RADIATION BIOLOGY

VOLUME I: HIGH ENERGY RADIATION

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PART I

CHAPTERS 1 TO 8

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PREFACE

These three volumes deal with the biological effects of radiations, corpuscular and electromagnetic, throughout the energy spectrum from the highest available energies to the near-infrared region. Radiation biology has progressed through important stages during the last fifty years. An upsurge of interest in the early years of the century was stimulated by developments which followed the discovery of X rays and radioactivity. In this era many of the fundamental phenomena in radiation biology were recognized, during the early growth of concepts in atomic and nuclear physics. Because much of the modern research had its roots in investigations of this period, a study of these early reports is still very rewarding. After World War I an important phase of research was reached with the discovery of (1) the genetic effects of radiation in *Drosophila* by Muller and, some time later, in maize by Stadler; (2) the effect of density of ionization; and (3) the exact action spectrum of the biological effects of ultraviolet. The unfolding of most of these early investigations is discussed in B. M. Duggar's most comprehensive review, "Biological Effects of Radiation." Significant aspects of radiation biology have been discussed in Lea's book, "Actions of Radiations on Living Cells"; the *British Journal of Radiology* supplement, "Certain Aspects of the Action of Radiation on Living Cells"; the Oberlin symposium on radiobiology, "The Basic Aspects of Radiation Effects on Living Systems"; and many monographs. Modern developments in biochemistry, biophysics, pathology, and related fields have established a profound and growing influence on research in the radiation field.

The discovery of the chain reaction in uranium initiated a new phase of scientific endeavor. The phenomenon of nuclear fission has become a practical instrument in the development of nuclear weapons; it gives great promise of becoming an economic factor as a power source; and it is outstanding as a contributor of important research tools. Many of the applications of nuclear energy are limited by their biological implications.

These volumes grew out of a tentative plan to revise the Duggar publication. However, the extraordinary expansion in radiation biology made it desirable to go beyond a straight-line biological discussion and to include in these volumes some discussions on the borderline subjects. Important developments in the field of ultraviolet radiation, especially in regard to its practical applications, justified extensive treatment. Widespread advances in photosynthesis, photoperiodism, vision, and related subjects demanded a complete volume on the effects of visible light.

PREFACE

The effects of the three types of radiation are presented in three volumes: Volume I, ionizing (high-energy) radiations; Volume II, ultraviolet; and Volume III, visible light. Since many biological effects are common to both ionizing and ultraviolet radiation, a sharp separation of these fields is no longer possible. The first two volumes might, therefore, be regarded as a whole. Both the ultraviolet and high-energy regions of the spectrum are discussed in individual chapters in both volumes. The radiation biology field, in general, is so active that, although only two years have elapsed since initiation of these publications, some of the discussions are not up to date. Space does not permit inclusion of all subjects of interest to the radiation biologists; some worthy topics are omitted for lack of an appreciable amount of new material. Studies on the use of radioisotopes as a research tool are not included because adequate texts are already available.

Gratitude is expressed to Dr. R. E. Cleland, who, during his tenure as chairman of the Division of Biology and Agriculture of the National Research Council, gave encouragement in the planning of these volumes; to Dr. Paul Weiss, the present chairman, who added his ready support to the project; and to the other members of the National Research Council. Acknowledgment is also made of the contribution of the members of the editorial boards of the separate volumes of "Radiation Biology." Without the generous support of the Division of Biology and Medicine of the Atomic Energy Commission and the Oak Ridge National Laboratory, the preparation of this work would not have been possible.

