

ATOMIC ENERGY IN MEDICINE

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The atomic bomb has demonstrated to the world in a dramatic fashion that great energies are stored up in atoms and that these energies can be liberated in many forms, such as mechanical, heat, light, ultra-violet radiation, roentgen rays, gamma rays, neutrons, and other sub-atomic particles. The demonstration of this destructive weapon has kindled in men the desire to use these energies for peaceful pursuits. Among these men the physician ranks first. He believes that the release of controlled atomic energy,¹ notably in the form of radiation, will widen his knowledge of the value of various types of radiant energy in diagnostic and therapeutic procedures.

Although many voices state that a new era, which should be measured in terms of atomic years, began with the year of the destruction of Nagasaki and Hiroshima, the physician knows that the science of atomic physics extends over the last fifty years and that the fundamental principle of atomic fission in particular, upon which the atomic bomb is based, was known before the start of the second World War. The technologic advance in the development of this principle to the point of controlled release of vast amounts of atomic energy is an important accomplishment. It has led to the production of large amounts and a great variety of radioactive materials. But at present only relatively few new radioactive substances or isotopes, such as radio-sodium, radio-carbon, radio-phosphorus, or radio-iodine, are available to the medical profession; they are used for so-called tracer studies as well as treatment purposes. Methods of dosage of such substances are to a large extent still experimental. Procedures for protection against the undesirable effect of such isotopes are known to but relatively few experts, although as a whole these methods are based mainly upon principles worked out in the past by radiologists.² A serious word of warning must be sounded against both careless use of any radioactive material and over-enthusiastic hopes regarding the possible cure of numerous diseases by their use. Only experience accumulated in fifty years of atomic physics combined with knowledge gathered from new improvements in the use of atomic energy and its by-products will lead toward a further successful attack on many obscure problems.

For twenty-five years the Research Division of Cleveland Clinic has been actively interested in studies on the use of various types of radiation in medicine. In 1933 this division collected material on the subject and

edited a book, *The Science of Radiology*,³ which presented a comprehensive picture of the status of atomic energies known at that time. Ten years later the division again collaborated on the publication of two additional books, *Medical Physics*⁴ and *Physical Foundations of Radiology*,² which brought up to date the picture of the use of atomic energy in medicine and illustrated the rapidly growing importance of this branch of science. A chapter on historic milestones in the fifty years of atomic energy was published in the latter book. That chapter, somewhat enlarged to include developments of the last three years, is presented here in order to familiarize the reader with the historic sequence of events. To many of these notations have been appended additional "Notes, 1946" in an attempt to evaluate past discoveries in the light of the 1946 knowledge of atomic energy.

- 1895 (November) W. C. Röntgen (Germany) discovered *x-rays* with a Hittorf-Crookes vacuum tube.
- 1896 (November) J. Perrin (France) measured by means of an air condenser the loss of electric charge caused by ionization produced by *x-rays*.
- 1896 A. H. Becquerel (France) presented the results of his discovery of radioactive radiations emitted by uranium compounds. *Radioactivity*.
- 1897 J. J. Thomson (England) studied deflection of cathode rays by a magnet and came to the conclusion that these rays are streams of discrete particles of negative electricity, considerably smaller than atoms. He applied the name *electrons* to these particles.
- 1897 E. Rutherford (England) examined Becquerel's radioactive radiations and found them to be composed of two types which he called *alpha* and *beta rays*. Later he found that alpha particles consist of nuclei of helium and beta rays of the electrons discovered by Thomson.
- 1898 Marie and Pierre Curie (France) announced the discovery of *polonium* in July and *radium* in December.
- 1898 P. Villard (France) discovered *gamma rays* of radium and found them to be of the same character as *x-rays*.
- 1901 M. Planck (Germany) proposed the *quantum theory*, according to which radiant energy is emitted or absorbed in discontinuous steps or quanta.
- 1905 A. Einstein (Germany) proposed that mass and energy are related by the equation $E=mc^2$, in which E signifies energy, m mass, and c the velocity of light, or 3×10^{10} cm. per second. (Note, 1946:

This famous equation has become of the greatest significance in the calculation of energies available in atomic energy releases. For example: What is the force that holds the helium nucleus together? The basic mass unit of each of the two protons in the nucleus is 1.00758, and of each of the two neutrons, 1.00893. Thus the total mass unit of the nucleus is 4.03302. But the real weight found in the atomic table is only 4.0028, which means that there is a difference of 0.0302. This difference in mass represents the binding energy holding the nucleus together. According to Einstein's formula it amounts to 28 million electron volts.)

