A MANUAL OF ARTIFICIAL RADIOISOTOPE THERAPY

Edited by

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PREFACE

The use of artificially produced radioactive isotopes in therapy of human disease dates back only a little over ten years. Until four years ago the supply of these materials was limited largely by the combined capacities of the cyclotrons in existence as well as by the nuclear reactions capable of being effected by that instrument. Yields were relatively low, and as a result few investigators obtained access to isotopes for clinical study. Those employed were chiefly P^{32} and I^{130} or I^{131}, the diseases treated being the leukemias, Hodgkin's disease, polycythemia vera, hyperthyroidism and thyroid tumors. This picture was potentially greatly altered by the advent of the chain reacting uranium pile. Many isotopes became available in many thousand times the previous quantities. Many new ones were produced either as a result of nuclear fission or by bombardment of thermal neutrons. In spite of this short time span many advances have been made in the application of therapeutic isotopes and the uses are multiplying at a rate limited only by the ingenuity of the investigators.

Restriction of isotopes to investigators experienced in handling these materials has undoubtedly slowed up their more universal acceptance and use, but allocation is gradually being placed on broader bases. It is with the wider therapeutic use of radioisotopes in mind that this manual has been prepared. Its purpose is to provide a conveniently available source of practical information to the radiologist, physician, radiobiologist and biophysicist and others interested in the isotope field. It is hoped the manual will help bridge the gap between the exploratory phases of isotope study and the conventional approaches to radiation therapy.

The radiologist should play an increasingly important role in the exploitation of the artificial radioactive materials. In the past there have been too few who had or were willing to acquire the necessary knowledge of the fundamentals of nuclear physics to do this. Instruction in the latter field should begin at the medical school level and be augmented in the residencies. If this is not done radiation therapy may become increasingly a part of the disciplines of internal medicine and surgery.

The new era of therapy opened up by application of radioisotopes requires medical and scientific teamwork of a degree which typifies the rapidly expanding field of radiation biology in general. It is to be hoped that through such cooperative efforts the field of radiation therapy will gradually become less of an art and more of a science.

P. F. HAHN

Nashville, Tennessee
December, 1950

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CHAPTER I

Introduction to Radiation Therapeutic Problems

BY ANDREW H. DOWDY, M.D.

INTRODUCTION TO RADIATION THERAPEUTIC PROBLEMS

The objective of radiation therapy is to bring about, or to assist in bringing about, a restoration of the normal physiological functions of an organ or organs for the benefit of the organism as a whole. This may require that we deliver amounts of radiation sufficient to depress markedly or to destroy hyperfunctional tissue. In the successful treatment of cancer by radiation, the objective is to destroy the cancer cells completely without doing irreparable damage to the surrounding normal tissue. Although radiation therapy and/or surgery all too often fail to be curative in many advanced cases, both types of therapy are extremely helpful as palliative agents in such instances when properly employed.

In a discussion of radiation therapy it becomes necessary to define the term "radiation." Radiation as employed here is confined to those particulate and nonparticulate emanations which have the ability to ionize tissue directly and to those which have the ability on interaction with tissue to displace from the atom, molecule, or compound, charged particles which in turn are able to ionize the tissues through which they pass.

Not infrequently these radiations are spoken of collectively as ionizing and penetrating radiations. Regardless of whether the primary beam of radiation, particulate or nonparticulate, is composed of x rays, gamma rays, electrons, neutrons, or emanations from a radioactive isotope, the resulting ionizations which take place in the tissues are the direct results of the presence of minute particles of matter having mass and carrying at least one net negative or positive electrical charge. These particles may be alpha particles, beta particles (negative electrons), positrons (positive electrons), protons, deuterons, or fission fragments.

For therapeutic purposes we have at hand a rather wide selection of penetrating and ionizing radiations. Some, such as roentgen rays, neutrons, and deuterons, are best suited to external or intracavitary applications. Perhaps in the near future, electron and proton beams may be available for this type of utilization. Gamma rays from radium and cobalt are most useful in specialized instances requiring the intracavitary or interstitial application of intensive radiation to localized areas.* Radioactive isotopes of suitable half-

*It seems probable that current technical developments will make cobalt available as a valuable high energy source for external radiation.

life are available for the technique of applying ionizing radiation systemically and interstitially.

