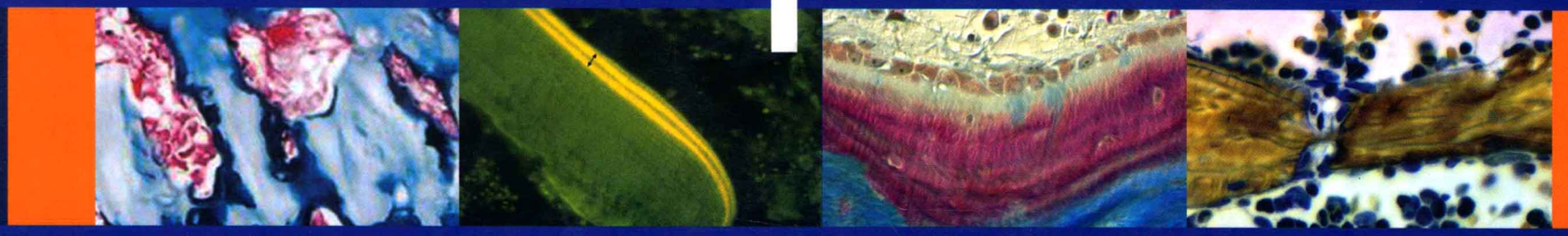
Eric S. Orwoll
Editor

Atlas of Osteoporosis



Third Edition

Springer

CD
INCLUDED

Atlas of Osteoporosis

Third Edition

Editor

Eric S. Orwoll, MD

Professor of Medicine
Department of Medicine
Director, Oregon Clinical and Translational Research Institute
Oregon Health and Sciences University
Portland, Oregon

Springer

CURRENT MEDICINE GROUP LLC, PART OF
SPRINGER SCIENCE+BUSINESS MEDIA LLC
400 Market Street, Suite 700 • Philadelphia, PA 19106

Senior Developmental Editor ..... Diana Winters
Developmental Editor ..... Stephanie Weidel Brown
Editorial Assistant ..... Juleen Deaner
Managing Editor ..... Megan Charlton
Design and Layout ..... Heather Hoch
Illustrators ..... Daniel Britt, Kim Broadbent, Marie Dean, Heather Hoch, Sara Krause, Wieslawa Langenfeld, Jacqueline Leonard, Maureen Looney
Production Coordinator ..... Carolyn Naylor
Indexer ..... Holly Lukens

Library of Congress Cataloging-in-Publication Data

Atlas of osteoporosis / editor, Eric S. Orwoll ; with 22 contributors. -- 3rd ed.
p. ; cm.
Includes bibliographical references and index.
ISBN 978-1-57340-296-5 (alk. paper)
1. Osteoporosis--Atlases. I. Orwoll, Eric S. II. Title.
[DNLM: 1. Osteoporosis--Atlases. WE 17 A8806331 2008]

RC931.O73.A856 2008
616.7'16--dc22

2008032873

ISBN 978-1-57340-296-5
ISBN 1-57340-296-6

www.springer.com

For more information, please call 1 (800) 777-4643
or email us at orders-ny@springer.com

www.currentmedicinegroup.com

10 9 8 7 6 5 4 3 2 1

Printed in China by L. Rex Printing Company Limited

This book was printed on acid-free paper

Preface

Osteoporosis has long been known to be a major health care problem, in both individual and public health terms, but in the last two decades tremendous increases in scientific inquiry have yielded a much greater understanding of the basic biology, clinical character, and epidemiology of the condition. These advances have been translated into much more sophisticated and effective tools for clinicians to use in the prevention and treatment of the disease. These tools, initially available only to specialists in endocrinology and rheumatology, are now available to a wide range of clinicians. Appropriately, the public is also becoming more educated and it is not uncommon for clinicians to have sophisticated discussions with well-read patients about the diagnosis, prevention, and treatment of osteoporosis.

The Third Edition of the *Atlas of Osteoporosis* builds on the foundation of previous editions and once again is designed to be useful to a broad readership. In a format that makes extensive use of graphical displays of important data, the authors have encapsulated not only the well-established basics of osteoporosis but also new developments in the field.

Exciting new chapters have been added, including the histology of bone remodeling and metabolic bone disorders. A chapter on emerging therapies reflects the considerable promise of new treatment approaches. The important problem of renal bone disease is now addressed in a chapter dedicated to that issue. Moreover, topics that are well known to be important to skeletal biology and osteoporosis have been updated, and the chapters that were new in the Second Edition (*eg*, genetics and biomechanics) have been expanded. Other chapters have been extensively revised to capture recent developments. For instance, the range of bisphosphonates drugs available for prevention and therapy has grown and parathyroid hormone treatment for osteoporosis, which was new at the time of the Second Edition, is now better understood. More information about both is provided.

Although osteoporosis has been recognized for millennia, knowledge regarding this disorder continues to evolve. The sheer volume of available information, as well as its complexity, poses considerable challenges to those attempting to summarize it. To whatever extent the *Atlas* has succeeded in this endeavor, it is a tribute to the many outstanding contributors who devoted time and considerable expertise to the effort.

Eric S. Orwoll, MD

Contributors

Diana Antoniucci, MD
Assistant Clinical Professor of Medicine
Department of Medicine
University of California
San Francisco, California

Laura K. Bachrach, MD
Professor of Pediatrics
Department of Pediatrics
Division of Endocrinology
Stanford University School of Medicine
Stanford, California

Neil Binkley, MD
Associate Professor
Department of Medicine
Section of Geriatrics and Endocrinology
University of Wisconsin
Madison, Wisconsin

Jane A. Cauley, DrPH
Department of Epidemiology
Graduate School of Public Health
University of Pittsburgh
Pittsburgh, Pennsylvania

Cyrus Cooper, MD, FRCP, FMedSci
MRC Epidemiology Resource Centre
University of Southampton
Southampton, United Kingdom
Botnar Research Center
University of Oxford
Oxford, United Kingdom

Jeffrey Curtis, MD, MPH
Assistant Professor of Medicine
Division of Clinical Immunology and Rheumatology
University of Alabama at Birmingham
Director
UAB Arthritis Clinical Intervention Program
Associate Director
UAB Center for Education and Research on the Therapeutics of Musculoskeletal Disorders (CERTs)
Associate Scientist
UAB Center for Metabolic Bone Disease
Birmingham, Alabama

Richard Eastell, MD, FRCP, FRCPath, FMedSci
Professor of Bone Metabolism
Head of Academic Unit of Bone Metabolism
School of Medicine and Biomedical Sciences
University of Sheffield
Metabolic Bone Center
Northern General Hospital
Sheffield, United Kingdom

Sol Epstein, MD
Mount Sinai School of Medicine
New York, New York

Dina E. Green, MD
Assistant Professor of Medicine
Division of Endocrinology, Diabetes, and Bone Disease
Mount Sinai School of Medicine
New York, New York

Karl J. Jepsen, PhD
Associate Professor
Leni and Peter W. May Department of Orthopaedics
Mount Sinai School of Medicine
New York, New York

David Kendler, MD, FRCPC
Associate Professor
Department of Medicine (Endocrinology)
University of British Columbia
Vancouver, British Columbia, Canada

Robert F. Klein, MD
Professor of Medicine
Division of Endocrinology, Diabetes, and Clinical Nutrition
Oregon Health and Science University
Chief
Endocrinology and Metabolism Section
Department of Hospital and Specialty Medicine
Portland VA Medical Center
Portland, Oregon

Philipp K. Lang, MD, MBA
Director, Musculoskeletal Radiology
Department of Radiology
Brigham and Women's Hospital
Harvard Medical School
Boston, Massachusetts

Michael R. McClung, MD, FACP
Assistant Director
Medical Education
Providence Portland Medical Center
Founding Director
Oregon Osteoporosis Center
Portland, Oregon

