

Abdelhamid H. Elgazzar
Editor

The Pathophysiologic Basis of Nuclear Medicine

Third Edition

 Springer

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Basis of Nuclear
Medicine

Third Edition

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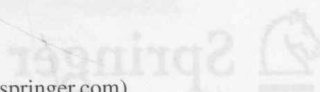
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Foreword to First Edition

Diagnostic imaging studies may be interpreted in one of two ways. The initial approach is that of the "imager", dealing solely with pattern recognition. In this respect, the experienced observer will surely out-perform the younger *To my children the superb humans* and of such knowledge in his or her memory bank. The other means of interpreting images draws basic pathophysiology and clinical knowledge of a disease entity into the interpretive process. Functional nuclear medicine-imaging studies are exquisitely sensitive but notoriously non-specific. For this reason, nuclear medicine is most often used as a screening tool or as a monitor of changes in function when therapeutic interventions are performed.

The non-specificity of radionuclide imaging studies makes it particularly important that nuclear medicine physicians have a broad, in-depth understanding of the basic pathophysiology of the disease processes which they are being asked to study. It is in this context that Dr. Abdelrazek H. Elgazzar and his many colleagues have succeeded in the following 24 chapters: they provide us with a basic reference presentation of the pathophysiology associated with various disease processes and how this knowledge is applied to the interpretation of the clinical presentation, coupled dealing with cell structure and function, radiopharmaceutical localization, biologic effects of ionizing radiation and radionuclide therapy provide very useful information. The format employed by this gifted international panel of authors provides us with an extraordinary text which differs from some of the other fine publications in our field. It remains true to the very essence of functional imaging which characterizes the field of nuclear medicine and distinguishes it from the more morphologically-based radiologic imaging procedures.

Both residents and active practitioners of nuclear medicine will profit from the enormous amount of clinically relevant information provided herein. This volume will surely enhance our role as well-rounded nuclear medicine physicians, as opposed to being more limited "imagers". It is only in this manner that we can fulfill our obligation as true consultants and play a pivotal role in assisting patient management decisions.

We are most indebted to Dr. Elgazzar and his co-authors for enhancing our diagnostic skills with this extraordinary textbook.

New York, NY, USA

Leonard M. Freeman, MD

Foreword to First Edition

Diagnostic imaging studies may be interpreted in one of two ways. The initial approach is that of the “imager”, dealing solely with pattern recognition. In this respect, the experienced observer will surely out-perform the younger physician who possesses a more limited fund of such knowledge in his or her memory bank. The other means of interpreting images draws basic pathophysiology and clinical knowledge of a disease entity into the interpretive process. Functional nuclear medicine imaging studies are exquisitely sensitive but notoriously non-specific. For this reason, nuclear medicine is most often used as a screening tool or as a monitor of changes in function when therapeutic interventions are performed.

The non-specificity of radionuclide imaging studies makes it particularly important that nuclear medicine physicians have a broad, in-depth understanding of the basic pathophysiology of the disease processes which they are being asked to study. It is in this area that Dr. Abdelhamid H. Elgazzar and his many colleagues have excelled. In the following 22 chapters, they provide us with a lucid, systemic presentation of the pathophysiology associated with various disease processes and how this knowledge impacts on scintigraphic interpretations. In addition to the clinical presentations, chapters dealing with cell structure and function, radiopharmaceutical localization, biologic effects of ionizing radiation and radionuclide therapy provide very useful information. The format employed by this gifted international panel of authors provides us with an extraordinary text which differs from some of the other fine publications in our field. It remains true to the very essence of functional imaging which characterizes the field of nuclear medicine and distinguishes it from the more morphologically based radiologic imaging procedures.

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New York, NY, USA

Leonard M. Freeman, MD

Kuwait City, Kuwait

Abdelhamid H. Elgazzar, MD, FCAP

Preface to Third Edition

Awareness of the impact of pathophysiology in particular on imaging studies is critical to the proper practice of nuclear medicine. The correlation of these basic aspects with the scintigraphic features of various diseases is further emphasized in this edition. Imaging specialist must appreciate the patient's clinical problem and the pathophysiologic changes to fully utilize nuclear images. Working from this clinical context, the specialist can then apply his/her understanding of the pathophysiologic basis of disease and the knowledge of how such pathology may translate into various imaging patterns. The difference between film reading dealing solely with pattern recognition and proper interpretation of a clinical scintigraphic image in the holistic approach integrating clinical, laboratory and pathophysiologic understanding should be appreciated to achieve proper clinical impact. New developments in molecular biology, radiopharmaceuticals and hybrid imaging have continued to contribute to the rapid change in the field of nuclear medicine and molecular imaging. To continue the efforts to accommodate these changes and be in line with the future direction of nuclear medicine and molecular imaging, the 3rd edition of *The Pathophysiologic Basis of Nuclear Medicine* was developed.