So far as is known, the radiation energy which is transferred to the tissue by virtue of ionization initiates a destructive process. Any reaction simulating stimulation is a result of compensatory responses on the part of the uninjured or less injured cells toward the taking over of the functions of the destroyed tissue. The destructive changes brought about by the various radiations are qualitatively similar but may differ quantitatively.

All living tissues in animals and plants are subject to damage from radiation if the total dose is sufficient. Radiation sensitivity is consequently a relative term. Some normal tissues are more susceptible than others and are damaged by smaller doses. Bone is considered to be very resistant, whereas the gonads are extremely sensitive to radiation effects. It is possible, of course, to render resistant tissues vulnerable indirectly by means of radiation injury to an intermediate tissue. Bone may thus become more radiation-sensitive following radiation injury to its blood supply.

Many factors, some of which are little understood, are operative in determining the degree of sensitivity of any cell or group of cells. These factors include the function of the cell or tissue, its life cycle, metabolic rate, enzyme system, blood supply (oxygen content), relative state of vigor, presence or absence of infection, rate of growth, total dose of radiation, and dose-time relationships.

The universal susceptibility of biological tissue poses one of the many problems confronting the radiation therapist. The problem is of particular importance in the treatment of cancer where of necessity the total dose of radiation is large. We may state for practical purposes that it is impossible to eradicate a cancer completely without injuring at least to a limited degree the adjacent normal tissue. However, it is possible in many instances to eradicate certain cancers with a minimal or scarcely detectable amount of damage to the healthy tissue and to have the patient continue to live a comfortable, unrestricted existence in so far as the previous cancer or the results of its therapy are concerned.

It must not be inferred that the universal susceptibility of biological tissue to radiation precludes the successful treatment of cancers, although it is frequently a very serious limiting factor. Neither must the converse be concluded with respect to the so-called radiation-sensitive tumors. Radiation sensitivity of a tumor is by no means synonymous with radiation curability. For example, the tumors of Hodgkin's disease and lymphosarcoma are radiation-sensitive. In their generalized form they involve such extensive body areas that the human organism as a unit cannot tolerate a systemic dose of radiation sufficient to destroy all the tumor. In contrast, squamous cell

carcinomata of the face and lip are composed of cells actually having a relatively high degree of resistance to radiation, but, in their localized form, without metastases, the limited volume of tissue involved permits curability by proper radiation methods.

With the types of equipment available at the present time, many deep-seated tumors are inadequately affected by external radiation within the tolerance limits of the overlying and surrounding normal structures. Consequently, our results at best by this method may be limited to palliative therapy. The many advances in neutron beam and supravoltage equipment have failed as yet to alter greatly our outlook in this respect.

The failure of radiation therapy in these instances has in part been a result of the following: (1) the natural radiation resistance of the tumor, (2) the large area of skin which is of necessity treated, (3) the large volume of intervening and adjacent normal tissue which must be intensively irradiated, (4) the mass or extent of the primary tumor and/or its metastases, and (5) the proximity of a less radiation-resistant organ. There are also many other factors which are important in assessing the probable results from radiation therapy of malignant tumors, including the general condition of the patient, the presence or absence of infection, the degree of vascularity of the tumor bed, the fixation of the tumor to the surrounding structures, and the presence or absence of bone invasion. For a more detailed discussion, the reader is referred to books and articles dealing with these factors.

Radiation and surgery as they are used at present cannot be expected to solve the cancer problem. However, they could be much more effective if patients would present themselves for definite treatment while the tumors are localized to their primary sites. Even then, our diagnostic tests and acumen in many instances are insufficient to detect small, localized, asymptomatic cancers of many of the internal organs. At other times, our diagnostic tests leave us in doubt as to the best method of treatment when all eventualities are carefully considered.

For example, the Papanicolaou smear and improved methods of cervical biopsy make possible the detection of what appears clinically to be an intraepithelial squamous cell carcinoma of the cervix. Yet can we be certain that the lesion is truly intraepithelial? Has it extended into the depths of the cervix or into the corpus? Can we be sure there are no metastases? Were we certain the lesion is truly localized to the cervix and free from metastases, adequate radiation therapy would be the method of choice in my opinion. Should there be metastases in the adnexa, then a radical panhysterectomy with its high percentage of complications would probably be indicated, but not a simple hysterectomy. However, sufficient experience with this type of early cancer is lacking, and one cannot be dogmatic concerning the most suitable treatment.

