RADIUM
THERAPY

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Its Physical Aspects and Extensions with Radioactive Isotopes

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SECOND EDITION

LONDON

BAILLIÈRE TINDALL AND COX

7 and 8 Henrietta Street, W.C.2

1956

RADIUM THERAPY—ITS PHYSICAL ASPECTS AND EXTENSIONS WITH RADIOACTIVE ISOTOPES

First Published 1945
(*Chapman & Hall Ltd.*)
Second Edition 1956

Foreword

DR. WILSON's book appeared in 1945, and now, eleven years later, this second edition is called for, not only by the natural development of radiotherapy, but equally by the development of hospital physics and the rapid increase in the number of hospital physicists engaged in it.

It is one of the great achievements in medicine that applied science should have been absorbed in the everyday practice of the doctor. In radium therapy, advances were made rapidly when the physicist gained access to the wards, the out-patients department and the operating theatre. From this partnership between the clinician and the scientist has emerged an accuracy of dosage, a precision in technique and an understanding of the inescapable relationship between treatment and the consequent biological effects. This book deals with the physical aspects of radium and radioistopes in therapy of cancer. By training or education and frequently by mental qualities, the physicist and the medical specialist have, of necessity, a different outlook on the same problem —the treatment of a patient. It is inevitable that much of what is clear to the physicist should remain obscure to the clinician. It is also true that the intricate problems of normal physiology and the aberrations caused by pathological processes should be outside the normal activities of the physicist. Once it is understood that the combined skill and specialised knowledge of both is essential, there no longer exists any rigidity or standardization of technique, or a reliance on a strictly mathematical conception of dosage. On the contrary, there results a collaboration which permits a rational application of principles to the individual needs of a given patient.

It is gratifying that in Great Britain there should have been such a rapid development of hospital physics with its own laboratories and workshops and autonomous departments. It is the recognition of the physicist as a "clinical" colleague which has transformed radiotherapy from a somewhat blind application of a patient to a piece of apparatus, into the flexible use of the apparatus as a therapeutic weapon, shaped to the individual needs of a patient. This welding of pathology, physics and therapy, made possible by the training of hospital physicists in the art of medical problems and the

similar training of doctors in the science of physics, has produced a happy partnership in "bio-physics." The intricate problems of a given tumour, its site, size, spread, structure and behaviour are brought into suitable focus, and thus dose-rate, total dose, overall length of treatment, and intermittency of application of radiation are no longer abstract problems, but vitally practical.

The various techniques of radium therapy are extended by the use of some radioistopes; these techniques are not static methods. There is a constant advance in apparatus used, in the methods employed and in the principles underlying the application of radiation. These advances are due in a great measure to the hospital physicist. The need for Dr. Wilson's book has increased since the publication of the first edition through the general increase in the use of radiotherapy and through the better training of the radiotherapist. The book is indispensable as a source of information to the student, and as a guide both to the radiotherapist and the hospital physicist.

The new edition will enlarge its scope of usefulness and is assured of a fully deserved popularity.

LONDON, *November* 1955 STANFORD CADE

Preface

ALMOST COINCIDENTLY with the appearance of the first edition of this book, events were occurring which have since led to considerable extensions and modifications of the therapeutic use of radioactive materials. The development of the atomic pile made available a great number and variety of radioactive isotopes. Some of these have such combinations of properties that they are being investigated and used as alternatives to radium and radon for therapeutic procedures requiring beta- or gamma-ray sources.

This does not mean that radium itself is being replaced entirely by the newer materials. It is agreed that there seems to be little point in a general replacement of well tried and most valuable radium needles and tubes by radioactive isotopes such as, say cobalt 60. It has meant, however, that in many ways we now have a greater flexibility of method in the clinical use of beta and gamma radiation. Projects which before the advent of radioisotopes might have been ruled out on account of expense, impracticability or safety, are often realised now relatively easily. In general, however, all such projects rest upon the firm base of past physical and clinical experience in radium therapy and are essentially a further development of this subject.

