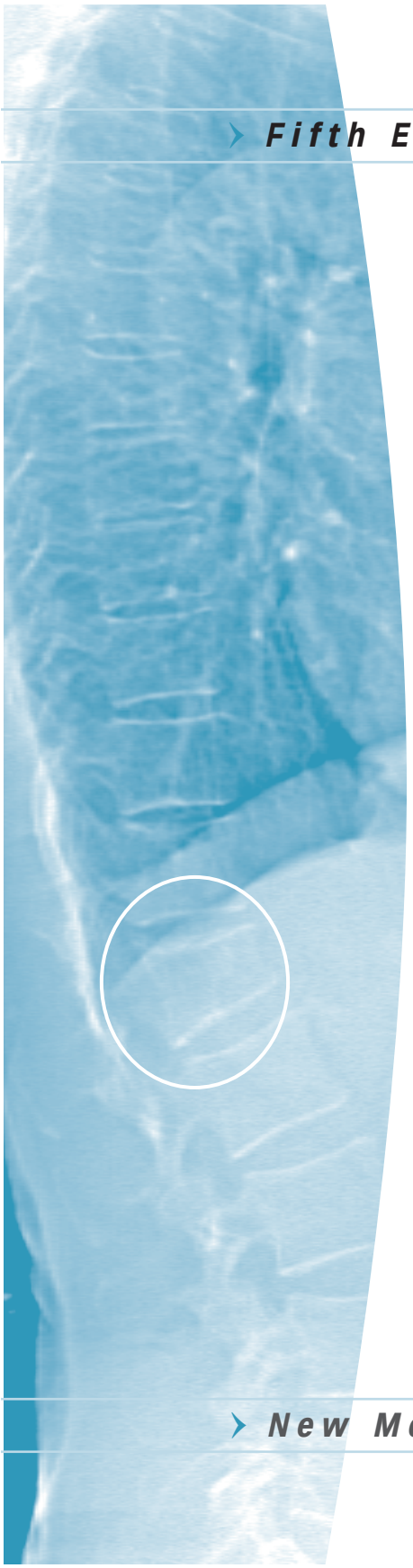

Fifth Edition

Mike's Manual

A Clinician's Guide to the Management of Osteoporosis

with

Bone Densitometry Referral Codes for Managed Care Organizations and Medicare

E. Michael Lewiecki, MD, FACP

New Mexico Version

Mike's Manual

Fifth Edition
New Mexico Version

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About the cover: The lateral spine DXA image shows an L1 compression fracture. This graphic was provided courtesy of Hologic, Inc., Bedford, MA. See page 48 for more information on this new technology for diagnosing prevalent vertebral fractures.

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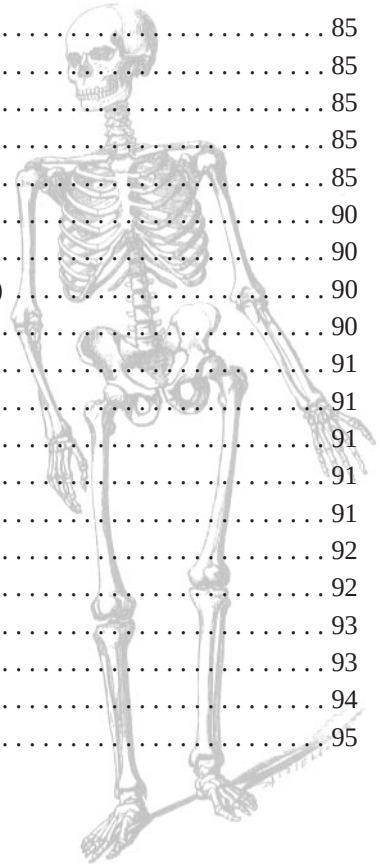


Preface

Welcome to the fifth edition of "Mike's Manual." Knowledge of osteoporosis continues to grow at a rapid rate. Exciting progress is being made in our understanding of basic bone metabolism. New medications for osteoporosis are emerging. Anabolic agents are ready to burst into the medical arena. Annual dosing of parenteral bisphosphonates is being investigated. Clinical standards for the use of bone densitometry are being developed. It is difficult for the busy practitioner to keep up with these changes. In preparing this manual, I have reviewed the medical literature, with special attention to large randomized controlled trials and published consensus guidelines. I have considered abstracts and presentations at osteoporosis and bone densitometry meetings. Where controversy exists, I have attempted to portray the issues evenhandedly. I hope I have succeeded in my goal of keeping the manual current, practical, and easy to use in daily practice.

This edition has been extensively edited, expanded and updated. Every clinical section has been revised to reflect advances in knowledge of osteoporosis and bone densitometry. In order to make the clinical portions more useful for healthcare providers, many new sections have been added. New topics include glucocorticoid-induced osteoporosis, anticonvulsant bone disease, metabolic effects of estrogen, clinical uses of estrogen, bone quality, lateral spine imaging by DXA, when to refer to an osteoporosis specialist, fall prevention guidelines, web sites of interest, publications of interest, and osteoporosis CME meetings.

I have had the help of many talented individuals in writing and editing this edition. My friend and colleague, Dr. Lance Rudolph, contributed two new sections on estrogen metabolism and clinical applications of estrogen therapy. His name appears below the title of sections he has written. I wrote the sections that have no named author. Julie Montano, our chief DXA technologist, and Deanna Reed, billing supervisor, updated the codes, criteria, and contact information for insurance coverage of bone density testing. This is a monumental task that requires ongoing diligence throughout the year. Yvonne Brusuelas, our osteoporosis education coordinator, has been instrumental in bringing the many pieces of the puzzle together to make the manual work. Finally, Yvonne Swartz-Lewiecki of Design Associates has taken my lackluster text and used her graphic design skills to create a publication that is easy on the eye.

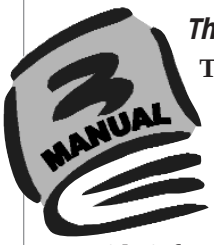
Preface

I am pleased to announce that this publication has received national recognition. It will serve as the model for a national bone densitometry reimbursement web site, managed by the International Society for Clinical Densitometry and funded by a generous grant from Merck. The web site will ultimately list bone density coverage information for all 50 states, with continual updates from volunteers in each state or region.

Special thanks to The Alliance for Better Bone Health (Aventis Pharmaceuticals and Procter & Gamble Pharmaceuticals); Novartis Pharmaceuticals and Eli Lilly and Company for unrestricted educational grants in support of this manual. Without their financial assistance, you would not be reading this now.

Please let me know what you like and don't like about this manual, and give me your thoughts for improvement in future editions. I need your feedback.

Mike Lewiecki
Albuquerque, NM
May 15, 2002

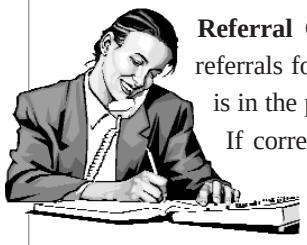


This Manual is Like the Yellow Pages

This manual is not for casual browsing or occasional reference. It is not to be read once and then filed on a shelf. It is for everyday use by anyone involved in osteoporosis care. The sections on clinical matters are meant to provide assistance in caring for patients, and the section on bone densitometry referral codes is designed to provide information about health plans and Medicare. This manual should be kept close at hand. If used correctly, the pages will become dog-eared, with scribbling on the cover and in the margins. Just like the Yellow Pages.

Examples of who should have this manual and how to use it:

Healthcare Providers. Keep a manual in each exam room. When ordering a bone density test, refer to the manual for the proper codes or categories to communicate medical necessity to the health plan. The patient can often provide helpful information on the spot. This type of information is often difficult for non-professionals to obtain after the patient has left the office. The patient will appreciate knowing at the time of the visit whether or not a bone density is likely to be covered by the health plan or Medicare. Keep another copy of the manual on the desk to help with clinical matters.



Referral Coordinators. Use the codes in the manual in processing referrals for bone densitometry. Coding can be confusing at best, but it is in the patients' best interest to have it accurately done the first time. If correct codes are given to the osteoporosis center, the procedure can be scheduled faster and is more likely to be covered by the health plan.

Osteoporosis Centers. ICD-9 codes used in billing for bone densitometry services must accurately reflect the condition of the patient. Osteoporosis center billing departments will find the section on bone densitometry referral codes very helpful. Bone density technologists and osteoporosis educators can use the clinical portions of the manual as an aid in counseling patients and answering their questions about osteoporosis.

History of Osteoporosis

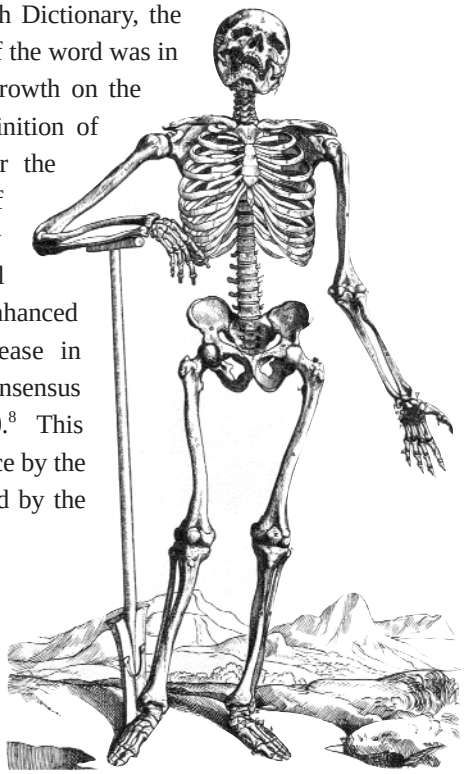
Paleopathology is the study of diseases in ancient skeletons. The bone density of ancient skeletal remains has been measured by a variety of methods, including DXA (dual energy X-ray absorptiometry), standard radiography, radiogrammetry, scanning electron microscopy, light microscopy, and stereoscopic photography. Most studies of archeological human skeletal remains have shown evidence of age-related bone loss. Age-related bone loss has been identified in paleopathological material from as early as 3200 BC.[1] It is likely that osteoporosis existed well before that time, but very old skeletons are sparse and technically difficult to evaluate for bone density. Bones with signs of osteoporosis have been found at Native American sites dated 2500-2000 BC.[2] Some Bronze-age European skeletons from 2000 BC have poor quality and quantity in trabecular bone,[3] with gender and age distribution similar to that seen in modern populations. A female skeleton dated to the XIIth Dynasty (1990-1786 BC) in Lisht, Upper Egypt, has been found with an osteoporotic fracture of the hip.[4] Numerous skeletons from medieval European populations have demonstrated age-related bone loss at a rate equal to or greater than modern times.[5] In addition to the paleopathological data, the art and literature of ancient times is replete with images and references that are compatible with kyphosis due to osteoporotic vertebral fractures.[6] It is clear from these studies that osteoporosis is not just a disease of modern society.

The word "osteoporosis" is derived from the Latin osteo, meaning bone, and the Greek poros, meaning porous or spongy. The word first made its appearance in French around 1820, and may have been coined by the French pathologist Jean George Chrétien Frédéric Maartin Lobstein "the Younger" (1777-1835).[7] According

1 Orter DJ. Disease and mortality in Early Bronze Age people of Bab edh-Dhra. Am J Phys Anthropol. 1979;51:589-597.
2 Perzigian AJ. Osteoporotic bone loss in two prehistoric Indian populations. Am J Phys Anthropol. 1973;39:87-96.
3 Kneissel M, Boyde A, Hahn M, et al. Age-and Sex-Dependent Cancellous Bone Changes in a 4000y BP Population. Bone. 1994;15(5):539-545.
4 Dequeker J, Ortner DJ, Stix AI, et al. Hip Fracture and Osteoporosis in a XIIth Dynasty Female Skeleton from Lisht, Upper Egypt. J BONE MINER RES. 1997;12:881-888.
5 Mays S. Age-dependent cortical bone loss in a medieval population. Int J Osteoarchaeol. 1996;6:144-154.
6 Appelboom T, Body J-J. The Antiquity of Osteoporosis: More Questions than Answers (Editorial). Calcif Tissue Int. 1993;53:367-369.
7 Schapira D, Schapira C. Osteoporosis: The Evolution of a Scientific Term. Osteoporosis Int. 1992;2:164-167.

History of Osteoporosis

to second edition of The Oxford English Dictionary, the first documented English language use of the word was in 1846, when it was used to refer to a growth on the cranium of an elderly patient. The definition of osteoporosis changed many times over the ensuing years. The modern definition of osteoporosis ("a disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk") was established at a consensus conference held in Copenhagen in 1990.[8] This definition achieved widespread acceptance by the medical community when it was adopted by the World Health Organization in 1994.[9]



The discovery of X-rays by Wilhelm Konrad Roentgen in 1895 marked the beginning of our ability to detect low bone density in the absence of clinical fractures. The current "gold-standard" technique for measuring bone density, dual energy X-ray absorptiometry (DXA), had its origins in single-photon absorptiometry, first described in 1963.[10] DXA is now commonly used to measure bone density, predict fracture risk, and follow the effects of therapy for osteoporosis.

[8] Consensus Development Conference: Prophylaxis and Treatment of Osteoporosis. Am J Med. 1991;90:107-110.

[9] Report of a WHO Study Group. Assessment of Fracture Risk and its Application to Screening for Postmenopausal Osteoporosis. WHO Technical Report Series 843. 1994.

[10] Cameron JR, Sorenson G. Measurements of bone mineral in vivo: an improved method. Science. 1963;142:230-232.

Definition of Osteoporosis

In the not too distant past, a diagnosis of osteoporosis could only be made after a fragility fracture occurred. In fact, in 1954 it was stated[1] that osteoporosis was an anatomical syndrome that could not be diagnosed unless "accompanied by at least one spontaneous vertebral compression." Even the authors recognized the absurdity of a chronic disorder not being present one day, but suddenly being there the next, even though bone mass had not changed in one day. It was also unsatisfactory to delay the diagnosis until a major adverse event occurred, just as it is unfortunate to diagnose coronary artery disease only after a patient has had a myocardial infraction.

In 1990, a Consensus Development Conference was held in Copenhagen, Denmark. One result of this meeting was agreement on the first modern definition of osteoporosis, setting the stage for making diagnosis of osteoporosis before a fracture occurs. This was reported[2] in 1991, and endorsed by the World Health Organization in 1994, as follows:

> *Osteoporosis is a disease characterized by low bone mass, microarchitectural deterioration of bone tissue leading to enhanced bone fragility, and a consequent increase in fracture risk.*

A few years later, the Consensus Development Conference was reconvened, and minor revisions[3] were made to this definition:

> *Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.*

The most recent consensus definition[4] comes from an NIH Consensus Development Conference, held March 27-29, 2000:

> *Osteoporosis is defined as a skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture. Bone strength primarily reflects the integration of bone density and bone quality. Bone density is expressed as grams of mineral per area or volume and in any*

1 De Seze L, Rickewaert A. Maladies des os et des articulations. 2 vols. Paris: Flammarion Medicine-Sciences. 1954.
2 Consensus Development Conference: Prophylaxis and Treatment of Osteoporosis. Am J Med. 1991;90:107-110.
3 Consensus Development Conference: Prophylaxis and Treatment of Osteoporosis. Am J Med. 1993;94:646-650.
4 NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. JAMA. 2001;285:785-795.

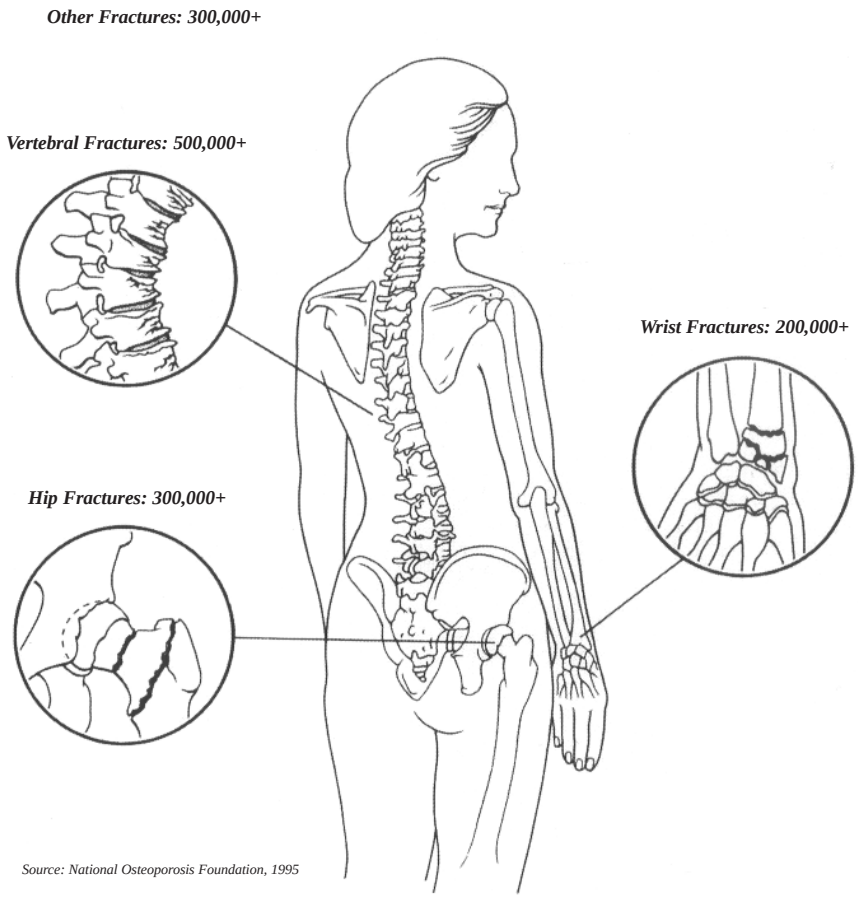
given individual is determined by peak bone mass and amount of bone loss. Bone quality refers to architecture, turnover, damage accumulation (e.g., microfractures) and mineralization.

Note that all of these definitions recognize two factors that cause diminished bone strength and increased risk of fracture: bone density and bone quality. Bone density can be measured easily, and ideally is done before a fracture occurs. In recent years, our understanding of bone quality has improved, and various components have been identified. We still have a great deal to learn about the nature of bone quality, and we need better ways to measure it.

In modern clinical practice, a densitometric diagnosis of osteoporosis is made using T-score of the spine, hip or forearm (see section on "Interpretation of Bone Densitometry"), or a clinical diagnosis is made when a patient has a known fragility fracture.

Osteoporosis Stats and Facts

Forty-four million Americans have osteoporosis or osteopenia. This represents 55% of the populations over age 50. Every year there are 1.5 million fragility fractures in the US, with about 700,000 vertebral fractures (only one-third of which are "clinically apparent"), 300,000 hip fractures, 200,000 wrist fractures and 300,000 fractures of other bones.



Statistics on this and the following page were obtained from multiple sources that are representative of the medical literature. In some cases there are different but equally valid values from other sources.

Osteoporosis Stats and Facts

Prevalence of osteoporosis in women by age:

- 60s: 20%
- 70s: 30%
- 80+: 70%

The prevalence of osteoporosis in white female nursing home residents is 64% for those age 65-75, and 86% for those over age 85.

Falls are 3 times more likely with nursing home residents than in the general population.

Each year, 30-40% of patients in long-term care facilities fall, with about 5% of those sustaining a fracture.

A 50 year-old woman has a 40% lifetime risk of any osteoporotic fracture and a 17% risk of hip fracture.

Women who are very physically active have a 36% decrease in fracture risk compared to sedentary women.

Hip Fractures

- 95% require surgery
- 50% lose the ability to walk independently after surgery
- 66% never regain pre-fracture level of ordinary activities
- 25-39% need long-term care institution
- Rate of hip fracture is 2-3 times higher in women than men
- Men have a one-year mortality rate twice as high as women
- A woman's risk of hip fracture is equal to her combined risk of breast, uterine and ovarian cancer

Vertebral Fractures

- Only 30% of vertebral fractures are clinically apparent
- Vertebral fractures that are not clinically apparent may nevertheless cause a 2-3-fold increase in back pain and functional limitation
- 5% of 50 year-old women and 25% of 80 year-old women have at least one vertebral fracture
- The five-year mortality rate for hip fracture and clinical vertebral fracture is about the same.
- For every T-spine fracture there is a loss of about 9% in FVC (forced vital capacity).

Osteoporosis Stats and Facts

Cost of osteoporotic fractures

- 2002: $17 billion
- 2040: projected to be $50 billion

Osteoporosis is a silent disease with no symptoms until a fracture occurs.