Paul D. Miller, MD
Distinguished Clinical Professor of Medicine
University of Colorado Health Sciences Center
Medical Director
Colorado Center for Bone Research
Lakewood, Colorado

Eric S. Orwoll, MD
Professor of Medicine
Department of Medicine
Director, Oregon Clinical Translational Research Institute
Oregon Health and Sciences Center
Portland, Oregon

Susan M. Ott, MD
Associate Professor
Department of Medicine
University of Washington
Seattle, Washington

Deborah E. Sellmeyer, MD
Associate Professor of Medicine
Division of Endocrinology
Department of Medicine
The Johns Hopkins Bayview Medical Center
Baltimore, Maryland

Elsa S. Strotmeyer, PhD, MPH
Assistant Professor
Department of Epidemiology
University of Pittsburgh
Pittsburgh, Pennsylvania

Jan E. Vandevenne, MD
Department of Radiology
Ziekenhuizen Oost-Limburg
Genk, Belgium

Chaim Vanek, MD
Department of Endocrinology, Diabetes, and Clinical Nutrition
Bone and Mineral Unit
Oregon Health and Science University
Portland, Oregon

Tjeerd-Pieter van Staa, MD
Head of Research
General Practice Research Database
London, United Kingdom
Associate Professor
Department of Pharmacoepidemiology
Utrecht Institute for Pharmaceutical Sciences
Utrecht University
Utrecht, The Netherlands

Connie M. Weaver, PhD
Department Head Foods and Nutrition
Purdue University
West Lafayette, Indiana

Robert S. Weinstein, MD
Professor of Medicine
Bone Morphometry Laboratory
Division of Endocrinology and Metabolism
Center for Osteoporosis and Metabolic Bone Diseases
Department of Internal Medicine
Central Arkansas Veterans Health Care System
University of Arkansas for Medical Sciences
Little Rock, Arkansas

Carl S. Winalski, MD
Head, Musculoskeletal MRI
Department of Radiology
Brigham and Women's Hospital
Harvard Medical School
Boston, Massachusetts

Contents

1

The Nature of Osteoporosis

Eric S. Orwoll and Chaim Vanek

The recent emergence of osteoporosis as a major focus of investigation in fields as diverse as mechanical engineering, pediatrics, and epidemiology has led to many important advances in the understanding of and therapeutics for this disease. Whereas the topic of osteoporosis formerly occupied just a few paragraphs in standard texts, it is now the primary focus of several journals and textbooks. This volume provides current information regarding skeletal health and its disruption. Attention is given to bone acquisition during growth years, mechanisms of adult bone loss, and new developments in osteoporosis diagnostics and therapeutics. In the final analysis, osteoporosis is a condition of bone, a complex tissue that undergoes physiologic repair throughout life. This chapter introduces the reader to the "nature" of osteoporosis, the physical characteristics of healthy and fragile bone. The study of bone transcends a measurement of its amount or mineral density to encompass aspects of its geometry and material properties. Bone remodeling is a continuous renewal process. Alterations in remodeling are the basis for the changes in the amount, geometry, and quality of bone during adult life.

Osteoporotic Bone

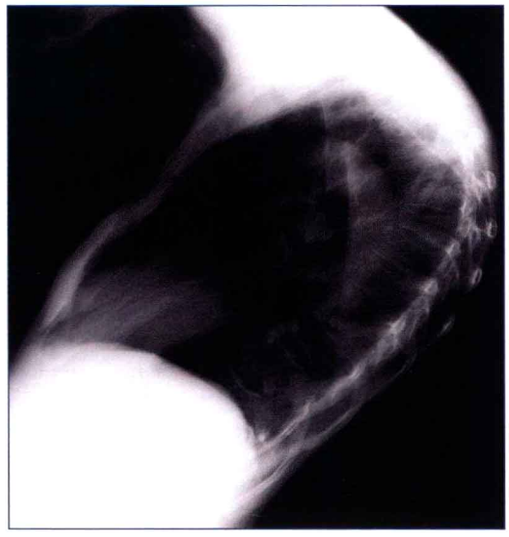


Figure 1-1. Lateral chest radiograph showing a classic spine deformity called kyphosis. Kyphosis is the end result of multiple vertebral compression fractures. *Osteoporosis* is defined as a skeletal condition of decreased bone quantity accompanied by abnormalities in the microscopic architecture of bone that renders a person more likely to sustain a fracture with little or no trauma. Osteoporosis frequently is considered in the context of specific fracture syndromes, including vertebral compression, Colles' (distal radial) fracture, and hip fracture. However, osteoporosis truly is a disease of global skeletal fragility, with increased risk of low-trauma fractures in all portions of the skeleton. (*Courtesy of* R. Marcus, MD.)

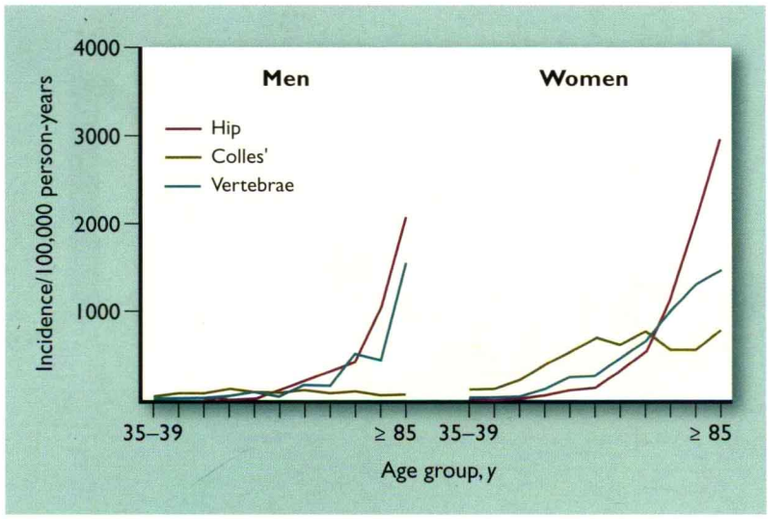


Figure 1-2. Incidence of osteoporotic fractures. The clinical consequences of bone fragility are fractures. Shown here are curves representing age-related incidences of vertebral, forearm, and hip fractures in North American men and women. The incidence of all fractures is about twice as great in women as it is in men, but osteoporosis is not exclusively a disease of women. The incidence of hip fracture increases rapidly in men older than 70 years of age. One-third of vertebral fractures result in pain sufficient to cause the patient to seek medical attention; however, many occur without obvious symptoms, becoming apparent only as there is a loss of height or development of curvature. Wrist fractures typically occur at a younger age than hip fractures. This may be explained by differences in the mechanism of the fall. Wrist fractures most commonly result when a person standing upright falls forward and attempts to break the fall by arm extension and pronation as happens in a younger subject. Older subjects commonly suffer hip fractures when they fall backwards and directly impact the femoral trochanter. Thus, the occurrence of fractures is a function not only of osteoporosis and intrinsic bone quality but also of the type and mechanism of the fall itself. (*Adapted from* Cooper and Melton [1].)