When a second edition of this book was contemplated it became obvious that the subject should now be treated in terms of the wider field indicated above. This necessitated a re-ordering of the original material and addition of new material and data so that ideas which were worked out with particular reference to radium might be expressed more generally in relation to the variety of radioactive materials now finding application. The extended title is thought to be an accurate description of the contents.

An essential characteristic of the types of therapy dealt with in the original book is that in all cases the radioactive sources are disposed in relation to the patient in a manner directly controlled by the therapist. Radioactive isotopes are now also being administered to patients either by injection or by mouth and in this form of radiation therapy a noteworthy fact is that once administered, the radioactive material is largely out of direct control by the therapist. This new edition does not deal at all with this latter form of therapy,

but concentrates, as did the first edition, upon therapy with controlled radioactive sources, these sources now being a selected variety of radioisotopes in addition to radium.

In the field of radium therapy itself a number of developments have occurred. In this country a national radium and radon service has been set up at the Radiochemical Centre, Amersham. After an interval of ten years there has been a resumption of International Radiological Congresses, the sixth being held in London in July, 1950, and the seventh in Copenhagen in July, 1953. These have brought modifications to our ideas of radiation dosage and of radiation protection which we have tried to embody in this new volume.

Radium therapy has also gained directly from atomic energy developments. A more intensive effort has been made in the production of instruments for the measurement of gamma-ray and beta-ray dose and the availability of large quantities of metallic uranium has led to its use as a highly efficient screening material in the design of radium and other beam units. Account is taken of this progress.

The first edition appears to have met the needs, as regards radium therapy physics, of the post-graduate student of radiology and to have provided a handy reference and data book for the practising radium therapist and the hospital physicist. I have tried to ensure that it still fulfils these functions in the wider field to be explored as a result of the advent of radio-isotopes, endeavouring to present the subject always with the patient in mind. The latter may account for certain deficiences from the viewpoint of the more academic reader but I hope it has led to a book more practically useful for all concerned with the application of radioactive materials to the treatment of disease.

In an attempt to increase the usefulness of the book additional appendixes have been included. For those appendixes that have been taken from the original publications which are referred to I am greatly indebted to both the authors and publishers who gave me permission so readily. I am equally indebted to the many authors of papers and publishers of journals, referred to in the text, who permitted me to use material which appears either as illustrations or tabulations of data. Mr. J. P. Nicholson very kindly assisted with the proof reading and I wish to take this opportunity of offering my thanks.

Finally, it gives me great pleasure to express my thanks to Baillière, Tindall and Cox Ltd., firstly for their willingness to produce this book and secondly for the most careful and courteous manner in which they have managed its production.

HENDON, *November* 1955. C. W. WILSON

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CHAPTER I

Radium—Its Properties and Medical Application

The Nature of Radium and its Radiations

A NUMBER of naturally occurring chemical elements, which are of high atomic weight and number, spontaneously change into other chemical elements possessing a different atomic number, and this change is accompanied by the emission of energy in the form of electromagnetic wave radiation together with corpuscular radiations. These elements are called radioactive and radium is one of them.

Chemically, radium reacts with other elements as a metal resembling barium, and it is usually used in medicine in the form of the compounds radium sulphate, radium chloride and radium bromide. The pure metal is not available, but the compounds behave with regard to their radioactive properties in the same way as does the element itself. It is the amount of radium element in a quantity of salt with which one is always concerned in medicine because it is this which gives rise to the radiations.

Radium is found in very small amounts in the black mineral pitchblende, which is chiefly uranium oxide. This is found mainly in Bohemia, Saxony, East Africa and Canada. Formerly most of the radium used derived from Katanga in the Belgian Congo, but in recent years the source discovered in the region of the Great Bear Lake in Canada has proved of some consequence and Canadian radium is now widely used.

