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BIOLOGICAL EFFECTS AND THERAPEUTIC POSSIBILITIES OF NEUTRONS

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IT IS now possible to obtain neutrons in sufficiently abundant intensities to make worth while the consideration of their biological and therapeutic possibilities. Enough knowledge of the remarkable behavior of neutrons has been accumulated through physical research to enable the prediction of certain biological effects, and to see, in a general way at least, certain therapeutic potentialities of this new kind of corpuscular radiation. The facility with which neutrons pass through matter, and penetrate and disrupt atomic nuclei, of which they are now believed to be fundamental constituents, gives them an importance in some fields of atomic physics which is not equalled by alpha, beta, or gamma rays. This naturally reflects on the various fields of biological application of corpuscular and quantum radiations.

I. NATURE AND BEHAVIOR OF NEUTRONS

Neutrons are electrically uncharged elementary particles which have very nearly the same mass as hydrogen atoms. They were discovered in 1932 by Dr. J. Chadwick, of Cavendish Laboratory, Cambridge University, who has very appropriately been awarded the Nobel Prize for the discovery. Neutrons are usually produced by bombarding beryllium metal with alpha particles from radium or radon, or by bombarding some element with deuterons (charged atoms of heavy hydrogen) which have been electrically accelerated to very high speeds. Although they are particles, neutrons pass through ordinary matter with facility resembling that of very hard gamma radiation. Their collisions, and other interactions, are with atomic nuclei, not with extra-nuclear electrons; hence they do not produce trails of ionization along their paths through matter, but collide, at intervals, with atomic nuclei. A nucleus struck by a neutron is either driven away as an (ionizing) recoil nucleus, or it captures the neutron, thereby being transmuted temporarily or permanently into another nucleus.

Since neutrons have no electric charge, they are not acted upon by the electronic fields of extra-nuclear electrons, nor are they stopped at nuclear boundaries, like other impinging particles; they may pass directly into atomic nuclei with little resistance.[1] Once a neutron has penetrated an atomic nucleus, it has considerable chance of disturbing the previous nuclear equilibrium. The particular kind of "disturbance" depends on the kind of nucleus and

[1] More exactly, the field of the neutron interacts with other atomic fields only through very short distances. Its "radius" is estimated to be of the order of 10^{-13} cm., as compared with atomic radii of 5 to 19×10^{-9} cm., and nuclear radii of about 1 to 10×10^{-13} cm.

on the velocity of the impinging neutron. Slow neutrons are most effective. If the velocity is very high, the neutron may simply pass through the nucleus and leave it unaltered. If the neutron stops, however, the nucleus may be disintegrated immediately, or it may be transmuted to another kind of nucleus. In the latter case, if the new nucleus is stable, the transmutation only results in the formation of a heavier nucleus from a lighter one, usually accompanied by the emission of a quantum of gamma radiation; but if it is unstable, it will disintegrate: hence the neutron has brought about induced radioactivity. The answer to the question of which of these processes will result from the penetration of the nucleus by a neutron depends on the kind of nucleus and the speed of the neutron.

To date, more than 40 elements have been made artificially radioactive by neutron bombardment; in some cases, two or more radioactive elements are created from a single bombarded element. The half-lives of the radioactivities vary from a few seconds to about fourteen days: the decay products are beta and gamma rays of singular energies, depending on the element. Whereas natural radioactivity is confined to three heavy elements, uranium, thorium, and actinium, and their descendants (except for the very feeble radioactivity of rubidium, potassium, and samarium), artificial radioactivity has been induced in elements throughout most of the atomic scale.