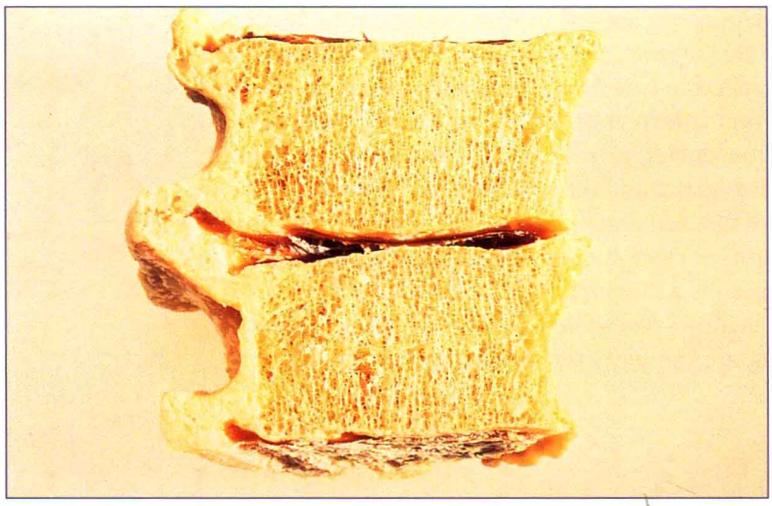


Figure 1-3. Normal vertebral bodies. Vertebral bodies are composed of a thin external cortical shell and a central honeycomb of vertical and horizontal bars, or trabeculae. Both the cortical shell and the central trabeculae contribute to the strength of the vertebrae and, thus, to its resistance to fracture. In adults, trabecular interstices of the axial (central) skeleton constitute the primary repository of red bone marrow. The trabecular surface is in proximity to the marrow cellular constituents responsible for bone turnover. Events leading to the loss of bone occur at these surfaces. Changes in bone mass occur earlier and to a greater extent in trabecular bone than they do in regions of the skeleton not adjacent to the marrow environment, such as cortical bone. (*Courtesy of* R. Marcus, MD.)

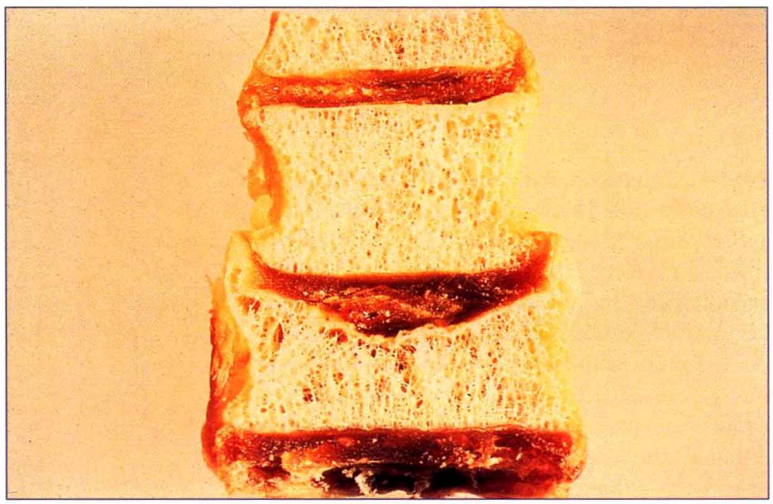


Figure 1-4. Osteoporotic vertebral bodies. Weakness of the trabecular structure results in mechanical failure, with collapse of the intervertebral disk into the underlying bony substance. This weakness reflects a decrease in the total amount of bone within the vertebral body and also a disruption of the normal trabecular microarchitecture, as is evident by the appearance of cavities where bone has been lost. A formal definition of the term *osteoporosis* is a skeletal condition characterized by low bone mass and abnormal microarchitecture, leading to increased risk of fracture with minimal trauma. (*Courtesy of* R. Marcus, MD.)

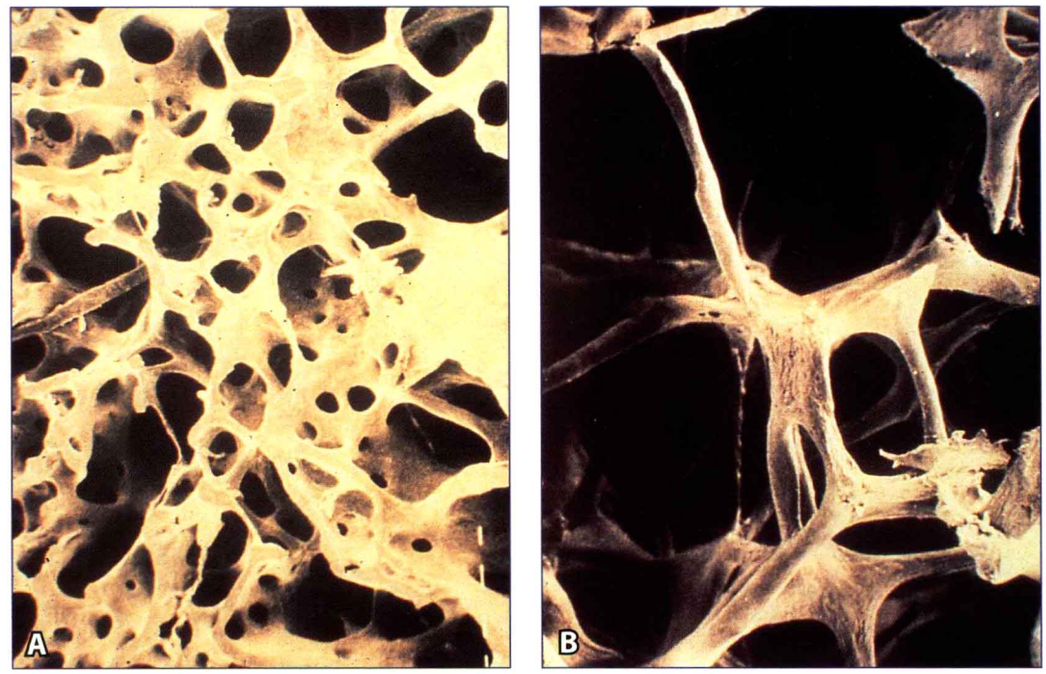
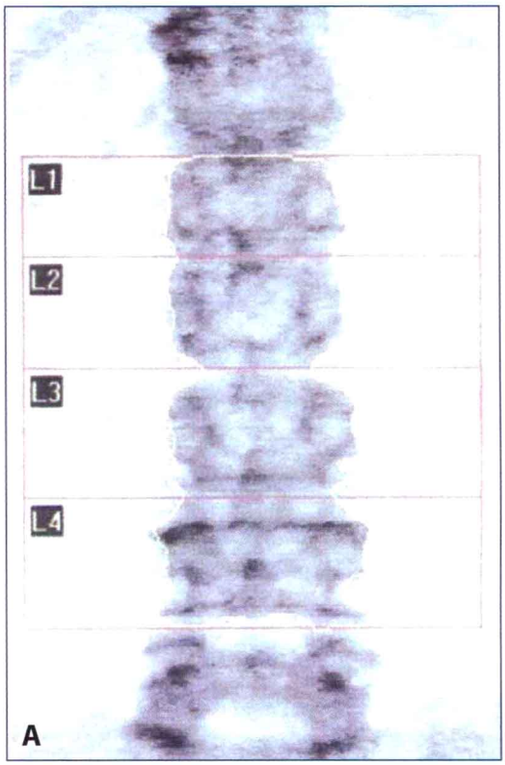


Figure 1-5. Scanning electron micrograph of normal (**A**) and osteoporotic (**B**) trabecular structures. In osteoporosis, the normal plate-like trabeculae have been replaced by thin rods. The microarchitecture and quality of the vertebral structure have been irreparably damaged by trabecular perforation resulting in loss of trabecular connectivity and continuity. (*Courtesy of* J. Kosek.)

Bone Mass Measurement



DXA Results Summary

Region	Area, cm^2	BMC, g	BMD, g/cm^2	T-score	Z-score
L1	11.01	8.27	0.751	−1.6	0.5
L2	12.25	8.97	0.733	−2.7	−0.3
L3	14.52	9.98	0.688	−3.6	−1.1
L4	16.47	12.64	0.768	−3.2	−0.6
Total	54.25	39.87	0.735	−2.8	−0.5

Total BMD CV 1.0%

B

Figure 1-6. Dual-energy x-ray absorptiometry (DXA). **A**, Printout from a lumbar spine bone density examination. Although low bone mass and architectural disruption are essential components of the diagnosis of osteoporosis, current applicable diagnostic tools provide measurements of bone mass (the amount of bone) only and do not address other aspects of bone quality that contribute to fragility, such as geometry, material properties, and microarchitecture. DXA is a technique that exploits the ability of bone mineral to attenuate the passage of x-rays through the body to provide estimates of the bone mineral density (BMD). **B**, Machine software estimates the area and mineral content of bones in the region scanned. A calculated areal BMD (measured in g/cm^2) is generated for the scanned region. For clinical purposes, the scanned regions generally include the lumbar spine, proximal femur, forearm, and whole body. For research purposes, any skeletal region can be assessed. BMC—bone mineral content.