Realizing the limitations of present day radiation therapy, one may well ask, "What are the prospects for the future and how will radioactive isotopes influence these prospects?" To answer this question we must have faith, hope, and charity. We must have faith that through the use of isotopes as a research tool in the hands of competent scientists we will learn more about cellular physiology, both normal and abnormal; that we will learn more about the actual mechanisms of the action of ionizing radiations on biological systems; that we will learn, if we are fortunate, how to intensify or suppress at will the responses of various tissues to radiation. We must have hope that definite progress will be made along these lines. Here there is real justification for hope, inasmuch as the amount of time, money, and energy being spent are unprecedented. Above all we must be charitable about the many seemingly false avenues into which our research may carry us. We must be charitable about the research problem which the individual experimenter may elect. Ideas cannot be regimented, neither can research be placed on a cost basis production. Often it is difficult adequately to evaluate the relative merits of a particular research proposal. Roentgen was not looking for x rays in his laboratory when he made his startling discovery of them. Had he been operating under present day panel and advisory board jurisdiction, doubtless a request by him for sponsorship of a project to discover a new and mysterious invisible ray which would pass through wood, metal, and other opaque substances would have been denied.

Radioactive isotopes are finding increasing usefulness as tracer elements in biological research. They are at the moment of more value as a tool in the hands of competent research workers than as therapeutic agents. Their use for research should not be limited. They should be available to all scientists sufficiently schooled in their proper use, storage, disposal, contamination possibilities, and the potential dangers involved.

Clinical applications of radioactive isotopes in other than tracer amounts should be limited to those physicians having adequate understanding of the biological reactions resulting from ionizing and penetrating radiations. The toxicity of a radioactive isotope, when given in therapeutic amounts, results from its radioactivity rather than from its chemical or pharmacological action. The biological actions will be qualitatively similar to those resulting from roentgen rays and radium. Regardless of the form or method of application, ionizing and penetrating radiations alter the tissues of the human body which they traverse by means of the release of energy from charged particulate matter.* The resulting effect depends upon the degree of specific ionization of the tissues, the dose, and the time-dose relationship. The therapeutic value

*Alpha particles, deuterons, electrons, positrons, protons, and fission fragments.

of any radioactive isotope will depend upon many factors: its degree of selective absorption and retention by the tumor or organ in question, its energy value, its physical and biological half-life, and its role in the general metabolism of the body.

One must not infer that the therapeutic use of radioactive isotopes will or should be limited to qualified radiologists. The main concern is that physicians inadequately trained in the basic underlying principles of radiation may assume responsibilities for which they are ill prepared and in their enthusiasm bring discredit upon a valuable therapeutic adjunct before it is fully developed and its possibilities explored.

Scientific advances in the past decade have made the diagnosis and treatment of human ills a very complex problem. The talents of no one individual can be expected to encompass the field. No one specialist can be completely versed in all the ramifications of his specialty. The therapeutic application of radioactive isotopes is not unique in this respect. The talents and cooperative participation of internists, surgeons, radiologists, pathologists, radiation biologists, biophysicists, radiation chemists, biochemists, physiologists, health physicists, biologists, physicists, electronic experts, and highly trained technicians are required for the most efficient exploration of the radiation therapeutic problem.

The following chapters will emphasize the complexities of the problem and indicate the progress which is being made through the cooperative type of approach.

CHAPTER II

Terminology and Standards*

BY ROBLEY D. EVANS

RADIO ACTIVITY UNITS AND STANDARDS

1. Electron volt. The electron volt (ev) and million electron volt (Mev) are units of energy.

1 ev $= 1.60 \times 10^{-12}$ erg $= 3.82 \times 10^{-20}$ g-cal
1 Mev $= 10^6$ ev
1 kev $= 10^3$ ev
1 atomic mass unit (amu) $= 931$. Mev/atom
$m_o c^2 = 0.51$ Mev (rest energy of the electron)
1 ion-pair in air $= 32.5$ ev (Gray, 1936, 1944; Binks, 1936)

2. Curie.† A curie is the quantity of radon (0.66 mm^3 at 0°C and 760 mm) in radioactive equilibrium with 1 g of radium. The International Radium Standard Commission in 1930 (Curie *et al.*, 1931) recommended extending the curie unit to include the equilibrium quantity of any decay product of radium, especially polonium. Thus "1 curie Po" is 2.24×10^{-4} g of Po, or the amount which has the same rate of emission of alpha particles as 1 g of radium. The Commission expressed its opposition to extension of the curie unit to radioactive substances outside the radium family.