- 1906 H. Geiger (Germany) with Rutherford (England) developed an instrument to detect and count alpha particles. He later improved this counter, at times assisted by Mueller, until it became a most sensitive device for the detection and measurement of many types of radiations. (Note, 1946: The technologic application of the *Geiger counter* in the atomic project program has brought this most valuable tool to the attention of wide scientific and lay circles with the result that it is often considered a new instrument. Actually it had been used successfully in scientific laboratories ^{2,5} for many years prior to this project.)
- 1908 P. Villard (France) proposed a dosage unit based upon ionization of air by roentgen rays.
- 1909 R. A. Millikan (U.S.A.) measured the electric charge of the electron.
- 1910 F. Soddy (England) suggested the existence of atoms with different atomic mass but identical chemical properties; such atoms would be called *isotopes* (same place).
- 1911 E. Rutherford (England) proposed an atomic theory according to which the mass and positive charge of the atom was concentrated in its nucleus.
- 1911 C. G. Barkla (England), in studying scattered roentgen rays, deduced that a number of electrons must exist outside the atomic center.
- 1912 M. von Laue, W. Friedrich, and P. Knipping (Germany) discovered that roentgen rays can be diffracted by crystals and thereby proved that roentgen rays belong in the group of electromagnetic wave radiations.
- 1912 C. T. R. Wilson (England) reported on studies of fog tracks produced by various types of corpuscular or wave radiations in his cloud expansion chamber. (Note, 1946: The Wilson cloud chamber has become another invaluable tool in the hands of the atomic

- physicists, and fundamental new discoveries have been made with it.)
- 1913 N. Bohr (Denmark) suggested an *atom model* with a central nucleus and electrons moving in certain orbits around it.
 - 1913 V. L. Moseley (England) studied many roentgen ray spectra of elements and assigned a number to each atom on the basis of these studies. *Atomic number*. (Note, 1946: The atomic number starting with 1 for the lightest element, hydrogen, and rising in sequence to the heaviest "pre-atomic" element 92 for uranium has become of the utmost importance in classifying atoms and in describing their structure.)
 - 1913 Th. Christen (Switzerland) suggested the expression of roentgen ray qualities in half value layers.
 - 1913 W. D. Coolidge (U.S.A.) built the first successful roentgen ray tube with hot filament and tungsten target.
 - 1914 W. H. and W. L. Bragg (England) reported on their roentgen ray spectrometer with crystals as reflecting or refracting diffraction grating.
 - 1914 W. Duane (U.S.A.) presented an "E" unit, based upon ionization, as a measure for roentgen ray intensities.
 - 1914 B. Szilard (France) demonstrated a dosimeter for the measurement of roentgen ray intensity, calibrated in mega-mega-ions.
 - 1916 W. Friedrich (Germany) suggested the e unit, or electrostatic unit, as a dosage unit for roentgen rays.
 - 1919 E. Rutherford (England) bombarded nitrogen atoms with alpha particles and found that the nuclei of these atoms disintegrated, giving off hydrogen, while oxygen atoms were left. The particles given off were found to be positively charged, and Rutherford named them *protons*. Historically this was the first experiment in which one element was artificially transformed into another element, namely nitrogen into oxygen. (Note, 1946: Atomic transmutations, of which Rutherford's experiment was the first, can be expressed in equations similar to chemical equations. Rutherford's transmutation reads: ${}_7\text{N}^{14} + {}_2\text{He}^4 \rightarrow {}_8\text{O}^{17} + {}_1\text{H}^1$, the letters representing chemical symbols of nitrogen, helium, oxygen, and hydrogen, the subscripts representing the atomic number, and the superscripts the atomic weight.)
 - 1920 F. W. Aston (England) reported exact measurements of masses of many atoms obtained with the mass-spectrograph. He offered evidence that many elements consist of a mixture of isotopes,

therewith furnishing experimental evidence for Soddy's original suggestion in 1910 that such fractions of ordinary elements exist. (Note, 1946: The name isotope has become the most important term in the science of atomic energies. There are *stable isotopes* which, like most elements, do not change with time, and there are unstable or *radioactive isotopes* which undergo changes associated with emission of radioactive radiations. For example, carbon with atomic number 6 has five isotopes, namely carbon-10, carbon-11, carbon-12, carbon-13, and carbon-14. Carbon-12 and 13 are stable, the other three radioactive.)

