

## BOOK REVIEWS

**NON-INVASIVE BONE MEASUREMENTS: METHODOLOGICAL PROBLEMS.** J. Dequeker, C. C. Johnston, Jr., Eds. Oxford, England and Washington, D.C., IRL Press Ltd., 1982, 255 pp, \$30.00

This book presents the *Proceedings of the Workshop on Non-Invasive Bone Measurements* held at the XVI European Symposium on Calcified Tissue Research, in Knokke, Belgium, 1981. The text is divided into three sections; noninvasive bone mass assays as viewed from the comparability of the different measurements, the proper expression of values obtained in these measurements, and the clinical relevance of measurements of peripheral, axial, and total skeletal mass. The purpose of the workshop associated with these proceedings was to discuss the methodological problems encountered in noninvasive bone measurements. As with many proceedings publications, however, the various topics covered are not given equal treatment. In spite of this, the text is an important contribution to the literature for investigators interested in the quantitative assessment of bone mass. There are 12 papers in the text on single- or dual-photon absorptiometry, seven on radiogrammetry, two each on neutron activation and TCT densitometry, in addition to three introductory presentations that compare the different methods of measurement. The variable attention given to these different topics reflects, in part, the general interest of the scientific and medical community. Radiogrammetry and absorptiometry have been used for many years and, only recently, has TCT been shown to offer considerable promise for the assay of bone mass.

The text is particularly useful from the standpoint of the numerous clinical examples of bone mass assays, especially in the study of metabolic bone disease. The different viewpoints expressed, both by the way of comparison of different approaches to the same method and by the reported findings from different methods provide the reader with good insight into the basis for selecting a procedure for a specific application. Those who have recently read Cohn's text, *Non-Invasive Measurements of Bone Mass and Their Clinical Application*, will find this an interesting and worthwhile companion volume. Whereas the book edited by Cohn stresses the theory underlying each of these bone assays, this volume emphasizes methodologic problems and clinical applications. The book provides an important compilation of up-to-date observations in this specialty area. It is a useful reference book for departmental libraries serving nuclear medicine specialists and radiologists interested in bone pathology and physiology.

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**BIOLOGIC APPLICATIONS OF RADIOTRACERS.** H. J. Glenn, Ed. Boca Raton, Florida, CRC Press, 1982, 208 pp, \$63.50

The title of this book could lead one to think it is another compilation of research results involving the applications of radiotracer methodology. *Biologic Applications of Radiotracers* is actually a "how-to" book for "the use of small animals in radiotracer research." As part of the CRC Press series *Radiotracers in Biology*

and Medicine, it is intended to be an updated presentation of material last available in the two-volume treatise *Radionuclides in Pharmacology*, published in 1971.

A perusal of the table of contents reveals that the eight contributing authors provided nine chapters that address virtually every aspect of the practical side of using small animals for radioisotope biodistribution studies including designing and organizing an animal radiopharmacology laboratory (Chapter 2), planning and carrying out biodistribution studies (Chapter 5), choosing an animal model (Chapter 1), animal handling, radiotracer administration, dissection and sampling techniques (Chapter 6), and obtaining the results using autoradiography (Chapter 4) and liquid scintillation counting (Chapters 7 and 8).

Concomitant with the multiauthor format is the expected unevenness and overlap. Often this overlap works to the reader's advantage, i.e., when a subject is only touched upon in one chapter, it is discussed at length in another. The extremes of the unevenness are exemplified by the presentation on autoradiography and the chapters on species biodistribution differences and the handling, maintenance, and disposal of radioactive animals.

One quarter of this volume is devoted to autoradiography, and provides a unique and valuable introduction to all aspects of this subject, including guidelines for choosing the appropriate technique, radioisotope and film, maximizing efficiency, and avoiding the common pitfalls. Although the depth of the information falls short of that needed to begin this type of experimental work, there are ample references to the literature. This chapter also includes 22 pages of black and white and color plates illustrating both the methods and equipment and the various applications of this powerful technique.

Another comprehensive chapter is that on animal handling, drug administration, dissection, and sampling techniques. This is a real "how-to" presentation on the correct procedures for rodent handling, injection, anesthetizing, killing, and dissection. Also given are detailed methods for obtaining fluid and tissue samples. Accompanying the text are clear, detailed photographs showing how these various procedures are carried out. Again, key references are provided to allow the researcher easy access to the primary literature.

Much less satisfying is the superficial treatment given the subjects of biodistribution differences between species (Chapter 3, three one-half pages, no references) and the handling, maintenance and disposal of radioactive animals (Chapter 9, five pages, four references). The latter subject is covered more thoroughly in the earlier chapter on the animal radiopharmacology laboratory, although this material is somewhat marred by the inclusion of several hastily executed drawings that are not up to the standards one would expect in a text such as this. This reviewer was also disappointed to discover that much of the material in the two chapters on liquid scintillation counting is reproduced verbatim from another CRC Press publication, *Principles of Radiopharmacology*.

These deficiencies, however, do not significantly detract from the fact that this text is an excellent compilation of all the basic information needed to plan and execute a basic research program

involving the generation of animal radiotracer biodistribution data. As such, it represents a unique resource both for those contemplating entering this field and for those who wish to update and expand their skills and knowledge.

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**BIOLOGICAL TRANSPORT OF RADIOTRACERS.** L. G. Colom-betti, Ed. Boca Raton, Florida, CRC Press, 1982, 329 pp. \$94.00

The scientific study of biological transport began in the middle of the last century with the qualitative descriptions by Naegely and Cramer on plant-cell membrane permeabilities and with the quantitative studies and mathematical studies of Fick on diffusive transport. While these and the subsequent early results were elegant and insightful, the prodigious growth of our knowledge of biological transport to its present breadth began with the introduction to radioisotopic methodology following the pioneering work of von Hevesy in the 1920s. The delicate sensitivity and ease of measurement offered by the new technique have made it the basis for much of the information on biokinetic phenomena we now possess.