The absolute disintegration rate of radium has been the subject of many measurements by a number of methods, giving individual values between 3.40 and 3.72, with some indication in the more recent measurements that the true value probably lies in the neighborhood of $3.63 \pm 0.03 \times 10^{10}$ disintegrating atoms/sec/g Ra. The Commission recommended the use of the arbitrary value 3.7×10^{10} until such time as agreement on the third figure could be reached.

Following the discovery of artificial radioactivity, the curie unit came into widespread unofficial use as a statement of the quantity of any radioactive isotope. Thus, 1 millicurie (1 mc $=$ 0.001 c) P^{32}, Na^{24}, or C^{14} meant the amount of the isotope necessary to provide 3.7×10^7 disintegrating atoms per second. Then the number of atoms and the weight of isotope required to make 1 mc is inversely proportional to the radioactive decay constant λ or directly proportional to the half-period T, or to the mean life $\tau (= 1.44T = 1/\lambda)$. If N is the number of atoms and M the number of grams in 1 mc, n is Avogadro's number, and W is the atomic weight, then

*Reprinted in part from *Advances in Biological and Medical Physics,* Vol. I, Academic Press, New York, 1948, pp. 176-191.

†As this book goes to press, the definition of the curie has been officially changed, as given in the footnote on page 10. The section above applies to the literature prior to July 1950.

$$N\lambda = 3.7 \times 10^7 \text{ sec}^{-1}$$
$$N = (M/W)n = 3.7 \times 10^7 \ \tau$$
$$M = 3.7 \times 10^7 \ \tau \ W/n$$

and 1 mc of P^{32} ($T = 14.30$ days $= 12.35 \times 10^5$ sec), would contain

$$N = (3.7 \times 10^7)\ (1.44 \times 12.35 \times 10^5) = 6.58 \times 10^{13} \text{ atoms of } P^{32}$$

or

$$M = (6.58 \times 10^{13})32/6.02 \times 10^{23} = 3.5 \times 10^{-9} \text{ g of } P^{32}$$

Actually, the absolute rate of disintegration is exceedingly difficult to measure accurately for any isotope, especially all those which do not emit alpha rays. It is necessary to know the "disintegration scheme" of the isotope, that is, the beta and gamma ray spectrum, and the relative abundance and energy of all the radiations emitted. At the beginning of 1947 the disintegration schemes of only about two dozen artificially radioactive isotopes were established with certainty. Representative examples are given in Fig. 1. When it is known that each disintegrating atom gives, say, one beta ray, and if calibrated beta ray counters (e.g., Peacock, 1944) are available, a good estimate of the absolute activity of the sample can be made. If conversion electrons are present, their abundance and energy must be known, and suitable corrections must be made.

If some of the transitions are by electron capture, instead of by beta ray emission, then 1 mc will emit less than 3.7×10^7 beta rays/sec. For example, the 6.5 day Mn^{52} decays by positron beta ray emission in 35% of the transitions, and by electron capture in 65% of the transitions; therefore, 1 mc of Mn^{52} emits only $0.35 \times 3.7 \times 10^7 = 1.3 \times 10^7$ beta rays/sec. The curie unit has been misused occasionally to denote 3.7×10^{10} beta rays/sec, instead of 3.7×10^{10} disintegrations/sec.