The possibility of applying artificially radioactive elements to biological research and radiation therapy has already aroused much interest; this field will doubtless be explored as fast as experimental facilities can be established and experiments performed. Indeed, it now seems very possible that artificially radioactive elements may eventually replace radium and radon for certain types of therapy. Their chief advantages would seem to lie in the homogeneity of their radiations, the suitability of their half-lives for therapeutic uses, and the non-toxicity of their decay products. But the production of these elements by neutron bombardment (directly or indirectly) is an extremely inefficient process: the average number of bombarding neutrons required to produce one atom of a radioactive element must be reckoned in powers of ten. Accordingly, the potential biological effects, useful or otherwise, of a given neutron source are necessarily larger than those, useful or otherwise, from any artificially radioactive material created by the same neutron source.

II. Biological Effects Expected from Neutron Irradiation

It is the purpose of this paper to call attention to some biological effects and possible uses of neutrons. I believe that very valuable applications may develop, particularly because of the peculiar absorption characteristics of different elements for neutrons. Thus, if a beam of slow neutrons traverses a heterogeneous mass of matter, the absorption does not follow the laws of absorption and scattering either of corpuscular or of quantum radiation. On the contrary, *certain elements absorb neutrons very strongly, and others, very little.* Moreover, the criterion for strong or weak absorption of neutrons of a given velocity is not the atomic number of the element (as with gamma or roentgen rays), but its particular nuclear structure. Thus boron (at. wt. 10.82) absorbs slow neutrons about 90 times as strongly as an equal amount of carbon (at. wt. 12); cadmium (112.41) absorbs about 825 times as strongly as tin (118.7), while tin has about the same absorption, per atom, as carbon.[2] From this contingency arises one of the most promising types of application of neutrons to biological processes. This will be discussed further on.

a. *Effects Due to Elastic Collisions.* For purposes of comparison, let us consider what would happen if two identical organisms are exposed, respectively, to a beam

[2] Taken from data of Dunning, Pegram, Fink, and Mitchell. Interactions of neutrons with matter, *Phys. Rev.*, 1935, *48*, 256.

of gamma radiation and to a beam of neutrons of heterogeneous energies. In the former case, the absorption is directly proportional to the number of electrons per atom, hence to the atomic number of the element, approximately. Consequently, the heavier elements absorb more strongly than the lighter ones. The energy goes into the ejection of electrons, and ultimately disappears as heat.

In the case of the organism exposed to heterogeneous neutrons, the absorption of energy is by a very different process. It is largely due to *hydrogen atoms*, except in regions where there are appreciable concentrations of atoms which absorb neutrons very strongly. The "absorption" by hydrogen atoms is mostly a scattering process: the neutrons undergo elastic collisions (i.e., non-capture collisions, or "billiard-ball collisions") with hydrogen nuclei, which recoil along short but highly ionizing paths, as compared with those of electrons ejected by gamma rays. A single neutron may be scattered many times before coming to rest. The large absorption of neutrons by hydrogen arises from two circumstances: the great abundance of hydrogen in organic matter, and the relatively large collision cross-section of hydrogen atoms, as compared with other atoms. (The nuclear cross-sections of carbon, nitrogen, and oxygen, for slow neutrons are, respectively 0.12, 0.32, and 0.09 times that of hydrogen.) A point of special interest, in this connection, in that the wide and rather uniform distribution of hydrogen throughout the organism tends to make the distribution of energy, absorbed by this recoil process, *uniform*, whereas the heavier elements, which absorb gamma rays and roentgen rays strongly, are localized to a considerable extent in bones and other special tissue.

It is only feasible to consider here the biological effects of neutrons as compared with effects of alpha rays, beta rays and electrons ejected by gamma type radiation. The major effects of fast neutrons should arise from the ejection of H-particles *within the tissue*. The ionization of an H-particle, per unit path-length, is about one-fourth that of an alpha particle, and the range is about four times that of an alpha particle of the same energy. Similarly, the ionization per unit path-length of an H-particle is of the order of 100 times that of an electron, and its range is, roughly, 1 per cent of the range of an electron of similar energy, ejected by a quantum of gamma radiation.

