1.1 Nuclear Medicine

Nuclear medicine can be defined quite simply as the use of radioactive materials for the diagnosis and treatment of patients, and perhaps the study of human disease (Wagner 1995a). Chemistry is the language of health and disease, since the entire body is a collection and vast network of millions of interacting molecules. If the definition of the disease is molecular, the diagnosis is also molecular. Because the treatment of many diseases is chemical, it becomes more and more appropriate that the chemistry be the basis of diagnosis and the planning and monitoring of a specific treatment. Nuclear medicine, therefore, is a medical specialty that is based on the examination of the regional chemistry of the living human body.

In the 1920s, George de Hevesy (Fig. 1.1) coined the term radioindicator or radiotracer and introduced the tracer principle in biomedical sciences. One of the most important characteristics of a true tracer is that it can facilitate the study of the components of a homeostatic system without disturbing their function. In the late 1920s, Hermann Blumgart and Soma Weiss, two physicians at the Massachusetts General Hospital, injected solutions of radium-C ($^{214}$Bi) into the veins of healthy persons and patients with heart disease to study the velocity of blood. Due to their pioneering work in nuclear medicine, Hevesy is regarded as the father of nuclear medicine, while Blumgart came to be known as the father of diagnostic nuclear medicine.

In the 1930s, the discovery of artificial radioactivity by Irene Curie and her husband Frederic Joliot, and the discovery of the cyclotron by Ernest Lawrence, opened the door for the production of radiotracers of practically every element, thus, enabling investigators to design radiotracers for the study of specific biochemical processes. Following the detection of radioactivity with the Geiger counter, it was discovered that thyroid accumulated $^{131}$I as radioiodide. Consequently it was soon realized that $^{131}$I can be used to study abnormal thyroid metabolism in patients with goiter and hyperthyroidism. More specifically, in patients with thyroid cancer, distant metastases were identified by scanning the whole body with the Geiger counter. The names radioisotope scanning and atomic medicine were introduced to describe the medical field’s use of radioisotopes for the purpose of diagnosis and therapy. The era of nuclear medicine, as a diagnostic specialty began following the discovery of the gamma camera based on the principle of scintillation counting, first introduced by Hal Anger in 1958. Since then, nuclear medicine has dramatically changed our view of looking at disease by providing images of regional radiotracer distributions and biochemical functions. Over the last four decades, a number of radiopharmaceuticals have also been designed and developed to image the structure and function of many organs and tissues.

1.2 Molecular Medicine

At the present time, the precise definition of the disease is as difficult as defining what exactly life is. Defining disease at the cellular and molecular level, however, is much easier than defining disease at the level of an individual. Throughout the history of medicine, two main concepts of disease have been dominant (Wagner 1995b). The ontological concept views a disease as an
entity that is independent, self-sufficient, and runs a regular course with a natural history of its own. The physiological concept 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 that are as close as possible to that of a person of the same sex and age of the patient. 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. Approximately 56% of the adult human body is fluid. Most of the fluid is intracellular, however, one third is extra-cellular, which is, in constant motion throughout the body and contains the ions (sodium, chloride, and bicarbonate) and the nutrients (oxygen, glucose, fatty acids, and amino acids) needed by cells for the maintenance of life. Claude Bernard (1813–1878) described extracellular fluid as the internal environment of the body and hypothesized that the same biological processes that make life possible are also involved in disease. In other words, the laws of disease are the same as the laws of life. All the organs and tissues of the body perform functions that help maintain homeostasis. As long as the organs and tissues of the body perform functions that help maintain homeostasis, the cells of the body continue to live and function properly.

At birth, molecular blueprints collectively make up a person’s genome or genotype, which is 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 referred to as pleiotropism. Several 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 (Cotran 1999).

In 1839, Theodor Schwann discovered that all living organisms are made up of discrete cells. In 1858, Rudolph Virchow observed that a disease cannot be understood unless it is realized that the ultimate abnormality must lie in the cell (Virchow 1958). Virchow correlated disease with cellular abnormalities as revealed by chemical stains and, thus, founded the field of cellular pathology. He also aptly defined pathology as physiology with obstacles.

Most diseases begin with a cell injury that occurs if the cell is unable to maintain homeostasis. Since the time of Virchow, gross pathology and histopathology have been a foundation of the diagnostic process and the classification of diseases. Traditionally, the four aspects of a disease process that form the core of pathology are etiology, pathogenesis, morphologic changes, and clinical significance (McCance and Huether 1998). The altered cellular and tissue biology, and all forms of loss of function of tissues and organs, are, ultimately, the result of cell injury and cell death. Therefore, knowledge of the structural and functional reactions of cells and tissues to injurious agents, including genetic defects, is the key for understanding the disease process. Disease may be considered a genetic or environmental reprogramming of cells to gain or lose specific functions that are characteristic of disease. Currently, diseases are defined and interpreted in molecular terms and not just with general descriptions of altered structure.

Pathology is evolving into a bridging discipline that involves both basic science and clinical practice. More specifically, pathology is devoted to the study of the structural and functional changes in cells, tissues, and organs that underlie diseases (McCance and Huether 1998). Molecular, genetic, microbiologic, immunologic, and morphologic techniques are also helping us to understand both, the ontological and physiological causes of disease. In molecular medicine, normal and disease states are defined at the cellular and molecular levels (Wagner 2006). Therapeutic drugs are designed based on these definitions of disease are being used to treat diseases by correcting abnormal cellular or molecular processes.