The average American consumes 500-600 mg dietary calcium per day, although the recommended daily intake is 1200-1500 mg per day.

25-40% of bone mass must be lost before osteoporosis is visible on conventional X-ray.

Osteoporosis in men: about 50% is due to factors such as corticosteroids, alcohol abuse, or hypogonadism; 50% is idiopathic.

Trabecular Bone

- 20% of total bone mass
- 80% of bone surface area
- 25% annual bone turnover

Cortical Bone

- 80% of total bone mass
- 20% of bone surface area
- 3% annual turnover

Composition of Bone

- Bone Matrix: 90% collagen (the rest is other proteins- osteocalcin, osteonectin, osteopontin)
- Bone Mineral: hydroxyapatite (calcium and phosphorous)
- Bone Cells: osteoclasts, osteoblasts, osteocytes

Bone Remodeling

- About 10% of the skeleton is being remodeled at any one time.
- The entire skeleton is replaced approximately every 10 years.
- About 0.027% of the skeleton is replaced each day.
- At any one time the human skeleton has about 1 million bone resorption pits, or cutting cones, called “basic multicellular units“, or BMUs.
- The lifespan of a BMU is about 6-9 months.
- About 4 million new BMUs are initiated each year, or about 1 BMU every 7 seconds.

Osteoclast

- Derived from hematopoietic cells of the monocyte-macrophage lineage in

red marrow
- These are multinucleated giant cells that will die by apoptosis (programmed cell death)
- Life span is about 3 weeks

Osteoblast
- Derived from pluripotent mesenchymal stem cells in red and yellow marrow (these stem cells also give rise to chondrocytes, myocytes, fibroblasts, and adipocytes)
- Some osteoblasts probably die by apoptosis, while others become lining cells or osteocytes
- Lifespan is about 3 months

Osteocytes
- Derived from osteoblasts that become buried in lacunae with the bone matrix
- About 30% of osteoblasts become osteocytes
- Over 90% of bone cells are osteocytes
- Osteocytes remain connected to the surface osteoblasts, lining cells and to each other by cell processes and gap junctions extending through fluid-filled channels called canaliculi
- The osteocyte-canalicular system may act as a transducer to detect changes in mechanical load and microfractures in order to activate the bone remodeling process
- Lifespan may be decades or even a lifetime

Lining Cells
- Derived from osteoblasts that become flattened to line the quiescent bone surface
- These cells retract during the activation process to allow osteoclast attachment

In women, the lifetime risk of hip fracture is greater than the risk of breast, endometrial, and ovarian cancer combined.

In men, the lifetime risk of hip fracture is greater than the risk of prostate cancer.

66% of women with osteoporosis are undiagnosed and untreated
15% are diagnosed and untreated
19% are diagnosed and treated

Risk Factors for Osteoporosis

Adapted from the guidelines of the National Osteoporosis Foundation

Demographics - Non-Modifiable

- **Age-** Once peak bone mass is attained (at age 20-30), aging accounts for 0.5% - 1% annual bone loss.
- **Caucasian, Asian-** These groups are more likely than African Americans or Hispanics to have osteoporosis.
- **Dementia-** Poor nutrition, more likely to fall.
- **Family history of osteoporosis-** Probably due to inherited tendency to have a low peak bone mass.
- **Female-** Of the 44 million Americans with osteoporosis or low bone density, 80% are women.
- **Low body weight (<127 lbs.)-** May be associated with poor nutritional status and low peak bone mass.
- **Personal history of fragility fracture-** Most adult fractures without major trauma are fragility fractures.
- **Poor health/frailty-** Poor nutrition, more likely to fall.

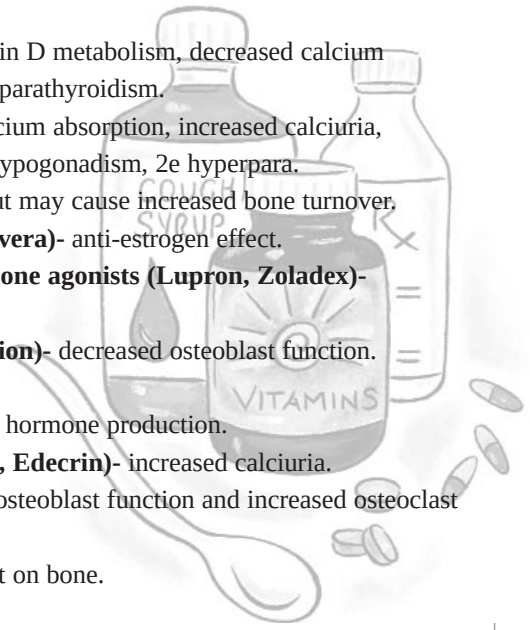
Lifestyle - Modifiable

- **Alcohol-** Poor nutrition, malabsorption, liver disease, and frequent falling all contribute.
- **Caffeine-** Excess urinary calcium loss.
- **Calcium deficiency-** Commonly begins in teenage years.
- **Estrogen deficiency-** May cause a bone loss of up to 3-5%/yr. for several years post menopause.
- **Excess dietary phosphate-** Causes decreased absorption of dietary calcium, mainly a problem in children.
- **Excess dietary sodium-** This can result in increased urinary loss of calcium.
- **Excessive exercise-** This can be harmful when amenorrhea and associated estrogen deficiency develops.
- **Lack of exercise-** This results in lower peak bone mass in children and more rapid bone loss in adults.
- **Smoking-** This has an adverse effect on estrogen metabolism and can result in earlier menopause.
- **Vitamin D deficiency-** Causes impaired calcium absorption and secondary hyperparathyroidism.

Risk Factors for Osteoporosis

Medications

- **Aluminum containing antacids-** decreased calcium and phosphate absorption, increased calciuria.
- **Anticonvulsants-** altered vitamin D metabolism, decreased calcium absorption and secondary hyperparathyroidism.
- **Corticosteroids-** decreased calcium absorption, increased calciuria, decreased osteoblast function, hypogonadism, 2e hyperpara.
- **Cyclosporine-** controversial, but may cause increased bone turnover.
- **Depo-progesterone (Depo-Provera)-** anti-estrogen effect.
- **Gonadotropin releasing hormone agonists (Lupron, Zoladex)-** decreased gonadal steroids.
- **Heparin (chronic administration)-** decreased osteoblast function.
- **Isoniazid-** increased calciuria.
- **Lithium-** increased parathyroid hormone production.
- **Loop diuretics (Lasix, Bumex, Edecrin)-** increased calciuria.
- **Methotrexate-** may decreased osteoblast function and increased osteoclast function.
- **Thyroid hormone-** direct effect on bone.



Surgery

- **Gastrectomy-** probably due to decreased calcium and vitamin D absorption with secondary hyperparathyroidism.
- **Intestinal bypass-** likely same mechanism as gastrectomy.
- **Thyroidectomy-** decreased calcitonin levels.
- **Organ Transplantation-** mainly due to immunosuppressive medications.

Other Diseases – Historical or Active

- **Acromegaly**
- **Adrenal atrophy and Addison's disease**
- **Amyloidosis**
- **Ankylosing spondylitis**
- **Anorexia nervosa**
- **Chronic obstructive lung disease**
- **Congenital porphyria**
- **Cushing's syndrome**
- **Diabetes mellitus**

Risk Factors for Osteoporosis

- **Endometriosis**
- **Epidermolysis bullosa**
- **Hemochromatosis**
- **Hemophilia**
- **Hypercalciuria**
- **Hyperparathyroidism**
- **Hyperprolactinemia**
- **Hyperthyroidism**
- **Hypogonadism (primary and secondary)**
- **Hypophosphatasia**
- **Idiopathic scoliosis**
- **Insulin-dependent diabetes mellitus**
- **Lymphoma and leukemia**
- **Malabsorption syndromes**
- **Mastocytosis**
- **Multiple myeloma**
- **Multiple sclerosis**
- **Nutritional disorders**
- **Osteogenesis imperfecta**
- **Parenteral nutrition**
- **Pernicious anemia**
- **Rheumatoid arthritis**
- **Sarcoidosis**
- **Severe liver disease, especially primary biliary sclerosis**
- **Thalassemia**
- **Tumor secretion of parathormone-related peptide**

Secondary Causes of Osteoporosis

Osteoporosis due to aging or postmenopausal estrogen deficiency is called "primary osteoporosis". When other contributing factors are identified, then "secondary osteoporosis" is said to be present. All patients with osteoporosis should be questioned about their risk factors and be examined to evaluate for associated medical disorders and complications. Secondary causes should be considered in any patient with osteoporosis, especially when the DXA study shows a T-score much lower than expected, or when the Z-score is < -2.0. Many of the known contributing factors are listed in the section entitled "Risk Factors for Osteoporosis." Depending on the patient population being studied, different factors may predominate. In general, the most likely secondary causes in women are long-term corticosteroid use and premature menopause. In men, the most common secondary causes of osteoporosis are long-term glucocorticoid use hypogonadism and alcoholism. Other common causes are malignancy (especially multiple myeloma), gastric surgery, anticonvulsant therapy, and malabsorption. Vitamin D deficiency occurs with regularity, especially in older patients. Treatable but easily missed secondary causes of osteoporosis include asymptomatic hyperparathyroidism, apathetic hyperthyroidism, mild Cushing's disease, male hypogonadism and occult malabsorption syndromes (that is, with no diarrhea or obvious GI symptoms). Keep in mind that low BMD may not be osteoporosis at all, but some other disease entity. The following table lists some of the causes of low BMD by category.

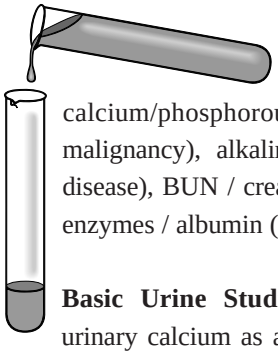
Many Causes of Low BMD				
Inherited	**Nutritional**	**Endocrine**	**Drugs**	**Other**
Osteogenesis imperfecta	Malabsorption	Hypogonadism	Glucocorticoids	Multiple myeloma
Homocystinuria	Chronic liver disease	Hyperthyroidism	Anticonvulsants	Rheumatoid arthritis
Marfan's syndrome	Alcoholism	Hyperparathyroidism	Long-term heparin	Systemic mastocytosis
	Calcium deficient diet	Cushing's syndrome	Excess thyroid	Immobilization
	Vitamin D deficiency	Eating disorder	GnRH agonists	

The type of "directed" work-up for low BMD depends on the patient's profile and the clinical suspicion of the physician. In all osteoporosis patients, it is reasonable to consider the following-

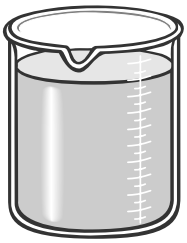
History- Family, diet, vitamins, alcohol, smoking, caffeine, fragility fractures, back pain, menstruation in women, erectile dysfunction in men, reproductive history, libido, medications, calcium intake, exercise, falling, loss of height, surgery, bowel habits, previous DXA studies.

Secondary Causes of Osteoporosis

Physical Exam- Height, weight, gait, posture, balance, skeletal tenderness, spinal deformity, distance between lower ribs and pelvic brim, testicle size and consistency, stigmata of hyperthyroidism or Cushing's syndrome, blue sclera / hearing loss / yellow-brown teeth (osteogenesis imperfecta), joint hyperelasticity (Erlos-Danlos syndrome), urticaria pigmentosa (systemic mastocytosis).



Basic Blood Studies- CBC (hematological malignancy, malnutrition), sedimentation rate (multiple myeloma), calcium/phosphorous (primary hyperparathyroidism, osteomalacia, malignancy), alkaline phosphatase (healing fracture, osteomalacia, Paget's disease), BUN / creatinine (renal insufficiency), TSH (hyperthyroidism), liver enzymes / albumin (alcoholism, malnutrition).

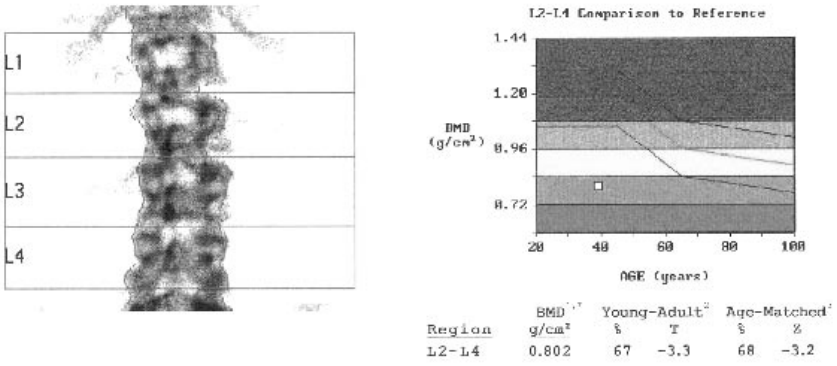


Basic Urine Studies- Some experts recommend using urinary calcium as a screening test for secondary causes of osteoporosis. A random urine calcium can be used, but a better test is a 24-hour urine for calcium, creatinine (to assure adequacy of collection), and sodium (increased urine sodium can cause increased urine calcium excretion). Urinary calcium is considered elevated when > 250 mg/24 hrs. in women; > 300 mg/24 hrs. in men; or > 4 mg/kg body weight per 24 hrs. in either sex. In the setting of normal renal function, normal serum calcium, and normal calcium intake, an elevated urinary calcium suggests a renal calcium leak ("renal hypercalciuria"), excess skeletal loss of calcium ("resorptive hypercalciuria"), or increased intestinal absorption of calcium ("absorptive hypercalciuria"). If urine calcium and sodium are both elevated, then a sodium-restricted diet may improve the hypercalciuria. A low urinary calcium (< 50 mg/24 hrs. in women or men) can be seen with dietary calcium deficiency, vitamin D deficiency, malabsorption, liver disease, and chronic renal failure. Note that malabsorption may be present without diarrhea or other GI symptoms, and that low urinary calcium may be the tip-off that further work-up is indicated.

Secondary Causes of Osteoporosis

In special situations, more extensive evaluation may be indicated-

Additional Studies in Selected Patients- Intact PTH level for patients with hypercalcemia or vitamin D deficiency. Dexamethasone suppression test or 24-hour urinary free cortisol for suspected Cushing's syndrome. Serum 25-hydroxyvitamin D level in the elderly or in anyone with intestinal malabsorption. Serum total testosterone level in men with osteoporosis. Serum and urine homocysteine when homocysteinuria is suspected. Serum and urine protein electrophoresis for possible multiple myeloma. Celiac disease antibodies (anti-endomysial antibody, anti-gliadin antibody) and upper endoscopy with duodenal biopsy in patients with suspected celiac disease. Radiographic studies to evaluate for pseudofractures (Looser's zones) in patients with possible osteomalacia. Serum tryptase and 24-hour urine for N-methylhistamine for suspected systemic mastocytosis. Serum bicarbonate may be low and urinary pH may be elevated in cases of renal tubular acidosis. Non-decalcified double tetracycline labeled iliac crest bone biopsy is rarely used in clinical practice, but may be helpful in the evaluation of renal osteodystrophy or atypical presentations of osteoporosis.



This DXA of a 39 year-old woman shows a very low T-score and Z-score. Evaluation for secondary causes of low BMD is indicated.

Osteoporosis in Men

Osteoporosis is a serious, but often unappreciated, health problem in men. The National Osteoporosis Foundation estimates that 20% of Americans that have osteoporosis are men. The Dubbo Osteoporosis Epidemiology Project suggests that a 60 year-old man has a 25% lifetime risk of osteoporotic fracture.[1] An elderly man with a hip fracture has a one-year mortality rate that is 26% higher than a woman of the same age with a hip fracture.[2] Despite the importance of osteoporosis in men, they are underrepresented in referrals for bone densitometry, underdiagnosed, and undertreated.

Men lose bone mass with age, albeit without the precipitous decline that women experience at the time of menopause. Men lose bone because of poor calcium intake, lack of exercise, declining testosterone levels, and age-related changes in bone metabolism. Interestingly, estrogen levels in men may also be related to changes in bone mass.[3] About 50% of men with osteoporosis have a contributing disease or condition that causes bone loss. Examples include hypogonadism, alcoholism, corticosteroid use, hyperparathyroidism, malabsorption, anticonvulsant therapy, malignancy, and immobilization. Cigarette smoking and low body weight may also play a role.

Loss of bone mass and increased risk of fracture[4] may occur in men treated for prostate cancer with gonadotropin releasing hormone (GnRH) agonists, such as Lupron® and Zoladex®. These patients should receive an adequate daily intake of calcium and vitamin D, periodic bone density tests to monitor for osteoporosis, and consideration of pharmacologic intervention if BMD is low.

1 Nguyen T, Sambrook P, Kelly P, et al. Prediction of osteoporotic fractures by postural instability and bone density. BMJ. 1993;307:1111-1115.

2 Osteoporosis and Related Bone Disease – National Resource Center. Osteoporosis Report. Washington, DC: National Osteoporosis Foundation, 1996.

3 Morishima A, Grumbach MM, Simpson ER, et al. Aromatase deficiency in male and female siblings caused by a novel mutation and the physiological role of estrogens. J Clin Endocrinol Metab. 1995;80:3689-3698.

4 Townsend MF, Sanders WH, Northway RO, Graham Jr. SD. Bone Fractures with Luteinizing Hormone-Releasing Hormone Agonists Used in the Treatment of Prostate Carcinoma. Cancer. 1997;79:545-550.

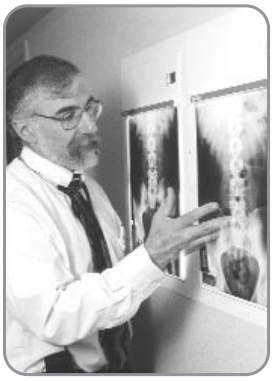
Osteoporosis in Men

The evaluation of osteoporosis in men is similar to women. Any fracture that occurs with minimal trauma should arouse suspicion. If a man has risk factors for osteoporosis, further evaluation should be considered. Keep in mind that disorders such as male hypogonadism may cause few symptoms, and may not be detected unless a serum testosterone is checked. If osteoporosis is suspected, a bone density measurement of the hip and spine should be ordered.

Treatment of osteoporosis in men includes regular weight-bearing exercise and adequate daily intake of calcium and vitamin D. Although the activity level of research with male osteoporosis pales in comparison to women, it can be expected that men will respond to most antiresorptive medications in a manner similar to women. If testosterone deficiency is detected in a man, then testosterone replacement therapy should be considered. Alendronate has been shown to be effective in treating men with osteoporosis,[5] and is FDA-approved for the treatment of osteoporosis in men. The beneficial effects of alendronate are not altered by the presence of testosterone deficiency, making it an attractive choice when testosterone replacement therapy is not a good option (such as when there is concern about prostate cancer). Aggressive treatment should be considered in men with a T-score < -2.0, and in men with a higher T-score (-2.0 to -1.0) if rapid bone loss is expected.

[5] Orwoll E, Ettinger E, Weiss S, et al. Alendronate Treatment of Osteoporosis in Men. J Bone Miner Res. 1999;14(suppl 1):S184.

Osteoporosis in Persons with Disabilities



by Lance A. Rudolph, MD

It has been well documented that patients with disabilities are at risk for fractures. This includes patients with developmental disabilities, epilepsy and physical disabilities. These patients are at risk for falls due to problems with mobility, decreased strength, poor balance and slow reaction times. It can be assumed that people with disabilities have the same risk factors for osteoporosis as those without disabilities but there have been no good studies on this issue. People with disabilities may be at higher risk for osteoporosis due to the more common occurrence of risk factors such as dietary deficiencies, lack of sun exposure with vitamin D deficiency, immobility and lack of weight-bearing activity, anticonvulsant therapy, medications used for behavior modification and metabolic defects that effect the structure of bone.

The prevalence of osteoporosis in the disabled is not well documented and may very well be quite high. In some patients with disabilities, specific trauma can be identified as a cause of fractures. In others, there is apparently no noticeable trauma. Fractures without noticeable trauma imply the diagnosis of pathologic fractures or fragility fractures. These are synonymous with the diagnosis of osteoporosis. When a disabled person sustains a significant fracture, a prolonged period of convalescence may be required. This often includes attendants, prolonged bed rest or chair confinement, hospitalization, absence from school or other day programs, or absence from work. Minimizing risk factors for falling and osteoporosis theoretically could have a significant impact on the cost of health care and the health and well being of the disabled.