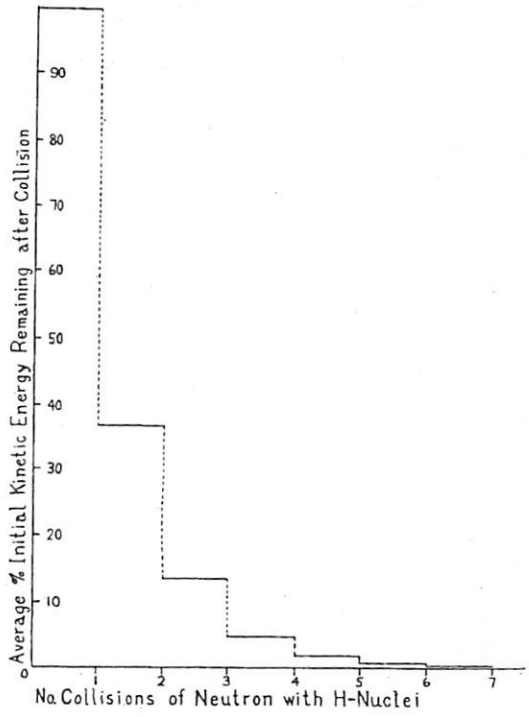

Fig. 1

Unfortunately, there are probably no experimental data on the biological effects of alpha particles (or H-particles) acting *within tissue* of appreciable thickness. Such experiments are made extremely difficult by the fact that, unless neutrons are used to generate them, heavy particles are only obtainable from certain radioactive chemical substances whose dissemination throughout animal or plant tissue would be attended with great difficulty.

When a neutron collides with a hydrogen nucleus, it imparts to the H-particle approximately 63 per cent of its kinetic energy, on the average. So the decline of kinetic energy of the neutron, with suc-

cessive H-collisions, is very rapid, as shown in Figure 1. Since the average distance between successive collisions of fast neutrons is relatively large (a matter of centi meters), the number of collisions of the particle will be rather few, in an organism of ordinary thickness; indeed, for a thickness of less than 1 cm., the number of cases in which a fast neutron makes more than one collision may be neglected, for a first-order approximation. With these facts available, one may calculate with reasonable accuracy the amount of energy dissipated within a given layer of matter, due to collisions with hydrogen atoms, if he knows the amount of hydrogen present, the number of kinetic energy of the incident neutrons, and the absorption (scattering) coefficient of hydrogen. Such a calculation is analogous to the calculation of roentgen- or gamma-ray absorption, where the nature of the absorber and wave lengths of the incident radiation are known, although the actual absorption processes are very different ones. Unfortunately, most practical sources of neutrons emit these particles with very heterogeneous energies. The problem of getting a homogeneous beam from such a source is, again, analogous to the problem of getting a beam of monochromatic roentgen rays from a roentgen tube: the beam can be filtered, to remove or diminish the less penetrating components, or a beam of homogeneous radiation can be selected by means of a spectrometer, for roentgen rays, or a velocity-selector, for neutrons. But the latter methods are of such low efficiency that their use cannot be considered unless the output required is very low, or the input very high.

Table I

Element	Atomic Number	Atomic Weight	Collison Cross-Section for Slow Neutrons, cm.^{2} $\times 10^{24}$	Relative Absorption, per Atom, Compared with Hydrogen	Relative Absorption, per Atom, Compared with Carbon	Relative Absorption *per Gram;* Based on Carbon = 1.00
Hydrogen	1	1.008	35.0	(1.00)	8.5	101.6
Carbon	6	12.00	4.1	0.12	(1.00)	(1.00)
Nitrogen	7	14.01	11.3	0.32	2.76	2.36
Oxygen	8	16.00	3.3	0.09	0.8	0.65
Sodium	11	23.00	4.2	0.12	1.0	0.53
Magnesium	12	24.32	3.5	0.10	0.85	0.42
Phosphorus	15	31.03	14.7	0.42	3.68	1.39
Chlorine	17	35.46	39.0	1.11	9.52	3.22
Calcium	20	40.07	11.0	0.31	2.68	0.80
Lithium	3	6.94	45.	1.3	11.	19.0
Boron	5	10.82	360.	10.3	88.	97.5
Yttrium	39	88.9	800.	22.9	195.	26.4
Cadmium	48	112.41	3300.	94.3	815.	86.0
Barium	56	137.37	140.	4.0	34.	3.
Samarium	62	150.43	4700.	134.3	1144.	92.
Europium	63	152.0	est. <1000.	<28.6	<244.	<19.
Gadolinium	64	157.6	30000.	857.0	7320.	557.
Terbium	65	159.2	est. <1000.	<28.6	<244.	<19.
Dysprosium	66	162.5	700.	20.0	171.	13.
Iridium	77	193.1	285.	8.1	69.	4.
Mercury	80	200.61	380.	11.0	93.	5.6
Lead	82	207.20	8.6	0.25	2.	0.1
Thorium	90	232.15	32.0	0.9	8.	0.4