*Biological Transport of Radiotracers* is an extensive collection of review articles by 19 well-qualified scientists addressing the large topic of mass transport in living entities, with emphasis on, but by no means limited to, the use of radiolabeled tracers and indicators. This book is part of a still larger undertaking, the publication of the CRC Series in radiotracers in biology and medicine, which at the present time comprises eight other related volumes of comparable scope.

As is frequently the case with books of multiple authorship, each contribution stands isolated from the others, and in this book, except for a brief preface by the editor, no very effective attempt at unification has been made. This makes a holistic description and evaluation of it difficult to accomplish. Accordingly, this review proceeds chapter by chapter, with groupings that reflect perceived similarities of content.

The first two chapters "Biological Transport: An Historical View," and "Solute Translocations" are introductory. The first reviews briefly the development of the study of biological transport, dividing the subject in the same fashion as is done in the rest of the book by treating separately transport into cells and transport in body fluids. The second is a concise and lucid summary of present understanding of the mechanisms of transmembrane transport. The author considers it to be "a list of topics to be considered before embarking on an investigation requiring solute translocation across a biological membrane."

The next three chapters "Dynamic Aspects of Cell Membrane Structure," "Transmembrane Transport as a Rate-Limiting Phenomenon in the Distribution of Pharmacological Agents," and "Membrane Transport," cite the evidence for mobility of membrane constituents in the plane of the membrane and describe the influence of this lateral mobility on transmembrane transport. Additionally, a review is provided of the experimental conditions and criteria that must be applied to differentiate true transmembrane transport from binding unrelated to transport that experimentally would be falsely interpreted as "uptake." A detailed review of the various modes of transmembrane transport is given, expanding on the more summarized exposition of Chapter 2.

Chapter 6, "Thermodynamic Aspects of Radiotracer Flow," reviews the concepts that lead to the use of radiotracer flows to define the driving forces in coupled transport processes. The ideas of nonequilibrium thermodynamics are used as the basis for the descriptions given. The author shows that ratios of unidirectional fluxes, which in the unperturbed state can be measured only

through the use of radiotracers, are a measure of the total Gibbs' free energy involved in the tracer transport process.

The chapter, "Kinetics of Blood To Cell Uptake of Radiotracers," in addition to being the most extensive is, at least from the point of view of the in vivo experimentalist investigating whole-organ or whole-body mass transport, one of the most fundamental. It seeks to provide answers to his question: "Given my observed laboratory or clinical data in the form of a temporal record of radiotracer response to a given radiotracer stimulus, how can I infer the parameters of biochemical or physiological importance that gave rise to my data?" The immediate answer is, of course, "By the judicious devising and use of mathematical models." The authors have provided a clearly written summary of much of the accomplishments in this difficult field since the early work of G. N. Stewart at the close of the last century. They point out that the techniques for obtaining information with relatively little disturbance in patients and animals has received great impetus in the last three decades with the advent of cardiac catheterization, and in the past few years, with the ever-increasing use of radionuclide-imaging techniques.

Included among the topics treated are descriptions of the general experimental and data-analysis methodologies that have evolved: single- and multicapillary distributed models, methods of accounting for blood-flow heterogeneities, estimation of flow by outflow- and residue-detection, and the delineation of conditions for the valid application of lumped-parameter or compartmental models. The chapter concludes with a brief review of whole-body kinetics of tracers taken up into cells.

Chapter 8, "Effect of Solute Structure on Transport of Radiotracers," and Chapter 9, "Effect of Transport on Distribution of Radioions and Radiometabolites," both by Y. Yano, are mutually complementary. One describes the pathways and binding sites of some of the radiopharmaceuticals commonly used in nuclear medicine, as influenced by the various mechanisms that bring about their transport and the other treats the inverse problem of designing radiopharmaceuticals to trace predetermined pathways and to bind to specific desired sites. From this viewpoint, it would seem reasonable to inquire why the two chapters were not combined into one. Chapter 8 gives some general principles of the relations between solute structure and transport. Effects such as lipid solubility, facilitated diffusion, and other structure-specific consequences are described. The possibility of designing radiotracers to predetermine their transport and binding behavior is considered and examples of successful efforts of this kind are described. Among these are the use of radiofluorinated deoxyglucose to effect "metabolic trapping" in brain and the use of similarly labeled fatty acids to study regional metabolism in the heart. No mention is made of the inherent limitations of analogs to study transport of endogenous substrates due to differences in kinetic behavior, especially in disease states. (This issue, however, is discussed fully in a general way in Chapter 13.) Chapter 9 reviews the effects of transport mechanisms on the spatial distribution of radiotracers used routinely in current clinical practice. Among the various labels discussed are those incorporating technetium-99m, iodine-123, -125, and -131, thallium-201, fluorine-18, xenon-127 and -133, krypton-81m, gallium-67, and indium-111 and -113m. Consideration is given to the interaction of the various radiolabels with plasma proteins and blood cells and to their mechanisms of uptake by cell-membrane permeation or by binding at specific sites. A short discussion is given on current developments in the use of the positron emitters carbon-11, nitrogen-13, and oxygen-15 to label biochemical compounds and blood-flow tracers for use in computer-aided, positron-emission tomography.

Chapter 10, "Transport of Protein-Bound Radiotracers into Tissues," and Chapter 12, "Transport of Radiolabeled Antibodies," includes an extensive review of kinetic factors, such as debinding rates, membrane permeabilities, and capillary transit