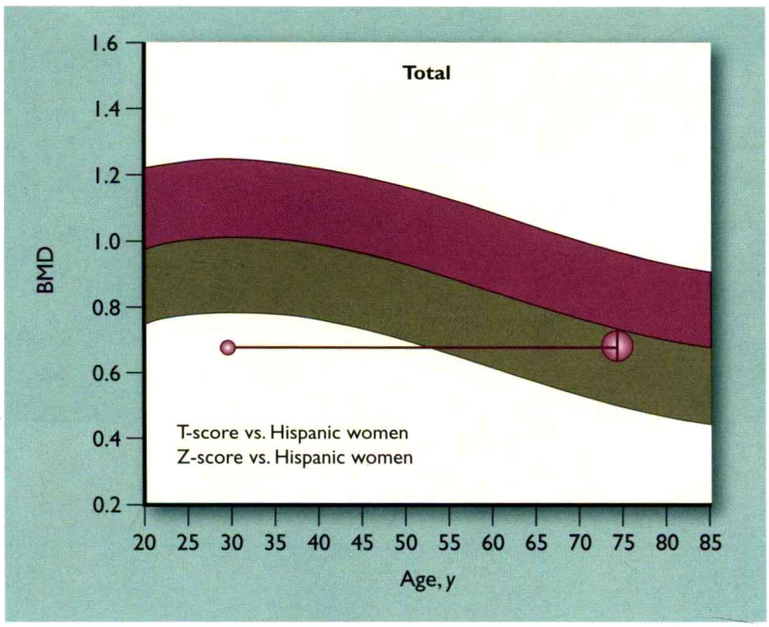


Figure 1-7. Bone mineral density (BMD) by dual-energy x-ray absorptiometry (DXA). Patient value (*cross*) is superimposed on a graph representing the mean ± 2 SD per age intervals for a healthy population. Absolute BMD results (g/cm^2) are commonly expressed in terms of units of SD from population averages. When comparing a patient with his or her age-matched population, these SD units are expressed as Z-scores. When a patient is compared with the average of a young population, SD units are expressed as T-scores. In this case, the patient's value is within 2 SD of the expected value for a 74-year-old person (Z-score = −0.5) and more than 2.5 SD below the peak bone density of a person 30 years of age (T-score = −2.8). Reference data for the young adult population are currently sex specific and are race specific for some densitometers. However, in the future, reference data from young white women may be used for all populations.

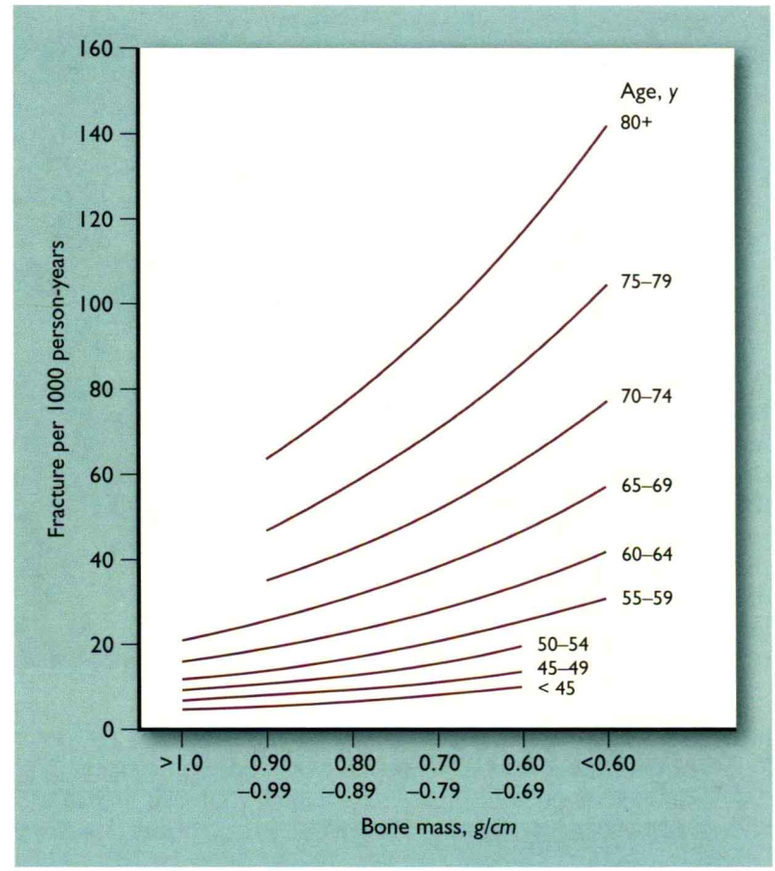


Figure 1-8. Interaction of age and bone mineral density (BMD) on fracture incidence. A large cohort of women was followed over time. Fracture incidence is shown on the vertical axis and the women are stratified by bone density along the horizontal axis. In addition, women are stratified by age, represented by a family of curves. At any given BMD, fracture incidence is higher with increasing age. In fact, the slope of the relationship to fracture is steeper for age than it is for BMD, which would not be expected if BMD itself were the sole determinant of fracture risk. For the oldest women, the incidence of falls is greater and contributes to the added fracture risk. However, falls and BMD do not entirely account for the added fractures that occur at older ages. These fractures may be the result of so-called qualitative or material properties of bone that affect fragility but are not accounted for by BMD measurement or other currently available imaging modalities. (*Adapted from* Hui *et al.* [2].)

Factors That Contribute to Bone Quality

- Altered mineral or matrix composition
- Cement lines
- Cortical porosity
- Fatigue accumulation
- Trabecular disruption

Figure 1-9. Factors that contribute to bone quality. This figure lists some of the qualitative properties of bone that could contribute to poor bone strength and increased fragility but are not well assessed by bone density measurements.

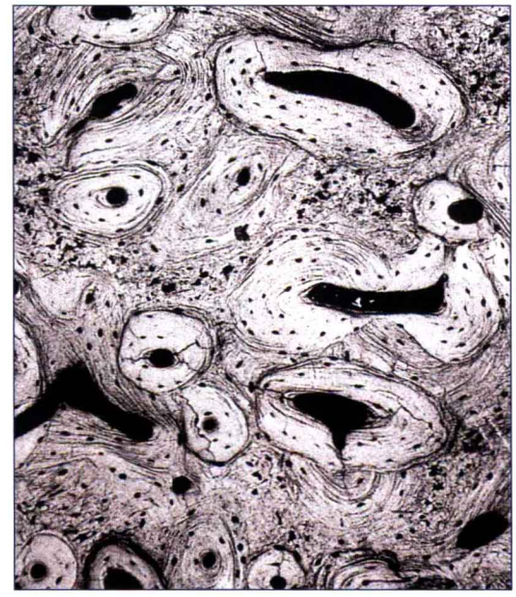
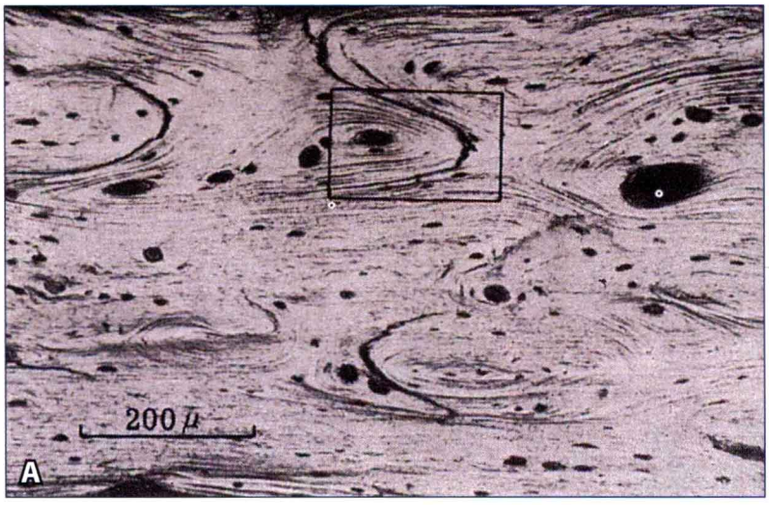