b. *Effects Due to Selective Absorption.*

Leaving, now, the elastic collisions of neutrons, we shall consider their absorption by a few particular elements whose absorption is very much higher than that of hydrogen. As previously mentioned, these elements evidently owe their strong absorption to their particular nuclear structures, which make them particularly susceptible to nuclear transformation (transmutation) due to bombardment by slow neutrons. Among these may be mentioned lithium, boron, yttrium, cadmium, barium, iridium, mercury, and some of the rare-earth elements, samarium, europium, gadolinium, terbium, and dysprosium. Table 1, prepared from data of Dunning, Pegram, Fink, and Mitchell,[3] gives the relative absorptions of slow neutrons by various elements with which we are here concerned. The upper part of the table includes the elements that constitute most organic tissue; the lower part is for some elements whose absorption is particularly high. The data for lead are included, for comparison.

Now it is immediately evident that if there is, in any particular part of the organic tissue which is irradiated with slow neutrons, an appreciable concentration of elements that absorb them strongly, there will be a greater dissipation of neutron energy in these regions than in the surrounding tissue. Even extremely small concentrations of some of these elements suffice to give strong absorption. On the other hand, the amounts of *any* of the elements listed in the lower part of the table are probably negligibly small, even in terms of their neutron absorption, in most organic matter. There exists, however, this important possibility: *a high absorber of neutrons may be introduced*, by injection or some other means, *into the regions of the organism wherein it is desired to dissipate a great deal of energy in the form of ionization*. The element chosen for the purpose must, obviously, be in the form of a nontoxic compound. The type of compound used is irrelevant, as far as the neutron absorption is concerned, since this absorption is purely an atomic phenomenon. An analogous procedure can be used for selective absorption of roentgen rays and gamma rays; but the elements of strong absorption are necessarily the *heavy* elements, whereas strong neutron absorbers include elements of *very low* atomic number, as shown in Table 1.

High selective absorption of slow neutrons seems, in all cases, to be connected with nuclear transformations in the absorbing element, brought about by neutron bombardment. In this connection, special attention should be called to the fact that *the energy released by the absorption of neutrons in matter is not the energy of the incident neutrons, except in cases of elastic collisions, such as those with hydrogen. Otherwise, the energy released is nuclear energy of the bombarded atoms. The neutrons serve, essentially, as trigger mechanisms which only start the nuclear transformations that release energy*. They differ from trigger mechanisms, in the ordinary sense of the expression, in that they become parts of the atomic nuclei in which they are absorbed. Since capture of the neutron is a fundamental part of the transformation, it is evident why slow neutrons are more efficacious than fast ones in bringing them about. The nuclear absorption of neutrons is a distinct phenomenon which has no counterpart in the absorption of gamma rays or roentgen rays.