Alexander Hollaender, Editor

CONTENTS

CHAPTER 1

Principles of Radiological Physics[1]

U. FANO

National Bureau of Standards

Properties and production of radiations: Corpuscular radiations—Production of corpuscular radiations—Electromagnetic radiation—Production of electromagnetic radiation. Action of radiations on atoms and molecules: Summary of information on atoms and molecules—Elementary processes involving radiation and free particles—Action of light and X rays on atoms and molecules—Action of charged particles on atoms and molecules—Nuclear collisions. Dissipation of radiation energy in matter: Activation by charged corpuscular radiations—Activation by X and gamma rays—Activation by neutrons—Activation by infrared, visible, and ultraviolet light—Action of far-infrared and radiofrequency radiation—Spatial distribution of activations—Summary. Penetration of radiations in matter: Heavy charged particles—Electrons—X rays—Neutrons—Light. Kinetics of radiation action: The radiation dose—Methods of expressing macroscopic effects—Simple dose-effect relations—Sigmoid dose-effect curves—Time-intensity factor—Comparative effectiveness of different radiations. References.

This chapter deals with facts and concepts of physics which underlie the action of radiations upon matter in general and upon biological materials in particular. It stresses the line of thought which may be followed in analyzing the radiation effects, but the reader will often be referred to other sources for technical details.

Physics has attained a fairly satisfactory understanding of the nature of radiations. The direct action of radiations on single atoms or small

[1] This chapter is designed to serve workers in biology and medicine as an introduction to the principles of radiological physics and to give an elementary but inclusive treatment of the broad question: What happens when radiation strikes a material? The attempt to present such a treatment has pointed up large gaps in our knowledge, the filling of which is a main goal of the current program of research in basic radiation physics at the National Bureau of Standards.

Some results of recent research supported by the Office of Naval Research and the Atomic Energy Commission are included. The Biophysics Branch of the AEC is supporting a project directed toward the survey and dissemination of information on the action of radiations on matter. Much work specifically required for the preparation and illustration of this chapter has been carried out as a part of that project.

The author wishes to thank the numerous colleagues who have contributed assistance and advice, especially M. Lewis, F. A. Stinson, and G. R. White for the calculation and preparation of numerous charts.

groups of atoms is also rather well understood. Moreover, an adequate over-all picture of the processes through which the action of radiations becomes distributed over macroscopic portions of matter may be drawn.

The nature of radiations and their action on small groups of atoms are the subject of the first two sections of this chapter. The over-all picture of the action on sizable amounts of matter constitutes the third section. The fourth section deals with the penetration of radiations to various layers of an irradiated material. Knowledge of this last field is far from satisfactory.

It should be emphasized from the outset that no detailed information exists regarding the effect of radiations on any but the smallest groups of atoms. Even less is known, of course, regarding the effects on complex biochemical substances or on the far more highly organized biological materials. The present treatment does not attempt to cover these topics which are more properly classed as radiochemistry or radiobiology.

Nevertheless, the relations between the physical characteristics of a radiation treatment and its eventual biological effects may be analyzed to some extent without any detailed knowledge of the mechanisms of radiobiological actions. The fifth and last section deals with the methods of this analysis.

1. PROPERTIES AND PRODUCTION OF RADIATIONS

The term "radiation" usually indicates a physical phenomenon in which energy travels through space, even though that space be empty of matter.

There are two classes of radiations, namely:

(1) *Corpuscular radiations*, consisting of streams of various kinds of atomic or subatomic particles, which can transfer their kinetic energy to anything they strike.[2]

(2) *Electromagnetic radiations*, consisting of self-propagating electric and magnetic disturbances, which affect the internal structure of matter and thus dissipate their energy.

Acoustic phenomena depend for their propagation upon the presence of an elastic material medium (e.g., air) and accordingly are not classified as radiations.

Table 1-1 gives a classification of biologically important radiations with references to the pertinent sections of the following treatment. Corpuscular radiations are classified according to the nature of the constituent particles. The classification of electromagnetic radiations has

[2] A stream of macroscopic particles, such as pebbles, fits, strictly speaking, the above definition of radiation, but it is not generally understood to be covered by that name.

practical rather than intrinsic significance (see Sect. 1–3c). Following are some notes on other radiations of lesser biological importance:

Cosmic rays consist of a complex of radiations which flow constantly through the earth's atmosphere in a general downward direction and achieve some penetration in the earth's crust. Several components of this complex are identical with corpuscular and electromagnetic radiations studied in the laboratory. Other components include particles of energies still not attained in the laboratory. Cosmic rays seem to have little biological significance because their over-all intensity is quite low.