Figure 1-10. Micrograph of a biopsy specimen of the iliac crest showing qualitative abnormalities in bone. Cortical porosity is seen in this specimen from an 80-year-old man. Porosity is evident as large Haversian canals (*dark areas*) that result from excess resorption. Also note the high prevalence of Haversian systems, indicating active remodeling events [3].



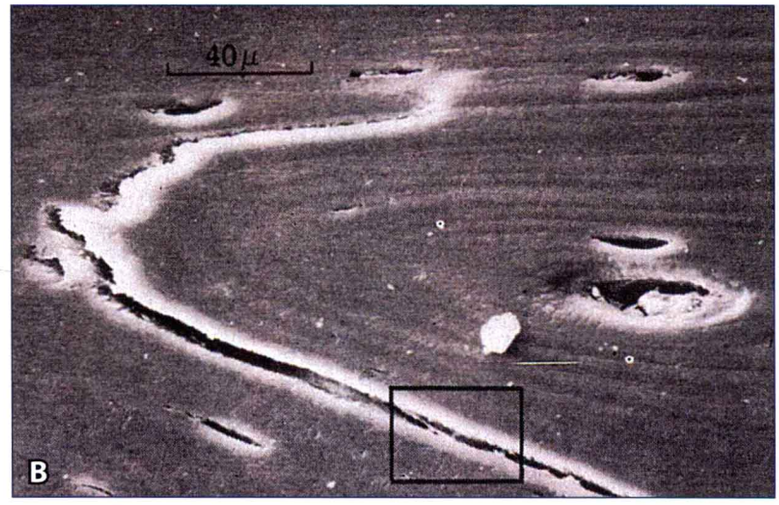


Figure 1-11. Micrograph of qualitative abnormalities in bone showing cement lines [4]. **A**, Cement lines are the residue of a previous bone resorption event. Composed of a filigree of woven, rather than dense, lamellar collagen, cement lines represent an area susceptible to structural failure. The *box* shows a Haversian system bounded by a curved cement line. **B**, Dehiscence of a cement line after application of a bending force to the whole bone. Bone breakage occurs as a propagation of fracture lines from one cement line to the next [5]. The *box* shows separation at the cement line between Haversian systems.

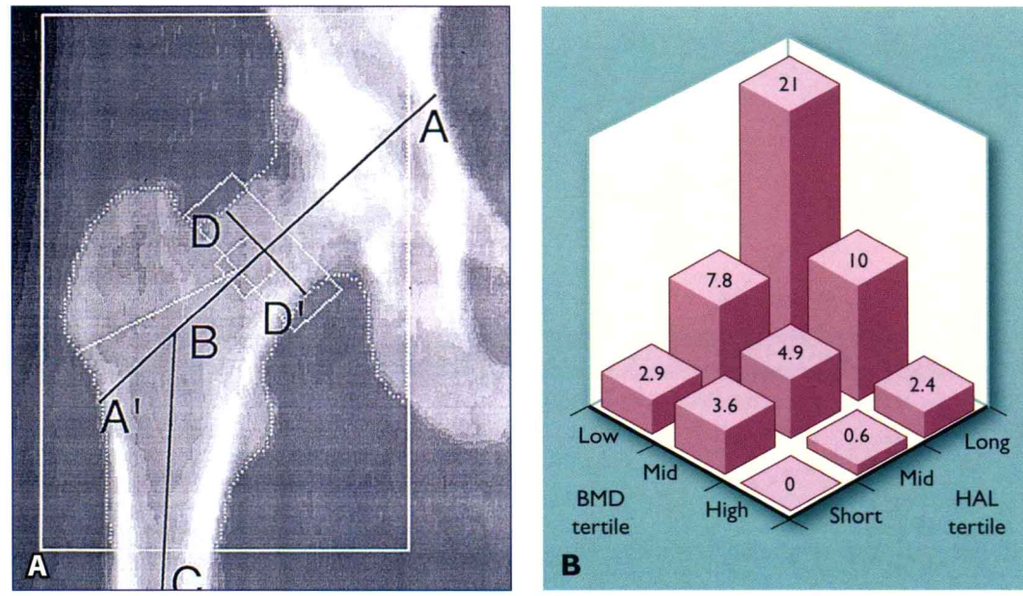


Figure 1-12. Geometric contributions to bone strength and fracture risk. Despite an undisputed relationship between bone mineral density (BMD) and fracture incidence, factors independent of BMD make important contributions to fractures. Of particular importance are bone geometry and the occurrence of falls. To illustrate the role of macroscopic bone geometry, this figure shows the important effect a measurement called the hip axial length (HAL) has on hip fracture risk. **A**, HAL is the length of a straight line connecting the inferior surface of the greater trochanter to the inner surface of the hip acetabulum (*line A-A′*). *Line D-D′* is the width of the femoral neck. **B**, Results of a large prospective observational study of elderly women showing that the incidence of hip fracture is dependent on HAL. At any level of BMD, women with longer HAL had significantly greater risk of hip fracture. Indeed, women with BMD in the lowest tertile who also had HAL in the longest tertile had a 21-fold increased relative risk of hip fracture. (**B** *adapted from* Faulkner *et al.* [6].)