This edition reflects new developments in the area of molecular imaging with more emphasis given to the basis and application of PET/CT. The chapter on tumor scintigraphy details PET/CT management of individual tumors. Furthermore the radiopharmaceuticals for PET imaging have been updated with more details and correlation with pathophysiologic changes such as hypoxia, angiogenesis and proliferation. The additional information about clinical and imaging correlation makes this text a very useful companion to those who are being trained in nuclear medicine technology and clinical nuclear medicine.

It is my hope that this book will help medical professionals to further understand what nuclear medicine technology can offer for the diagnosis and treatment of disease. Deep understanding of the scientific and clinical basis of the new directions in medical imaging will certainly lead to further improvements and innovations in this important field of medicine. This updated edition will hopefully help in the understanding of the field of nuclear medicine in depth and further advance and improve current diagnostic and therapeutic modalities in the treatment of disease.

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Abdelhamid H. Elgazzar, MD, FCAP
Abdelhamid H. Elgazzar, MD, FCAP

Preface to Second Edition

The field of nuclear medicine is continuing to grow rapidly and incorporating advances in molecular biology, molecular imaging, and pathophysiology. In an effort to accommodate these changes and be in line with the future direction of nuclear medicine, we have updated the first edition of *The Pathophysiologic Basis of Nuclear Medicine*, building on its strengths and making modifications to remedy any weak areas.

To reflect new developments in the area of molecular imaging, a separate chapter on the basis of positron emission tomography has been included, more information about therapy using radionuclides has been added, and the chapters on the cell, radiopharmaceutical uptake, inflammation, bone, respiratory and neurology have been expanded. Furthermore, the clinical aspects of the role of molecular imaging in nuclear imaging are emphasized, since an imaging specialist must appreciate the patient's clinical problem for a full utilization of nuclear images. For instance, the difference between superficial film reading and proper interpretation of a clinical scintigraphic image by a holistic approach has been highlighted. Working from this clinical context, the specialist can then apply his/her understanding of the pathophysiologic basis of disease and the knowledge of how such pathology may translate into various imaging patterns. Awareness of the impact of pathophysiology on imaging studies is critical to the proper practice of nuclear medicine. The additional information about clinical and imaging correlation makes this text an invaluable companion to those who are being trained in nuclear medicine technology and clinical nuclear medicine.

We extend our appreciation to reviewers of several journals as well as members of the nuclear medicine community from around the world for their helpful and motivating feedback, both published and private. It is my sincere hope that this book will help medical professionals to further understand what nuclear medicine technology can offer in the diagnosis and treatment of disease. A deeper understanding of the scientific and clinical basis of new directions in medical imaging will certainly lead to further modifications and new innovations. I also hope that this revised text will help to advance knowledge in the field of nuclear medicine and improve currently available diagnostic and therapeutic tools in the treatment of patients with various diseases.

Kuwait City, Kuwait

Abdelhamid H. Elgazzar, MD, FCAP

Preface to First Edition

There is a great difference between superficial reading of a film and proper interpretation of a clinical scintigraphic image by an imaging specialist. Fully utilizing the clinical image, the imaging specialist evaluates both the anatomical and the physiological structure of the human body. First the specialist must appreciate the patient's clinical problem. Working from this clinical context, he then applies his understanding of the pathophysiological basis of disease and his knowledge of how such pathology may translate into various imaging patterns. This awareness of the impact of pathophysiology on imaging studies is critical to the proper practice of nuclear medicine.

Nuclear medicine is a unique and growing medical specialty that contributes most significantly to our understanding of the functional changes which accompany disease. In this way, nuclear medicine helps to advance scientific understanding. Both the diagnostic and the therapeutic aspects of nuclear medicine rely for their efficacy on the physiological changes produced by disease. Clearly, a detailed understanding of both normal and morbid pathophysiology is prerequisite to a successful career in this growing field of medicine.

Today nuclear medicine is one of the medical specialties with great opportunities for innovation and creative thinking. We are fortunate to be practicing nuclear medicine at a time of rapid scientific progress and significant growth in our contributions to patient care and well-being. The resources devoted to nuclear medicine, however, will be most profitably used when both researchers and practicing physicians have taken the time to understand the pathophysiological basis of scintigraphy and radionuclide therapy.

