

9-1988

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### Recommended Citation

Krane, Stephen M. (1988) "Allied Disciplines," *Henry Ford Hospital Medical Journal* : Vol. 36 : No. 3 , 145-146.

Available at: <https://scholarlycommons.henryford.com/hfhmedjournal/vol36/iss3/5>

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# Allied Disciplines

Stephen M. Krane, MD\*

In the course of planning the 1988 International Bone and Mineral Symposium, several of us thought it would be valuable to discuss certain problems of the skeleton that might not be considered to be related to what have been perhaps arbitrarily defined as metabolic bone diseases. We reasoned that principles are emerging from recent research that eventually might be applicable to the care of patients with these diseases or understanding pathogenesis.

There is little question that in order to maintain exquisite control of skeletal metabolism it will be necessary to establish what factors regulate the function of bone cells and their interactions. For example, regulation of the rate at which osteoblasts deposit bone matrix and effect its mineralization is critical for maintenance of adequate bone mass during remodeling and the degree and quality of repair in response to injury or tumor. The quality and amount of the organic matrix deposited in bone are critical as demonstrated by the profound pathological consequences of single amino acid substitution in the helical portion of the type I collagen chains in instances of osteogenesis imperfecta.

## Application of Molecular Genetics to Osteopenic Bone Disease

Tsipouras and Rowe (1) presented an analysis of the genetic approach to understanding collagen structure and synthesis in human disease, particularly the use of analysis of restriction fragment length polymorphisms. This technique has made it possible to demonstrate linkage in several kindreds with multiple members affected with some forms of osteogenesis imperfecta.

## Bone Induction

Glowacki (2) described what is known about some of the mechanisms that govern induction of new bone, particularly the system in which the endochondral sequence is induced by implantation of fragments of demineralized bone. This model, described first by Urist and Huggins, not only permits dissection of controls at each phase in the sequence, but application of some of the principles derived from its study also provides new therapeutic approaches to such clinical problems as nonunion of fractures and reconstitution of various types of skeletal discontinuity.

## Hematopoietic Growth Factors

Considerable progress has now been made in understanding what governs proliferation and differentiation of hematopoietic precursor cells. Not only have several of the specific growth fac-

tors involved been isolated, the cDNAs cloned and expressed and their receptors characterized, but sufficient quantities of the recombinant polypeptides are available specifically to treat some anemias and neutropenias. Sufficient promise has now been shown using some of these colony stimulating-factors to relieve the bone marrow failure after irradiation or chemotherapy. Osteoclasts are also derived from hematopoietic precursors, and knowledge of factors that govern the differentiation of these cells is critical to understanding physiological and pathological bone resorption. Roodman (3) presented an up-to-date general description of hematopoietic growth factors, particularly in the context of therapeutic potential and the relationship to osteoclast differentiation.

## Musculoskeletal Magnetic Resonance Imaging

The introduction of computed tomography and magnetic resonance imaging has revolutionized clinical care by providing more accurate means for assessing the type and extent of all sorts of pathological lesions in soft tissues. The application of magnetic resonance imaging techniques to analysis of musculoskeletal disorders has recently been achieved. Dr. Murphy from the Mallinkrodt Institute of Radiology at Washington University in St. Louis discussed some of his experience with musculoskeletal magnetic resonance imaging to illustrate the power of the method.

## Surgical Management of Patients with Skeletal Tumors

Bone tumors are rare, and physicians who care for adults with metabolic bone diseases usually do not have the chance to develop any experience in the diagnosis or management of these neoplasms. Even in patients with Paget disease, osteosarcomas develop as a complication of the skeletal lesions with a frequency of well under 1%. Nevertheless, these are still important cancers in pediatric orthopedic practice, and there has been considerable improvement in outlook as a result of better procedures to evaluate the lesions and proper appreciation of the usefulness of surgery and chemotherapy. Understanding the biology of osteosarcomas will provide us with useful information about the biology of osteoblasts, since in these tumors the ma-

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lignant cells are certainly related to osteoblasts. McGuire (4) discussed surgical management of patients with skeletal tumors, particularly from the point of view of management, but he also described his attempts to identify specific components on the surface of the malignant cells using monoclonal antibodies.

### Final Note

These presentations provide a flavor of the research accomplishments in disciplines that relate in some way to metabolic bone disease. The application of principles and methodology of modern cell and molecular biology to these clinical problems will be even more widespread in the future. Other technologies particularly derived from the physical sciences will continue to offer new approaches to diagnosis and management of skeletal disorders. Further development of some of these approaches and

the introduction of new surprises will certainly influence the program of the next Henry Ford Hospital International Bone and Mineral Symposium.

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