A second and much more serious misuse of the curie unit has been its widespread use as an ambiguous unit of gamma radiation. This has arisen from the radiological use of radon, whose absolute disintegration rate is properly measured in curie units. Radon gives rise to the decay products RaB and RaC whose complex gamma radiations (Fig. 2) have long been used in radiological practice. Many laboratories have misused the curie unit to describe any radioactive source which produces the same gamma ray response as 1 c of radon. An outstanding technical objection to this practice is that the gamma ray response depends profoundly on the detection instrument used. For example the ratio of the apparent gamma ray intensity of a source of 8-day I^{131} to a source of radium (or of radon) is 4 times as great if a platinum cathode counter is used for both measurements as if a copper cathode counter is used with the same sources, geometry, and filtering. Moreover,

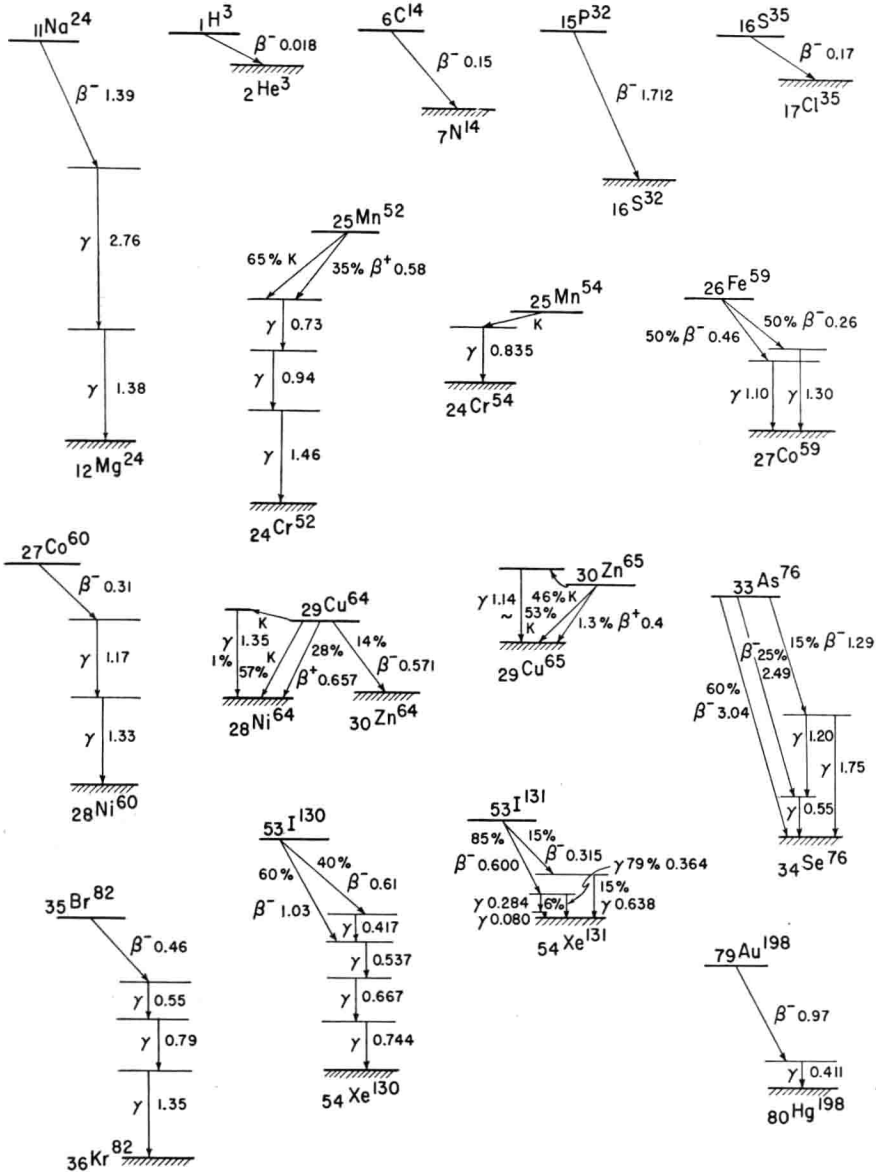
11Na24
β⁻ 1.39
γ 2.76
γ 1.38
12Mg24
1H3
β⁻ 0.018
2He3
6C14
β⁻ 0.15
7N14
15P32
β⁻ 1.712
16S32
16S35
β⁻ 0.17
17Cl35
25Mn52
65% K
35% β⁺ 0.58
γ 0.73
γ 0.94
γ 1.46
24Cr52
25Mn54
K
γ 0.835
24Cr54
26Fe59
50% β⁻ 0.46
50% β⁻ 0.26
γ 1.10
γ 1.30
27Co59
27Co60
β⁻ 0.31
γ 1.17
γ 1.33
28Ni60
29Cu64
K
γ 1.35
1%
K
57%
28%
14%
β⁺ 0.657
β⁻ 0.571
28Ni64
30Zn64
30Zn65
γ 1.14
46% K
53%
K
1.3% β⁺ 0.4
29Cu65
33As76
β⁻ 25%
15% β⁻ 1.29
2.49
60%
β⁻ 3.04
γ 1.20
γ 1.75
γ 0.55
34Se76
53I130
60%
40%
β⁻ 1.03
β⁻ 0.61
γ 0.417
γ 0.537
γ 0.667
γ 0.744
54Xe130
53I131
85%
15%
β⁻ 0.600
β⁻ 0.315
γ 79% 0.364
15%
γ 0.284
6%
γ 0.638
γ 0.080
54Xe131
35Br82
β⁻ 0.46
γ 0.55
γ 0.79
γ 1.35
36Kr82
79Au198
β⁻ 0.97
γ 0.411
80Hg198