In one study of institutionalized developmentally disabled individuals 18 years of age and older, there was an overall 1.7 times higher incidence of fracture than the average population.[1] There was a 2.8 times higher incidence of fracture in those who had

1 Lohiya, G, Crinella FM, Tan-Figueroa T-F, et al. Fracture Epidemiology and Control in a Developmental Center. West J Med. 1999;170:203-209.

documented osteoporosis. Other risks for fracture included epilepsy, male gender, Caucasian race, older age, ambulatory status and intermediate level of care (as opposed to skilled level of care). The cause of fracture was not identified in 58% of the cases. Bone loss in a paretic extremity may be as rapid as 1-2% per month with 20-50% over the first 1-2 years after the acute injury.

In conclusion, more attention should be addressed to fracture prevention in disabled individuals. Emphasis should be placed on fall prevention for ambulatory and wheelchair bound individuals, and the screening and treatment of osteoporosis. Currently, there are no established guidelines for osteoporosis screening in the disabled. At this point, I recommend screening for osteoporosis in the disabled if one or more risk factors are present. If an abnormal screening test is obtained with pDXA or ultrasound, then a full central DXA should be done. If the risk of osteoporosis is considered very high, then go directly to central DXA. All patients with disabilities should maintain an adequate daily intake of calcium and vitamin D. Disabled individuals should be as physically active as possible with weight-bearing activities as tolerated. Patients at high risk for developing osteoporosis, such as those with paresis (para-, quadra- or hemi-), should be considered for prophylactic antiresorptive therapy with bisphosphonates.

Glucocorticoid-Induced Osteoporosis

Bone loss and increased fracture risk are well-recognized consequences of glucocorticoid therapy. This occurs regardless of the disease for which they are being used, and is related to the dose and duration of treatment. The pathophysiology of glucocorticoid-induced osteoporosis (GIOP) is multi-factorial:

1. **Decreased bone formation.** Glucocorticoids are associated with decreased osteoblast differentiation, lifespan, and function. The amount of bone replaced in each remodeling cycle is reduced by about 30%. This effect on osteoblasts begins soon after glucocorticoids are started and continues as long as they are taken. In addition, increased apoptosis of osteocytes and lining cells may be an important factor in the development of osteonecrosis, or avascular necrosis.
2. **Increased bone resorption.** Glucocorticoids, at least early in the course of therapy, cause increased RANKL and decreased OPG. The result is increased osteoclast differentiation, lifespan, and activity. Chronic glucocorticoid therapy may result in decreased osteoclast activity, but net loss of bone continues due to uncoupling of bone resorption and formation.
3. **Abnormal mineral metabolism.** Calcium absorption is decreased and renal calcium excretion is increased is some, but not all studies. These changes in mineral metabolism may result in secondary hyperparathyroidism with elevated PTH levels, which can also contribute to bone loss.
4. **Hormonal changes.** Gonadal hormone levels are decreased in both men and women. This is due to a combination of inhibition of pituitary function and direct effects on ovaries and testes.

It was formerly thought that large doses (> 7.5 mg prednisone/day, or equivalent) and long-term administration (> 3 months) were required for bone toxicity to develop. However, a very large retrospective cohort study[1] from the UK has demonstrated that smaller doses for shorter duration may still be a problem. Doses < 2.5 mg/day were associated with increased risk of vertebral and nonvertebral fractures compared to controls, with increased fracture risk becoming apparent in the first three months of treatment. Fracture risk rapidly decreased within one year of cessation of treatment. Another study,[2] using the same UK general practice database, showed that inhaled glucocorticoids are also associated with increased fracture risk, but suggests that this increased risk may be related more to the underlying respiratory disease than to the inhaled glucocorticoids.

1 Van Staa TP, Leufkens HGM, Abenhaim L, et al. Use of Oral Corticosteroids and Risk of Fractures. J Bone Miner Res. 2000;15:993-1000.

2 Van Staa TP, Leufkens HGM, Cooper C. Use of Inhaled Corticosteroids and Risk of Fractures. J Bone Miner Res. 2001;16:581-588.

Glucocorticoid-Induced Osteoporosis

The American College of Rheumatology has the following recommendations[1] for the prevention and treatment of GIOP.

<u>Patient beginning therapy with glucocorticoid</u> (prednisone equivalent of ≥ 5 mg/day with plans for treatment duration of ≥ 3 months):

- **Modify lifestyle risk factors for osteoporosis.**
  - **Smoking cessation or avoidance**
  - **Reduction of alcohol consumption if excessive**
- **Instruct in weight-bearing physical exercise.**
- **Initiate calcium supplementation.**
- **Initiate supplementation with vitamin D (plain or activated form).**
- **Prescribe bisphosphonate (use with caution in premenopausal women).**

<u>Patient receiving long-term glucocorticoid therapy</u> (prednisone equivalent of ≥ 5 mg/day):

- **Modify lifestyle risk factors for osteoporosis.**
  - **Smoking cessation or avoidance**
  - **Reduction of alcohol consumption if excessive**
- **Instruct in weight-bearing physical exercise.**
- **Initiate calcium supplementation.**
- **Initiate supplementation with vitamin D (plain or activated form).**
- **Prescribe treatment to replace gonadal sex hormones if deficient or otherwise clinically indicated.**
- **Measure bone mineral density (BMD) at the lumbar spine and/or hip.**
  - **If BMD is not normal (i.e., T-score <-1.0), then**
    - **Prescribe bisphosphonate (use with caution in premenopausal women).**
    - **Consider calcitonin as second-line agent if patient has contraindication or intolerance to bisphosphonate therapy.**

  If BMD is normal, follow-up and repeat BMD measurement annually or biannually.

[1] American College of Rheumatology Ad Hoc Committee on Glucocorticoid-Induced Osteoporosis. Recommendations for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis: 2001 Update. Arthritis Rheum. 2001;44:1496-1503.

Anticonvulsant Bone Disease

Anticonvulsant bone disease was first described[1] in 1967, and subsequently validated in numerous reports and investigations. The older literature typically reported institutionalized patients with fractures, hypocalcemia and hypophosphatemia due to florid osteomalacia or rickets. In recent years, the clinical presentation is more likely to be an osteoporotic fracture or low BMD in an asymptomatic patient, with few, if any, biochemical abnormalities. The medications most often implicated are phenytoin, phenobarbita[l], and carbamazepine. Valproic acid is also associated with low BMD. There are far less data on newer anticonvulsant medications, such as gabapentin, lamotrigine, oxcarbazepine, topiramate, and zonisamide.

Risk factors[2] identified with anticonvulsant bone disease are:

1. High-dose, multiple drug regimens
2. Long-term therapy
3. Low vitamin D intake
4. Limited sunlight exposure
5. Chronically ill, elderly, or institutionalized patients
6. Reduced physical activity levels
7. Adjuvant therapy to induce chronic metabolic acidosis (acetazolamide or ketogenic diets)
8. Concomitant therapy with drugs that induce hepatic enzymes (rifampin, gluterimide)

The prevalence of anticonvulsant bone disease is difficult to determine, but it seems to be common in institutionalized patients and dependent on the above risk factors in outpatients. Epilepsy patients have lower BMD[3] and more fractures than controls. Fracture risk is probably due to higher risk of trauma as well as low BMD. The Study of Osteoporotic Fractures[4] showed that current use of anticonvulsant drugs was associated with a relative risk of hip fracture of 2.8. Epidemiological studies in other countries have confirmed this relationship.

1 Schmid F. Osteopathien bei antiepileptischer Dauerbehandlung. Fortschritte der Medzin. 1967;85:381-382.
2 Hahn TJ. Steroid and drug-induced osteopenia, in Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism. (Favus MJ, Ed.), 1993. pp. 252-255. Raven Press, New York.
3 Stephen LJ, McLellan AR, Harrison JH, et al. Bone Density and antiepileptic drugs: a case-controlled study. Seizure. 1999;8:339-342.
4 Cummings SR, Nevitt MC, Browner WS, et al. Risk Factors for Hip Fracture in White Women. N ENGL J MED. 1995;3323:767-773.

Anticonvulsant Bone Disease

The pathogenesis of anticonvulsant bone disease is multifactorial. Phenytoin, phenobarbital, and carbamazepine stimulate hepatic mixed function oxidase enzymes. This has adverse effects on vitamin D metabolism and may result in vitamin D deficiency and secondary hyperparathyroidism. Phenytoin has also been shown to directly inhibit intestinal calcium transport, inhibit vitamin D mediated calcium absorption, inhibit collagen synthesis, and have toxic effects on human osteoblast-like cultured cells. Valproic acid has an undefined mechanism of action on bone, and is not known to effect hepatic enzymes.

Pediatric and adult neurologists usually do not evaluate their seizure patients for bone disease,[1] and there is lack of consensus among neurologists as to the clinical significance of anticonvulsant bone disease. Although consensus guidelines for the evaluation and treatment of anticonvulsant bone disease are not yet available, a recent editorial[2] suggests the following:

1. Evaluation for all adults who are or will be prescribed long-term anticonvulsant therapy
   - Measure baseline serum calcium, phosphate, and alkaline phosphatase
   - Measure BMD
   - If biochemical abnormalities are present, or BMD is low, or musculoskeletal symptoms are present, then more extensive evaluation or referral to a specialist is indicated
   - Further investigation may include measuring bone turnover markers, 24-hour urinary calcium, serum 25-hydroxyvitamin D level, and intact PTH

2. Evaluation for children who are or will be prescribed long-term anticonvulsant therapy
   - Similar to adults, except that the role of BMD testing and bone turnover markers is not clear

3. Prevention and Treatment
   - Adequate calcium and vitamin D intake based on standard dietary references

1 Valmadrid C, Voorhees C, Litt B, et al. Practice Patterns of Neurologists Regarding Bone and Mineral Effects of Antiepeptic Drug Therapy. Arch Neurol. 2001;58:1369-1374.

2 Heller HJ, Sakhaee K. Anticonvulsant-Induced Bone Disease. Arch Neurol. 2001;58:1352-1353.

- Some patients require vitamin D intake more than five times the dietary reference
- Monitor serum calcium, phosphorous, and alkaline phosphatase
- Adjust calcium and vitamin D intake according to serum and urinary levels
- Monitor BMD annually initially, then at increasing intervals if stable

Some authorities suggest that an ideal serum 25-hydroxyvitamin D level is in the range of 30-57 ng/ml. A level below this range may be associated with rising PTH levels and increased bone turnover due to secondary hyperparathyroidism, and a level above this range may be toxic. Consider adjusting vitamin D intake to reach this range.

Basic Science of Bone Metabolism

by Lance A. Rudolph, MD

Bone is a dynamic tissue with an active metabolism that not only provides form and structure for the body's muscles and organs, but also is the body's reservoir for calcium. Bone is in a constant state of turnover, being resorbed by osteoclasts and formed by osteoblasts. Osteoclasts come from macrophage precursors (scavenger cells) and osteoblasts come from mesynchymal cell lines (connective tissue cells). Formation and resorption are linked in part by the interaction of osteoclasts and osteoblasts via cytokines, small chemical messengers. Osteoblasts lay down a base of collagen (braided proteins) in osteoid (uncalcified bone) which then becomes calcified, trapping the osteoblasts inside the new bone, where they are then called osteocytes. These cells can communicate with other cells and tissues through cytokines diffusing through the bony matrix and through cellular connections via small channels in the bone. Bone metabolism is an exciting and challenging area for osteoporosis specialists. New information arrives almost daily that challenges our knowledge of the way bones are formed, reabsorbed, and remodeled, and the way they interact with the body's internal and external environment.

A landmark discovery was the common pathway for osteoclast activation and bone resorption through the action of RANKL (pronounced rank-el). This stands for receptor activator of NK-kB ligand. It is a cytokine produced by osteoblast precursors that stimulates the proliferation, maturation and migration of osteoclast precursors and retards apoptosis (programmed cell death) of osteoclasts. RANKL is up-regulated by IL-1β and IL-11 (interleukins 1β and 11), TNF-α (tumor necrosis factor alpha), PTH (parathyroid hormone) and PGE_2 (prostaglandin E_2). TNF-α (tumor necrosis factor beta) down-regulates RANKL. The receptor for RANKL is RANK. This is a transmembrane receptor on the cell surface of the osteoclast that initiates the intracellular mechanisms that lead to increased bone resorption. OPG (osteoprotegerin) is a decoy receptor for RANKL. It is produced by osteoclasts and binds RANKL so it cannot bind to RANK. Thus, OPG slows down bone resorption. OPG analogs are now being investigated as a possible powerful therapeutic antiresorptive agent. Other cytokines that are involved in osteoblast precursor proliferation, maturation and migration are such chemicals as heparin-binding growth factors, BMP-2 (bone morphogenic protein 2), IGF-1 and IGF-2 (insulin-like ◗

growth factor 1 and 2), TGF-β (transforming growth factor beta), osteocalcin, platelet-derived growth factor and collagen itself.

In another discovery, newer bisphosphonates such as alendronate and risedronate were found to act through the mevalonic acid pathway, the same pathway that produces cholesterol. These compounds interfere with enzymes involved in the production of structural proteins necessary for the osteoclast to reabsorb bone. Incidentally, statin drugs, which are used to lower cholesterol, are also being investigated as possible adjunctive therapeutic antiresorptive agents. They interfere with earlier enzymes in the same pathway.

A breakthrough in osteoporosis therapy may be on the horizon. Parathyroid hormone (PTH), released from the parathyroid glands in a continuous stream, normally regulates calcium levels in the body by controlling calcium release from bone. Hyperparathyroidism increases bone resorption and causes secondary osteoporosis, especially in cortical bone. Paradoxically, when PTH is given in small daily doses by injection, it causes an increase in trabecular bone formation. Trabecular bone provides the majority of the strength for bones in the spine and hip. Intermittent PTH is the only clinical agent on the horizon that builds bone and may help return bone density to normal in some patients. The mechanism of intermittent PTH action is unknown but it appears to uncouple the formation and resorption of bone, favoring formation over resorption. Some clues are beginning to emerge as to how this happens. Intermittent PTH increases activation of BMUs (bone metabolic units), the basic unit of cells that is involved in bone formation and resorption. Osteoblastic cell lines contain PTH receptors. Intermittent PTH stimulates the expression of type I procollagen (which eventually forms the collagen that makes up the underlying framework of bone) and quiescent osteoblastic cell lines on the bone surface. Intermittent PTH also may stimulate matrix metalloproteinases (MMP). These enzymes, produced by osteoblasts and osteoclasts, degrade the extracellular bone matrix, promote bone cell migration and prepare the bone for the formation of new osteoid (uncalcified bone).

Researchers are also learning more about the effects of immobilization on BMD. Three mechanisms have been proposed that link stress to bone formation and

remodeling: streaming potentials, mechanical strain and fluid sheer stress. Streaming potentials occur when bone is flexed in the ionic environment of the bone matrix. The displacement of ions generates local electrical fields that can change bone cell metabolism. When mechanical strain is applied to cell membranes, stretch activated ion channels and other membrane-associated proteins are activated. These channels and proteins are linked by the cytoskeleton to cellular processes and eventually to the nucleus. Fluid sheer stress occurs when flexion of bone causes fluid in the canaliculi around extension processes of osteocytes to produce a force on the cell membrane. Bone loading must be cyclical to produce an increase in bone density and the effects are dose dependent and cumulative. Cyclical mechanical loading has been associated with an increase in bone-building cytokines such as nitric oxide, prostaglandins, IGF-1, TGF-β and collagen.

As researches learn more, we realize how many organ systems use a similar language of messengers, cytokines and intracellular mechanisms to function normally. Discoveries on a metabolic and cellular level should lead to better treatment and prevention strategies for osteoporosis.

Metabolic Effects of Estrogen

by Lance A. Rudolph, MD

Postmenopausal estrogen deficiency is the most common cause of low bone density in women. Estrogen replacement therapy is often used to treat menopausal symptoms and prevent postmenopausal bone loss. As knowledge of the effects of estrogen at the molecular and cellular level grows, our understanding of the clinical applications of therapy with estrogen and its analogues improves.

Estrogen is a steroid hormone derived from the conversion of cholesterol into estrogen precursors. It diffuses through the cell membrane into the nucleus where it undergoes binding to an estrogen receptor, dimerization, association with an adaptor protein and a transcription apparatus, before it finally attaches to a steroid response element on DNA.

There are 2 estrogen receptors, α and ß. ER-α has high levels in uterus, breast, kidney, pituitary and epididymis. ER-ß has high levels in prostate, vasculature, ovary, brain and bladder and low levels in uterus, kidney, pituitary and epididymis. Bone has both ER-α and ER-ß receptors.

Estrogen targets all major bone cells: osteoblasts, osteoclasts and osteocytes. Estrogen blocks bone marrow stromal and mononuclear cell production of IL-1, TNF-α, MCSF, PGE_2 and IL-6, cytokines that stimulate the nucleus of the osteoblastic cell line to produce RANKL, the ligand that promotes osteoclast differentiation and maturation while it decreases osteoclast apoptosis (programmed cell death). In a feedback loop, estrogen also stimulates the osteoblast to produce TGF-β, a cytokine that directly acts on the osteoblast nucleus to decrease RANKL production. These actions lead to decreased bone resorption by osteoclasts, decreased bone turnover and maintenance of bone mass. Other possible positive effects of estrogen on bone include increasing mRNA for type I procollagen, a precursor to the type of collagen that serves as the backbone for calcium deposition in bone. Finally, estrogen may decrease apoptosis of osteocytes, the cells that sense and transduce mechanical loads. Thus estrogen deficiency may impair the skeletal response to loads.

Estrogen has extra-skeletal effects on calcium homeostasis. There are estrogen receptors in the small intestine, renal tubules and the parathyroid gland. Estrogen may increase calcium absorption in the small intestine. There may be a renal calcium

leak in estrogen deficiency. Also, estrogen may have variable effects on PTH secretion. Acutely, estrogen may increase PTH secretion but when used long term, it may act to decrease PTH secretion.

Estrogen has both good and bad effects on the body's metabolic and biochemical processes apart from its effects on bone metabolism. Some of the beneficial effects include a decrease in LDL; increase in HDL; decrease in Lp(a)-high levels; decrease in fibrinolysis; restoration of normal vasodilation in response to acetylcholine in coronary arteries; increase in nitric oxide production; stimulation of endothelial production of prostacyclin, a vasodilator and platelet aggregation inhibitor; and a decrease in plasma viscosity. All of these are associated with or possibly associated with decreased cardiovascular mortality. Detrimental effects include an increase in triglycerides, C-reactive protein and microalbuminuria, all of which are associated with higher cardiovascular mortality. There may be good tissue effects such as on the brain, mucosal linings and vasomotor system and there may be bad tissue effects on the uterine lining and breast.

When choosing estrogen for preventative or therapeutic uses in patients with low bone density, the benefits versus risks are ultimately a result of estrogen's multiple cellular and metabolic effects. Knowledge of these biologic processes may be helpful in determining who may benefit from postmenopausal ERT.

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Clinical Use of Estrogen

by Lance A. Rudolph, MD

The decision to use estrogen replacement therapy in postmenopausal women has become increasingly complex. Providers are faced with evaluating multiple conflicting studies suggesting indications for starting, continuing and stopping ERT. In the absence of consensus guidelines, it is helpful to understand the strengths and weaknesses of the published trials. The following information is provided to assist in making patient care decisions regarding estrogen therapy for bone health.

ERT is FDA-approved for osteoporosis prevention, not for treatment. There is no question that ERT improves bone density in both the spine and hip, and decreases markers of bone turnover. Although a meta-analysis shows a 50% reduction in vertebral and non-vertebral fractures, there is no large, prospective, randomized, blinded trial that shows fracture reduction with ERT. Another meta-analysis suggests that ERT is not effective at preventing non-vertebral fractures if it is started over the age of sixty. Therefore, questions remain about the efficacy of ERT in fracture prevention.