TABLE 1-1. CLASSIFICATION OF BIOLOGICALLY IMPORTANT RADIATIONS

Corpuscular			Electromagnetic		
Electrically charged		Electrically neutral			
Light	Heavy				
Cathode rays (electrons), positrons (Sects. 1-1b and 1-2b)	Protons, deuterons, and other ion beams (Sects. 1-1b and 1-2b)	Neutrons (Sects. 1-1b and 1-2d)	Radio waves, micro-waves (Sects. 1-3c and 1-4)	Light (infra-red, visible, and ultra-violet) (Sects. 1-3c and 1-4a)	X (or roentgen) rays (Sects. 1-3c and 1-4b)
Special names of radiations from atomic nuclei					
β rays.......	α rays (beams of helium ions)	....	....	....	γ rays

Mesons include a variety of subatomic particles heavier than electrons but lighter than protons or neutrons. They arise from the collision of very-high-energy radiations with atomic nuclei but have only a brief existence and presumably no biological significance.

The *neutrino* is the constituent of a radiation which is presumed to arise from the emission of β rays and from other subatomic processes (see Sect. 1-1b). A certain amount of energy and momentum remains unaccounted for in these processes. The circumstances indicate that the balance of energy and momentum is removed by a still undetected but otherwise well-defined radiation whose carrier element is electrically neutral and is called a "neutrino." The circumstances also indicate that this radiation ought to exert an exceedingly small action on matter and thus explain why this action has not yet been detected.

Molecular rays are beams of mono- or polyatomic molecules which escape from an enclosure into a high vacuum, carrying little energy and no electric charge.

1-1. CORPUSCULAR RADIATIONS

Material corpuscles (or "particles") are physical entities endowed with a *mass*. Because of their mass atomic particles behave like macroscopic bodies, at least in so far as their velocity can be varied to a great extent by physical means. Any change of velocity is accompanied by energy transformations. Acceleration of a particle is effected by a force which imparts to the particle a certain amount of energy to be stored in the form of kinetic energy. This energy is returned when the particle slows down owing to the action of a force opposing its motion. The storage of kinetic energy constitutes the main mechanism for energy transport by corpuscular radiation. (The internal structure of each traveling particle may contain additional energy.)

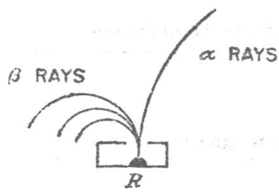

FIG. 1-1. Deflection of the α and β rays from a material located in a magnetic field perpendicular to the drawing and pointing outward.

The deflection of radiation particles is effected by a force perpendicular to their line of motion. The observation of such deflections serves to analyze the radiation response to various forces and thereby to analyze the nature of the radiation. For example, the α and β rays ejected by certain radioactive substances turn in opposite directions when they traverse a magnetic field (see Fig. 1-1). The deflection indicates that the α rays carry a positive charge, and, in these cases, the β rays a negative charge.

The analysis of corpuscular radiations progresses also through the study of their penetration in various materials (see Sects. 2, 3, and 4). Determination of the nature and velocity of the constituent particles marks the completion of this analysis.

1-1a. *Methods of Detection.* Corpuscular radiations are detected by the effects produced by their impact on matter. For instance, the electric charge delivered to a body by a radiation, the heat dissipated in the body, the luminescence caused in certain materials, or the blackening of photographic films can be measured. Electrically charged radiation particles are generally easier to detect than electrically neutral ones, because they interact electrically with the atoms of matter even from a considerable distance.

It is possible to demonstrate directly that a radiation consists of discrete particles, for example by detecting the arrival of individual particles upon a luminescent screen. This method of observing "scintillations" served as a basis for the early study of α rays. It has become much more practical since the introduction of improved luminescent materials and of devices which record the scintillations automatically.

