Special Topic: Prospectus on Research Advances

Prospectus: Research Advances

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OUR KNOWLEDGE of bone structure and its function in health and disease has grown considerably. Key advances in bone biology include the development of methods for studying human bone cells, the provisional demonstration of estrogen receptors in bone, a delineation of the impact of mechanical loading on bone tissue, and the finding that bone contains a variety of growth factors for bone cells. Major clinical advances relevant to osteoporosis have been a new appreciation of osteoporosis as a public health problem, new insights into the clinical epidemiology of osteoporosis, and the development of novel techniques for bone mass and density measurement.

The preliminary evidence for estrogen receptors in bone cells is particularly exciting. Heretofore, estrogen was thought to inhibit bone resorption indirectly, by modifying its production, release, or turnover of other osteotropic hormones. With this new evidence, it is possible to conceptualize a model in which estrogen acts directly, by blocking the activation of new remodeling events or the perpetuation of already initiated units. Should estrogens have such a direct action, it would set the stage for the development of strategies to perturb the estrogen receptor in a selective fashion, preserving the skeletal while eliminating the nonskeletal effects of the hormone.

The demonstration that bone matrix contains, and bone cells elaborate, multiple proteins which can stimulate bone cell growth or specialization (or both) has enhanced our understanding of bone healing and remodeling. Local release of these factors from bone matrix is likely to expedite fracture healing, and may serve to link the processes of bone resorption and bone formation. A reduction in the synthesis and matrix storage of the growth factors may underlie the progressive loss of bone tissue with advancing age. Several of these factors have been purified and characterized; they hold considerable promise as agencies for promoting and treating osteoporosis.

A major accomplishment has been the development of accurate, precise, and sensitive methods for measuring bone mass and density, including single and dual photon absorptiometry and computed axial tomography. These methods have enabled clinical investigators to test, prospectively and cross-sectionally, the efficacy of agents in reducing the loss of bone tissue, thus obviating the cumbersome use of fracture frequency as an endpoint. Studies have shown that bone mass at menopause is a predictor of subsequent low bone mass—certainly more reliable than the assessment of clinical risk factors. Further refinements, such as dual energy radiography, have reduced precision errors and the cost per test to the point where frequent clinical use is feasible.

Despite these advances, additional information is most urgently needed in all aspects of osteoporosis. Of vital importance are studies directed toward understanding the regulation of bone remodeling at the cellular and supracellular organizational level, the nature of bone tissue and the determinants of its mechanical integrity, the epidemiology of osteoporosis, and the mechanisms of bone loss in the various forms of primary and secondary osteoporosis. Much more must be learned about the impact of nutrition and calcium intake on bone growth and maturation, and on aging-associated bone loss. We need improved strategies to determine risk for low bone mass and fractures; even better clinical methods for estimating bone mass and density, and bone turnover; and safe, effective, inexpensive, and easily accepted modes of prevention and treatment. Since falls are the precipitating events in most if not all hip fractures, and all fractures of the wrist among the elderly, it is crucial that we understand the causes of, and risk factors for, falling, and develop effective strategies for fall prevention.

Osteoporosis has received increased research support within the past year, largely through the funding of specialized centers and centers of excellence. Currently available funds, however, are insufficient to enhance research efforts substantially. Federal support for research in osteoporosis per year amounts to less than 0.25 percent of the estimated annual cost of the disorder in the United States. Clearly, additional funds will be required to solve this major public health problem.