Non-skeletal factors are important when deciding weather or not to start ERT. The FDA has approved ERT for relief of postmenopausal vasomotor instability, and most experts use ERT for relief of vaginal dryness. It is well known that unopposed estrogen stimulation of the endometrium increases the risk of endometrial cancer 2-8 fold, and that the addition of a progestin eliminates the additional risk. Ovarian cancer risk may increase with current or prior use of ERT for 10 years or more. There is 2-4 fold increase in the incidence of thromboembolic disease (DVT and pulmonary embolism) with ERT. ERT has favorable effects on lipids in postmenopausal women, with a decrease in total cholesterol, an increase in HDL and a decrease in LDL. It increases triglycerides, which may or may not be important in increasing cardiac risk. ERT appears to decrease the expected age-related rise in systolic blood pressure for women between the ages of 45 and 65. Women with postmenopausal vasomotor instability may experience some cognitive improvement with ERT. Although there are cohort and case-controlled studies that suggest a 34% decrease in the development of Alzheimer's disease in women on ERT, design flaws make these studies inconclusive.

It is well known that postmenopausal women have a higher incidence of coronary artery disease and myocardial infarction. What is not clear is what effect ERT has on

the prevention and progression of coronary artery disease. Studies that have looked at the progression of coronary artery disease with ERT are contradictory. The Framingham Heart Study suggests that ERT does not confer cardioprotection, while the Nurses Heart Study concludes that it does. Both these studies are observational studies and have inherent problems with design. A recent meta-analysis suggests that ERT reduces the risk of cardiovascular disease by 35-50%. The HERS study, a prospective randomized double blind study of secondary prevention in myocardial infarction for patients who have known coronary artery disease, showed increased risk of a second event during the first year but near-benefit by the 4th year of ERT.

Because of these conflicting findings, the American Heart Association has recommended that ERT not be used for secondary prevention of cardiovascular disease. Continuation of ERT in a patient who has had a coronary event should be based on non-coronary considerations and patient preference. There are no firm recommendations on its use in the primary prevention of cardiovascular disease. They recommend stopping ERT in the setting of an acute coronary event or prolonged immobilization, or adding DVT prophylaxis for immobilization if ERT is continued.

Controversy remains regarding the association of ERT with an increased risk of breast cancer. When is it safe to start ERT for osteoporosis prophylaxis and how long should it be continued? What dosage is safe? Does the type of estrogen influence the risk of breast cancer? Does the addition of a progestin affect breast cancer risk?

With no conclusive answers, some general comments are indicated. Although there are studies on both sides of the issue, there may be a slightly higher risk of breast ➧

cancer in women who choose ERT. The risk may be related to the duration of therapy and recedes within 5 years after ERT is stopped. Combined estrogen-progestin therapy may increase the risk of breast cancer more than estrogen alone. Even if there is an increased risk of breast cancer with ERT alone or with progestin therapy, overall mortality is reduced, perhaps due to less cardiovascular and osteoporosis related deaths.

The decision to start ERT should be made conjointly by both the patient and physician, taking into account potential risks, benefits and patient preferences. At this time, ERT should be the first choice for young postmenopausal females who desire osteoporosis prophylaxis or who have vasomotor complaints, provided there are no contraindications. Well recognized relative or absolute contraindications include cardiovascular disease, smoking, family history of breast cancer, known or suspected breast cancer or estrogen-dependent neoplasia, thromboemboloic disease or undiagnosed vaginal bleeding. After 5 years of ERT, the patient should be given the option to discontinue or continue ERT with documentation of a discussion of the potential risks in the patient's chart. The older the patient, the less inclined the provider should be to recommend ERT. Finally, consider using lower doses of ERT, especially in older individuals.

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Biochemical Markers of Bone Turnover

Bone is a living organ that is continually being resorbed and formed. When both of these factors are evenly balanced, the bone mass is stable. If bone formation is greater than resorption, there is a net gain in bone mass, as occurs in growing children. If bone resorption is greater than formation, there is a net loss of bone, as occurs in postmenopausal women and aging men. Increased bone turnover is an independent risk factor for fragility fracture,[1] regardless of BMD.

Biochemical markers of bone turnover, or bone markers, are by-products of bone resorption or formation that can be detected in the urine or blood. These are commonly measured in clinical trials to evaluate the effects of medications on bone metabolism. Their role in clinical practice for the management of individual patients is not well established, but many clinicians find them helpful in selected patients.

Markers of bone formation include serum alkaline phosphatase, serum bone specific alkaline phosphatase, and serum osteocalcin. Markers of bone resorption include urine and serum N-telopeptide (NTx), urine C-telopeptide (CTx), and urine pyridinolines (PYR). The markers of bone resorption are most often used in the evaluation of osteoporotic patients.

The three possible uses of bone markers in clinical practice are-

1. To predict fracture risk.
   All other things being equal, a patient with greater bone turnover (i.e., higher value for marker of bone resorption) has a higher fracture risk. This knowledge may be helpful in determining the aggressiveness of therapy.

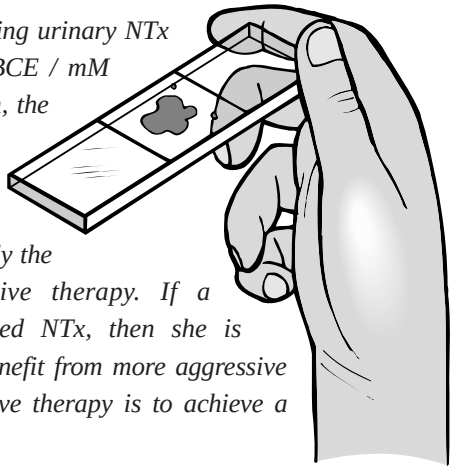
2. To aid in the selection of treatment, and serve as a baseline for monitoring treatment.
   Patients with high values for a marker of bone resorption can be predicted to respond better to antiresorptive therapy than those with a low value.

3. To monitor the effectiveness of treatment, and evaluate patient compliance.
   A decrease of 30% or more in the value for a marker of bone resorption, or a single post-therapy value in the low range, suggests a response to therapy. ➧

[1] Garnero P, Hausherr E, Chapuy M-C, et al. Markers of Bone Resorption Predict Hip Fracture in Elderly Women: The EPIDOS Prospective Study. J Bone Miner Res. 1996;11:1531-1538.

This can be checked as early as 3 months following the start of treatment. A smaller amount of change may mean the patient is not taking the medication, is not taking it correctly, or is a "non-responder."

Several assays for markers of bone resorption are now commercially available, with more sure to come along soon. These are usually collected from a fasting second morning void or a 24-hour urine. It is important that a follow-up test is collected under identical conditions, so that the comparison is as valid as possible. Some investigators suggest averaging the results from duplicate baseline and follow-up tests, in order to increase the level of precision.



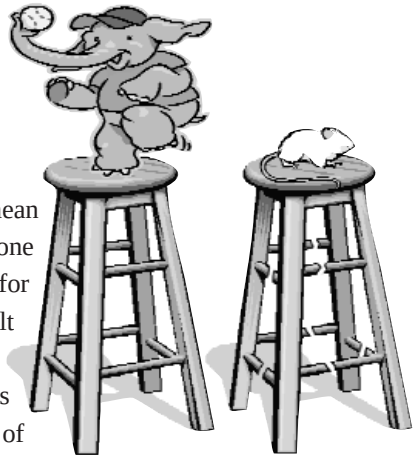
Clinical Tip: The average 2nd void morning urinary NTx for a premenopausal women is 35 nM BCE / mM creatinine, with a range of 5-65. For men, the average is 27, with a range of 3-51. The higher the NTx (even within the "normal" range), the greater the risk of low BMD and fracture, and the more likely the patient is to respond to antiresorptive therapy. If a postmenopausal woman has an elevated NTx, then she is probably a rapid bone-loser and may benefit from more aggressive therapy. A good target NTx for aggressive therapy is to achieve a value < 35 after 3 months of therapy.

Bone Quality

Bone density is strongly correlated with fracture risk. In the absence of a fragility fracture, BMD is the best clinical tool for estimating future fracture risk. There is an approximate doubling of relative risk of fracture for each standard deviation decline in BMD. However, the reverse is not necessarily the case. In order to cut fracture risk in half, it is not required that BMD increase by one standard deviation. In fact, raloxifene and nasal calcitonin cause minimal increases in bone density, yet substantially reduce fracture risk. Conversely, sodium fluoride causes large increases in BMD, but does not always reduce fracture risk. It is clear that factors other than bone density play a role in determining bone strength and susceptibility to fracture. The term "bone quality" has been designated to represent these factors.

The WHO definition of osteoporosis[1] refers to "microarchitectural deterioration of bone tissue", as well as low bone mass, as characteristic of osteoporosis. This early concept of bone quality is further refined by the NIH definition of osteoporosis,[2] which identifies four categories of bone quality:

1. Architecture,
2. Turnover,
3. Damage accumulation (e.g., microfractures), and
4. Mineralization.



Cutting the horizontal rungs of a barstool dramatically reduces the load capacity of the stool, with a minimal change in stool mass. Similarly, small changes in the integrity of horizontal trabeculae can have large effects on bone strength.

Bone "architecture" can be interpreted to mean microarchitecture as well as bone size and bone shape. Architects and engineers have known for centuries that small changes in mass can result in large changes in strength. The flying buttress is a practical example of this, as represented in buildings such as the Cathedral of Notre Dame in Paris. In trabecular bone, the horizontal strut is nature's version of the flying buttress. The spatial orientation of trabeculae in vertebral bodies develops in response to load-bearing forces, with ➧

[1] Consensus Development Conference: Prophylaxis and Treatment of Osteoporosis. Am J Med. 1993;94:646-650.

[2] NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. JAMA. 2001;285:785-795.

horizontally oriented trabecular struts being responsible for a disproportionate amount of bone strength. As a consequence, small changes in thickness and connectivity of horizontal trabeculae may result in large changes in bone strength.[3]

Bone size plays a role in bone strength.[4] Engineers have known this for years and have used it to their advantage in the design of building materials. A tube of larger diameter is stronger than a smaller tube, even when the total mass is the same. By the same token, the larger bones of men tend to be stronger than the bones of women, even when volumetric bone density is the same.

Bone shape may be related to bone strength and fracture risk. It has been suggested that genetically determined traits such as hip axis length and femoral neck-shaft angle are correlated with hip fracture risk.[5] Other studies have shown no relationship between hip axis length and fracture risk.[6]

Bone turnover is an independent risk factor for fragility fracture,[7] regardless of BMD. With an increase in bone turnover, as typically occurs in estrogen-deficient postmenopausal women, there is an increase in the number and size of bone remodeling units. This results in loss of bone strength due to trabecular thinning, trabecular perforation, and "stress-risers." Just as scoring, or creating a stress-riser, on the surface of a glass pipette makes it easy to make a clean break, so does an increase in the number of bone remodeling units create weakened areas in a bone that makes it more likely to fracture.

Microfractures are asymptomatic events that may be normal occurrences in response to load-bearing forces. They probably stimulate osteocytes to initiate the bone remodeling process, allowing weight-bearing bones to maintain strength that is appropriate for the mechanical demands. With increased bone turnover, it is likely

3 Guo XE, Kim CH. Mechanical Consequence of Trabecular Loss and Its Treatment: A Three-dimensional Model Simulation. Bone. 2002;30:404-411.

4 Looker AC, Beck TJ, Orwoll ES. Does Body Size Account for Gender Differences in Femur Bone Density and Geometry? J Bone Miner Res. 2001;16:1291-1299.

5 Gnudi S, Ripamonti, Gualtieri G, Malavolta N. Geometry of proximal femur in the prediction of hip fracture in osteoporotic women. Br J Radiol. 1999;72:729-733.

6 Pande I, O'Neill, Pritchard C, et al. Bone Mineral Density, Hip Axis Length and Risk of Hip Fracture in Men: Results form the Cornwall Hip Fracture Study. Osteoporosis Int. 2000;11:866-870.

7 Garnero P, Hausherr E, Chapuy M-C, et al. Markers of Bone Resorption Predict Hip Fracture in Elderly Women: The EPIDOS Prospective Study. J Bone Miner Res. 1996;11:1531-1538.

that more microfractures occur. The role of microfractures in the pathogenesis of osteoporotic fractures is not well defined,[1] but evidence is accumulating that they play a role. There has been concern that overly aggressive treatment with antiresorptive drugs could impair bone remodeling at microfracture sites, with a resulting increase in fracture risk. Fortunately, this has not yet been observed with the doses of FDA-approved antiresorptive agents currently in clinical use.

Lastly, bone mineralization has been identified as a component of bone strength.[2] Bone is a composite of an organic matrix, called osteoid, that is composed of collagen, and inorganic material composed largely of crystallized calcium phosphate. There is a correlation between optimal mineralization of bone and bone strength. In the bone remodeling, bone resorption is followed by osteoid deposition and then primary mineral apposition, a process that takes several months. This is then followed by secondary mineralization, which may take years to complete. If there is a state of rapid bone turnover, the shortened lifespan of the bone remodeling unit may not allow enough time for complete mineralization, and ultimately there will be a decline in bone strength. Antiresorptive medication increases the lifespan of the bone remodeling unit, so that there is more time for mineralization. Indeed, it has been hypothesized that increased mineralization is a major mechanism of action for the anti-fracture effect of antiresorptive medication.

Investigators differ on the relative importance of bone density and bone quality in determining fracture reduction in response to therapy. In meta-analyses of similar studies, Wasnich and Miller[3] suggest that most of the anti-fracture effect of antiresorptive therapy is due to an increase in BMD, while Cummings et al[4] propose that only a small portion of fracture reduction is due to an increase in BMD. As our understanding of bone quality expands, will be able to apply this knowledge to the development and clinical application of new treatments for osteoporosis.

1 Burr DB, Forwood MR, Fyhrie DP, et al. Bone Microdamage and Skeletal Fragility in Osteoporotic and Stress Fractures. J Bone Miner Res. 1997;12:6-15.

2 Meunier PJ, Boivin G. Bone Mineral Density Reflects Bone Mass but Also the Degree of Mineralization of Bone: Therapeutic Implications. Bone. 1997;21:373-377.

3 Wasnich RD, Miller PD. Antifracture Efficacy of Antiresorptive Agents Are Related to Changes in Bone Density. J Clin Endocrinol Metab. 2000;85:231-236.

4 Cummings SR, Karpf DB, Harris F, et al. Improvement in Spine Bone Density and Reduction in Risk of Vertebral Fractures during Treatment with Antiresorptive Drugs.Am J Med. 2002;112:281-289.

Who Should Have a Bone Density Test?

Many guidelines for bone density testing have been published. The one that has received the widest distribution in the USA was developed by the National Osteoporosis Foundation (NOF), in collaboration other medical societies and organizations.[1] These guidelines apply only to postmenopausal women, and therefore are limited in application. The NOF recommends that BMD testing should be performed on:

1. All postmenopausal women under age 65 who have one or more additional risk factors[2] for osteoporotic fracture (besides menopause).
2. All women aged 65 and older regardless of additional risk factors.
3. Postmenopausal women who present with fractures (to confirm diagnosis and determine disease severity).
4. Women who are considering therapy for osteoporosis, if BMD testing would facilitate the decision.
5. Women who have been on hormone replacement therapy for prolonged periods.

In July 2001, the International Society for Clinical Densitometry (ISCD) held a Scientific Position Development Conference to consider this issue, and others. The ISCD recommendations[3] are more comprehensive than those of the NOF, and may be more useful in clinical practice. It was the consensus of the ISCD panel of experts that BMD testing be done for:

1. All women age 65 and older.
2. All men age 70 and older
3. Anyone with a fragility fracture
4. Anyone with a disease, condition or medication associated with osteoporosis
5. Anyone who is considering therapy for osteoporosis, if BMD testing would facilitate the decision

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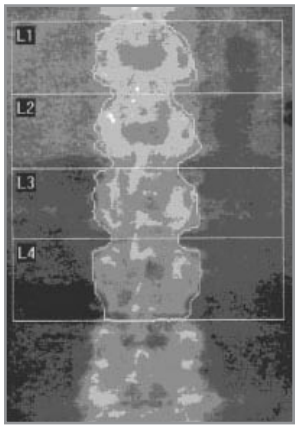
1 Physicians Guide to Prevention and Treatment of Osteoporosis. National Osteoporosis Foundation. 1999.

2 Personal history of fracture as an adult; history of fracture in a first-degree relative; Caucasian; advanced age; dementia; poor health / frailty; current cigarette smoke; low body weight (<127 lbs); lifelong low calcium intake; alcoholism; impaired eyesight despite attempts at correction; recurrent falls; inadequate physical activity.

3 International Society for Clinical Densitometry. Scientific Position Development Conference. 2002. In Press

Who Should Have a Bone Density Test?

6. Women who have been on HRT for prolonged periods.
7. Anyone being treated for osteoporosis, to monitor the effects of therapy



The decision to test for BMD should be based on an individual's risk profile, and testing is never indicated unless the results could influence a treatment decision.

Frequency of testing. The appropriate interval between bone density tests depends on the precision of the test, the expected rate of change in BMD, and the level of statistical confidence desired. The ISCD recommends that each center calculate precision for each instrument and each technologist, and that "Least Significant Change" be calculated for the 95% confidence level. For monitoring the response to therapy, a repeat test in 1-2 years is usually sufficient. An increase or no change in BMD is considered to be a good response. A significant loss of BMD is worrisome. In situations where a rapid change in BMD is possible, such as initiation of high dose glucocorticoid therapy, a baseline study is suggested, with a follow-up test every 6 months until stable.

Interpretation of Bone Densitometry

Components of a DXA Printout

Each DXA manufacturer of DXA instruments has its own style of printout. There are usually three parts- an image of the skeletal site, a colorful graph, and numerical data.

1. **Image.** The image of the skeletal site being measured provides important information for the bone densitometrist. For the spine, it shows the labeling of vertebral levels, location of computer-generated lines separating bone from soft tissue, and possible artifacts that could increase or decrease BMD. For the hip, the degree of internal rotation is estimated (about 15∞ is ideal), placement of lines for hip regions of interest is checked, and possible artifacts are evaluated. When comparing baseline and follow-up studies, the hip and spine must be put in exactly the same position, if possible. This is sometimes a challenge for the hip, and highly dependent on the skill of the technologist.

2. **Graph.** The printout of the DXA report often includes a graph that plots the patient's age against BMD, with bars or lines to indicate mean BMD with standard deviations. Despite the colorful appearance, this graph offers no useful clinical information beyond that shown on the data table. It can also be confusing and misleading, since it may show a BMD value for a region of interest different than the one that is most appropriate for interpretation.

3. **Data.** The most important number on the DXA printout is the T-score. This is the number that is used to diagnose osteoporosis or osteopenia. The Z-score is more limited in value, but may be helpful in certain clinical situations.

T- score (also called young-adult T-score and young-adult Z-score)

This is the variation of the patient's bone mineral density (BMD) from the mean BMD of a young-adult reference population, expressed as standard deviation. The lower the T-score, the greater the risk of fracture. The T-score is used to define normal, osteopenia, and osteoporosis.

Z-score (also called age-matched Z-score)

This is the variation of the patient's bone mineral density from an age-matched reference population, expressed as standard deviation. The Z-score should not be used to assess risk of fracture. A low Z-score (< -2.0) suggests that investigation for possible secondary causes for bone loss may be indicated.

Interpretation of Bone Densitometry

World Health Organization (WHO) Definitions[1]

Normal:	T-score ≥ -1
Osteopenia:	T-score between -1 and -2.5
Osteoporosis:	T-score ≤ -2.5
Severe Osteoporosis:	T-score ≤ -2.5 and personal history of fragility[2] fracture

The WHO definitions apply to DXA measurement of the hip, spine or mid-radius, and are not applicable to other skeletal sites and other technologies for measuring BMD. See the section on Peripheral Bone Density Testing for more information.

Clinical Tip: A T-score ≤ -2.5 does not always mean osteoporosis. Sometimes a local bone disease, such as a bone cyst or osteolytic bone lesion may be present, or the patient may have another disease, such as osteomalacia. And a patient may have osteoporosis with a T-score > -2.5. A clinical diagnosis of osteoporosis may be made if the patient has had a fragility fracture, regardless of T-score.

1 Report of a WHO Study Group. Assessment of Fracture Risk and its Application to Screening for Postmenopausal Osteoporosis. WHO Technical Report Series 843. 1994.

2 What is a fragility fracture? Most experts agree that a fragility fracture is any fracture occurring after trivial trauma. Most fractures in adults, except those from major trauma (such as auto accident or falling off a ladder), are fragility fractures.