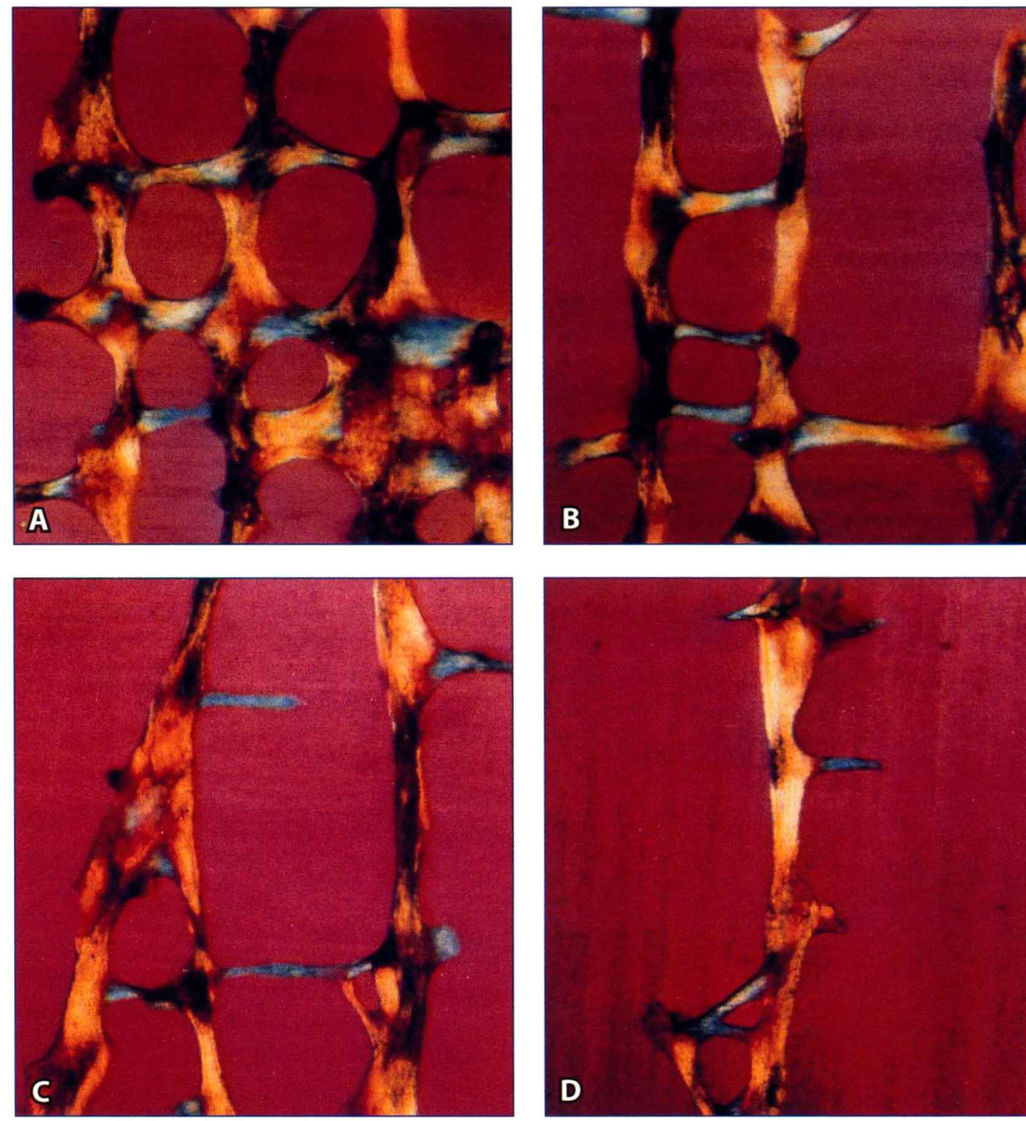


Figure 1-13. Geometric contributions to bone strength and fracture risk. During the development of osteoporosis, the loss of horizontal connections between the trabeculae is more prominent than the loss of vertical elements; this loss is a major factor in the loss of resistance to compressive forces. The microscopic architecture is shown in a 50-year-old man (**A**), a 58-year-old man (**B**), a 76-year-old man (**C**), and an 80-year-old woman (**D**) [7].

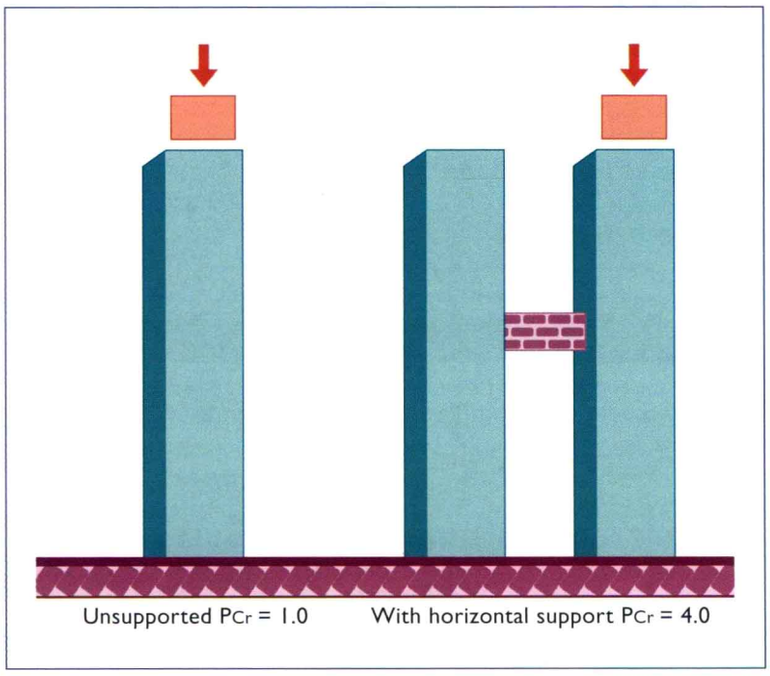


Figure 1-14. Geometric contributions to bone strength and fracture risk showing the consequences of horizontal trabecular loss. A single horizontal connecting strut increases by fourfold the maximum load (Pcr) that can be carried by a vertical bar without buckling. Thus, loss of horizontal trabeculae with age has a profound independent effect on vertebral trabecular strength. (*Adapted from* Snow-Harter and Marcus [8].)

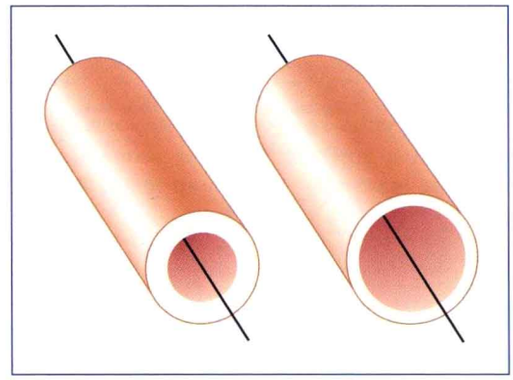


Figure 1-15. Geometric contributions to bone strength and fracture risk showing the effect of cortical mass distribution on strength in a long bone. Assume that the two cylinders have equal mass. The one on the right has a greater distribution of mass farther from the axis of bending compared with the left; this is called the cross-sectional moment of inertia (CSMI). Despite the thinner walls of this structure, the distribution results in a substantially increased resistance to bending along the length of the cylinder. The long bones of men generally are larger and thus have larger CSMI compared with those of women. The increased CSMI confers on them relative greater protection against fracture at any given value of bone mineral density. (*Adapted from* Snow-Harter and Marcus [8].)

