Nuclear Medicine in Motion

As they left the Garden of Eden, Adam is reported to have told Eve: "We are living at a time of great change." Ever since then, it seems, human beings have experienced anxiety and tension directly related to the speed of the cultural, scientific, and political changes they experience. The field of nuclear medicine is in a period of rapid change, perhaps experiencing a crisis of identity. Some in the field are suffering from *tomographic shock*. For a long time, many people in nuclear medicine, and outside the field as well, have equated nuclear medicine with radioisotope scanning, which can be defined as the visualization of previously invisible internal organs by portrayal of the distribution of gamma-emitting radioactive tracers within the body. As ultrasonography, thermography, and finally computerized axial tomography developed, the nuclear medicine community awoke one morning to find that they were no longer running "the only game in town." They were confronted with the idea that they might not be able to continue growth rates of 15% or more per year, and they began to review their historical growth curves.

Perhaps more than other scientists, biologists are familiar with the sigmoid or S-shaped curves that describe the birth, growth, development, and death of many biological processes. Such curves can be seen in human activities of all sorts and are useful in planning. While it is difficult to predict accurately the rate of growth of human activities, it is at times possible and often exceedingly helpful to be able to predict when a human activity will move from a latent phase into a period of exponential growth and, perhaps even more important, to be able to detect the first signs of plateauing, cessation of growth, and decline. In interpreting growth curves, we must recognize at the outset that the sigmoid curve showing overall growth is the integrated sum of a family of smaller curves. Certain activities may plateau and decline, while overall growth continues at an exponential rate. It is necessary to differentiate the entire curve into its component parts. Let us consider an example. At Johns Hopkins Hospital, after a latent period of 4 years, the number of brain scans began to increase at an exponential rate in 1963 and continued this growth until 1972 when it plateaued, 3 years before the introduction of computerized axial tomography. In 1975–76, the number of brain scans decreased by 15% while the total number of imaging studies continued to increase at an exponential rate, as a result of a steady increase in the number of new procedures, particularly bone scans, but also liver, kidney, lung, and other studies.

Such data are essential in planning for the future, because we must make decisions now that will be of greatest importance in the future. Long-range planning is the making of decisions and carrying out of actions *today*, not simply trying to predict events that are likely to occur.

The difficulty in predicting what lies ahead can be illustrated from our experiences with lung and bone scanning. In 1960 we had no idea that lung and bone imaging would be invented. We didn't predict the development of these procedures as we indulged in "blue sky" forecasting of what was needed to help solve medical problems. As in the case of most innovations, lung and bone scanning developed in response to recognized needs, not in terms of solutions, but in terms of problems. In 1963 lung scanning developed in response to the need for a rapid diagnostic test to permit proper selection of patients for pulmonary embolectomy that was popular at that time; bone scanning developed in response to rising interest in cancer chemotherapy.

Pressures for change now occurring have the potential of revitalizing the field of nuclear medicine in a very beneficial way. In our hospital, this seems to be the case. Throughout history, human progress has required a crisis atmosphere to change the status quo, to shake the self-satisfied out of their complacency, and to stimulate innovations without which a field will decline. This phenomenon can be expressed as an aphorism: "No crisis, no progress."

Undoubtedly, social, economic, political, and cultural factors will play a major role in the future growth of nuclear medicine. For example, we may be approaching a plateau in the size of the health services' share of the gross national product. We may also be in the process of changing some of our values. Wilson has stated that the present medical system in the United States seems to be based to a large degree on

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the following assumptions: (A) The cure of disease is more important than the care of patients. (B) The medical and hospital administrative staffs call the tune as to which health care services are delivered. (C) Only experts can provide these services. (D) Every problem has a solution. (E) Death is the worst thing that can happen to a person. Some of these attitudes may soon change, and the changes are likely to affect nuclear medicine, some tending to increase, others to decrease growth rates.