Lateral Spine Imaging by DXA

Lateral spine imaging by DXA is a recently developed technology with potentially useful clinical applications. This procedure goes by several acronyms, including MXA (morphometric X-ray absorptiometry- a generic term), IVA (instant vertebral assessment, the trademarked term used for Hologic instruments), and LVA (lateral vertebral assessment, the trademarked term used for GE Lunar instruments). Regardless of the terminology, the principle is the same. A lateral spine DXA image is obtained with the patient in the supine or lateral decubitus position. This can be done with some of the recently manufactured DXA machines, but may not be possible with older equipment. It takes just a few minutes to do and can be done at the time of a visit for DXA BMD testing of the spine and hip. The radiation exposure to the patient is a small fraction of that received with standard spine X-rays. The image is used to evaluate for previously unrecognized vertebral fractures. The presence of any fragility fracture results in a "clinical" diagnosis of osteoporosis, regardless of results on bone density testing.

The rationale for doing lateral spine imaging by DXA is the following:

1. Vertebral fractures are the most common type of fragility fracture- about 700,000 in the USA annually.
2. Most vertebral fractures are not clinically apparent- only 30% are clinically diagnosed.
3. Vertebral fractures, even those that are not clinically recognized, are associated with increased morbidity and mortality- 5-year mortality rates about 20% over expected have been reported.
4. Prevalent vertebral fracture is a strong predictor of future fracture risk.
5. Lateral spine imaging by DXA is a convenient low-radiation means of evaluating high-risk patients for prevalent vertebral fractures at the same time DXA BMD testing is done.
6. Knowledge of prevalent vertebral fractures may alter the patient's diagnostic classification, fracture risk stratification, and therapy.

Lateral Spine Imaging by DXA

A cross-sectional study[1] of 482 ambulatory, community-dwelling, postmenopausal women with no prior knowledge of vertebral fractures found 18.3% with vertebral fractures on lateral spine DXA imaging. Using BMD testing alone, the prevalence of osteoporosis in this cohort was 31.7%. By combining BMD results and vertebral fracture assessment, the prevalence increased to 43.2%. Another study[2] showed that this technique is comparable to morphometric radiography for reliability in diagnosing vertebral deformities.

In summary, lateral spine imaging is a fast, noninvasive, low radiation technique for identifying vertebral previously undiagnosed vertebral fractures. It's role in clinical practice, and parameters for patient selection, remain to be determined.

1 Greenspan SL, von Stetton E, Emond SK, et al. Instant Vertebral Assessment- A Noninvasive Dual X-ray Absorptiometry Technique to Avoid Misclassification and Clinical Mismanagement of Osteoporosis. J Clin Densitometry. 2001;4:373-380.

2 Ferrar L, Jiang G, Eastell R. Longitudinal Evaluation of Morphometric X-ray Absorptiometry for the Identification of Vertebral Deformities. Osteoporosis Int. 2001;12:661-671.

Peripheral Bone Density Testing

What is peripheral bone density testing?

This is the measurement of bone mineral density (BMD) at "peripheral" sites, such as heel, wrist, finger, or tibia, as opposed to measuring a "central" site, such as the spine or hip.

How is it done?

Many devices are now available to measure peripheral BMD. These machines are becoming less expensive, more portable and more widely accessible. Several different technologies are used, the most common being peripheral dual energy X-ray absorptiometry (pDXA) and quantitative ultrasound (QUS). The most popular measurement site at this time is the calcaneous (heel). These devices are now being seen in physicians' offices and health fairs, as well as some non-traditional settings, such as pharmacies and grocery stores.

Who should be tested?

Since these tests are relatively inexpensive, and sometimes free, they are appropriate for screening large numbers of people. Early recognition of bone loss in asymptomatic individuals may allow therapeutic intervention to occur in time to prevent fragility fractures. The most appropriate people for screening are postmenopausal women who have not had a central DXA study.

Possible clinical uses of peripheral bone density testing:

Osteoporosis awareness. The availability of peripheral testing, regardless of the results of the test, offers healthcare providers an opportunity to discuss bone health with patients and improve osteoporosis awareness.

Prediction of fracture risk. A low peripheral bone density measurement is clearly associated with increased risk of fragility fractures. A "normal" result, however, does not necessarily mean fracture risk is normal. It is quite possible to have normal bone density at the measured site, but to have low bone density at other sites.

Diagnosis of osteoporosis. Peripheral tests, with the exception of a mid-radius measurement, cannot technically be used to diagnose osteoporosis, since that would not be consistent with the WHO definition. It would be more appropriate to use the peripheral test in combination with a risk factor questionnaire to estimate a patient's risk of osteoporosis. Depending on the estimation of risk, a

recommendation for follow-up evaluation and care can be made.

Monitoring patients being treated for osteoporosis. Peripheral skeletal sites cannot be used to monitor treatment. For baseline and follow-up of patients being treated for low bone density, a central bone mass measurement is necessary, since a BMD response may not be detected by measuring a peripheral site.

How do I interpret the T-score results of peripheral bone density testing? The answer is - very carefully. It is probably wise to take care not to over-interpret peripheral results, and especially not to assume that a "normal" T-score necessarily means that the patient has normal bones. Although there are no well-accepted standards for interpretation of peripheral tests, here is one method to assist in dealing with this issue.

T-score is ≥ -1.0: This is "normal" for the site measured, according to the World Health Organization (WHO) definition, but does not preclude a low value at another site. A recent study[1] has shown that using this definition for a single peripheral site will miss 24-37% of patients with significant bone loss. The authors suggest that the definition of "normal" for a single peripheral site be raised to T-score > 0.0. Additional BMD testing should be done for patients at high risk for osteoporosis. A panel of world leaders in this field[2] has recommended that the following subset of patients with "normal" peripheral BMD should proceed with a central bone mass measurement:

1. Postmenopausal women not on ERT, concerned about osteoporosis, and concerned about prevention, who would consider ERT, bisphosphonates, or SERMs if a low bone mass is discovered.
2. Maternal history of hip fracture; smoking; tall (> 5'7"); or thin (< 125 lbs.).
3. Patients on medications associated with bone loss (corticosteroids, anticonvulsants, etc.).

1 Fogarty CD, Nodine K, Fogarty CM. Peripheral Screening: 50% Decrease in False Negative Rate using Two Sites. Poster Presentation at the Annual Meeting of the International Society of Clinical Densitometry, New Orleans. 1999.

2 Miller PD, Bonnick SL, Johnstone CC Jr., Kleerekoper M, Lindsay RL, Sherwood LM, Siris ES. The Challenges of Peripheral Bone Density Testing, Which Patients Need Additional Central Density Skeletal Measurements? J Clin Densitometry. 1998;1:211-217.

4. Patients with secondary conditions associated with bone loss (hyperthyroidism, organ transplantation, malabsorption, hemigastrectomy, hyperparathyroidism, prolactinoma, immobilization, etc.).
5. Patients found to have a high urinary marker of bone resorption (NTx, CTx, DpD).
6. History of fragility fracture.

T-score between -1.0 and -2.5: This is "osteopenia" for the site measured, by the WHO definition. Pharmacological intervention is suggested if postmenopausal and not on ERT, and in the presence of secondary conditions associated with bone loss or history of fragility fracture. A central BMD measurement should be considered as a baseline prior to initiating treatment, and to monitor the effectiveness of therapy.

T-score ≤ -2.5: This is "osteoporosis" for the site measured, by the WHO definition. Pharmacological intervention is indicated if postmenopausal and not on ERT, and in the presence of secondary conditions associated with bone loss or history of fragility fracture. A central BMD measurement should be considered as a baseline prior to initiating treatment, and to monitor the effectiveness of therapy.

Body Composition Testing

The measurement of body composition is a valuable tool in the evaluation of nutritional disorders, with applications in both research[1] and clinical practice,[2] In addition, body composition testing is often done for health club members, recreational athletes, and competitive athletes, to monitor the effects of training and physical conditioning programs, and to aid in the attainment of peak athletic performance. Numerous techniques for measuring body composition are available, each with its own advantages and disadvantages. Testing skinfold thickness, for example, is convenient and inexpensive, but lacking in sensitivity.[3] Underwater weighing is accurate, but inconvenient and difficult to perform.[4] Bioelectrical impedance analysis is fast and portable, but subject to variability due to state of hydration.[5]

Dual energy X-ray absorptiometry (often called DXA or DEXA) is a very accurate non-invasive technique for measuring body composition, with results showing much more than just total % body fat. It also shows body fat and lean body mass by region of the body, so that sport-specific and training-specific effects can be monitored. In addition, bone mass is measured with great accuracy, making this an excellent test to check for osteoporosis. In fact, the primary use of DXA machines is to evaluate and follow patients with osteoporosis, and to predict future risk of fractures. DXA has been recommended as the "gold standard" for validating other techniques for measuring body composition.[6] It has been used to study body composition in many types of athletes, including weight trainers, competitive swimmers, and long-distance runners. With DXA technology the entire body is scanned with X-ray generated photons at two different energy levels. Since different types of body tissue absorb ➧

1 Heymsfield SB, Wang Z, Baumgartner RN, et al. Human Body Composition: Advances in Models and Methods. Ann Rev Nutr. 1997;17:527-58.

2 Fogelholm GM, Sievanen HT, van Marken Lichtenbelt WD, Westerterp KR. Assessment of fat-mass loss during weight reduction in obese women. Metabolism. 1997;46:968-75.

3 Newby MJ, Fein NC, Brown DL. Body composition of adult cystic fibrosis patients and control subjects as determined by densitometry, bioelectrical impedance, total body conductivity, skinfold measurements and deuterium oxide dilution. Am J Clin Nutr. 1990;52:209-13.

4 Lubaski HC. Methods for assessment of body composition: traditional and new. Am J Clin Nutr. 1990;52:438-41.

5 Formica C, Atkinson MG, Nyulasi I, et al. Body composition following dialysis: studies using dual energy X-ray absorptiometry and bioelectrical impedance analysis. Osteoporosis Int. 1993;3:192-97.

6 Revilla RM, Hernandez ER, Villa F, et al. Total body bone measurements in spinal osteoporosis by dual energy X-ray absorptiometry. Calcif Tissue Int. 1997;61:44-47.

the photon beams differently, a detector connected to a sophisticated computer program can distinguish three different types of body tissue- fat mass (% body fat), fat-free mass (lean body mass), and bone mass (bone mineral density). DXA is a "high-tech" test, done by an experienced technician on a very expensive machine. The cost, therefore, is more than that of some of the simpler methods that measure only body fat, and is usually not covered by insurance, except is situations where it is used to evaluate a medical problem.

The DXA scan time is only a few minutes. The test is safe and comfortable. The patient need not even remove clothes, provided there are no metal objects or fasteners, such as zippers, buttons, or bra hooks. A loose-fitting sweat suit is ideal for this test. There are no injections and no underwater submersion. The patient simply lies down on the table and remains still during the time of scanning. Radiation exposure is extremely small- about .02 mRem. This is 1/1,500th the radiation exposure of a standard chest X-ray (30 mRem), and 1/10,000th the annual background radiation in Albuquerque (200 mRem). Despite the very tiny radiation exposure, it is best not to do this test on women who may be pregnant. The results of the test are immediately available, in the form of a printout that includes an image of the body and skeleton.

Who Should Be Treated?

Treatment thresholds are different than diagnostic cutoff points. The T-score cutoff points for defining osteoporosis and osteopenia are not the same as the T-score thresholds for initiating drug therapy. For example, the Federal Drug Administration (FDA) approves starting medications, such as bisphosphonates or calcitonin, for the treatment of osteoporosis, if the T-score is < -2.0, even though the WHO cutoff for defining osteoporosis is -2.5. Several organizations have developed helpful guidelines for initiation of pharmacologic therapy. All patients should be advised about non-pharmacologic therapy, such as weight-bearing exercise, fall prevention, calcium, vitamin D, avoidance of smoking and alcohol abuse, and other lifestyle modifications. Some may benefit from additional interventions, such as balance training or hip protectors. The key to making a bone density report clinically useful is to look at T-score values in the light of the patient's total clinical profile and to have a good working understanding of the risks and benefits of all the recognized therapeutic options.

Here are some guidelines from two prominent medical organizations on when to consider starting pharmacologic therapy for postmenopausal women:

National Osteoporosis Foundation[1]

> **Initiate therapy to reduce fracture risk in women with BMD T-scores below -2 in the absence of risk factors and in women with T-scores below -1.5 if other risk factors are present.**

American Association of Clinical Endocrinologists[2]

> **The following women may benefit from pharmacologic treatment of osteoporosis:**
>
> 1. **Women with postmenopausal osteoporosis**
>   - **Women with low-trauma fractures and low BMD**
>   - **Women with BMD T-scores of -2.5 and below**
> 2. **Women with borderline low BMD (e.g., T-=scores of -1.5 and below) if risk factors are present**
> 3. **Women in whom nonpharmacologic preventive measures are ineffective (bone loss continues or low trauma fractures occur)**

[1] Physicians Guide to Prevention and Treatment of Osteoporosis. National Osteoporosis Foundation. 1999.

[2] Osteoporosis Task Force. AACE 2001 Guidelines for Clinical Practice for the Prevention and Management of Postmenopausal Osteoporosis. Endocrine Practice. 2001;7:293-312.

When to Refer to an Osteoporosis Specialist

In the vast majority of cases, a well-informed primary healthcare provider is the best person to manage the prevention and treatment of osteoporosis. However, an occasional patient will require the expertise of a physician with special knowledge and training in osteoporosis and metabolic bone disease. To address this issue, the following guidelines have been developed.[1]

Referral to an osteoporosis specialist is appropriate when the patient is in any of the following circumstances:

1. **Has osteoporosis that is unexpectedly severe or has unusual features at the time of initial assessment**
   - **Has very low BMD (a T-score below -3.0 or a Z-score below -2.0)**
   - **Has osteoporosis despite young age (premenopausal)**
   - **Has fractures despite borderline or normal BMD**

2. **Has a suspected or know condition that may underlie the osteoporosis (for example, hyperthyroidism, hyperparathyroidism, hypercalciuria, Cushing's syndrome, or hypogonadism)**

3. **Is a candidate for combination therapy**

4. **Is intolerant of approved therapies**

5. **Fails to respond to treatment**
   - **Takes estrogen yet has low baseline BMD**
   - **Is undergoing treatment yet shows an apparent loss of BMD on serial studies**
   - **Has fractures on treatment**

[1] Osteoporosis Task Force. AACE 2001 Guidelines for Clinical Practice for the Prevention and Management of Postmenopausal Osteoporosis. Endocrine Practice. 2001;7:293-312.

Non-pharmacological Therapy for Osteoporosis

Non-pharmacologic therapy is the foundation of any program for the prevention and treatment of osteoporosis. The cost is low and there may be non-skeletal benefits as well. For example, weight-bearing exercise may improve cardiovascular fitness, and avoidance of smoking will lower the risk of many smoking-related diseases. Pharmacologic therapy is likely to be less effective in the setting of nutritional deficiencies and unhealthy lifestyle.

Nutrition

Calcium: at least 1200 mg. per day[1] (elemental calcium in diet + supplements).

This recommendation applies to all adults. Since the typical American diet contains less that 600 mg. calcium per day, most of us need calcium supplements. The most commonly used calcium supplements contain calcium carbonate or calcium citrate. Many other forms of calcium are available as well. Absorption is usually best when taken with a meal. Even patients with achlorhydria and those taking medications to decrease gastric acid can expect to absorb the calcium supplements, provided they are taken with food. Patients with a history of calcium oxalate kidney stones usually generally do not need to restrict calcium intake, and in fact, doing so may actually increase the risk of future stones. Renal calcium loss may be minimized by a low sodium diet. Major brand-name calcium products meet USP standards, but some other products may not be manufactured with the same level of quality control. There is evidence that calcium and vitamin D supplementation has beneficial effects on bone density[2] and reduces fracture risk[3] in elderly ambulatory patients.

Vitamin D: 400 - 800 I.U. per day.[1]

This is the advisable intake for adults at risk for vitamin D deficiency. Most multivitamin pills contain 400 I.U. vitamin D. When in doubt about vitamin D status, the best test is a serum 25-hydroxyvitamin D level. Contrary to the "normal" range typically given by laboratories, the desirable level is between 30 and 57 ng/ml. Levels less than 30 ng/ml may be associated with bone loss due to secondary hyperparathyroidism, and levels greater than 57 ng/ml ➧

1 Physicians Guide to Prevention and Treatment of Osteoporosis, National Osteoporosis Foundation, 1999.

2 Dawson-Hughes B, Harris SS, Krall E, et al. Effect of Calcium and Vitamin D Supplementation on Bone Density in Men and Women 65 Years of Age or Older. N ENGL J MED. 1997;337:670-676.

3 Chapuy MC, Arlot ME, Duboeuf F, et al. Vitamin D3 and Calcium to Prevent Hip Fractures in Elderly Women. N ENGL J MED. 1992;327:1637-1642.

may be associated with vitamin D toxicity. Very low levels of vitamin D may cause osteomalacia as well as osteoporosis, and may require treatment with large doses of vitamin D (50,000 I.U. once or twice a week). Vitamin D deficiency is much more common than previously recognized, especially in older adults. There is accumulating evidence that calcium and vitamin D supplementation may stabilize or increase bone density and lower fracture risk in some patients.

Lifestyle

- Regular weight-bearing exercise
- Fall prevention
- No smoking
- Limit dietary sodium
- Limit alcohol intake
- Adequate protein intake
- Avoid medications associated with osteoporosis

Hip Protectors

External hip protectors are pads that are placed over the greater trochanter, usually as an insert into pocketed under-shorts. Since most hip fractures result from sideways falls with direct impact on the greater trochanter, an external device to attenuate the force of impact might be expected to prevent fractures. Several controlled studies[1,2] have shown that hip protectors are remarkably effective at reducing the risk of hip fracture in elderly frail patients, with a reduction in fracture risk of over 80% if worn at the time of the fall. They are cost-effective and work immediately. The challenge is patient acceptance. They will not work if not worn, and only a minority of patients started on hip protectors will continue to wear them daily[3]. Hip protectors should be considered in elderly frail patients at high risk of falling.

1 Kannua P, Parkkari J, Niemi S, et al. Prevention of Hip Fracture in Elderly People with Use of a Hip Protector. N ENGL J MED. 2000;343:1506-1513.

2 Lauritzen JB, Petersen MM, Lund B. Effect of External Hip Protectors on Hip Fractures. Lancet. 1993;341:11-13.

3 Hubacher M, Wettstein A. Acceptance of Hip Protectors for Hip Fracture Prevention in Nursing Homes. Osteoporosis Int. 2001;12:794-799.

Fall Prevention Guidelines

Falling is a very common and serious problem in the elderly. Falling results in increased morbidity and mortality, more hospital and nursing home admissions, and great expense. The frequency of falling and the severity of complications related to falling rises steadily after the age of 60. In healthy community-dwelling patients over age 65, the annual rate of falling is about 35-40%. Complications of falling include contusions, lacerations, fractures, and head injuries. Guidelines to assist healthcare providers in the assessment of fall risk and the management of elderly patients who at high risk of falling have been published.[1] Here is a summary of these guidelines, edited for easy reference:

Assessment of persons who have fallen or are at risk of falling

- **Older persons presenting for routine care**
  - **Ask annually about falls**
  - **If a fall is reported, then**
    - **Perform a "Get up and Go Test"- Patient stands up from chair without using arms, walks a few steps, and returns. If patient has difficulty doing this, further evaluation is required.**
- **Older persons who have fallen, or who have abnormalities of gait and/or balance**
  - **Perform fall evaluation as follows**
    - **History of fall circumstances**
    - **Medications**
    - **Acute and chronic medical problems**
    - **Mobility**
    - **Examine vision, gait, balance, lower extremity joint function**

[1] American Geriatrics Society, British Geriatrics Society, and American Academy of Orthopedic Surgeons Panel on Falls Prevention. Guideline for the Prevention of Falls in Older Persons. JAGS. 2001;49:664-672.