As a practicing nuclear medicine physician and teacher, I know that beginning students and physicians in both radiology and nuclear medicine have in the past lacked a concise textbook which focuses on the pathophysiological basis of nuclear medicine. I feel that the contributing authors to this book have collectively fulfilled this need. In addition, I hope that this book will serve as a practical reference for practicing radiologists and nuclear medicine physicians. Given the rapid pace of research in the field of nuclear medicine, keeping up to date after the completion of formal training is a challenge for all of us.

Along with the contributing authors, I hope that this book will help to spread medical knowledge and enhance patient care within the field of nuclear medicine.

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1.1 Introduction

Understanding pathophysiology of disease is essential for all who study and work in any field of medicine. Since nuclear medicine deals with functional and molecular changes, it becomes crucial to understand the pathophysiologic changes of relevant diseases and disease-like conditions to properly study and practice the field.

Pathophysiology has been changing and expanding with added new knowledge. Since the late 1970s, tremendous developments in molecular biology and genetics have provided medical science with an unprecedented chance to understand the molecular basis of disease. Disease can now be defined on the basis of abnormal deviation from normal regional biochemistry. Since pathophysiology is a bridge between pathology and physiology, it is imperative to understand the principles of both disciplines.

1.2 Pathology

Pathology is concerned with the study of the nature of disease, including its causes, development, and consequences with emphasis on the structural changes of diseases. Specifically, pathology describes the origin of disease, its etiologies, how it progresses and manifests clinically in individuals in order to determine its treatment. Pathology plays a vital role across all facets of

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Pathophysiology: General Principles

Abdelhamid H. Elgazzar

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1.1 Introduction

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medicine throughout life, and currently it extends to the examination of molecules within organs, tissues, or body fluids.

1.3 Definition of Disease

The precise definition of disease is as complex as an exact definition of life. It may be relatively easier to define disease at a cellular and molecular level than at the level of an individual. Throughout the history of medicine, two main concepts of disease have predominated: ontological and physiological [1].

The ontological concept views a disease as an entity that is independent and self-sufficient and runs a regular course with a natural history of its own. The physiological concept on the other hand defines disease as a deviation from normal physiology or biochemistry; the disease is a statistically defined deviation of one or more functions from those of healthy people under circumstances as close as possible to those of a person of the same sex and age of the patient. Most diseases begin with cell injury, which occurs if the cell is unable to maintain homeostasis.

1.3.1 Homeostasis

The term homeostasis is used by physiologists to mean maintenance of static, or constant, conditions in the internal environment by means of positive and negative feedback of information. About 56 % of the adult human body is fluid. Most of the fluid is intracellular, and about one-third is extracellular fluid that is in constant motion throughout the body and contains the ions (sodium, chloride, and bicarbonate) and nutrients (oxygen, glucose, fatty acids, and amino acids) needed by the cells to maintain life. Extracellular fluid was described as the internal environment of the body and hypothesized that the same biological processes that make life possible are also involved in disease [1]. As long as all the organs and tissues of the body perform functions that help to maintain homeostasis, the cells of the body continue to live and function properly [1].

1.3.2 The Genome

At birth, molecular blueprints collectively make up a person's genome or genotype that will be translated into cellular structure and function. A single gene defect can lead to biochemical abnormalities that produce many different clinical manifestations of disease or phenotypes, a process called pleiotropism. Many different gene abnormalities can result in the same clinical manifestations of disease – a process called genetic heterogeneity. Thus, diseases can be defined as abnormal processes as well as abnormalities in molecular concentrations of different biological markers, signaling molecules, and receptors.

1.4 Physiology

Physiology is the study of normal, healthy bodily function. It is concerned with the science of the mechanical, physical, bioelectrical, and biochemical functions of humans in good health, their organs, and the cells of which they are composed. It is a broad science which aims to understand the mechanisms of living, from the molecular basis of cell function to the integrated behavior of the whole body.

1.5 Pathophysiology

Pathophysiology is a convergence of pathology and physiology. It deals with the disruption of normal mechanical, physical, and biochemical functions, either caused by a disease or resulting from a disease or abnormal syndrome or condition that may not qualify to be called a disease, and now includes the molecular mechanisms of disease. In the year 1839, Theodor Schwann discovered that all living organisms are made up of discrete cells [2]. In 1858, Rudolph Virchow observed that a disease could not be understood unless it was realized that the ultimate abnormality must lie in the cell. He correlated disease with cellular abnormalities as revealed by chemical stains, thereby founding the field of cellular