Radium was first isolated from pitchblende by Madame Curie in 1898. The separation, which involves a large number of fractional crystallizations, is a costly and laborious process, since less than 1 g. of radium is present in a ton of even the richest mineral.

The radioactivity of radium and all other radioactive elements is independent of their physical state and of their chemical combination. Because of this, natural radioactivity was taken to be an atomic phenomenon peculiar to the atoms of these heavier elements.

For an appreciation of the principles of radioactive transformation it is necessary to discuss briefly present ideas concerning the structure of atoms. It is believed, in view of the evidence available,

that every atom consists of a central, positively charged, heavy nucleus which contains practically all the mass of the atom, around which a number of comparatively light *electrons* rotate in various orbits. Electrons are negatively charged particles which exist in various states of binding in the various atoms and in certain circumstances they may be removed from their atoms, as is the case in the cathode ray tube, the thermionic valve and photo-electric cell.

Since every atom is electrically neutral there is a sufficient number of electrons in each atom for their total negative charge to balance exactly the positive charge of the nucleus. The simplest atom is that of hydrogen, which has a single orbital electron so that its nucleus has a positive charge equal to that on the electron. The latter may be considered as a unit of electric charge. This hydrogen nucleus is known as a *proton*. Its mass is practically equal to that of the whole atom, which is unity (to a very close approximation) on the chemists' scale. The proton is therefore a heavy particle of unit atomic mass bearing unit positive charge.

Next in simplicity of structure is the atom of helium, which has two orbital electrons, so that its nucleus bears two positive units of charge. The mass of this nucleus, however, is four of the atomic units. In certain circumstances, as we shall see, the atom of helium may be obtained free of its outer electrons. It is then referred to as an *alpha particle*. An alpha particle is, therefore, a heavy particle of four units of atomic mass bearing two units of positive charge.

At one time it was considered that protons and alpha particles were the main building units from which all atomic nuclei are constructed but research carried out since 1930 has shown that an alpha particle is itself made up of two protons and two other particles, which have the same mass as a proton, but which are electrically neutral. These particles are known as *neutrons*, and it is now considered that every atomic nucleus is built of specific numbers of protons and neutrons.

A quantity that is used a great deal in the physics of radioactivity is the atomic number of an element. The atomic number of any element is the number of unit positive charges on the nuclei of the atoms of that element. Thus, for instance, the atomic number of hydrogen is 1, that of helium 2. It follows, naturally, that the atomic number is also equal to the number of extra-nuclear electrons in the individual atoms.

All the natural radioactive elements are of high atomic number and atomic weight, the values being 88 and 226 respectively in the

case of radium. The nuclei of these elements therefore consist of quite large numbers of protons and neutrons, and this complexity results in considerable instability. Because of this instability the elements undergo spontaneous disintegration in which an atom changes into a different atom which is less complex than its parent. These transmutations are accompanied by the emission of energy of one form or another. A series of such disintegrations may occur until a stable nuclear structure is reached.

The energy released in the process of such transmutation is emitted as radiation, which may be of three types. It may be emitted in the form of alpha rays, beta rays and gamma rays.

Alpha rays are alpha particles which are ejected from the nuclei of the disintegrating atoms with velocities of the order of one-twentieth of that of light (the velocity of light is 186,000 miles/sec.). Alpha rays are, therefore, really helium nuclei, a fact which has been confirmed by passing a spark discharge through a vacuous space into which alpha rays had been allowed to pass. The spectrum obtained from the discharge was that of helium.

In their passage through air or other gas alpha rays ionize the gas very intensely so that they quickly lose energy. The fastest alpha particles from radium travel up to 7 cm. in air, but are stopped by a few thicknesses of cigarette paper. Because of their small penetrating power alpha rays are of little therapeutic value.