FIG. 1. Nuclear energy level diagrams and disintegration schemes for some representative isotopes. Symbols: β^- = negative beta rays; β^+ = positron beta rays; K = orbital electron capture; γ = gamma ray. Internal conversion transitions will be associated competitively with the gamma ray transitions shown. The actual order of emission of cascade gamma rays is unknown in all cases. The numbers beside each transition show the energy of the gamma rays in Mev, or the maximum energy E_m of the continuous beta ray spectrum, in Mev. The diagrams are to scale. Therefore, the nuclear energy separation plotted for each beta ray transition is the total energy of the disintegration (E_m + 0.51 Mev) = (maximum kinetic energy + rest energy) of the beta ray emitted. In electron capture transitions the final nuclear level may lie above the initial level, as in the 46% transition of Zn^{65}, because the reaction receives 0.51 Mev from the rest energy of the captured electron. The nuclear energy change in the electron capture disintegration of Mn^{54} is unknown, but is probably less than 0.51 Mev because no competing positron beta rays can be observed.

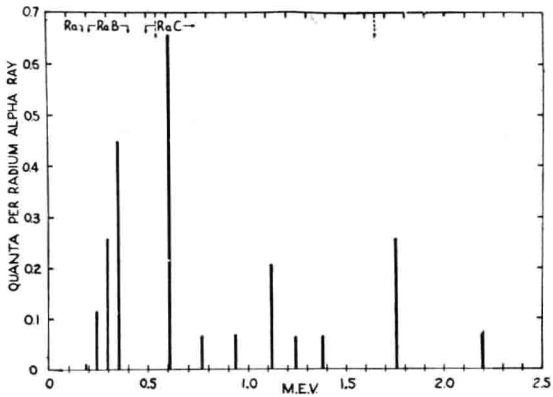

FIG. 2. The principal gamma ray lines of radium and its equilibrium decay products. Note that radium itself emits only a low-energy gamma ray of 0.184 million electron volts (Mev) and then only in 1.2% of the disintegrations, 98.8% of the radium alpha rays being unaccompanied by any gamma radiation (Stahel and Johner, 1934). The decay product radium B emits beta rays and three important but low-energy gamma rays. Radium C emits beta rays and eight important gamma rays having energies as high as 2.2 Mev. On the average, each atom which decays through all the stages shown in Table I will have emitted 2.3 quanta of gamma radiation (Ellis and Aston, 1930; Gray, 1937; Ellis, 1933; Sizoo and Willemsen, 1938). Significantly different results for the relative intensity and energies of the lines in RaC at energies greater than 1.1 Mev have been reported by Latyschev *et al.*, 1940.

many istopes emit no gamma rays at all, e.g., C^{14}, P^{32}, S^{35}. An educational effort should be made by everyone to eliminate the conflicting, confusing, and irrational use of the curie as a unit of gamma ray source intensity.

In the meantime, caution is advised in interpreting the meaning of curie (c), millicurie (mc), and microcurie (μc) in the past and current literature.

Even when the reader can assure himself that "curie" is used in the sense of disintegrating atoms per second, he must ascertain whether the number 3.7×10^{10} or some other popular contender, especially 3.47×10^{10}, has been the author's intent.