- 1920 N. Bohr (Denmark) modified Rutherford's and his own original concept of the atom model, made in 1913, and assigned the electrons to orbits around the nucleus with certain levels of energy. The number of protons in the nucleus determined the number of electrons on orbits outside the nucleus and therewith the place of the atom in the periodic system of elements.
- 1922 A. H. Compton (U.S.A.) discovered the "Compton effect".
- 1925 L. DeBroglie (France) suggested that fast-travelling electrons are accompanied by a train of waves. C. J. Davisson and L. H. Germer (U.S.A.) stated that under certain circumstances beams of electrons behave as waves and not as particles.
- 1925 H. Fricke and Otto Glasser^{2,6} (U.S.A.) developed the thimble ionization chamber with "air wall".
- 1928 Otto Glasser, U. V. Portmann, and V. B. Seitz^{2,7} (U.S.A.) constructed the condenser dosimeter for the measurement of roentgen and radium radiations.
- 1930 W. Bothe and A. Becker (Germany) bombarded beryllium atoms with alpha rays from polonium and obtained carbon-13 and very penetrating rays with no electric charge which they thought to be gamma rays. (Note, 1946: This experiment written in an atomic equation reads: ${}_4\text{Be}^9 + {}_2\text{He}^4 \rightarrow {}_6\text{C}^{13} + \gamma$.)
- 1930 C. C. Lauritsen (U.S.A.) developed a supervoltage single section roentgen ray tube for atomic investigation.
- 1931 W. D. Coolidge (U.S.A.) built multisection "cascading" super-voltage roentgen ray tubes.
- 1931 E. O. Lawrence (U.S.A.) invented the *cyclotron*.⁸ In 1933, collaborating with M. S. Livingstone (U.S.A.), he built a cyclotron capable of producing five-million-volt deuterons. In further constructions sixteen-million-volt and then 100-million-volt deuterons were attained. (Note, 1946: A 200-million-volt deuteron cyclotron is scheduled to be in operation shortly.)

- 1932 H. C. Urey (U.S.A.) discovered heavy hydrogen, which he called *deuterium*. Its nucleus, *deuteron*, has mass 2 and consists, as was established later, of 1 proton and 1 neutron. This nucleus plays an important role as a bullet in atomic-smashing experiments.
- 1932 J. Chadwick (England) announced discovery of the *neutron*, a neutral nuclear particle of about the same mass as the positively charged proton. This experimental proof of the existence of the neutron confirmed speculations made by Rutherford in 1919. (Note, 1946: The formula for Chadwick's discovery is essentially the same as Bothe and Becker's formula, described previously under the year 1930: ${}_4\text{Be}^9 + {}_2\text{He}^4 \rightarrow {}_6\text{C}^{12} + {}_0\text{n}^1$, but it contains Chadwick's discovery of a new particle, the neutron, which in certain respects behaves like gamma rays. Bothe and Becker did not realize that they dealt with a new type of radiation in their experiment and they narrowly missed making the great discovery of the neutron.)
- 1932 W. Heisenberg (Germany) explained theoretically that the atomic nucleus consists of protons and neutrons.
- 1932 J. D. Cockroft and E. T. S. Walton (England) disintegrated lithium with 700 kv. protons and found that mass is converted into energy during the disintegration.
- 1932 D. H. Sloan and E. O. Lawrence² (U.S.A.) constructed a radio-frequency supervoltage roentgen ray generator. (Note, 1946: L. W. Alvarez is building a "linear accelerator" on this same principle, which promises to produce radiations of more than 300 million electron volts.)
- 1932 L. S. Taylor (U.S.A.) developed an American standard air ionization chamber to determine the value of the *roentgen*.
- 1933 R. J. Van de Graaff (U.S.A.) built electrostatic generators capable of producing voltages up to 10 million volts.
- 1933 C. D. Anderson (U.S.A.) discovered the *positron*, the electric counterpart of the electron.
- 1934 F. Joliot and Irene Joliot-Curie (France) produced *artificial radioactivity* by bombarding aluminum with alpha particles and observing that neutrons and positively charged particles were emitted from the aluminum during this process. (Note, 1946: The formula for this experiment is: ${}_{13}\text{Al}^{27} + {}_2\text{He}^4 \rightarrow {}_{15}\text{P}^{30} + {}_0\text{n}^1$. The produced isotope of phosphorus, being unstable, disintegrates into silicon accompanied by emission of positrons according to the formula: ${}_{15}\text{P}^{30} \rightarrow {}_{14}\text{Si}^{30} + {}_{+1}\text{e}^0$.)