A useful method of detecting alpha particles is by means of the fluorescence they produce on striking various minerals such as zinc sulphide. If the alpha particles are sufficiently few it is possible to observe individual impacts of alpha particles on the fluorescent materials by means of a low power microscope. It is possible to count alpha particles by means of such scintillations. Another useful method for the detection of these particles is by means of their photographic effect.

Beta rays are electrons which are emitted from the disintegrating nuclei with various velocities. The slowest (soft beta rays) have a velocity of about one-sixth of that light, while the speed of the fastest (hard beta rays) is only slightly less than that of light. The beta rays are identical in character with the cathode rays which produce X-rays in the sense that they are high-speed electrons. Since their mass is only one-eighteen-hundredth of the mass of an alpha particle, beta rays have a penetrating power about 100 times greater than that of alpha rays, and the fastest can pass through 1 cm. of aluminium and an even greater thickness of tissue. For this reason beta rays are sometimes used in the treatment of superficial

lesions, the radium source being lightly screened to permit the passage of these rays. Such use, however, is strictly limited.

Like alpha rays, beta rays affect a photographic plate and ionize gases. The intensity of ionization, however, is much less for beta rays than for alpha rays. Since alpha rays and beta rays are electrically charged, they can both be deflected by a magnetic field, the alpha rays being bent in a direction opposite to that of the beta rays.

Gamma rays are different from alpha rays and beta rays in that they are undeflected in a magnetic field. They are a true electromagnetic radiation similar in nature to visible light and X-rays, and they travel with the same velocity. The gamma rays which derive from radium and its products consist of radiations having a wide range of penetrating power. The most penetrating or hardest of the gamma rays are able to pass through 15 cm. of lead, having a very short wave-length.

It is with the gamma rays that modern radium therapy is primarily concerned, and it is upon these that we shall chiefly fix our attention throughout this book. In their passage through matter the gamma rays interact with the electrons of the atoms, the interaction giving rise to high-speed electrons, which are called secondary corpuscular radiation. It is this secondary corpuscular radiation which is responsible for the effects produced by the radiation such as ionization in gases and the biological effect in tissues. Gamma rays may, therefore, be used as an agent to convey energy to deep-seated tissues, where this energy is transformed into a biologically active radiation.

Natural Radioactive Series

Radium is a member of a series of naturally radioactive elements. It derives from the successive transformation of parent substances, and, as a result of its own decay, is itself a parent to a number of radioactive substances. There are three main natural radioactive series: the uranium, actinium and thorium series. Radium belongs to the first of these series, which is the only one used in practical radiotherapy. The members of this series are listed in order of their sequence in Table 1, together with the radiations emitted at each transformation, the rates of decay and the amounts of each in equilibrium with 1 g. of radium.

It will be seen from Table 1 that the radium first transforms into radon, which is a gas, by the emission of an alpha particle. The radon atoms emit alpha particles and thereby are transformed into radium A, which is a solid. Radium A in turn emits alpha particles to produce

radium B, another solid. Radium B transforms into the solid, radium C, with the emission of beta rays and weak gamma radiation. Radium C changes into another solid, radium D, with the emission of alpha particles, beta rays and a strong gamma radiation. These transformations take place within a relatively short space of time. Those which follow (*see* Table 1) take much longer and give rise to little gamma

Table 1. Elements of the Uranium Series (Eddy & Oddie[1])

Element	Atomic weight	Atomic number	Particle emitted	Gamma rays	Rate of decay	Amount in equilibrium with 1 g. of radium
Uranium I	238	92	α	—	0·000000015% per year	2,830 kg.
Uranium X	234	90	β	Weak	3·3% per day	0.04 mg.
Uranium X_2	234	91	β	Weak	1·0% per sec.	0·0013 μg.
Uranium II	234	92	α	—	0·0003% per yr.	1·18 kg.
Ionium	230	90	α	—	0·001% per yr.	41 g.
Radium	226	88	α	—	0·044% per yr.	1 g.
Radon	222	86	α	—	0·75% per hr.	0·25 μg.
Radium A	218	84	α	—	0·38% per sec.	0·0034 μg.
Radium B	214	82	β	Weak	2·6% per min.	0·030 μg.
Radium C	214	83	β	Strong	3·5% per min.	0·022 μg.
Radium C′	214	84	α	—	Very fast	Very small
Radium D	210	82	β	Weak	4·3% per yr.	9·8 mg.
Radium E	210	83	β	Weak	0·60% per hr.	8·1 μg.
Polonium	210	84	α	—	0·51% per day	0·22 mg.
Lead	206	82		—	Stable	