Two other very effective methods for detecting and studying individual fast charged particles are the Wilson cloud chamber and the Geiger counter. They rely on the ability of radiation particles to eject electrons when they collide with gas molecules and thus to create pairs of separated charges of opposite sign, i.e., pairs of "ions."

The cloud chamber (Fig. 1-2) is a vessel filled with a gas which is saturated with water vapor. The chamber is suddenly expanded, at intervals, by the action of a piston. As a result, the gas is cooled and the vapor becomes supersaturated. In the absence of impurity particles which act as condensation centers, the vapor does not condense into water droplets. However, since ions act as condensation centers, the ionized path of a charged particle which has recently traversed the chamber is marked by a line of fine water droplets. This line of cloud can easily be seen or photographed (Fig. 1-3) (see Gentner *et al.*, 1940).

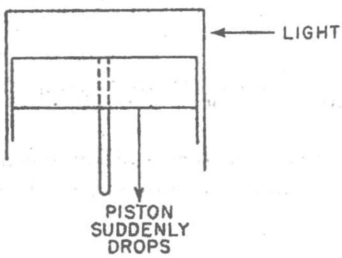

FIG. 1-2. Diagram of a cloud chamber.

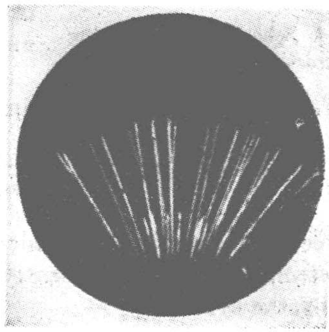

FIG. 1-3. Tracks of α particles in a cloud chamber. (*Gentner et al.*, 1940. *Vested in the U.S. Attorney General.*)

A Geiger counter consists essentially of a wire with a tube surrounding it. An electric potential difference is established between wire and tube which is not quite sufficient to cause a discharge under normal conditions. When a particle traverses the counter and creates a pair of ions in the filler gas, the electric force accelerates the ions and thereby starts a sudden discharge. After this, the wire and the tube recharge and no discharge passes until a new ionizing particle comes by. Thus one counter detects the passage of a single particle at a time, while a set of counters may serve to trace the path of a particle.

For information on counting devices the reader is referred to a report by Wilson, Corson, and Baker (1950).

Another method of observing radiations, similarly based on the ejection of electrons from gas molecules, becomes possible at somewhat higher levels of intensity when the total separation of positive and negative electric charges ("ionization") is adequate for measurement by electric techniques. Ionization is measured by attracting the charges of opposite sign toward two electric terminals (Fig. 1-4). Vessels designed for this purpose are called "ionization chambers" and constitute basic dependable tools for radiation detection and measurement (see, for example, Halliday, 1950, p. 170).

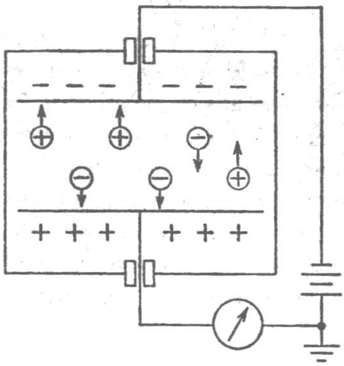

FIG. 1-4. Schematic functioning of an ionization chamber.

Neutrons are detected indirectly, through the effect of secondary radiations arising from the collision of neutrons with atomic nuclei (see Sect. 2-5).

1-1b. *Types of Corpuscular Radiations.* As stated before, any stream of atomic or subatomic particles constitutes a corpuscular radiation. The main characteristics of the various kinds of particles are their masses and their electric charges.