- **Basic neurologic function- mental status, muscle strength, lower extremity peripheral nerves, proprioception, reflexes; tests of cortical, extrapyramidal, and cerebellar function**
- **Basic cardiovascular function- heart rate and rhythm, postural pulse and blood pressure changes**

Intervention to prevent falls

- **Multifactorial**
  - **Community-dwelling older persons**
    - **Gait training**
    - **Assistive devices**
    - **Review and modify medications, especially psychotropic medications**
    - **Exercise program with balance training**
    - **Treatment of postural hypotension**
    - **Modification of environmental hazards**
    - **Treatment of cardiovascular disorders, including cardiac arrhythmia**
  - **Long-term care and assisted living settings**
    - **Staff education programs**
    - **Gait training and advice on assistive devices**
    - **Review and modification of medications, especially psychotropic medications**
  - **Acute hospital setting**
    - **Insufficient evidence to make recommendations**
- **Single intervention**
  - **Exercise**
    - **Many proven benefits**
    - **Optimal type, duration and intensity for fall prevention is unclear**
  - **Environmental modification**
    - **Home assessment should be considered**
    - **May reduce falls in some patients**
- **Medications**
  - **Pay particular attention of older persons taking 4 or more medications or psychotropic medications**
- **Assistive Devices**
  - **Consider bed alarm, cane, walker, hip protectors**

- **Few studies showing benefit in preventing falls**

- **Behavioral and educational programs**
  - **Beneficial when part of comprehensive multifactorial intervention**
- **Cardiovascular intervention**
  - **Orthostatic hypotension**
  - **Carotid sinus syndrome**
  - **Vasovagal syndrome**
- **Visual intervention**
  - **Ask about vision, and assess if any problem is present**
- **Footwear intervention**
  - **No specific recommendations**
- **Restraints**
  - **No evidence to support their use for fall prevention**

FDA-Approved Medications for Osteoporosis

At the time of this printing, all medications approved by the FDA for prevention or treatment of osteoporosis are antiresorptive agents. A new anabolic agent that stimulates formation, teriparatide (Forteo®), is widely expected to receive final FDA approval before the end of 2002. Prices listed are "approximate retail prices" from www.drugstore.com.

Estrogen Replacement Therapy (ERT)

Drug Class: Hormonal therapy.
Examples: Premarin® tablets (conjugated estrogens), Ogen® tablets (estropipate), Estrace® tablets (micronized estradiol), Estraderm® / Vivelle® / Alora® / Climara® patches (estradiol transdermal systems), and others, as well as combination therapy such as Prempro™ (conjugated estrogens and medroxyprogesterone acetate), Premphase® (conjugated estrogens and medroxyprogesterone acetate) and femhrt™ (norethindrone acetate and ethinyl estradiol).
Mechanism of Action: Antiresorption
FDA: Approved for prevention of postmenopausal osteoporosis.
Typical Dose: Premarin® .625 mg. tab PO qday, Ogen® .625 mg. tab PO qday, Estrace® .5 mg. PO qday, Estraderm® / Vivelle® / Alora® .05 mg./day patches 2 x per week, Climara® patch .025 mg./day patch 1 x per week, Prempro™ .625 mg/2.5 mg tab qday, Premphase® tab PO qday, and femhrt™ 1/5 tab PO qday.
Comment: The above doses will usually stabilize or increase BMD in early postmenopausal women, and may benefit older postmenopausal women as well. Lower doses may also be effective in some cases, but to a lesser extent. Some women, especially smokers, may require a higher dose. Bone densitometry is the only way to know for sure that the dose is sufficient. Consider ERT in all postmenopausal women with no contraindication. Patient compliance may be enhanced by using a continuous daily oral dosing regimen or a once a week patch. In women with a uterus, ERT should be combined with a progestin for at least 10 days of each estrogen cycle, in order to prevent endometrial hyperplasia. It has long been felt that discontinuation of ERT is followed by accelerated bone loss, although a recent report[1] suggests this may not be the case. The literature concerning the risk of breast cancer and cardiovascular disease in patients receiving ERT continues to expand. The non-skeletal effects of ERT should be carefully considered before prescribing.

[1] Greendale GA, Epseland M, Slone S, et al. Bone Mass Response to Discontinuation of Long-term Hormone Replacement Therapy: Results From the Postmenopausal Estrogen/Progestin Interventions (PEPI) Safety Follow-up Study. Arch Int Med. 2002;162:665-672.

BMD, Bone Markers & Fracture Risk: The PEPI (Postmenopausal Estrogen Progestin Intervention) Trial[2] showed 6.8 % increased spine BMD and 3.4 % increased hip BMD for ERT compared to placebo over 3 years. Although the definitive large prospective multi-center randomized double-blind placebo-controlled study to evaluate ERT and fracture risk is yet to be completed, numerous observational studies[3] and meta-analysis have shown a 40-60% decreased risk of fracture of the spine, hip and wrist in women taking ERT. Urinary markers of bone resorption may decrease by about 50% on ERT. Without ERT, expect 2-5% per year decreased BMD for first 5 years after menopause and a 40-50% lifetime risk of fragility fracture.

Cost: ~ $18-26 per month for oral estrogens or $28 per month for estrogen patches.

Raloxifene

Drug Class: Selective Estrogen Receptor Modulator (SERM)

Brand Name: Evista®

Mechanism of Action: Antiresorption

FDA: Approved for prevention and treatment of postmenopausal osteoporosis.

Dose: 60 mg. tab PO qday (anytime, with or without meals).

Comment: Contraindicated in women who are or who may become pregnant, and in women with a history of venous thromboembolic events. Positive effect lipids-decreased total and LDL cholesterol, no effect on HDL. There is evidence that raloxifene decreases the risk of cardiovascular events by 40% in high-risk patients.[4] No effect or slight increase in hot flashes. No effect on uterus. May lower risk of breast cancer. Not yet evaluated in patients with baseline breast or uterus cancer, or with severe liver disease. Not contraindicated in breast cancer.

BMD, Bone Markers & Fracture Risk: The MORE (Multiple Outcomes of Raloxifene) Study[4] showed that raloxifene 60 mg. per day resulted in 2.6% increased spine BMD and 2.1% increased femoral neck BMD compared to placebo in ➧

2 The Writing Group for the PEPI Trial. Effects of Hormone Therapy on Bone Mineral Density. JAMA. 1996;276(17):1389-1396.

3 Cauley JA, Seeley DG, Ensrud K, et al. Estrogen Replacement Therapy and Fractures in Older Women. Ann Int Med. 1995;122:9-16.

4 Barrett-Conner E, Grady D, Sashegyi A, et al. Raloxifene and Cardiovascular Events in Osteoporotic Postmenopausal Women: Four-Year Results From the MORE (Multiple Outcomes of Raloxifene Evaluation). JAMA. 2002;287:847-857.

5 The Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. Reduction of Vertebral Fracture Risk in Postmenopausal Women with Osteoporosis Treated with Raloxifene. JAMA. 1999;282:637-645.

osteoporotic postmenopausal women treated for 3 years. Urinary CTx decreased by 34.0%, compared to an 8.6% decrease in the placebo group. There was a 30% decreased in risk of vertebral fracture risk in the treated group, but no difference in non-vertebral fractures.
Cost: ~ $63 per month.

Alendronate

Drug Class: Bisphosphonate (formerly called diphosphonate)
Brand Name: Fosamax®
Mechanism of Action: Antiresorption
FDA: Approved for treatment of postmenopausal osteoporosis, prevention of postmenopausal osteoporosis in women who are at risk, treatment of osteoporosis in men, and treatment of glucocorticoid-induced osteoporosis in men and women who are taking the equivalent of at least 7.5 mg prednisone per day and have low BMD. Approved for 70 mg. weekly dosing and 35 mg. twice-a-week dosing.
Dose: For prevention of postmenopausal osteoporosis use 5 mg. tab PO qAM. For treatment of postmenopausal osteoporosis and for treatment of osteoporosis in men use 10 mg. tab PO qAM. For glucocorticoid-induced osteoporosis in men and women, use 5 mg. tab PO qAM, except in postmenopausal women not taking ERT, for whom the 10 mg. dose is recommended. Dosing with a 70 mg tab once a week is equivalent to 10 mg. qAM, and 35 mg once a week is equivalent to 5 mg. qAM.
Comment: Must be taken at least one-half hour before the first food, beverage or medication of the day because of poor bioavailability (only about 0.66% of ingested medication is absorbed), and must be upright for at least 30 min. after taking to minimize GI irritation. Use in women unable or unwilling to take ERT. Avoid with severe renal insufficiency (creatinine clearance < 35 ml/min). Weekly dosing of 70 mg. has an effect on BMD identical to daily dosing of 10 mg., and weekly dosing of 35 mg. has an effect on BMD identical to daily dosing of 5 mg., with greater dosing convenience and no difference in GI tolerability.
BMD, Bone Markers & Fracture Risk: The EPIC (Early Postmenopausal Intervention Cohort) Study[1] showed that alendronate 5 mg per day given to early postmenopausal women with normal baseline BMD for four years resulted in about

[1] Ravn P, Didstrup M, Wasnich RD, et al. Alendronate and Estrogen in the Long-Term Prevention of Bone Loss: Four Year Results from the Early Postmenopausal Intervention Cohort Study. Ann Int Med. 1999;131(12):935-942.

6.7% increased spine BMD and 4.4% increased total hip BMD compared to placebo. Urinary NTx decreased by about 80% compared to baseline. The four-year FIT (Fracture Intervention Trial)[2] data for osteoporotic women without baseline vertebral fractures show 6.6% increased spine BMD and 4.6% increased femoral neck BMD compared to placebo, with 44% decreased in radiographic vertebral fractures and 36% decreased femoral neck fractures. In another arm of the same study,[3] looking at women with baseline vertebral fractures, there was a 55% decreased in clinical vertebral fractures and 48% decreased hip fractures. A phase III open label trial[4] of alendronate treatment with 10 mg. per day extended to 7 years showed that spine BMD continues to improve (by 11.4% compared to baseline), and the benefit at other skeletal sites is maintained. Alendronate has been shown to stabilize or improve BMD and to lower vertebral fracture risk in patients on long-term glucocorticoids.[5]
Cost: ~ $64 per month.

Risedronate

Drug Class: Bisphosphonate (formerly called diphosphonate)
Brand Name: Actonel®
Mechanism of Action: Antiresorption
FDA: Approved for prevention and treatment of postmenopausal osteoporosis, and prevention and treatment of glucocorticoid-induced osteoporosis.
Dose: 5 mg. qday.
Comment: Efficacy and tolerability are similar to alendronate. Same dosing precautions as alendronate.
BMD & Fracture Risk: Three-year North American data[6] with risedronate 5 mg per day in the treatment of postmenopausal osteoporosis have shown a 4.3% increased spine BMD and 2.8% increased femoral neck BMD compared to placebo, with 41% ➧

2 Cummings SR, Black DM, Thompson DE, et al. Effect of Alendronate on Risk of Fracture in Women with Low Bone Density but Without Vertebral Fractures. JAMA. 1998;280:2077-2082.
3 Watts NB. Treatment of osteoporosis with bisphosphonates. Endocrinol Metab Cllin N Amer. 1998;27:419-439.
4 Tonino RP, Meunier PJ, Emkey R, et al. Skeletal Benefits of Alendronate: 7-Year Treatment of Postmenopausal Osteoporotic Women. J CLIN ENDOCRINOL METAB. 2000;85:3109-3115.
5 Adachi JD, Saag KG, Delmas PD, et al. Two-year effects of alendronate on bone mineral density and vertebral fracture in patients receiving glucocorticoids: a randomized, double-blind, placebo-controlled extension trial. Arthritis Rheum. 2001;44:202-11.
6 Harris ST, Watts NB, Genant HK, et al. Effects of Risedronate Treatment on Vertebral and Nonvertebral Fractures in Women with Postmenopausal Osteoporosis. JAMA. 1999;282:1344-1352.

decreased in radiographic vertebral fractures and a 39% decreased in non-vertebral fractures. Three-year multinational data[1] showed a 5.9% increased spine BMD and 3.1% increased femoral neck BMD compared to placebo, with a 49% decreased in radiographic vertebral fractures and a 33% decreased in non-vertebral fractures. In elderly women with osteoporosis, a 40% decreased in hip fracture risk has been demonstrated.[2] Risedronate has been shown to stabilize or improve BMD and to lower vertebral fracture risk in patients on long-term glucocorticoids.[3]
Cost: ~ $58 per month

Nasal Salmon Calcitonin

Drug Class: Hormonal therapy
Brand Name: Miacalcin® Nasal Spray
Mechanism of Action: Antiresorption
FDA: Approved for treatment of postmenopausal osteoporosis in women more than 5 years postmenopausal who are unable or unwilling to take ERT.
Dose: 1 spray (200 IU) per day, alternating nostrils. One container lasts 2 weeks. Must be refrigerated prior to opening.
Comment: Not proven effective in first 5 years after menopause. An analgesic effect[4] has been demonstrated in the immediate post-fracture period.
BMD & Fracture Risk: In women with postmenopausal osteoporosis, two year treatment with nasal calcitonin has resulted in 2% increased spine BMD compared to placebo.[5] The PROOF (Prevent Recurrence of Osteoporotic Fracture) study[6] 5-year data showed 36% decreased spine fractures with 1.2% increased spine BMD. Hip BMD remained stable, with a 48% decreased in hip fracture risk that was not statistically significant.
Cost: ~ $63 per month.

1 Reginster J-Y, Minne HW, Sorensen OH, et al. Osteoporosis Int. Randomized Trial of the Effects of Risedronate on Vertebral Fractures in Women with Established Postmenopausal Osteoporosis. 2000;11:83-91.
2 McClung MR, Geusens P, Miller PD, et al. Effect of Risedronate on the Risk of Hip Fracture in Elderly Women. N ENGL J MED. 2001;344:333-340.
3 Wallach S, Cohen S, Reid DM, et al. Effects of risedronate on bone density and vertebral fracture in patients on corticosteroid therapy. Calcif Tissue Int. 2000;67:277-85.
4 Pun KK, Chan LW. Analgesic effect of intranasal salmon calcitonin in treatment of osteoporotic vertebral fractures. Clin Ther. 1989;11(2):205-9.
5 Overgaard K, Hansen MA, Jensen SB, et al. Effect of calcitonin given intranasally on bone mass and fracture rates in established osteoporosis: a dose-response study. BMJ. 1992;305:556-561.
6 Chesnut, CH, Silverman S, Andriano, K, et al. A Randomized Trial of Nasal Spray Salmon Calcitonin in Postmenopausal Women with Established Osteoporosis: The Prevent Recurrence of Osteoporotic Fractures Study. Am J Med. 2000;109:267-276.

Injectable Salmon Calcitonin

Drug Class: Hormonal therapy
Brand Name: Miacalcin® Injectable
Mechanism of Action: Antiresorption
FDA: Approved for treatment of osteoporosis.
Dose: 1/2 cc. (100 IU) subq or IM qday.
Comment: Very expensive. Alternative dosing schedules can help to cut cost. Some experts use a more frequent dosing schedule, such as q8h, in the initial treatment of painful vertebral compression fractures in hospitalized patients, then switch to the nasal preparation. Concomitant anti-nausea medication may be required.
BMD & Fracture Risk: Similar to calcitonin nasal spray.[1]
Cost: ~ $250 per month.

Teriparatide[1] (recombinant human PTH 1-34)

Drug Class: Hormonal therapy
Brand Name: Forteo®
Mechanism of Action: Anabolic. Stimulates bone formation.
FDA: Not approved for treatment of osteoporosis, but approval and release anticipated soon.
Dose: 20 µgm subq qday.
Comment: There is evidence that, in addition to increasing BMD and reducing fracture risk, PTH therapy may improve bone quality. This is demonstrated by increased trabecular volume, increased trabecular connectivity, and no increase in cortical porosity. This drug is an exciting addition to the management of osteoporosis, but many questions remain about its clinical use. Patient selection, combination with other drugs (simultaneously or sequentially), and duration of therapy are issues that are being investigated. It should be noted that Fischer 344 rats treated with large doses of teriparatide for near-lifespan were observed to have a high risk of osteosarcoma. There is no evidence of increased risk of osteosarcoma in humans, who are treated with a lower dose for a much shorter period of time. It is also comforting to note that there is no evidence for increased risk of osteosarcoma in patients with primary hyperparathyroidism. Observed changes in serum and urinary calcium have been mild and transient.

[1] At the time of this writing, teriparatide has not yet received final FDA approval and has not been released. It is expected that this will happen before the end of 2002. It is included here in anticipation of this event.

BMD & Fracture Risk: The pivotal teriparatide fracture trail[2] showed that 20 mgm per day given for an average of 18 months resulted in 8.6% increased spine BMD and 3.5% increased femoral neck BMD compared to placebo, in osteoporotic postmenopausal women with at least one prevalent vertebral fracture. There was a 65% decreased in new vertebral fractures and a 53% decreased in non-vertebral fragility fractures in the treated group compared to controls. Urinary CTx decreased by 34.0%, compared to an 8.6% decrease in the placebo group.

Cost: Not yet announced.

Summary of FDA Approved Medications for Osteoporosis (4/02)

		Postmenopausal Osteoporosis		Glucocorticoid-Induced Osteoporosis			
Generic Name	**Brand Name**	**Prevention**	**Treatment**	**Prevention**	**Treatment**	**Men**	**Weekly Dosing**
Estrogens	Various	✔					
Alendronate	Fosamax	✔	✔		✔	✔	✔
Risedronate	Actonel	✔	✔	✔	✔		
Raloxifene	Evista	✔	✔				
Calcitonin	Miacalcin		✔				
Teriparatide[1]	Forteo						

[2] Neer R, Arnaud CD, Zanchetta JR, et al. Effect of Parathyroid Hormone (1-34) on Fractures and Bone Mineral Density in Postmenopausal Women with Osteoporosis. N ENGL J MED. 2001;344:1434-1441.

[3] At the time of this writing, teriparatide has not yet received final FDA approval and has not been released. It is expected that this will happen before the end of 2002. It is included here in anticipation of this event.

Non FDA-Approved Medications for Osteoporosis

Etidronate

Drug Class: Bisphosphonate (formerly called diphosphonate)
Brand Name: Didronel®
Mechanism of Action: Antiresorption
FDA: Not approved for prevention or treatment of osteoporosis, although it is used in some other countries for this purpose. It is approved in the USA for Paget's disease of bone and for heterotopic ossification.
Dose: The usual dose used for the treatment of osteoporosis is 400 mg. tab qday for 2 weeks every 3 months (14 days of Didronel® only, followed by 76 days of calcium only).
Comment: Remember to hold calcium during the 2 weeks of taking Didronel®. It should be taken at least 2 hours before or after food, vitamins, supplements, or other medications. It is acceptable to take it at bedtime.
BMD & Fracture Risk: Studies in women with postmenopausal osteoporosis with as long as seven-year follow-up have shown about 8% increased spine BMD and 50% decreased in new vertebral fractures.[1]
Cost: ~ $78 per month.

Pamidronate

Drug Class: Bisphosphonate (formerly called diphosphonate)
Brand Name: Aredia®
Mechanism of Action: Antiresorption
FDA: Not approved for prevention or treatment of osteoporosis. It is approved for Paget's disease and hypercalcemia of malignancy.
Dose: 30 mg. IV infusion every 3 months for the treatment of osteoporosis is commonly used. Other dosing regimens have been used as well.
Comment: Consider this only in patients who cannot tolerate or have not responded to FDA approved mediations.
BMD & Fracture Risk: Pamidronate has been shown to increase BMD at the spine and hip.[2] Fracture data is not available.
Cost: ~ $200 per dose plus cost of IV infusion.

1 Watts NB, Miller PD, Licata AA, et al. Seven Years of Cyclical Etidronate: Continued Improvement in Spine BMD and Progressive Decline in Vertebral Fracture Incidence. Bone. 1995;17(6):597-618.
2 Tohme JP, Bilezikian JP, Sutherland B, et al. Treatment of Osteoporosis with Cyclic Intravenous Pamidronate. J Bone Miner Res. 1999:14(suppl 1):F343.

Zoledronic Acid

Drug Class: Bisphosphonate (formerly called diphosphonate)
Brand Name: Zometa®
Mechanism of Action: Antiresorption
FDA: Not approved for prevention or treatment of osteoporosis. It is approved for hypercalcemia of malignancy. It is approved for the treatment of hypercalcemia of malignancy, and for the treatment of patients with multiple myeloma and patients with documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy.
Dose: 4 mg. IV infusion over 15 minutes has been used for the treatment of osteoporosis.
Comment: Consider this only in patients who cannot tolerate or have not responded to FDA approved mediations. Renal toxicity has been reported. Fracture studies are underway.
BMD & Fracture Risk: Zoledronic acid has been shown to increase BMD at the spine and hip.[1] Fracture data is not available.
Cost: ~ $860 per dose plus cost of IV infusion.