3. Rutherford. In view of the justifiable position held by the International Radium Standard Commission that the curie unit be used only for radium (1 g Ra = 1 c), radon, polonium, and other members of the radium series, a carefully defined new unit, the rutherford (rd), has been proposed for general use. Ambiguities due to choice of numerical values, due to failure to distinguish between beta rays/sec and disintegrations/sec, and due to extensions to arbitrary and undefined gamma ray intensities, can then be avoided. A joint committee of the Divisions of Chemistry and Chemical Technology and of Mathematical and Physical Sciences of the National Research Council has proposed (Curtiss, Evans, Johnson, and Seaborg, 1950) that the amount of any radioactive isotope which disintegrates at the rate of 10^6 disintegrations/sec be called 1 rutherford, abbreviated rd, and that the amount which disintegrates at the rate of 3.7×10^{10} disintegrations/sec be called 1 curie.*

4. Roentgen. The roentgen unit was originally developed for use as a unit of radiological dose. Workers in physics and in radiobiology have made use of the roentgen and a number of units derived from it.

The roentgen unit (r), as redefined at the Radiological Congress at Chicago in 1937, is "that quantity of x- or γ-radiation such that the associated corpuscular emission per 0.001293 g of air, produces, in air, ions carrying 1 electrostatic unit of quantity of electricity of either sign."

*In 1948 the International Council of Scientific Unions asked the International Union of Chemistry and the International Union of Pure and Applied Physics to nominate representatives to a new Joint Commission on Standards, Units and Constants of Radioactivity. The new Joint Commission is the official successor of the International Radium Standard Commission, and includes the surviving members of the former commission as advisory councilors. At its meeting in Paris in July 1950, the Joint Commission officially redefined the curie unit. The new definition of the curie is as follows: *"The curie is a unit of radioactivity defined as the quantity of any radioactive nuclide in which the number of disintegrations per second is 3.700×10^{10}."* This new definition divorces the curie unit from its former special association with radon and radium. For example, if it were later agreed that 1 g of radium has say 3.63×10^{10} disintegrations/sec then 1 g of radium would have an activity of $3.63/3.700 = 0.98$ curie. The arbitrary coefficient 3.700 (instead of, say, unity) was chosen so that the new curie will be substantially equivalent to the old curie when radon is involved, and will be identical with the unofficial curie which was previously used widely by many workers in artificial radioactivity. The curie has now become an official unit of disintegration rate, and the previous necessity for the rutherford unit vanishes.

The mass of air referred to is 1 cc of dry air at 0°C and 760 mm Hg. One electrostatic unit is $1/(3 \times 10^9)$ coulombs, or $1/(4.80 \times 10^{-10}) = 2.083 \times 10^9$ ion pairs. Therefore, 1 r produces $2.083 \times 10^9/0.001293 = 1.61 \times 10^{12}$ ion pairs/g of air. If an average of 32.5 ev is expended (Gray, 1936, 1944; Binks, 1936) to form each ion pair in air, then 1 r corresponds to the absorption of 5.24×10^{13} ev of energy (or 5.24×10^{13} ev $\times$ 1.60×10^{-12} erg/ev $= 83.8$ ergs)/g of air. This ionization is produced by the secondary electrons (photo (τ), Compton (σ_a), and pair (κ)) produced in 1 g of standard air. Of course the relative proportion of photo, Compton, and pair electrons will vary with the energy of the gamma radiation.

Correct use of the roentgen as a unit of "quantity of gamma radiation" requires us to realize that the term "quantity" is used here in its common, or household, sense of "amount," and does not connote any exact physical magnitude involving the energy per photon, or the total number of photons, or the total energy of the beam of photons. Indeed, the roentgen does not involve any precise physical information at all about the quality (energy per photon) or intensity (energy flowing through unit area in unit time) of the gamma radiation. The "quantity" to which the roentgen really refers with physical exactness is the "*quantity of ionization*" produced in air by the secondary electrons formed in gamma ray collisions with air molecules. Thus, the roentgen is a unit of energy dissipation, by gamma rays or x rays, in a standard arbitrary material, air. A schematic representation of the roentgen unit is shown in Fig. 3.