Role of Remodeling in Lifelong Acquisition and Loss of Bone

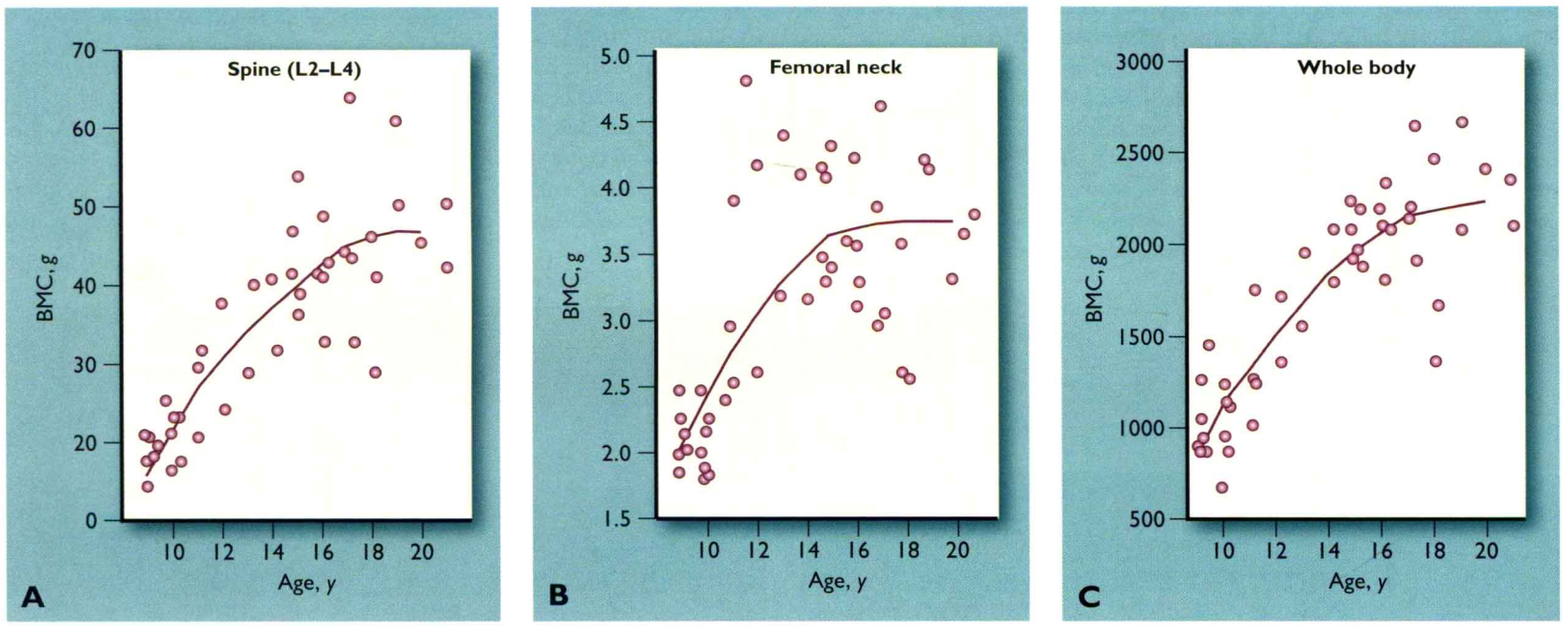


Figure 1-16. **A–C**, Acquisition of bone during adolescence. At any time during adult life, bone mass reflects bone that has been gained during years of growth minus bone that subsequently has been lost. Previous theories about osteoporosis have not adequately considered the role of bone acquisition in determining lifelong fracture risk. This study of healthy white girls aged 9 to 21 years shows that about 60% of final adult "peak" bone mass is acquired during the adolescent growth spurt. Only about 5% of peak bone mass is acquired after 18 years of age. Thus, adolescence constitutes a window of opportunity when genetic, dietary, hormonal, and other factors determine the magnitude of bone gain. About 80% of peak bone mass is genetically determined. Important environmental factors include dietary calcium intake, reproductive endocrine status, and habitual physical activity. However, adolescence is also a window of vulnerability when inadequate attention to these same factors can lead to low bone mass at skeletal maturity. Persons who have not gained adequate bone mass would not need to lose very much bone in adulthood to have a substantially increased risk of osteoporosis and fracture. Of particular concern are dietary calcium intake (which is generally low in American teenaged girls), a relatively sedentary lifestyle, and the high prevalence of anorexia nervosa and other eating disorders. BMC—bone mineral content. (*Adapted from* Katzman *et al.* [9].)

Acquisitional Osteopenia

- Delayed puberty
- Immobilization or therapeutic rest
- Specific disorders
  - Anorexia nervosa
  - Cystic fibrosis
  - Intestinal or renal disease
  - Marfan syndrome
  - Osteogenesis imperfecta

Figure 1-17. Acquisitional osteopenia. This list includes some childhood conditions that are known to interfere with the acquisition of peak bone mass. Low peak bone mass may result in an increased risk for fractures later in life.

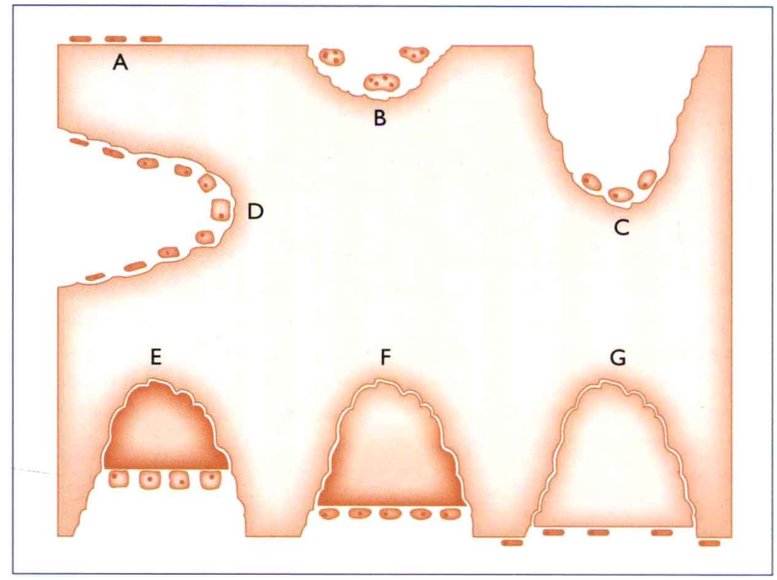


Figure 1-18. Bone remodeling. Once new bone is laid down, it is subject to a continuous process of breakdown and renewal called remodeling that continues throughout life. After linear growth stops and peak bone mass has been reached, remodeling constitutes the final common pathway by which bone mass is adjusted throughout adult life. Remodeling is carried out by thousands of individual and independent "bone remodeling units" on the surfaces of bone throughout the skeleton.

A, About 90% of bone surface is normally inactive, covered by a thin layer of lining cells. **B**, In response to physical or biochemical signals, recruitment of marrow precursor cells to a site at the bone surface results in their fusion into the characteristic multinucleated osteoclasts that resorb, or dig a cavity into, the bone. In cortical bone, resorption creates tunnels with haversian canals, whereas trabecular resorption creates scalloped areas of the bone surface called Howship lacunas. **C**, On termination of the resorption phase, a 60-μm cavity remains and is bordered at its deepest extent by a cement line, a region of loosely organized collagen fibrils. **D**, Completion of resorption is followed by ingress of preosteoblasts derived from marrow stromal stem cells into the base of the resorption cavity. **E**, These cells develop the characteristic osteoblastic phenotype and begin to replace the resorbed bone by elaborating new bone matrix constituents, such as collagen, osteocalcin, and other proteins. **F**, Once the newly formed osteoid reaches a thickness of about 20 μm, mineralization begins.

The remodeling cycle normally is completed in about 6 months (**G**). No net change in bone mass occurs as a result of remodeling when the amount of resorbed bone replaced equals the amount removed. Persistence of small bone deficits on the completion of each cycle, however, reflects an inefficiency in remodeling dynamics. The lifelong accumulation of remodeling deficits underlies the phenomenon of age-related bone loss. (*Adapted from* Marcus [10].)

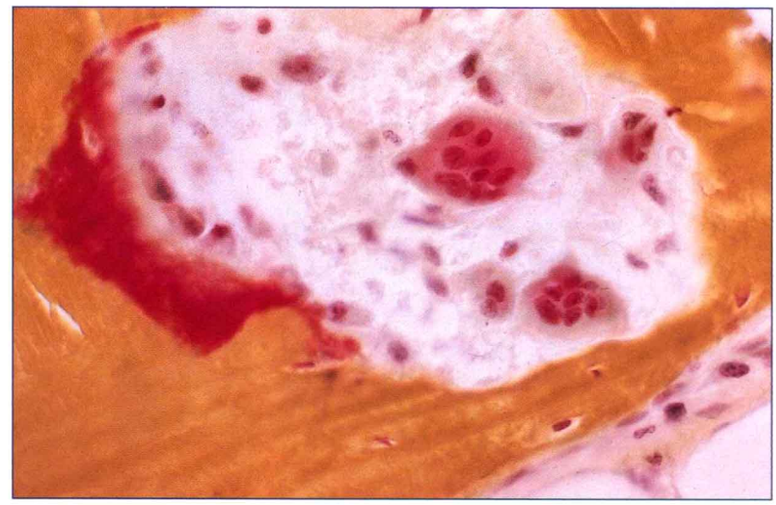


Figure 1-19. Bone biopsy specimen from the iliac crest showing the cellular participants in bone remodeling. Large multinucleated cells seen in the middle of the field are osteoclasts. Derived from a mononuclear macrophage precursor, these cells migrate to a locus on the bone surface, become adherent to the surface with the participation of a number of adherence molecules, and resorb bone (both organic matrix and mineral). The layer of cuboidal mononuclear cells at the bone surface is osteoblasts and the thick red band beneath them represents organic matrix that has not yet been mineralized (osteoid). Mineralized bone is olive in color (Goldner stain). (*Courtesy of* J. Kosek.)