Combination Therapy

Evidence is accumulating that some combinations of medications may increase BMD more than either medication alone. Examples of efficacious combinations include

1 Reid IR, Brown JP, Burkhardt P, et al. Intravenous Zoledronic Acid in Postmenopausal Women with Low Bone Mineral Density. N ENGL J MED. 346:653-661.
2 Wimalawansa SJ. A Four-Year Randomized Controlled Trial of Hormone Replacement and Bisphosphonate, Alone or in Combination, in Women with Postmenopausal Osteoporosis. Am J Med.1998;104:219-226.
3 Lindsay et al, FACET (Fosamax Added to Continuous Estrogen Therapy) Study. ECO. 1998.
4 Harris ST, Wasnich R, Ettinger M, et al. The Effects of Risedronate Plus Estrogen Compared with Estrogen Alone in Postmenopausal Women. J Bone Miner Res. 1999;14(supppl 1):S410.
5 Roe EB, Sanchez SD, del Puerto, GA, et al. Parathyroid Hormone 1-34 (hPTH 1-34) and Estrogen Produce Dramatic Bone Density Increases in Postmenopausal Osteoporosis – Results from a Placebo-Controlled Randomized Trial. J Bone Miner Res. 1999;14(suppl 1):S137.
6 Watts NB, Notelovitz M, Timmons MC, et al. Comparison of oral estrogens and estrogens plus androgen on bone mineral density, menopausal symptoms, and lipid/lipoprotein profiles in surgical menopause. Obstet Gynecol. 1995;85(4):529-537.
7 Meschia M, Brincat M, Barbacini P, et al. Effect of hormone replacement therapy and calcitonin on bone mass in postmenopausal women. Eur J Obstet Gynecol Reprod Biol. 1992;47(1):53-7.
8 Johnell O, Scheele W, Lu Y, Lakshmanan M. Effects of Raloxifene (RLX), Alendronate (ALN) and RLX + ALN on Bone Mineral Density (BMD) and Biochemical Markers of Bone Turnover in Postmenopausal with Osteoporosis. J Bone Miner Res. 1999:14(suppl 1):S157.

estrogen plus etidronate[2], estrogen plus alendronate,[3] estrogen plus risedronate,[4] estrogen plus PTH,[5] estrogen plus testosterone[6] (Estratest®), estrogen plus calctonin[7]and alendronate plus raloxifene.[8] There are no fracture data on these combinations. The role of combination therapy in clinical practice is promising but not yet well established. Combination therapy should be used with great discretion, since it may add considerable extra expense and increase risk of toxicity, with no proven therapeutic benefit in terms of fracture reduction.

Under Investigation

Bisphosphonates- ibandronate, zoledronic acid
SERMs (Selective Estrogen Receptor Modulators)- lasofoxifene, bazedoxifene
Regulators of Bone Metabolism- osteoprotegerin (OPG) analogues
Anabolic Agents- recombinant human PTH, statins
Synthetic Steroids- tibolone

Vertebroplasty and Kyphoplasty

Background. There are 28 million Americans with osteoporosis or osteopenia, resulting in 1.5 million fragility fractures per year with direct health care costs of approximately $13 billion.[1] About 700,000 of these fractures are vertebral compression fractures, of which about 270,000 are clinically diagnosed.[2] New vertebral fractures that are not clinically detected nevertheless cause a two to three-fold increase in back pain and functional limitation.[3] Five percent of 50 year-old women and 25% of 80 year-old women have had at least one vertebral fracture.[4] Clinical consequences of vertebral compression fractures include pain, loss of height, deformity, reduced pulmonary function,[5] disability, diminished quality of life,[6] and a 15% increased mortality rate.[7]

Treatment of vertebral fractures. Conventional medical therapy for vertebral fractures includes bed rest, narcotic analgesics, salmon calcitonin, external back bracing, physical therapy, hospitalization, and skilled nursing care. Unfortunately, medical management of painful fractures may itself compound the problem, since lack of mobility can increase the rate of bone demineralization and increase the risk of additional fractures.[8] Although most patients respond to conservative treatment and heal within weeks or months, a minority of patients continue to suffer pain. When there is concurrent spinal instability or neurologic deficit, open surgery with fracture reduction and stabilization has been used. Due to the high risk of surgery, minimally invasive techniques, such as vertebroplasty and Kyphoplasty™ have been developed.

1 Ray NF, Chan JK, Thamer M, Melton LJ III. Medical expenditures for the treatment of osteoporotic fractures in the United States in 1995: Report from the National Osteoporosis Foundations. J Bone Miner Res. 1997;12:24-35.

2 Cooper C, Atkinson EJ, O'Fallon WM, Melton LJ III. Incidence of clinically diagnosed vertebral fractures: a population-based study in Rochester, Minnesota, 1985-1989. J Bone Miner Res. 1992;7:221-7.

3 Nevitt MC, Ettinger B, Black D, Stone K, Jamal SA, Ensrud K, Segal M, Genant HK, Cummings SR. The association of radiographically detected vertebral fractures with back pain and function: a prospective study. Ann Int Med. 1998;128(10):793-800.

4 Melton LJ III, Kan SH, Frye MA, Wahner HW, O'Fallon WM, Riggs BL. Epidemiology of vertebral fracture in women. Am J Epidemiol. 1989;10:283-96.

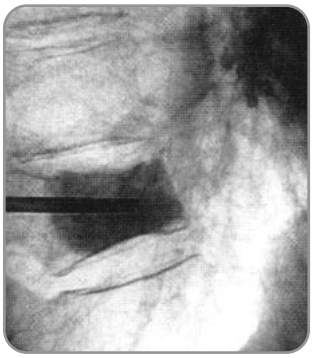
5 Schlaick C, Minne HW, Bruckner T, Wagner G, Gebest HJ, Grunze M, Ziegler R, Leidig-Bruckner G. Reduced pulmonary function in patients with spinal osteoporotic fractures. Osteoporosis Int. 1998;8:261-67.

6 Cortet B, Houvenagel E, Puisieux F, Roches E, Garnier P, Delcambre B. Spinal curvatures and quality of life in women with vertebral fractures secondary to osteoporosis. Spine. 1999;24(18):1921-25.

7 Kado DM, Browner WS, Palermo L, Nevitt MC, Genant HK, Cummings SR. Vertebral fractures and mortality in older women: a prospective study. Arch Intern Med. 1999;159:1215-20.

8 Heaney RP. The natural history of osteoporosis: Is how bone mass an epiphenomenon? Bone. 1992;18(3):S23-26.

Vertebroplasty and Kyphoplasty



Vertebroplasty. This procedure was first performed by interventional radiologists in France in 1984, and in the USA in 1995. The minimally invasive procedure involves the high-pressure injection of bone cement (polymethylmethacrylate) through a 10 or 11 gauge needle through both pedicles into the vertebral body, usually using biplane fluoroscopic control.[9] Vertebroplasty has been used to treat fractures caused by osteoporosis, metastatic tumors, multiple myeloma and vertebral hemangiomas.[10] It is a safe and effective method of treating disabling pain in selected patients who are refractory to conservative measures. Pain relief often occurs within one hour of the procedure, which can be performed with local, regional, or general anesthesia.

In a series of 80 patients with osteoporotic vertebral fractures treated and followed for one month to ten years, more than 90% had immediate results that were excellent, with complete relief of symptoms within 24 hours.[11] There was one complication- an intercostal neuralgia treated by local anesthetic infiltration. In another study,[12] 29 patients with 47 osteoporotic vertebral fractures were treated over a period of three years. Twenty-six (90%) of patients treated experienced pain relief and improved mobility with 24 hours after treatment. The only clinical complications were two non-displaced rib fractures resulting in limited chest pain, which subsequently resolved. As many as 7 vertebral bodies have been injected in one patient, with excellent results.[13]

Indications: Painful vertebral fracture(s) due to osteoporosis, multiple myeloma, metastatic malignancy, or aggressive vertebral hemangiomas.

9 Garfin S, Mermelstein L, Mirkovic S, Sandu H, Vaccaro A. Challenges of spine fixation in the adult. Presented at the North American Spine Society meeting, October 31, 1998.

10 Cotton A, Boutry N, Cortet B, Assaker R, Demondion X, Leblond D, Chastanet P, Duquesnoy B, Deramond H. Percutaneous vertebroplasty: state of the art. Radiographics. 1998;18:311-20.

11 Deramond H, Depriester C, Galibert P, Le Gars D. Percutaneous vertebroplasty with polymethylmethacrylate: technique, indications and results. Radio Clin North Am. 1998;36:533-46.

12 Jensen ME, Evans AJ, Mathis JM, Kallmes DF, Cloft HJ, Dion JE. Percutaneous polymethylmethacrylate vertebroplasty in the treatment of osteoporotic vertebral compression fractures: technical aspects. AJNR. 1997;18:1897-1904.

13 Mathis JM, Petri M, Naff N. Percutaneous vertebroplasty treatment of steroid-induced osteoporotic compression fractures. Arth Rheum. 1998;41(1):171-5.

Vertebroplasty and Kyphoplasty

Absolute contraindications: Asymptomatic stable fracture; patient clearly improving on medical therapy; osteomyelitis of target vertebra, acute traumatic fracture of non-osteoporotic vertebra; uncorrectable bleeding disorder.

Relative contraindications: Radicular pain significantly in excess of vertebral pain; retropulsed fragment causing significant spinal cord compromise; tumor extension into the adjacent epidural space with significant spinal cord compromise; very severe vertebral body collapse (>70%); stable fracture known to be more than two years old.

Risks: Infection; transient or permanent neurological deficit; transient or permanent radicular pain; pulmonary cement embolus; epidural cement embolus; rib fracture; allergic/idiosyncratic reaction.

Benefits: Pain relief and fracture stabilization.

Kyphoplasty™. Kyphon Inc. has developed a bone tamp, similar to an angioplasty balloon, which can be inserted through a small cortical window in the vertebral body or pedicle and inflated to reduce vertebral compression fractures. The procedure creates a void in the trabecular bone and restores vertebral body height, thereby allowing a stabilizing material to be injected under low pressure. This device is similar to other devices that have been used for other types of fractures for many years, and on this basis received FDA approval in 1998. Preliminary reports have shown that this procedure is similar to vertebroplasty in safety and efficacy, with the added benefit of vertebral fracture reduction and partial reversal of skeletal deformity. A randomized controlled study is now underway at approximately 30 centers in the USA, comparing Kyphoplasty™ to conventional medical therapy for the treatment of acute osteoporotic vertebral fractures.

Indications, Contraindications & Risks: Similar to vertebroplasty, although Kyphoplasty™ can be expected to have the greatest potential to correct skeletal deformities in the setting of an acute, rather than chronic, vertebral compression fracture.

Benefits: Pain relief, fracture stabilization, fracture reduction, correction of skeletal deformity.

Osteoporosis Community Services in New Mexico

Osteoporosis Support Group

The National Osteoporosis Foundation Albuquerque Support Group is an organization devoted to providing education and emotional support in the area of osteoporosis. Its meetings are for anyone who has osteoporosis, has a loved one with osteoporosis, or is interested in osteoporosis. To volunteer to give an expert presentation, or to get more information for patients wishing to attend, call the support group coordinator at (505) 855-5627.

Osteoporosis Speakers' Bureau

This program provides speakers and educational materials for osteoporosis presentations to lay groups, medical office personnel, or health care organizations. Topics can be varied to meet the needs of the group. To schedule a presentation or obtain more information, call (505) 855-5627.

New Mexico Osteoporosis Society

NMOS is an organization composed of healthcare providers with an interest in osteoporosis. Quarterly educational presentations with CME credit have gained tremendous popularity, and are a convenient way to keep up with the latest developments in osteoporosis. For more information call Dr. Lewiecki at (505) 855-5525.

Osteoporosis Foundation of New Mexico

This is a 501(c)(3) non-profit foundation dedicated to research and education for osteoporosis and metabolic bone disease. For information on foundation activities, or to learn how to make a tax-deductible donation to the foundation, call (505) 855-5627, or visit www.osteoporosisfoundationnm.org.

New Mexico Osteoporosis Prevention Program

This is a program funded by the state legislature for the purpose of educating residents of New Mexico about the prevention and treatment of osteoporosis. At the present time, the contract for administering the program is with the New Mexico Medical Review Association (NMMRA). For information, call JoAnna Weiss, Project Director and Communications Specialist, at 1-800-279-6824.

Osteoporosis Coalition

The Osteoporosis Coalition is an advisory committee composed of representatives from state agencies, managed care, hospitals, pharmaceutical companies, industry, and provider organizations. The committee works closely with NMMRA to offer guidance to the activities of the state's Osteoporosis Prevention Program.

Web Sites of Interest

American Association of Clinical Endocrinologists
www.aace.com

American College of Rheumatology
www.rheumatology.org

American Society for Bone and Mineral Research
www.asbmr.org

European Calcified Tissue Society
www.ectsoc.org

Federation of American Societies for Experimental Biology
www.faseb.org

International Bone and Mineral Society
www.IBMSonline.org

International Myeloma Foundation
www.myeloma.org/imf.html

International Osteoporosis Foundation
www.osteofound.org

International Society for Clinical Densitometry
www.iscd.org

Journal of Bone and Mineral Research
www.jbmronline.org

National Osteoporosis Foundation
www.nof.org

New Mexico Clinical Research & Osteoporosis Center
www.nmbonecare.org

North American Menopause Society
www.menopause.org

Osteogenesis Imperfecta Foundation
www.oif.org

Osteoporosis and Bone Physiology, Univ. of Washington
www.washington.edu/bonephys

Osteoporosis and Related Bone Diseases, National Resource Ctr.
www.osteo.org

Osteoporosis Foundation of New Mexico
www.osteoporosisfoundationnm.org

Osteovision
www.osteovision.org

Paget Foundation
www.paget.org

The Endocrine Society
www.endo-society.org

Publications of Interest

Journals. Many medical journals occasionally publish review articles, research studies, and guidelines for the management of osteoporosis. The following journals are exclusively devoted to osteoporosis, metabolic bone disease, or bone densitometry. Anyone with a special interest in osteoporosis should consider subscribing to some of these, or monitoring the articles published in them.

Bone
The journal of the International Bone and Mineral Society.
Published monthly by Elsevier Science Inc., 655 Avenue of the Americas, New York, NY 10010.
To subscribe call 212-633-3950 or4 email ibms@dc.sba.com.

Calcified Tissue International (CTI)
The journal of the European Calcified Tissue Society.
Published monthly by Springer-Verlag, 175 Fifth Avenue, New York, NY 10010.
To subscribe call 800-SPRINGER or email journals@springer-ny.com.

Journal of Bone and Mineral Research (JBMR)
The journal of the American Society for Bone and Mineral Research.
Published monthly by ASBMR, 2025 M Street NW, Suite 800, Washington, DC 20036-3309.
To subscribe call 202-367-1161 or contact www.asbmr.org

Journal of Clinical Densitometry (JCD)
The journal of the International Society for Clinical Densitometry.
Published quarterly by Humana Press Inc., 999 Riverview Dr., Suite 208, Totowa, NJ 07512.
For subscription information call 202-367-1132 or contact www.iscd.org

Osteoporosis International (OI)
A joint initiative of the International Osteoporosis Foundation and the National Osteoporosis Foundation of the USA.
Published monthly by Springer-Verlag, 175 Fifth Avenue, New York, NY 10010.
To subscribe call 212-460-1500 or email orders@springer-ny.com.

Publications of Interest

Other journals with content that reflects a more than passing interest in osteoporosis and metabolic bone disease include Arthritis & Rheumatism (journal of the American College of Rheumatology), Endocrine Practice (journal of the American Association of Clinical Endocrinologists), and Journal of Clinical Endocrinology & Metabolism (journal of The Endocrine Society).

Textbooks. There are many excellent references that can be an invaluable source of information for those who want to learn more. Some textbooks to consider are-

Dynamics of Bone and Cartilage Metabolism. Ed. Markus Seibel, Simon Robins, John Bilezikian. 1999. Academic Press, 525 B Street, Suite 1900, San Diego, CA 92101-4495.

Osteoporosis. Ed. Robert Marcus, David Feldman, Jennifer Kelsey. Second edition, 2 volumes. 2001. Academic Press, 525 B Street, Suite 1900, San Diego, CA 92101-4495.

Osteoporosis in Men. Ed. Eric Orwoll. 1999. Academic Press, 525 B Street, Suite 1900, San Diego, CA 92101-4495.

Nutritional Aspects of Osteoporosis. Ed. Peter Burckhardt, Bess Dawson-Hughes, Robert Heaney. 2001. Academic Press, 525 B Street, Suite 1900, San Diego, CA 92101-4495.

Principles of Bone Biology. Ed. John Bilezikian, Lawrence Raisz, Gideon Rodan. Second edition, 2 volumes. 2002. Academic Press, 525 B Street, Suite 1900, San Diego, CA 92101-4495.

Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism. Ed. Murray Favus. Fourth edition. 1999. Lippincott Williams & Wilkins, 227 East Washington Square, Philadelphia, PA 19106-3780.

Osteoporosis CME Meetings

There are times when nothing can offer as much professional reward or advance our clinical skills as much as attending a meeting or conference with colleagues that share similar interests. There are more and more regional, national and international meetings that address issues related to osteoporosis and metabolic bone disease. Here is a sampling of annual meetings that are primarily or partly concerned with osteoporosis and metabolic bone disease. Updated information on meetings is often listed in journals concerned with osteoporosis, and these meetings are usually listed on the web sites of the sponsoring organization.

Annual meetings

International Society for Clinical Densitometry

- 2002- Feb 13-16. Atlanta, GA
- 2003- Feb 13-16, Los Angeles, CA

American Society for Bone and Mineral Research

- 2002- Sept 20-24, San Antonio, TX
- 2003- Sept 19-23, Minneapolis, MN

National Osteoporosis Foundation

- 2002- March 6-9, Honolulu, HI

International Osteoporosis Foundation

- 2002- May 10-15, Lisbon, Portugal

Santa Fe Bone Symposium

- 2002- Aug 2-3, Santa Fe, NM

North American Menopause Society

- 2002- Oct 3-5, Chicago, IL
- 2003- Sept 18-20, Miami, FL

American Association of Clinical Endocrinologists

- 2002- May 1-4, Chicago, IL
- 2003- May 14-18, San Diego, CA

The Endocrine Society

- 2002- June 19-22, San Francisco, CA
- 2003- June 18-21, Philadelphia, PA

Basic Principles for Ordering Bone Densitometry

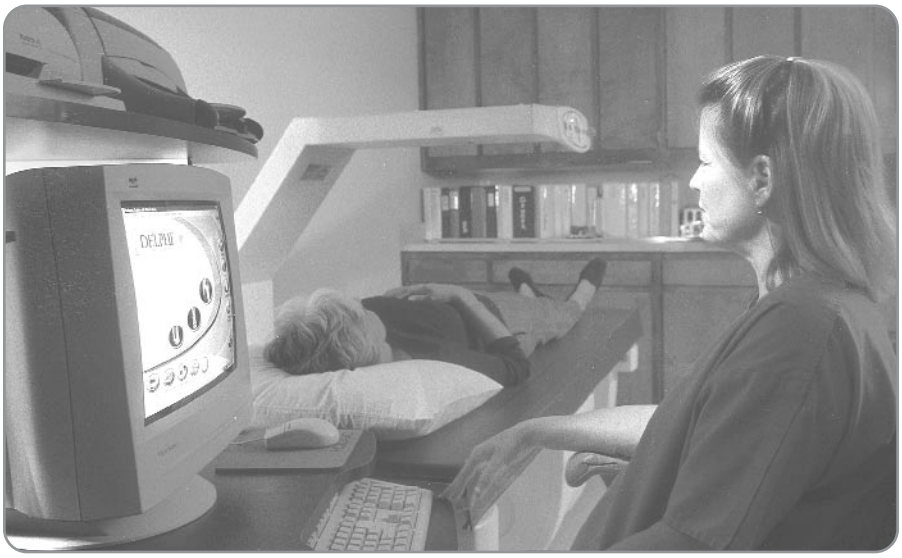
1. Most payers will not pay for "screening" in healthy individuals, but they may pay for testing in patients who meet their criteria for being at high risk for osteoporosis, or for monitoring of treatment for osteoporosis.

2. Health plans can, and will, change their criteria for coverage of bone densitometry on a moment's notice.

4. Many health plans require prior authorization. This must be done before the bone density test in order to be certain that the procedure is covered.

5. To increase the chances for approval of a DXA, it is helpful to identify and submit any other diagnoses or risk factors that are associated with osteoporosis. Refer to the "Risk Factors for Osteoporosis" section for more information.