radiation, so they are of little consequence to gamma-ray therapy. The various solids which derive from the decay of the gas radon are usually referred to as the active deposit of radon.

We see that gamma rays are not emitted in the disintegration of radium itself; they are only emitted by the solids radium B and radium C, which are formed as a result of the decay of radium. These solids really derive from the gas radon, which is produced by the disintegration of radium. Thus, if a radium source is to reach its condition of maximum gamma-ray activity, it must be hermetically sealed to prevent the loss of radon. Further, the gas radon, so far as gamma radiation is concerned, may be looked upon as the "radiation essence" of radium. This fact is made much use of in radium therapy for, as we shall see, it enables one to use a source of radon in cases where it is undesirable to use a source containing radium element.

When radium is sealed in a container such as a needle so that none of its subsequent products can become dispersed, a state of affairs is reached, after a suitable interval of time, when the rate at which a disintegration product is formed is equal to the rate at

which it decays. This state of affairs, when there will be fixed amounts of each of the disintegration products present, is termed *radioactive equilibrium*. Thus when equilibrium is established in a radium needle, the radium C, which is the important source of gamma rays, has reached its maximum value. About one two-thousandth of the radium atoms in the needle per year pass through the series of transformation products. Thus the available energy in the needle is dissipated at the rate of one two-thousandth per year, and the intensity of the radiation also decreases at this practically negligible rate.

When freshly prepared radium is sealed in a needle some time is required for the disintegration products to accumulate and reach radioactive equilibrium. Hence the gamma-ray emission of a new tube may be quite small, but gradually increases with time, reaching within one-thousandth of its equilibrium strength in about thirty-five days after sealing.

Isotopes

An examination of Table 1 shows that some of the elements of the series have identical atomic numbers but their atoms have different atomic weights. Thus, for example, radium A, radium C′ and polonium all have an atomic number of 84. Their respective atomic weights, however, are 218, 214 and 210. Similarly, radium B, radium D and lead all have an atomic number of 82 but atomic weights of 214, 210 and 206 respectively. This phenomenon, which is also found among the better known stable elements, is described by saying that radium A, radium C′ and polonium are isotopes of a common element of atomic number 84. Similarly radium B, radium D and lead are isotopes of the element of atomic number 82.

A considerable number of the stable elements have been shown to consist of mixtures of isotopes. The gas chlorine, for example, which has an atomic number of 17, is made up of two isotopes, of masses 36 and 37 respectively. The metal molybdenum, of atomic number 42, consists of seven isotopes of masses 92, 94, 95, 96, 97, 98 and 100. Many other examples could be quoted. Even hydrogen consists of two isotopes of masses 1 and 2. Only a very small proportion consists of the heavier isotope which is known as heavy hydrogen. Water, in which the hydrogen is heavy hydrogen, is known as heavy water.

By bombarding stable elements with accelerated hydrogen and heavy hydrogen nuclei, or with alpha particles and more especially with beams of neutrons, it is possible to transmute elements by

changing the atomic mass and number of the bombarded elements. In this way a very large number of previously unknown isotopes of the various elements have been produced. Many of these are radioactive. In other words, it is possible by these means, to produce artificial radioactivity or radioactive isotopes.

The development of atomic energy and especially the atomic pile has made it possible easily to irradiate stable elements with neutrons at high intensity so that quite large quantities of many radioactive isotopes are available. As will be seen later, some of these have such properties that they may be used for radiotherapy.