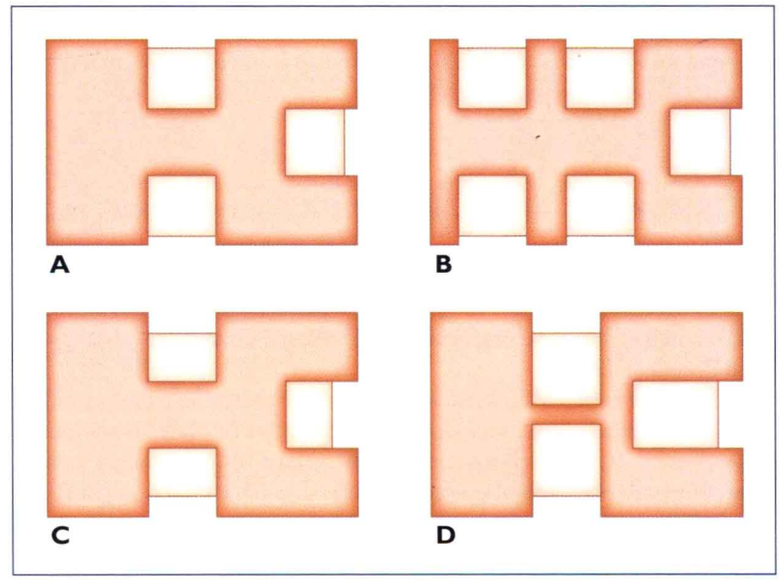


Figure 1-20. Perturbations in remodeling. Alterations in remodeling activity represent the pathway through which diverse stimuli such as dietary insufficiency, hormones, and drugs affect bone balance. A change in the whole body remodeling rate can be brought about through distinct perturbations in remodeling dynamics.

A representation of normal remodeling is shown in **A:** three areas of remodeling activity, each with identical resorption lacunae that have filled in with new bone (*shaded area*). Identical small bone deficits are shown with each remodeling area, reflecting remodeling insufficiency. **B**, Increased remodeling, as shown by five remodeling units, such as is seen in conditions that increase the activation or birthrate of new remodeling units. Examples include hyperparathyroidism, hyperthyroidism, and hypervitaminosis D. Although each remodeling unit is similar to those in **A**, the total bone mass is reduced. **C,** Exaggerated inefficiency of osteoblastic response. The number of remodeling units is similar to **A**; however, the magnitude of the bone deficit is increased due to poor osteoblastic bone formation. Such changes are typical of osteoblastic toxins such as ethanol and glucocorticoids. Progressive age may also be associated with increasing deficits in osteoblast recruitment and function. **D**, Exaggerated osteoclastic activity. A variety of conditions (*eg*, estrogen deficiency or immobilization) may augment osteoclastic resorptive capacity. If the resorption cavities perforate the trabeculae, no scaffold remains for new bone formation to take place. Such resorption becomes a permanent loss of bone.

At any given time, a transient deficit in bone called the remodeling space exists, which represents sites of bone resorption that have not yet been filled. In response to any stimulus that alters the birth rate of new remodeling units, the remodeling space will either increase or decrease accordingly until a new steady state is established. This adjustment is seen as an increase or decrease in bone density. (*Adapted from* Marcus [10].)

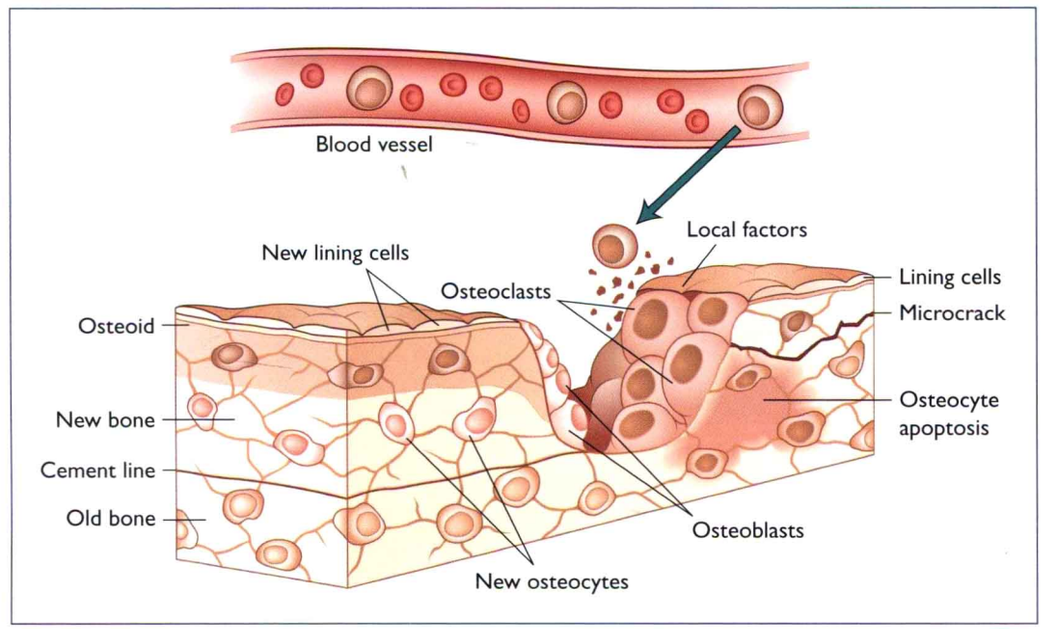


Figure 1-21. Remodeling cycle. After the completion of bone formation, osteoblasts that remain within the newly formed osteoid become osteocytes. Osteocytes have cytoplasmic processes that extend through the matrix in canaliculi. Osteocytes and their network of processes detect strain and microfractures and transmit this information to induce new bone remodeling and repair. For instance, microfractures sever osteocyte processes and initiate a cascade of growth factors and cellular migration that begets osteoclast bone resorption followed by osteoblast bone formation. (*Adapted from* Seeman and Delmas [11].)

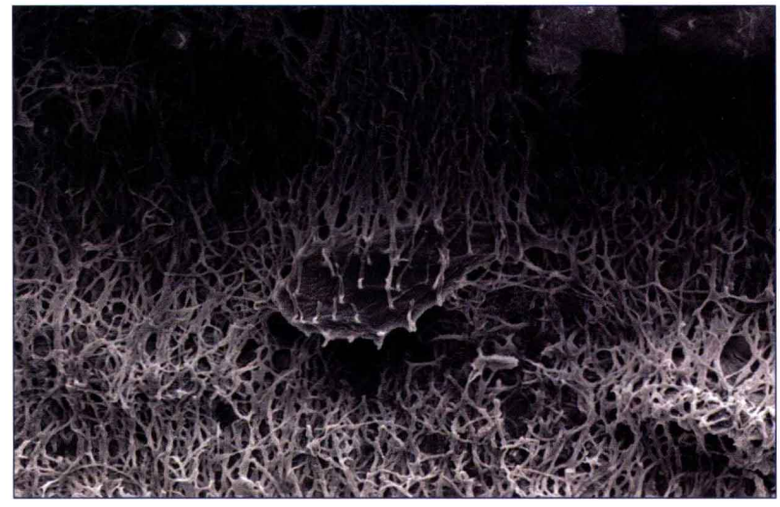


Figure 1-22. Osteocytes are the most numerous and longest living cells in bone [12]. They connect with one another and bone surfaces through a network of canalicular processes. There are approximately 10,000 osteocytes per cubic millimeter of bone with 50 processes per cell. Canalicular processes orchestrate focal bone remodeling by detecting bone strain. (*Courtesy of* L. Bonewald and J. Feng.)