The masses are conveniently expressed in the scale of atomic weights in which

$$1 \text{ unit atomic weight} = \frac{1 \text{ gram}}{\text{Avogadro's number}} = 1.66 \times 10^{-24} \text{ gram} \qquad (1)$$

The electric charges are conveniently expressed in terms of the charge of an electron, whose sign is negative and whose magnitude is usually indicated by the symbol

$$e = 4.80 \times 10^{-10} \text{ esu} = 1.60 \times 10^{-19} \text{ coulomb} \qquad (2)$$

The charges of atomic particles may be positive or negative but are always integral multiples of the charge of an electron.

The corpuscular radiations listed in Table 1-1 fall into the following three groups:

(1) Light charged particles, namely:

(*a*) The *electron*, with atomic weight $\frac{1}{1823}$ and a negative charge equal to e. Electrons are a normal constituent of all kinds of matter. They spring out from matter when sufficient energy becomes available for them to overcome the attraction of the positive charges carried by the atomic nuclei. This energy may be supplied by radiation or simply by heat. Classical studies have been made of electrons as they emerge from the negative terminal ("cathode") of an electric circuit inserted in an evacuated vessel and form a beam of cathode rays (see, for example, Richtmyer and Kennard, 1947, pp. 80 ff.). Electrons are also called "negative β particles."

(*b*) The *positron*, with atomic weight $\frac{1}{1823}$ and a positive charge equal to e. Positrons are the positively charged counterpart of the electrons and are also called "positive electrons" or positive β particles. They are not a normal constituent of matter because they quickly vanish by combining with one of the ever-present electrons of matter (see the following paragraph and Sect. 2-2b). Positrons may emerge from atomic nuclei as a result of nuclear transformations (see next paragraph) or from matter exposed to high-energy radiations (see Sect. 2-2b). For further data see Richtmyer and Kennard (1947), pp. 598 ff.

(2) Heavy charged particles, which are atoms of any kind of matter stripped of some or all of their electrons, i.e., turned into positive ions. They are produced and studied conveniently when an electric discharge passes through a rarefied gas or vapor in a suitable arrangement (see, for example, Richtmyer and Kennard, 1947, pp. 542 ff.). The following types of ions are widely used as the constituents of radiations:

(c) The *proton*, a bare nucleus of the common isotope of hydrogen, with atomic weight 1.008 and a positive charge equal to e.

(d) The *deuteron*, a bare nucleus of the heavy isotope of hydrogen, with atomic weight 2.015 and a positive charge equal to e.

(e) The *alpha particle*, a bare nucleus of helium, stripped of both electrons, with atomic weight 4.003 and a positive charge equal to $2e$.

(3) Neutral particles, one of which has great practical importance, namely:

(f) The *neutron*, with atomic weight 1.009 and no electric charge. Neutrons are a normal constituent of the nuclei of all kinds of matter except the common isotope of hydrogen. They are released from nuclei only in the course of transformations induced by high-energy radiations (see, for example, Richtmyer and Kennard, 1947, pp. 615 ff.).

The constituent particles of radiations are by no means strictly unchangeable entities, even though some of them are normal constituents of matter. In fact, none of the particles is strictly unchangeable, and some have only a fleeting existence under ordinary conditions. Thus any positron quickly vanishes, together with an electron, giving rise to high-energy electromagnetic radiation. Similarly, electrons would disappear quickly if the world contained an excess of positrons.

Isolated neutrons are intrinsically unstable. They can turn into protons, ejecting at the same time a negative electron and, presumably, a neutrino (see notes in the first part of Sect. 1). Neutrons, if left to themselves, undergo this transformation at random, now one neutron and then another, at irregular intervals. On the average, half the neutrons existing at any one time are expected to turn into protons in approximately a quarter of an hour. However, the great majority of free neutrons disappear by capture in some atomic nucleus in a much shorter time, i.e., before changing into protons.

Protons may turn into neutrons through a similar transformation, ejecting a positive electron and, presumably, a neutrino. However, this transformation is energetically impossible unless the proton is part of a nucleus and the rest of the nucleus supplies the necessary energy.