- 1935 E. Fermi (Italy) bombarded uranium and other atoms with deuterons and neutrons and observed many phenomena of artificial transmutation and radioactivity. Shooting slow neutrons into uranium he produced new "trans-uranium" elements, notably one with the atomic number 93.
- 1936 J. H. Lawrence, R. E. Zirkle, and P. Aebersold (U.S.A.) found that neutrons have profound biologic effects.
- 1937 The Fifth International Congress of Radiology accepted the *roentgen* as an international dosage unit.
- 1939 The treatment of cancer patients with the neutron beam from a cyclotron was started by E. O. Lawrence and R. S. Stone (U.S.A.).
- 1939 O. Hahn and F. Strassman (Germany) bombarded uranium-235 with neutrons and demonstrated that it broke into two large fragments with atomic masses of about 142 and 91. L. Meitner and O. Frisch (Germany) reasoned theoretically that in this "fission" of uranium great amounts of energy are released. O. Frisch, F. Joliot, N. Bohr, J. R. Dunning, H. O. Nier, and others confirmed experimentally the prediction that uranium-235 can undergo fission.
- 1940 Two new elements were created from uranium by neutron bombardment; they are neptunium, atomic number 93, and plutonium, atomic number 94. (Note, 1946: The formulae for the production of these new elements are:

$${}_{92}\text{U}^{238} + {}_0\text{n}^1 \rightarrow {}_{92}\text{U}^{239} + \gamma \rightarrow {}_{93}\text{Np}^{239} + {}_{-1}\text{e}^0$$

$${}_{93}\text{Np}^{239} \rightarrow {}_{94}\text{Pu}^{239} + {}_{-1}\text{e}^0 + \gamma.$$
)
- 1940 Several hundred artificially created *radioactive isotopes*⁹ had been discovered. Some were used for treatment, others served as tracer substances to trace physiologic processes.
- 1940 D. W. Kerst (U.S.A.) constructed the *betatron*,¹⁰ with which electrons are accelerated to energies of 20 million electron volts by magnetic induction. (Note, 1946: A number of betatrons were constructed, the largest at present delivering electrons with energies up to 100 million electron volts. An improved betatron, called *synchrotron*, proposed by McMillan and promising energies up to 300 million electron volts, is under construction now.)
- 1942 (December 2) First self-maintaining nuclear chain reaction in an *uranium graphite pile* was initiated.
- 1945 Atomic bombs were exploded on July 16 in New Mexico, August 6 in Hiroshima, and August 11 in Nagasaki. Official report on *Atomic Energy for Military Purposes* was published.¹

- 1945 G. T. Seaborg (U.S.A.) announced discovery of elements americium, atomic number 95, and curium, atomic number 96.
- 1946 Headquarters, Manhattan Project, Washington,¹¹ announced the availability of a number of tracer and therapeutic radioisotopes to scientific laboratories. First shipment of fission products for scientific research was made from Oak Ridge, Tennessee.
- 1946 G. T. Seaborg (U.S.A.) announced the discovery of neptunium-237, a slow isotope of neptunium-239, discovered in 1940. Neptunium-237 is the fourth element in which atomic energy is released by nuclear fission; the other three are uranium-235, plutonium-239, and uranium-233.

To the medical profession, the great scientific events condensed in the preceding chronology of developments in atomic energy offer many new opportunities in the endeavor to fight disease. Developments of the last few years have considerably enhanced the scope of these possibilities.

Atomic energy as used in medicine may be divided into two parts, *electronics* and *nucleonics*. Electronics comprises that part which has to do with the electrons revolving around the nucleus of atoms. Most phenomena observed by the physician, such as chemical reactions, optical, electric, magnetic effects, have to do with these electrons. In the roentgen ray tube, electrons emitted from the cathode are accelerated by the applied high voltage and, when suddenly stopped at the target, are transformed into roentgen rays. When roentgen rays hit the fluoroscopic screen, the photographic film, or tissue, they first knock out electrons from the matter hit. These electrons are subsequently responsible for the reactions observed, such as fluorescence, darkening of the film, erythema, or other biologic reaction of tissues. Multimillion-volt Van de Graaff electrostatic generators, betatrons, or synchrotrons capable of producing high energy roentgen rays and electrons will enlarge the field of application of roentgen rays and lead to new observations in medical radiology. Other electronic devices in medicine consist of the application of improved amplifier circuits to such well known devices as the electrocardiograph, the electrostethoscope, and the electro-encephalograph. Improved photo-electric devices such as the multiplier photo-cell have greatly improved roentgen ray exposure meters, plethysmographs, and other devices. An ingenious use of steering devices for electrons has led to the development of electromagnetic lenses and condensers, which in their practical development have resulted in the construction of electron microscopes which have multiplied many times the amplification powers of standard microscopes. A whole new branch of science has been built upon this foundation, the science of electron optics.