The so-called "competing technologies" have already begun to affect nuclear medicine, particularly imaging techniques. Some have suggested that *imaging* departments should be established, so that all procedures involving diagnostic images could be centralized, compared, and controlled. In my opinion this would be a mistake. For a medical specialty to develop into a true scientific and clinical discipline, it must be concerned with measurement of function as well as visualization of structure. Historically, biomedical research has moved progressively from descriptive anatomy to a description of function. Clinically, continued dependence upon visualization of form and structure persists, but perhaps now is the time for a leap forward in our ability to visualize function, both global and regional. As Cooke has said: "A fundamental reorientation in approach must occur if the advantages of nuclear medicine are to be exploited. We must conceptualize abnormality rather than visualize it. We must reconstruct anatomy from our measurements of function—the converse of how our thought processes operated in the past."

The concept of motion is essential to physiology, indeed to life itself. Nuclear imaging techniques can provide a new way to perceive functional anatomy, to reveal patterns and changes in body constituents. A medical discipline based only on visualizing spatial patterns and ignoring temporal patterns is unlikely to be creative, because creativity is the reflection of movement. Nuclear medicine can portray both space and time in unique and exciting ways.

The pioneers of nuclear medicine, Georg von Hevesy, Joseph Hamilton, and others, emphasized the chemical and physiological nature of the field and thus extended or developed the concepts of the constancy of the internal environment and the dynamic state of body constituents. For the first time the study of the site of physiological processes became possible where previous studies had been limited to morphological information. The principle of the dynamic state of body constituents, first stated by Hevesy and expanded by Schonheimer and Rittenberg, could never have been discovered at the autopsy table or looking through a microscope, but required the invention of radioactive tracers. In 1942 Hamilton stated that "the discovery of artificial radioactivity and the development of the cyclotron have given the biologist the most useful tool since the discovery of the microscope." At that time, although radioiodine uptake of the thyroid was being measured, "images" had not yet been invented.

These were the forefathers of the modern "nuclear physician" who emphasized the physiological and biochemical information provided by nuclear medicine procedures, whether or not they were imaging procedures. To them, whole-body counting or radionuclide imaging were applications of the same principle, the only difference being the degree of spatial resolution needed to study a given physiological process. For years, we have stressed to students that when we look at a brain scan, we are not seeing the brain per se, but the distribution of the blood–brain barrier; when we look at a lung scan, we see the distribution of regional perfusion or ventilation; when we look at a liver scan, we are not looking at the liver, but at the distribution of phagocytic or hepatocellular function, and so on.

The invention of computerized transmission axial tomography is leading to a redefining of the scientific, clinical, and academic focus of nuclear medicine. As with other disciplines, nuclear medicine must constantly review its origins, accomplishments, limitations, and opportunities for future advances. The most fundamental principle of the field remains the tracer principle, for which Georg von Hevesy was awarded the Nobel Prize in 1944. Its application elucidated the principle of the dynamic state of body constituents, which in turn was translated into today's clinical nuclear medicine.

The direction that nuclear medicine is now taking is exemplified by cardiovascular nuclear medicine. Cardiologists have long been among the most physiologically oriented of all physicians, insisting on quantification and validation of the data whenever possible. The increasing use of computers in nuclear medicine has permitted us to meet their strict requirements for quantification of functional information, both regional and global, to help solve their patients' problems. One of the most striking new developments in cardiovascular nuclear medicine is imaging of the beating of the right and left ventricles by motion-picture display of the intraventricular distribution of technetium-99m albumin during 16 or more phases of the cardiac cycle. To be able to obtain noninvasively and with reasonable accuracy measurements of the pre-ejection period of the ventricle, the rates of filling and emptying of the ventricles, the ejection fraction, and the adequacy of regional wall motion are major accomplishments.