In order to designate more clearly which isotope is being referred to it is customary to add the mass as an index number to the chemical symbol or name. Thus, phosphorus 32 or P^{32} is written for the radioactive isotope of phosphorus of mass 32. Similarly Na^{24} or sodium 24 is written for the radiosodium isotope of mass 24 and so on.

Growth and Decay of Radioactive Elements

In general, any radioactive substance decays at a fixed rate, which is characteristic of the substance. The decay follows an exponential

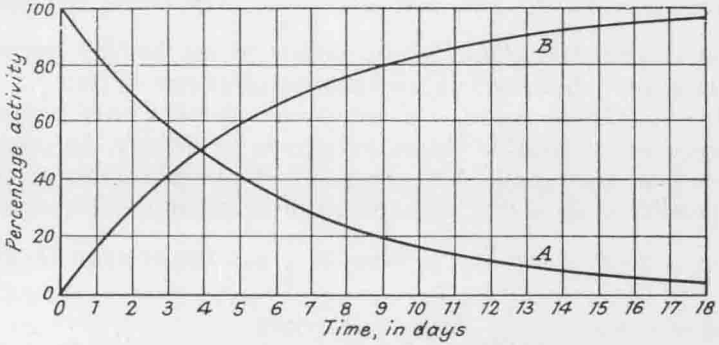

FIG. 1. Curves showing the growth (B) and decay (A) of radon.

law, that is, if within a certain time half the number of atoms of a particular substance have disintegrated, then in a following equal time half of the remainder will disintegrate, and so on. This law is indicated more clearly in the curve A of Fig. 1, which illustrates the decay of radon.

The exponential law of disintegration may be expressed mathematically by the equation:

$$N = N_o e^{-\lambda t} \quad . \quad . \quad . \quad . \quad (1)$$

where N_o is the original number of atoms, N is the number remaining after a time t, e is the base of Naperian logarithms (= 2·718)

and λ is a constant for the particular substance being considered, which is known as the transformation constant. This constant has different values for different substances and is a measure of the fractional decay per unit time.

The growth of a new substance as the result of the decay of its parent is expressed by the equation:

$$N = N_o (1 - e^{-\lambda t}) \quad . \quad . \quad . \quad (2)$$

where N_o now is the maximum number of atoms that is finally attained and N is the number after a time t. The curve of growth for radon is given as curve B of Fig. 1, from which it may be seen that the radon produced by its parent radium is approaching its maximum amount after a period of about eighteen days or more. The transformation or decay constant λ of radon is 0·181 per day.

The time required for one-half of the atoms of a radioactive substance to have undergone disintegration is known as the *half-life period* of the substance. It may be shown that the half-life period, which we shall call T, is related to the transformation constant of the substance by the equation $T = \frac{0{\cdot}693}{\lambda}$. For radon the half-life period is 3·82 days. Usually one prefers to use half-life period of a radioactive substance as a specification of its rate of decay.

The individual atoms of a radioactive element have periods of existence of all possible values from zero to infinity. In practice, however, we may speak of the *average life* of a large number of atoms. It is possible to show that the average life of the atoms of a substance having a decay constant λ is equal to $\frac{1}{\lambda}$, *e.g.* the average life of the atoms of radon $= \frac{1}{0{\cdot}181}$ days $= 5{\cdot}52$ days.

The element gold has an artificially produced radioactive isotope gold 198 (Au^{198}) which emits beta and gamma rays and has a half-life of a similar magnitude to that of radon, *viz.* 2·69 days. The decay constant for this radio-element is 0·258 per day and the average life of the atoms of Au^{198} is $\frac{1}{0{\cdot}258}$ days or 3·88 days. This isotope is referred to in more detail in Chapter II.

Radon and Its Measurement—The Curie

Radon, the substance immediately produced by the transformation of radium, is a heavy, colourless, inert gas belonging to the