The transformations of protons into neutrons and of neutrons into protons within a nucleus constitute the processes of "β disintegration."

1-1c. *Potency of Corpuscular Radiations.* The ability of a corpuscular radiation to affect the properties of matter clearly depends not only on the nature of its constituent particles and on their total energy but also on the kinetic energy of each single particle. A few particles of high kinetic energy can produce effects which a far larger number of particles of low kinetic energy cannot possibly achieve. Therefore an indication of the speed or of the kinetic energy of individual particles serves as a measure of what we may call the "potency" of the radiation.

The basic unit employed with reference to the kinetic energy of atomic particles is the "electron volt" (ev), i.e., the increase of kinetic energy experienced by an electron while being accelerated across a potential difference of 1 volt. This unit has a direct significance when applied to a particle carrying the same quantity of electric charge as an electron, but it is currently used as a unit of energy with reference to particles carrying any quantity of charge or no charge at all.

$$1 \text{ ev} = 1.6 \times 10^{-19} \text{ joule} = 1.6 \times 10^{-12} \text{ erg} \qquad (3)$$

When the kinetic energy E of a particle is expressed in electron volts and its mass M in units of atomic weight, its velocity is given by

$$v = 1.4 \times 10^{6} \sqrt{E/M} \text{ cm/sec} \qquad (4)$$

(This formula is valid only if its result is much less than 10^{10} cm/sec; otherwise it must be replaced by a more complicated formula of relativistic mechanics.)

The kinetic energy of individual particles may also be expressed in terms of the chemical energy unit "calorie per mole." One mole of a substance consists of Avogadro's number, $N = 6.0 \times 10^{23}$, of molecules. If each of these molecules has, for example, a kinetic energy of 1 ev, the entire mole has a kinetic energy equal to

$$6.0 \times 10^{23} \times 1.6 \times 10^{-12} \text{ ergs} = 9.6 \times 10^{11} \text{ ergs} = 23{,}000 \text{ cal}$$

In the same way, if a chemical reaction yields 1000 cal/mole, this means that each molecule participating in the reaction has yielded $\frac{1}{23}$ ev.

The equation

$$1 \text{ ev} = 23{,}000 \text{ cal/mole} \qquad (5)$$

serves to estimate the chemical "potency" of a radiation. For example, if a certain gas reaction requires an activation energy of 50,000 cal/mole,