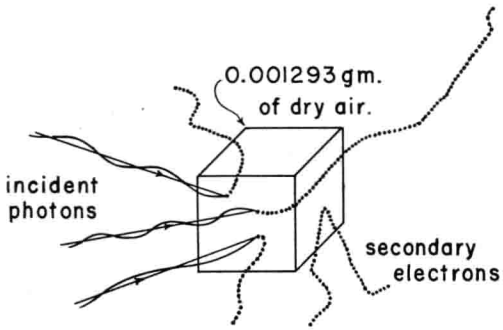

FIG. 3. A schematic representation of the roentgen unit of photon energy dissipation. Photons, of any energy, are incident from any directions, over any time interval. Even if the photons are collimated, the cross-sectional area of the beam is unspecified. The absorption of these photons in 0.001293 g of dry air (1.000 cc at 0°C, 760 mm; 1.073 cc at 20°C, 760 mm), produces secondary electrons which, if completely absorbed in air, would produce a total ionization of 1 electrostatic unit of charge (1 statcoulomb), that is $1/4.80 \times 10^{-10}$ or 2.083×10^9 ion pairs. This ionization would be distributed along the relatively long individual paths of the secondary electrons.

The roentgen does not depend on the *time* required for the production of the ionization. Consequently *gamma ray* dosage rates are represented in terms of roentgens per unit time. For example an unvarying dosage rate of 12.5 mr/hr if continued for 8 hours, would give a total dose of 100 mr, or 0.1 r. The maximum permissible daily dose for laboratory personnel exposed to gamma radiation over the entire body, is commonly taken in the United States as 100 mr in a 24-hr day (Burnam, 1938; Cantril, 1946). Again, an ionization rate of 1 ion pair/cm^3 of standard air/sec is $(1/2.08) \times 10^{-9}$ r/sec or 1.73 microroentgens (μr)/hr. The cosmic radiation produces about 2.4 ion pairs/cm^3 of standard air/sec at sea level, or 0.10 mr/24-hr day. The cosmic and local gamma radiation at sea level is usually equal to or greater than 0.2 mr/24 hr.

In summary, the official 1937 definition of the roentgen, when combined with current values of physical constants, leads to the following equivalent quantities:

$$\begin{aligned} 1\ \text{r} &= 1\ \text{esu/cc standard air} \\ &= 2.083 \times 10^9\ \text{ion pairs/cc standard air} \\ &= 1.61 \times 10^{12}\ \text{ion pairs/g air} \\ &= 6.77 \times 10^4\ \text{Mev/cc standard air} \\ &= 5.24 \times 10^7\ \text{Mev/g air} \\ &= 83.8\ \text{erg/g air} \end{aligned}$$

5. Gamma Ray Intensity. The unit of dosage rate, r/sec, is often loosely used in the older literature as a unit of gamma ray intensity. Really, the roentgen per second is a unit of *ionization intensity* in a particular reference medium, dry air at 0°C and one atmosphere pressure.

True gamma ray intensity is the rate at which photon energy flows past any point (or small region). True gamma ray intensity can be expressed only in absolute units such as ergs/cm^2 sec, or as Mev/cm^2 sec. The ionizing effects depend not merely on the true intensity, but on the number and energy of the photons involved. Thus if 1000 photons/cm^2 sec, each of 1 Mev quantum energy, traverse an area of 1 cm^2, the gamma ray intensity at this surface is 1000 Mev-cm^2 sec. The same intensity would be given by 500 photons/cm^2 sec, each of 2 Mev quantum energy. The Compton absorption coefficient σ_a for 1 Mev photons is 3.60×10^{-5} cm^{-1} in standard air. Similarly, for 2 Mev, the linear Compton absorption coefficient σ_a is 3.00×10^{-5} cm^{-1} in air. For air ($Z_{av} = 7.22$), photoelectric and pair-production absorption will be negligible at these energies. Consequently, the energy absorbed per centimeter of travel in air, or per cubic centimeter of air, for these two photon beams of equal gamma ray intensity will be:

$$\begin{aligned} &\text{For 1 Mev: } 1000 \times 1 \times 3.6 \times 10^{-5} = 0.036\ \text{Mev/cm}^3\ \text{sec} \\ &\text{For 2 Mev: } 500 \times 2 \times 3.0 \times 10^{-5} = 0.030\ \text{Mev/cm}^3\ \text{sec} \end{aligned}$$