The widespread application of electronics in medical instruments is being overshadowed at present by nucleonics. The reason for this lies in

the fact that the amount of energy stored up in the atomic nuclei is millions of times greater and has, therefore, if released, effects which supercede by far those produced by electronic energies. To a limited extent the radiologist has been familiar with the release of atomic energies, since he has used radioactive substances for decades and has known that they decay continuously and in doing so emit alpha, beta, and gamma rays. In decaying, a transmutation takes place. The fact that metallic radium element, for instance, decays into two gases, namely radon and a helium nucleus, has demonstrated that by atomic changes one element can be transformed into another of entirely different physical properties. Beta and gamma rays have long been used for therapeutic purposes. Radium dosages had to be measured properly and precaution taken for protection against undesired radiation effects upon patient and operator. In principle, established dosage units and terms such as the curie, the roentgen, and tolerance dose have been maintained in recent radioactive isotope work. Similarly, protection methods against undesirable radiations are like those used in pre-fission days, although the technologic improvements in ionization chambers and Geiger counters have been great.

However, the process of fission developed in atomic research of the last few years, in addition to radioactive decay and transmutation, has furnished the medical profession not only with new methods of producing radioactive substances but with a large variety of such substances of great intensities. Powerful uranium and plutonium piles in themselves produce numerous radioactive fission products, i.e. radioactive isotopes with atomic numbers near the middle of the periodic atomic table. Neutrons released in these piles, furthermore, can activate any materials placed into the pile. This artificial radioactivity may be used in various ways. One might, for instance, use penetrating radiations emitted from the pile for therapeutic purposes. Such a radiation beam might possibly be a neutron beam similar to that emitted from the cyclotron, and such a beam might activate chemicals introduced into certain parts of the body. Other elements made radioactive in the pile may subsequently be used as radiation sources for treatment similar to the technic employed in the radium pack. And finally, given atoms might be made radioactive and introduced into the body with the plan to have them absorbed selectively in organs or in tumors or any place where specific radiation doses could be applied at the desired site of the tissue. In the same way atoms could be made radioactive or they could be "tagged" to act as tracers in the human body. As long as they are active they could be traced throughout body fluids or tissues in a way rather similar to the tracing of a lost radium container by means of sensitive devices such as a Geiger counter. Long before the era of tracing radioactive isotopes through the body with Geiger counters, physicists have tracked

down lost radium through furnaces, ash cans, trucks, city dumps, and final resting places of cinders miles away from the furnace through which the radium tube passed.¹² Modern tracing hunts are very similar. They permit the investigator to follow certain given isotopes in a compound or a mixture through liquids, gases, or solids. Blood flow and blood volumes can thus easily be measured. Circulation and its impairments in peripheral vascular diseases can be studied with radioactive sodium and the extent of such diseases revealed. Similarly, the path of drugs, poisons, and anesthetics can be followed throughout the body to their elimination or final resting place. Radioactive dyes can easily be localized. Tracing radioactive iron or phosphorus in blood cells has revealed important information on their formation and life. Radioactive carbon has helped studies on basal metabolism, breaking down of food, of diabetes, tooth decay, and other bodily changes. Radioactive gases such as krypton have opened new roads to studies on respiration, vascular diseases, and arteriosclerosis.

Accumulation of such radioactive isotopes in certain locations has helped in the treatment of leukemias and polycythemia with radioactive phosphorus, of thyroid diseases with radioactive iodine, of arthritis with radioactive gold, and of cancers with radioactive strontium.

In conclusion, it may be stated that scientific research in releasing and controlling atomic energy and related problems has vastly enlarged the field of medical radiology and has presented medicine with a great number of new materials and new tools for use in medical research as well as for practical application in clinical problems.

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