6. Sometimes a patient who needs a DXA will pay out-of-pocket if it is not covered by the health plan.



Coverage for Bone Densitometry

The information in this section applies only to New Mexico.
Health plans in other states may have different criteria for coverage.

Please note that some health plans state that prior authorization is not required if BMD testing is "medically necessary." This is a managed care "code phrase" that may mean that a copy of the progress note from the chart, documenting the necessity for the test, must be sent to the testing facility. Submission of this note may be required in order for the testing facility to be reimbursed for the BMD test.

CPT Codes for Bone Densitometry

76070 Computerized axial tomography bone mineral density study, one or more sites

76075 Dual energy x-ray absorptiometry (DXA), bone density study, one or more sites; axial skeleton (e.g., hips, pelvis, spine) [this code is used whether one, two or three skeletal sites are measured, including forearm if done by central DXA device]

76076 Dual energy x-ray absorptiometry (DXA), bone density study, one or more sites, appendicular skeleton (peripheral) (e.g., radius, wrist, heel)

76977 Ultrasound bone density measurement and interpretation, peripheral site(s), any method

Modifiers

-26 Professional component
-TC Technical component
-GA Waiver on file
-59 Distinct procedural service

AARP

Prior authorization: Not required
Telephone: 1-800-523-5800
Web site: www.aarphealthcare.com
Criteria: N/A
Comment: Medicare "straight supplemental policy"

Admar

Prior authorization: May or may not be required, depending on the plan
Telephone: 1-800-422-0294, option #3 (member services)
Criteria: Vary according to plan

Comment: This is a managed care network- call insurance carrier listed on member ID card

Aetna

Prior authorization: Not required
Telephone: 1-888-342-3862
Criteria: N/A

Affordable Benefit Administration

Prior authorization: May or may not be required, depending on the plan
Telephone: 1-800-350-0148
Criteria: Vary according to plan
Comment: This is a 3rd party administrator

American Republic

Prior authorization: Not required
Telephone: 1-800-247-2190
Criteria: N/A
Comment: Medicare "straight supplemental policy"

Bankers Life

Prior authorization: May or may not be required, depending on the plan
Telephone: (505) 275-2131
Criteria: Variable
Comment: Medicare "straight supplemental policy"- no PA required if covered by Medicare

Beech Street

Prior authorization: Variable- call number on insurance card to determine requirement
Telephone: 1-800-227-7464
Criteria: Variable
Comment: This is a provider network

Blue Cross Blue Shield of New Mexico

Prior authorization: Not required if "medically necessary"
Telephone: 1-800-432-0750

Web site: www.bcbsnm.com
Criteria: N/A

CIGNA Healthcare PPO

Prior authorization: Depends on account
Telephone: 1-800-251-0670
Website: www.cigna.com
Criteria: Same as Medicare

Cimarron Health Plan (commercial product)

Prior authorization: Required except for state groups (state group accounts begin with ST)
Telephone: (505) 858-3461; Fax: (505) 856-2950
Web site: www.cimarronhealthplan.com
Criteria: See table and comment below
Comments: To qualify for DXA prior authorization, there must be a "Yes" answer to at least one category in this table-

Risk Factor	ICD-9 Code	Yes	No
Premature menopause (<45 years)	256.3		
Prolonged secondary amenorrhea	626.0		
Primary hypogonadism	256.0		
Corticosteroid therapy (> 7.5 mg/day x 1 yr. or more)	V58.69		
Anorexia nervosa	307.1		
Malabsorption	579.9		
Primary hyperparathyroidism	252.0		
Organ transplantation	V42		
Chronic renal failure	586		
Myelomatosis	203.0		
Hyperthyroidism	242.9		
Prolonged immobilization	718.59		
Radiologic evidence of osteopenia or vertebral deformity or both	733.90		
Previous fragility fracture of the hip, spine, or wrist	733.10		
Previously diagnosed osteoporosis follow-up	733.0		
Lupron therapy for men	V58.69		
Cushing's syndrome	255.0		

Coverage for Bone Densitometry

Cimarron HMO

Prior authorization: Required
Telephone: (505) 342-4680; Fax (505) 856-2950
Web site: www.cimarronhealthplan.com
Criteria: See Cimarron Health Plan

Cimarron Salud (Medicaid product)

Prior authorization: Required
Telephone: (505) 342-4681; Fax (505) 856-2950
Web site: www.cimarronhealthplan.com
Criteria: See Cimarron Health Plan

Government Employees Hospital Association (GEHA)

Prior authorization: Not required if "medically necessary"
Telephone: 1-800-821-6136
Web site: www.geha.com
Criteria: Only "approved codes" are covered. GEHA will not reveal what these codes are. The PCP must call GEHA to ask if a specific code is covered before a DXA is scheduled. In the past, these disorders have been covered, but that is not a guarantee that they will work in the future-

- Cushing's Syndrome
- Hyperparathyroidism
- Osteoporosis (established)
- Osteoporosis (suspected and confirmed on study)
- Osteomalacia
- Pathological Fracture (Fragility Fracture)
- Renal Osteodystrophy
- Unspecified Intestinal Malabsorption

Comment: This is a managed care "Catch-22" situation. Do the best you can.

Great West (POS)

Prior authorization: May or may not be required, depending on the plan
Telephone: 1-800-313-9010 (AZ) or 1-800-685-1030 (CA)
Web site: www.onehealthplan.com
Criteria: Based on "medical necessity"
Comment: Third party administrator

Coverage for Bone Densitometry

HMO New Mexico

Prior authorization: Not required if "medically necessary"
Telephone: 1-800-325-8334, Option 4
Web site: www.bcbsnm.com
Criteria: N/A

Lovelace / CIGNA Flexcare

Prior authorization: Not required
Telephone: (505) 262-3100
Web site: www.cigna.com
Criteria: N/A

Lovelace Salud (Medicaid product)

Prior authorization: Not required
Telephone: (505) 232-9888 for information
Web site: www.cigna.com
Criteria: N/A

Lovelace Senior Plan

Prior authorization: Not required
Telephone: (505) 262-3100
Web site: www.cigna.com
Criteria: N/A

Medicaid (Consultec)

Prior authorization: Not required
Telephone: (505) 246-9988
Criteria: Same as Medicare

Medicare

Prior authorization:
Not required if the patient is Medicare only
May be required by Medicare supplemental insurance, if applicable
Telephone: 1-877-567-9230
Web site: http://www.oknmmedicare.com/provider/provinfo.html
Comment: The Bone Mass Measurement Act of 1998 mandates coverage for 5 groups-

Coverage for Bone Densitometry

- Estrogen-deficient women at clinical risk for osteoporosis
  - *As determined by the healthcare provider*
- Individuals with vertebral abnormalities
  - *X-ray showing osteopenia or vertebral fracture*
- Individuals receiving long-term glucocorticoid therapy
  - *Equivalent of 7.5 mg prednisone, or greater, per day for more than 3 months, or beginning treatment expected to be longer than 3 months*
- Individuals with primary hyperparathyroidism
  - *As determined by healthcare provider*
- Individuals being monitored to assess the response to or efficacy of an FDA-approved osteoporosis drug therapy
  - *See frequency standard*

Some of the items have no corresponding ICD-9 code. Allowable codes vary according to the Medicare carrier. Listed below are codes for New Mexico.

Criteria (revised by the New Mexico Medicare carrier March 2000):

252.0 Primary hyperparathyroidism
255.0 Cushing's syndrome, including unspecified and iatrogenic
256.2 Postablative ovarian failure (iatrogenic, postirradiation, postsurgical)
256.3 Other ovarian failure (premature menopause, primary ovarian failure)
259.3 Ectopic hormone secretion, not elsewhere classified
627.2 Menopausal or female climacteric state (menopausal symptoms)
627.4 States associated with artificial menopause
627.9 Unspecified menopausal and postmenopausal disorder
731.0 Osteitis deformans without mention of bone tumor
733.00-733.09 Osteoporosis
733.00 Osteoporosis, unspecified (includes vertebral wedging)
733.01 Postmenopausal osteoporosis
733.02 Idiopathic osteoporosis
733.03 Disuse osteoporosis
733.09 Drug induced osteoporosis
733.13 Pathologic fracture of vertebrae
733.90 Disorder of bone and cartilage, unspecified
758.6 Gonadal dysgenesis
805.00-805.98 Fracture of vertebral column without mention of spinal cord injury
Fifth-digit subclassification for use with codes 805.0-805.1

0 cervical vertebra, unspecified level
1 first cervical vertebra
2 second cervical vertebra
3 third cervical vertebra
4 fourth cervical vertebra
5 fifth cervical vertebra
6 sixth cervical vertebra
7 seventh cervical vertebra
8 multiple cervical vertebrae

805.0 Cervical, closed
805.1 Cervical, open
805.2 Dorsal (thoracic), closed
805.3 Dorsal (thoracic), open
805.4 Lumbar, closed
805.5 Lumbar, open
805.6 Sacrum and coccyx, closed
805.7 Sacrum and coccyx, open
805.8 Unspecified, closed
805.9 Unspecified, open

806.00-806.09 Fracture of vertebral column with spinal cord injury, cervical, closed

806.00 C1-C4 level with unspecified spinal cord injury
806.01 C1-C4 level with complete lesion of cord
806.02 C1-C4 level with anterior cord syndrome
806.03 C1-C4 level with central cord syndrome
806.04 C1-C4 level with other specified spinal cord injury
806.05 C5-C7 level with unspecified spinal cord injury
806.06 C5-C7 level with complete lesion of cord
806.07 C5-C7 level with anterior cord syndrome
806.08 C5-C7 level with central cord syndrome
806.09 C5-C7 level with other specified spinal cord injury

806.10-806.19 Fracture of vertebral column with spinal cord injury, cervical, open

806.10 C1-C4 level with unspecified spinal cord injury
806.11 C1-C4 level with complete lesion of cord
806.12 C1-C4 level with anterior cord syndrome
806.13 C1-C4 level with central cord syndrome

806.14 C1-C4 level with other specified spinal cord injury
806.15 C5-C7 level with unspecified spinal cord injury
806.16 C5-C7 level with complete lesion of cord
806.17 C5-C7 level with anterior cord syndrome
806.18 C5-C7 level with central cord syndrome
806.19 C5-C7 level with other specified spinal cord injury
806.20-806.29 Fracture of vertebral column with spinal cord injury, dorsal (thoracic), closed
806.20 T1-T6 level with unspecified spinal cord injury
806.21 T1-T6 level with complete lesion of cord
806.22 T1-T6 level with anterior cord syndrome
806.23 T1-T6 level with central cord syndrome
806.24 T1-T6 level with other specified spinal cord injury
806.25 T7-T12 level with unspecified spinal cord injury
806.26 T7-T12 level with complete lesion of cord
806.27 T7-T12 level with anterior cord syndrome
806.28 T7-T12 level with central cord syndrome
806.29 T7-T12 level with other specified spinal cord injury
806.30-806.39 Fracture of vertebral column with spinal cord injury, dorsal (thoracic), open
806.30 T1-T6 level with unspecified spinal cord injury
806.31 T1-T6 level with complete lesion of cord
806.32 T1-T6 level with anterior cord syndrome
806.33 T1-T6 level with central cord syndrome
806.34 T1-T6 level with other specified spinal cord injury
806.35 T7-T12 level with unspecified spinal cord injury
806.36 T7-T12 level with complete lesion of cord
806.37 T7-T12 level with anterior cord syndrome
806.38 T7-T12 level with central cord syndrome
806.39 T7-T12 level with other specified spinal cord injury
806.4 Fracture of vertebral column with spinal cord injury, lumbar, closed
806.5 Fracture of vertebral column with spinal cord injury, lumbar, open
806.60-806.69 Fracture of vertebral column with spinal cord injury, sacrum and coccyx, closed
806.60 With unspecified spinal cord injury
806.61 With complete cauda equina lesion
806.62 With other cauda equina injury

806.69 With other spinal cord injury
806.70-806.79 Fracture of vertebral column with spinal cord injury, sacrum and coccyx, open
806.70 With unspecified spinal cord injury
806.71 With complete cauda equina lesion
806.72 With other cauda equina injury
806.79 With other spinal cord injury
806.8 Fracture of vertebral column with spinal cord injury, unspecified closed
806.9 Fracture of vertebral column with spinal cord injury, unspecified open

The words *in italics and underlined* below are not part of the ICD-9 description.

E932.0 Drugs, medicinal and biological substances causing adverse effects in therapeutic use, adrenal cortical steroids (cortisone derivatives, desoxycortisone derivatives, fluorinated corticosteroids). *To be used with ICD-9-CM 733.09 for reporting an individual receiving (or expecting to receive) glucocorticoid therapy equivalent to 7.5 mg of prednisone, or greater, for 3 months. Medicare does not recognize this diagnosis as a covered diagnosis. You will need to use another diagnosis for coverage.*

V58.69 Long-term (current) use of other medications (high risk medications). *To be used for reporting individuals on long term chronic corticosteroids (E932.0 should be added as a second diagnosis.)*

V67.51 Following completed treatment with high-risk medication, NEC. *To be used for reporting an individual who has completed drug therapy for osteoporosis and is being monitored for response to therapy.*

V67.59 Following other treatment, other. *To be used for reporting an individual who is receiving ongoing drug therapy for osteoporosis and is being monitored for effectiveness.*

Frequency Standard: Once every 2 years, if at least 23 months have passed since the last bone mass measurement was performed. However, if medically necessary, Medicare may cover a bone mass measurement more frequently than every 2 years. Examples of such situations include, but are not limited to, the following situations:

- Monitoring long-term glucocorticoid therapy of more than 3 months
- Allowing for a confirmatory baseline bone mass measurement (either central or peripheral) to permit monitoring in the future if the initial test was performed with a technique that is different from the proposed monitoring method (for example, if the initial test was performed using bone sonometry and monitoring is anticipated using bone densitometry, Medicare will allow coverage of baseline measurement using bone densitometry).
- One year after the initiation of an FDA approved therapy for osteoporosis.
- Allowing for evaluation of therapy 12 months after therapy with an FDA approved medication has been changed, or
- 12 months after a bone mass measurement did not show response to therapy with an FDA approved medication.

Medicare / Medicaid (Consultec)

Prior authorization: Not required
Telephone: 1-877-567-9230 for Medicare, (505) 246-9988 for Medicaid
Criteria: See Medicare listing

Mutual of Omaha

Prior authorization: Not required if "medically necessary"
Telephone: 1-800-775-1000
Web site: www.mutualofomaha.com
Criteria: N/A

National Association of Letter Carriers (NALC)

Prior authorization: Not required if "medically necessary"
Telephone: 1-800-433-6252
Web site: www.nalc.org/depart/hbp
Criteria: N/A

Physicians Mutual

Prior authorization: Not required for most policies
Telephone: 1-800-228-9100 or 1-402-633-1111
Criteria: N/A
Comment: Medicare "straight supplemental policy"

Coverage for Bone Densitometry

Presbyterian Health Plan

Prior authorization: Not required as long as PCP and provider are contracted with Presbyterian
Telephone: (505) 923-5757
Web site: www.phs.org
Criteria: N/A
Comment: Screening peripheral BMD measurements are not covered

Presbyterian Salud

Prior authorization: Not required as long as PCP and provider are contracted with Presbyterian
Telephone: (505) 923-5757
Web site: www.phs.org
Criteria: N/A
Comment: Screening peripheral BMD measurements are not covered

Presbyterian Senior Care

Prior authorization: Not required as long as PCP and provider are contracted with Presbyterian
Telephone: (505) 923-5700
Web site: www.phs.org
Criteria: N/A
Comment: Screening peripheral BMD measurements are not covered

St. Joseph Medicare Plus

Prior authorization: Not required
Telephone: (505) 727-4595
Criteria: N/A

Standard Life

Prior authorization: Not required
Telephone: 1-888-350-1488
Criteria: N/A
Comment: Medicare "straight supplemental policy." Will cover whatever Medicare covers.

Tri-Care / Tri-West

Prior authorization: Not required except for "Prime Program"

Telephone: 1-888-908-9378

Web sites: www.mytricare.com, www.triwest.com

Criteria: See table and comments below.

Comment: Screening bone density studies not covered. The following guidelines are provided to determine who qualifies for a DXA study. All patients must qualify with a "Yes" answer to at least one of these questions. For "Prime Program" patients, this information should be submitted to Tri-Care / Tri-West, along with "any supporting clinical notes, X-ray report, lab, or other pertinent supporting data," for prior authorization before the DXA is scheduled. For other patients, this information should be documented in the medical record of the referring healthcare provider and provided to the DXA facility when the appointment is scheduled.

Tri-Care / Tri-West DXA Criteria	Yes	No
Is patient over age 50?		
Does patient have X-ray documented osteoprosis?		
Previous fargility fracture of hip, spine, wrist?		
Is this a request for follow-up on a therapy program?		
Chronic renal failure?		
PRemature menopause (before age 45)?		
History of steroid use of 7.5 mg prednisone (or equivalent) per day for over 12 mo?		
Hyperthyroidism or thyroid replacement for over 5 years?		
Primary hypogonadism?		
Anorexia nervosa?		
Malabsorption?		
Primary hyperparathyroidism:		
Organ transplantation?		
Prolonged immobilization?		
Male hypogonadism?		

United American

Prior authorization: Not required

Telephone: 1-972-529-5085 or 1-214-328-2841

Web page: www.medicalUA.com

Criteria: N/A

Comment: Medicare "straight supplemental policy"

Coverage for Bone Densitometry

United Healthcare

Prior authorization: Depends on plan.
Telephone: 1-800-552-3232, Option 6.
Web site: www.unitedhealthcareonline.com or www.myuhc.com
Criteria: Not disclosed.

USAA

Prior authorization: Not required
Telephone: 1-800-531-9017
Criteria: N/A
Comment: Medicare "straight supplemental policy"

DENIAL OF COVERAGE

The International Society for Clinical Densitometry (ISCD) is keeping a database of cases where patients are denied bone density tests by Medicare or private insurers.

If you have such cases, please fax the appropriate information to:

ISCD Executive Director
Fax 202-367-2132

About the Author

E. MICHAEL LEWIECKI, MD, FACP, is a board-certified internist in Albuquerque, New Mexico. He is Osteoporosis Director of New Mexico Clinical Research & Osteoporosis Center, Clinical Assistant Professor of Medicine at University of New Mexico School of Medicine, and President-Elect of the International Society for Clinical Densitometry (ISCD). His responsibilities include the daily supervision and interpretation of bone density and body composition tests, consultation for osteoporosis patients, and education of healthcare providers and the public on osteoporosis issues. He is principal investigator for the center's osteoporosis clinical trials.

Dr. Lewiecki is founder and president of the Osteoporosis Foundation of New Mexico. He was one of the founders of the New Mexico Osteoporosis Society, and continues to direct its educational programs. He advises healthcare systems on developing osteoporosis policies, and works with legislators on bone densitometry legislation. He established and supervises the educational activities of the National Osteoporosis Foundation Albuquerque Support Group. He founded New Mexico's annual Osteoporosis Awareness Walk, which has evolved into the "Stroll & Roll for Osteoporosis and Arthritis". He established and is program director of the annual Santa Fe Bone Symposium. He is actively involved in clinical research of new medications and procedures for the prevention and treatment of osteoporosis. He has a special interest in bone densitometry and new minimally invasive treatments for vertebral fractures.

Dr. Lewiecki is certified by the ISCD and sits on its Board of Trustees. He is chairman of the ISCD Interspecialty Council. As an ISCD faculty member, Dr. Lewiecki frequently lectures on bone densitometry. He is a member of the American Society for Bone and Mineral Research, the International Bone and Mineral Society, the National Osteoporosis Foundation, and the American Association of Clinical Endocrinologists.

He was awarded "Young Internist of the Year" by the American Society of Internal Medicine in 1986, and "Physician of the Year" by the ISCD in 2002. He is a fellow of the American College of Physicians, and former president of the New Mexico Society of Internal Medicine.

About the Author

Dr. Lewiecki, who was raised in the Boston area, graduated with honors from Amherst College and received his medical degree from Northwestern University Medical School. His internal medicine training was at University of New Mexico Health Sciences Center. He then served two years as a medical officer in the United States Air Force. In 1977, he began practicing medicine in Albuquerque, where he has remained ever since.

Dr. Lewiecki has been writing and rewriting *Mike's Manual* since 1997.

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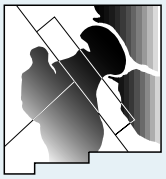

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