Now in its third edition, Osteoporosis is the most comprehensive, authoritative reference on this disease. Written by renowned experts in the field, this two-volume reference is a must-have for academic and medical libraries and physicians. Worldwide, 200 million women between 60-80 years of age suffer from osteoporosis and have a lifetime risk of fracture between 30 and 40 percent continuing to make osteoporosis a hot topic in medicine. This newest edition covers everything from basic anatomy and physiology to diagnosis, management and treatment in a field where direct care costs for osteoporotic fractures in the U.S. reach up to $18 billion each year. Academic and medical libraries, as well as professionals in bone biology, endocrinology, osteology, neuroendocrinology and drug companies developing osteoporosis medications will find all of their information needs met in this classic reference.

NEW TO THIS EDITION:
✦ Offers critical reviews of reproductive and hormonal risk factors, ethnicity, nutrition, therapeutics, management, and economics comprising a tremendous wealth of knowledge in a single source not found elsewhere
✦ Examines essential updates on estrogen prevention and treatment and the recent results from the Women’s Health Initiative
✦ Recognizes the critical importance of the Wnt signaling pathway for bone health
✦ Incorporates new chapters on osteocytes, phosphatonins, mouse genetics, and CNS and bone
✦ Discusses the controversial topics of screening and clinical trial design for drug registration
✦ Includes essential updates on therapeutic uses of calcium, vitamin D, SERMS, bisphosphonates, and parathyroid hormone
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A. M. Parfitt

I. INTRODUCTION

The cells of bone influence its structure by means of four processes: growth, repair, modeling, and remodeling, the last being the basis of bone tissue turnover in the adult skeleton. The purposes of growth and repair are obvious. Modeling serves to adjust bones to changing mechanical loading [1], and remodeling serves to thicken trabeculae in the growing skeleton [2], processes that are most effective during adolescence [3]. But why does a tissue that can survive for thousands of years after death need to be maintained for replacement during life? Most of those interested in bone, whether as physicians, as clinical investigators, or as basic scientists, show remarkably little interest in the fundamental question. Many articles and book chapters discuss the regulation of bone remodeling, but regulation, at least in the physiologic sense, implies a target [4]. The target value of any regulatory process in biology has been optimized by natural selection. Mechanisms have evolved which ensure that deviations from the target values are detected and that corrective measures to restore the target value are carried out. In this sense, body temperature, extracellular fluid osmolality, tissue oxygen tensions, and countless other physiologic quantities are regulated, but the mechanisms of regulation could not be determined until the existence of the target had been recognized and its precise nature defined. Is there a target for bone remodeling or for some characteristic of bone that is influenced by remodeling?

The piecemeal, spatial nature of bone remodeling is well known. The process is carried out by temporary anatomic structures known as basic multicellular units, or BMUs [5-8], which excise and replace tunnels through cortical bone (osteoclastic remodeling) or trenches across the surface of cancellous bone (endosteal remodeling). Each BMU includes a team of executive cells (osteoclasts and osteoblasts), supported by blood vessels, nerves, and bone connective tissue. The life span of the BMU is measured in months, but the life span of osteoclasts while they are making bone is measured in weeks, and the life span of osteoblasts is measured in days. During progression of the BMU through or across the surface of bone, the spatial and temporal relationships between its components are maintained by the combined growth of the central cavity, in cortical bone [9], and extension of the remodeling front in cancellous bone [10], together with recruitment of new cells [9-11]. These cells, like the formed elements of the blood, originate from stem cells in the bone marrow [12] except the cells that provide local progenitors and are found in bone-derived, differentiated, and mature cells. More information about this process is needed.

Each type of blood cell is normally produced at a basal rate that is sufficient for ordinary purposes but can be increased when needed [13]. For each cell, the circumstances under which demand is met and is well known, and are related to the function of the particular cell. Although the cell types differ from the response, the relative importance of reactive and hematopoietic [14], and the extent to which different hematopoietic mechanisms have been elucidated. The key relationships between supply and demand for bone cell function, applies a cells. For osteoclasts in the adult organism, the demand is created by bone receptor function of osteoblasts to replace lost bone. However, the circumstantial evidence that this is the case is the secreted factors, such as mechanical strain, that influence the activity of osteoclasts and osteoblasts.

II. SKELETAL HETERONEGITY

A. Structure and Function

The structural differences between cortical bone, in which density and surface-to-volume ratio are low, and cancellous bone, in which these geometric quantities are high [15], are now widely recognized. All intermediate values of these quantities can occur, but they are infrequent, implying that transitional structures tend to be temporary and short-lived [16]. Less often noted are the differences between the axial and appendicular skeleton and the pelvic skeleton and apophyses. The daily activity of the skeleton (Table 5.1), the spine as an appendicular, behaves as an axial skeleton, so that the central axis is the most central with peripheral consequences. The consequences of this division differ from the central and peripheral components. The peripheral components (including locomotion), and provide protection for the soft tissues. Subchondral slips are a characteristic of our own living bone, and often referred to as "mechanical" [17]. It is commonly believed that the mechanical functions of bone are carried out mainly by cortical bone and the metabolic functions mainly by cancellous bone, regardless of their central or peripheral locations. In fact, the
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