The Evolution of Nuclear Medicine


Frederick J. Bonte, MD

Many people in nuclear medicine believe that our discipline started with the Big Bang. Those were exciting times. In the beginning there was a soup of energy, out of which particles resolved, including quarks, baryons, leptons, hadrons and, of course, positrons—and no government to regulate them. Out this swirl of matter, mankind evolved, and out of mankind evolved that unique breed, the scientist. The eighteenth and nineteenth centuries saw the appearance of the scientific method of investigation, which as far as nuclear physicians are concerned, culminated in the experiments of Wilhelm Conrad Roentgen. This year marks the 100th anniversary of the discovery of radiation and next year is the 100th anniversary of the beginning of nuclear medicine.

Early Uses of Radiation

On November 8, 1895, Roentgen, using a Hittorf tube, identified the existence of a powerful radiation, which he called x-rays. He found that hidden parts of the human body, such as the bones of the hand, could be photographed in all of their structural detail. Roentgen issued his first report on December 28, 1895, and gave a paper on January 23, 1896, to the Wuerzburg Physico-Medical Society, during which he made an x-ray film of the program chairman's hand by way of demonstration. Never has a scientific discovery been so immediately and widely accepted and used. Otto Glasser, the physicist-historian, tells us that during 1896 more than 1000 papers were published on the subject of x-ray; he further notes that Thomas Edison developed the fluoroscope within the same year from principles laid down by Roentgen in his original paper. For his achievement, Roentgen received the first Nobel Prize in Physics in 1901.

During 1896, Antoine Henri Becquerel identified rays, similar to those discovered by Roentgen, which were emitted from a sample of uranium ore. It was at this time that nuclear medicine had its first stirrings. In 1898, Pierre and Marie Curie looked for the source of these emanations and found that they were the property of the unstable chemical elements radium and polonium. They named this property radioactivity, and for this work they shared the Nobel Prize with Becquerel. Within a few years Lord Rutherford began to characterize radiation from naturally occurring elements, identifying alpha particles and beta rays, while Villard identified the x-ray-like radiation as gamma rays.

The Rise of Nuclear Medicine

From Rutherford's laboratory in Manchester, England, came the patron saint of nuclear medicine, the physicist-chemist Georg de Hevesy. De Hevesy was born in Hungary and educated in a number of physics laboratories, including Rutherford's institution in Manchester. Rutherford assigned de Hevesy the problem of separating what were regarded as radium isotopes and prepared him for one of the great events of history, which featured the Manchester landlady and the hash that changed the world.

On his arrival at his new assignment, de Hevesy found a room in a boarding house where the landlady served a grand roast for dinner each Sunday. Since the roast was never entirely consumed, de Hevesy suspected, that it turned up again in the hash served on Wednesday. When de Hevesy questioned the landlady on the subject, she vigorously denied recycling Sunday dinner. To find out for certain, de Hevesy brought home a tiny sample of a radium isotope, which he sprinkled on a bit of meat that he left on his plate on the following Sunday. On Wednesday, when the landlady marched majestically into the dining room bearing a large pot of hash, de Hevesy appeared at the other doorway with a charged electroscope. Placing the instrument dramatically over the hash, de Hevesy and the astonished landlady saw the leaves collapse, identifying the hash as radioactive. This established once and for all, not only the landlady's cupidity, but the tracer principle.

De Hevesy was later to use this principle in studying the passage of a radioisotope of lead from the soil through a plant's roots, stem and leaves. Following the creation of artificial radionuclides in the early 1930s, he used ^{32}P to study phosphorus metabolism in living organisms. For his ingenious invention, the radiotracer method, de Hevesy received the Nobel Prize in 1943.

Lesser known scientists contributed to the evolution of nuclear medicine: In 1927 the imaginative Herman Blumgart used de Hevesy's tracer method to measure a dynamic function in a living human subject. He injected what is euphemistically described as "a small amount of radium salt" into a vein in the subject's left arm and timed its arrival in the right arm with a Wilson cloud chamber. This was but one of a number of striking experiments performed by this sometimes forgotten but most original pioneer.

Radionuclide Production Boom

Tracer research was given formidable impetus with the construction of cyclotrons at the University of California in the 1930s by Lawrence and his colleagues. They created many families of radionuclides, the properties of which permitted investigators to begin to identify the chemical processes that run biological systems. By the 1940s, radioisotopes of iodine and phosphorus were used not only for diagnostic purposes but for therapeutic purposes as well. The development of reactors during World War II opened the world of radionuclide production, further spurring the introduction of tracer research into medicine.

Several landmark accomplishments helped launch the medical discipline of nuclear medicine. Consider the development of photon imaging by Benedict Cassen and Hal Anger and positron imaging by investigators such as Brownell, Anger and Ter Pogossian. The basic concepts of three-dimensional biological imaging were laid down by Kuhl and Oldendorf. One of its ultimate refinements, the imaging of brain receptor system chemistry, was developed by Wagner and his associates, and the mapping of the circuitry of the brain itself was initiated by Raichle, Fox and Frackowiak.

Another notable example of the tracer principle in action was the development of radioimmunoassay by Rosalyn Yalow and Solomon Berson, for which Yalow received the Nobel Prize. Many other discoveries, great and small, defined the field of nuclear medicine and continue to advance its applications. They have been chronicled by historians such as Glasser, Eisenberg, Grigg, Myers, Croll, and Brucer and Buntaine.

Future Directions

Since the trail of nuclear medicine is marked by the award of Nobel Prizes to investigators who forged the directions of scientific biomedical research, I consulted several laureates as oracles of what is to come. At the University of Texas Southwestern Medical Center, we have four laureates: Michael Brown, Joseph Goldstein, Johann Deisenhofer and, most recently, Alfred Gilman. Their collective opinions about the most important work to be done in biomedical research in the coming century are divided equally between characterization of the human genome, to be followed by the diagnosis and treatment of all genetic diseases, and of equal importance, the mapping and characterization of the human brain, so that mankind may at last understand how the mind works.

The research supporting the annual award of the Nobel Prize in Physiology or Medicine, or in Chemistry, is almost invariably based, in some measure, upon de Hevesy's radiotracer technique. It is fundamental to more than 80% of the funded research at our institution, as at most others.

Lastly, I consulted nuclear medicine's own oracle, Dr. Yalow, whose concern was not for what might comprise key research in the future, but the public's attitude toward radiation and the risk inherent in it. Misperception of this risk can bring work of decisive value to a halt, as has already happened in several institutions. Dr. Yalow believes that there is no substitute for a knowledgeable public as an ally in scientific progress.

Withal, this progress in biomedical science will be achieved largely with the help of the de Hevesy radiotracer method, opening the door to nuclear medicine for the development of new diagnostic and therapeutic procedures based on the new knowledge. The future of nuclear medicine could be bright indeed.

Frederick J. Bonte, MD

Dr. Bonte is the director of nuclear medicine at the University of Texas Southwestern Medical Center at Dallas. He presented this commentary as the Radiology Centennial Hartman Lecture at the 1995 Annual Meeting of the Society of Nuclear Medicine. He dedicated the lecture to the memory of Glen W. Hartman, MD.

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