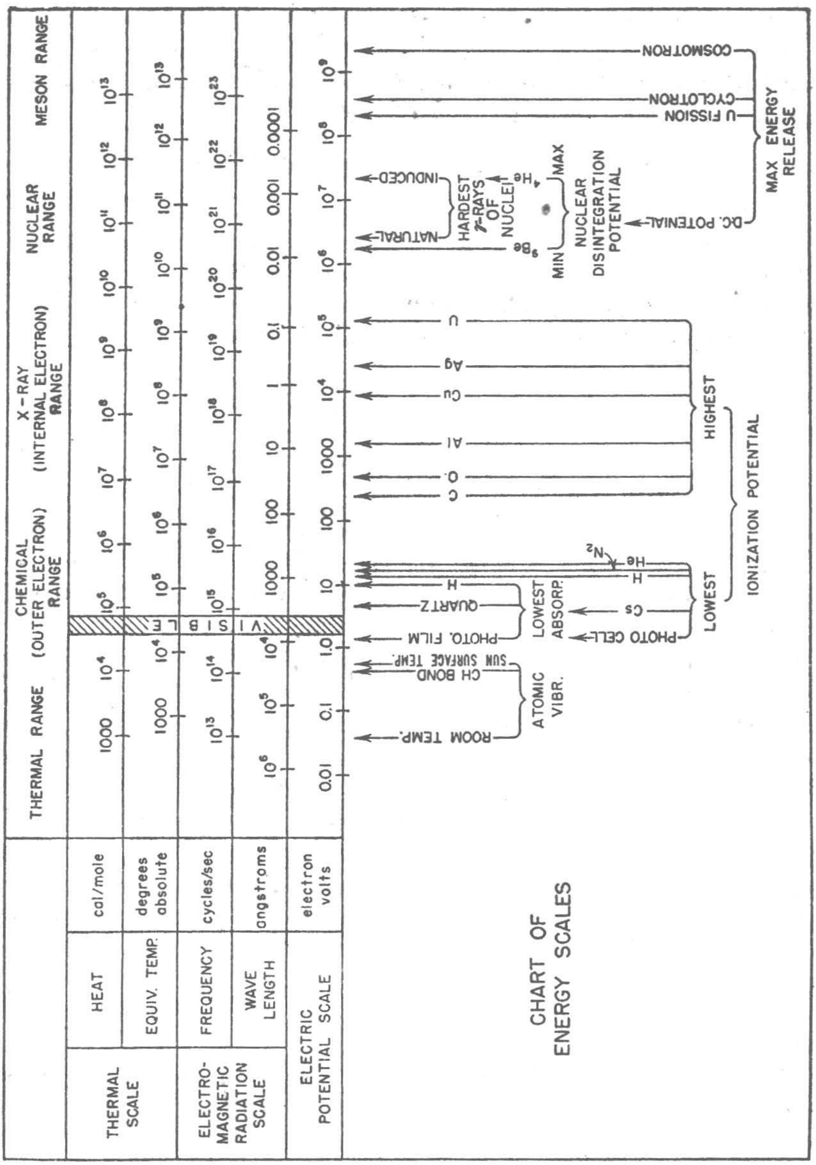

FIG. 1-5. Chart of energy scales.

each molecule can be activated by the impact of a particle only if this particle has a kinetic energy equal to at least $50/23 = 2.2$ ev.

There is yet another method of expressing the "potency" of a radiation with reference to familiar thermal concepts. Vapor molecules which filter out of an oven at a temperature of T degrees absolute have a kinetic energy of the order of magnitude of kT, where

$$k = 1.4 \times 10^{-16} \text{ erg/degree} = 8.5 \times 10^{-5} \text{ ev/degree} \tag{6}$$

and is the "Boltzmann constant." The formula indicates that it would take an oven at about 12,000°C to emit particles with a kinetic energy of the order of 1 ev. Any radiation source may thus be characterized from the thermal standpoint by means of an "equivalent temperature" which is proportional to the kinetic energy of the radiation particles at a rate of 12,000°C/ev.

A comparison of the various scales of radiation potency is shown in Fig. 1-5.

1-2. PRODUCTION OF CORPUSCULAR RADIATIONS

Electrically charged particles can be directed into a beam and then accelerated to a desired velocity under the action of electric forces. Neutral particles, on the contrary, cannot be controlled easily; the main device to form a beam of neutral particles is to let the particles pass from the space where they are produced to another portion of space through collimating holes or slits.

1-2a. *Sources of Charged Particles.* Electrons are easily produced in a vacuum by heating a metal. The hot metal emits electrons in quantities limited only by the mutual repulsion of the electrons in the surrounding space ("space-charge effect"). Rates of emission of the order of amperes, i.e., of 10^{19} electrons per second, are practicable.

Positrons have to be emitted by radioactive nuclei or produced by X rays. Their rate of production is much smaller than that of electrons from a hot wire. For example, a "strong" radioactive source, of the order of curies, yields only 10^{11} positrons per second, i.e., about 10^{-8} amp.

Protons and other positive ions are produced by stripping electrons off the atoms or molecules of a gas at low pressure. The stripping results from the violent atomic collisions which accompany an electric discharge. Usable ion-beam intensities of the order of a milliampere have been obtained.

Charged particles produced by these methods can be formed into a beam by attracting them toward a conductor charged with electricity of opposite sign. Thence they can be canalized into empty space. Suitably distributed electric and magnetic forces also serve to concentrate or "focus" beams of charged particles. Still, the achievement of good focusing at a high intensity level offers difficulties.