Stimulated by viewing ventricular function as a motion picture, we have begun to make other "fast motion" pictures of a whole variety of body functions, extending from the cerebral circulation to the study of the kidneys. In the future, motion pictures of regional function, displayed on a TV screen, will become commonplace in nuclear medicine. This new concept is, in a sense, a descendent of the previous concept of *functional imaging*, defined as a single image portraying data from a series of images obtained over a period of time. I now believe that data showing regional physiological processes should *not* always be compressed into a single image but should be compressed into a "fast motion" moving picture using fast framing rates when the images are viewed. At present we are compressing the data obtained over periods of minutes, hours, and days into 16 frames per second. These "compressed time images" are shown over and over on a color TV screen to improve our perception of regional dysfunction. We look for patterns in the spatial distribution of the radioactive tracers as well as changes in these spatial patterns. This is the essence of physiology.

In 1795 the German philosopher Hegel made a statement that was quite remarkable. He said that he didn't like to look at mountains because they were lifeless; he preferred the movement of waterfalls. I get the same feeling when I look at electron microscope pictures. The structural detail is exquisite, but something is lacking—the red blood cells don't move, gases can't be seen diffusing back and forth across the magnificently detailed membranes, the cilia of the bronchial tree are as motionless as the trees in a burned-out woods. We in nuclear medicine can use the photons available to us to examine both space and time. Rather than putting all our photons into a single high-spatial-resolution image, we spread them out over the time of the process under study, e.g., the slow metabolic activity of bone or the rapid emptying and filling of the heart.

One of the first lessons learned in using photons to provide diagnostic information is that you can't have everything. Since the number of photons (whether from an x-ray machine or an administered radiochemical) is limited by the unwanted biological effects of radiation, we must decide whether we need high spatial resolution, high temporal resolution, or some intermediate compromise. Diagnostic roentgenology is an anatomical science and is of greatest help to surgeons; nuclear medicine is based on chemistry and physiology and, properly used, can help not only the surgeon, but, perhaps even more, the pharmacologist, internist, pediatrician, and other physiologically oriented physicians.

Nuclear "imaging devices" permit us to measure regional as well as total organ function. This ability helps us to solve one of the most important problems in diagnostic medicine, biological variability. No two persons look alike, behave alike, or have identical values for physiologic parameters that we measure. How can we get around this problem of biological variability as we try to solve our patients' problems? One way is to use what I call the "homogeneity principle." It turns out that we can use the symmetry of paired organs, such as the kidneys or lungs, and the homogeneity of functions, such as cerebral blood flow and the phagocytic function of the liver, to detect regional abnormalities. For example, the earliest sign of renal disease is often revealed by one kidney's having significantly reduced function compared to the other, while overall renal function is still within the normal range of bilateral kidney function among other people. The study of functional homogeneity is implicit in nuclear medicine, but should perhaps be made more explicit. It can be stated: "Regional abnormalities can often be detected while the overall function of an organ remains within normal limits."

L. A. Appley has described four kinds of people in the world: those who make things happen; those to whom things happen; those who watch things happen; and those who don't even know that things are happening. If we in nuclear medicine wish to be in the first category, several things must be done now. We must (A) more clearly define our origins, accomplishments, and directions; (B) define the scientific, clinical, and academic focus of our discipline; (C) strengthen our organizational identity, calling ourselves nuclear physicians instead of radiologists, internists, or pathologists; (D) increase research support; (E) attract talented young people; (F) interact as equals with other scientific and clinical disciplines; (G) define our discipline to other professionals and the public; and (H) realize our full potential. Most of all, we need continued confidence and enthusiasm to continue our important contributions to health care and biomedical research. Unwarranted pessimism is a self-fulfilling prophecy.

A final word to those who still view nuclear medicine simply as a means to visualize organs not able to be seen by roentgenography and who are therefore frightened by the revolutionary developments in computerized axial tomography. Sometimes it takes a sock in the eye in order to be able to see stars.

Confucius has been quoted as saying that it is difficult to make predictions, especially about the future. Wouldn't it be very sad if nuclear medicine were to reach a turning point and not turn?

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