The form in which energy is released by nuclear absorption of neutrons depends on the absorber. In the case of light elements, particularly lithium and boron, low-range alpha particles are emitted; in the case of heavy elements, the products are (so far as we now know) beta rays and gamma rays. In some cases, the emission is simultaneous with the absorption of the neutron; in others, namely those elements in which artificial radioactivity is induced, the emission will succeed the absorption, according to the laws of radioactive decay of the element concerned. The *amount* of energy released in any element, due to neutron absorption, is the product of the number of

[3] Dunning, Pegram, Fink, and Mitchell, *loc. cit.*

neutrons absorbed, N, and the energy released by the absorption of a single neutron, e. Approximate relative values of e are known for a few light elements;[4] others will doubtless be measured soon. The energy released, e, may be either positive or negative, depending on the element and transformation involved. The release of energy by naturally or artificially radioactive elements is, of course, a release of nuclear energy without external stimulus. Instantaneous disintegrations of elements by neutrons (if they are ever truly "instantaneous") may be regarded as "induced radioactivity of zero half-life," without departing from the truth in any way.

c. *Summary of the Effects to be Expected from Neutron Irradiation.* The biological effects to be expected from the action of neutrons are of two kinds: (*a*) those produced in the bulk of tissue, due to elastic collisions of neutrons, especially those with hydrogen nuclei, and (*b*) those produced in specific regions where (even small) concentrations of highly absorbing atoms are present. In either case, the ionizing action which arises from neutron bombardment, like that from gamma and roentgen irradiation, will probably be chiefly *destructive*, hence applicable to problems such as the production of mutations in animals and plants, and to the destruction of malignant cells, such as those of cancerous tissue. Any constructive stimulation will probably be, as in the case of other radiations, at best an open question. The action of neutrons differs conspicuously from those of other radiations in that the effects are, broadly speaking, greatest in *light elements*, particularly hydrogen, as contrasted with the heavy element absorption of gamma type radiation. The scattering of neutrons by hydrogen results in the production of short-range, but highly ionizing particles, as compared with the long-range, low-ionizing paths of electrons ejected by gamma rays. Finally, slow neutrons can be subjected to strong selective absorption by certain elements; this absorption may result in the spontaneous release of atomic energy from the atoms in which absorption occurs, and is not furnished by the neutrons themselves.[5]

[4] Thus H. J. Taylor (*Proc. Roy. Soc. A 47*, 1935, 873) has shown that boron, when disintegrated by slow neutrons, emits alpha rays whose energy is about 2×10^6 electron volts; this corresponds to a range of about 1.1 cm. in air, or about 7.6 microns in the gelatine of a photographic plate.

III. SOME PHYSICAL PROBLEMS THAT SHOULD BE SOLVED

Much remains to be done in the way of purely physical research before it will be possible to calculate the exact amount, form, and distribution in which energy will be liberated in any given mass of material irradiated with a neutron beam from a (practical) source of neutrons. Several types of such physical problems may be cited:

(1) The development of simple and reasonably accurate means of measuring the number of neutrons, per second, in any beam, and the distribution of their velocities.

(2) The neutron "absorption," in any absorber, is divided into two parts: nuclear absorption (true absorption), and scattering. The ratios of these, for different elements and for neutrons of various energies, must be determined. Some data on this subject are already available;[6] others will doubtless appear soon.

(3) The scattering of neutrons of various velocities by various substances must be further examined for the purpose of finding the mean free paths between successive collisions, under various conditions. This information would be very desirable for determining the amount and distribution of energy released by scattering, in any absorber, and for designing appropriate scatterers and filters to surround neutron sources.

(4) The processes and energy relations in nuclear transformations must be further

[5] Neutrons, like alpha particles, never exist free in nature. Alpha particles eventually capture electrons and become helium atoms; neutrons eventually enter, and attach themselves to atomic nuclei, thereby producing nuclear transformations.

[6] Mitchell, A. C. G., and Murphy, E. J., *Phys. Rev.*, 1935, *48*, 653; also *Bull. Amer. Phys. Soc.*, 1935, *11*, 13.

investigated. In some cases, artificial radioactivity is induced; in others, instantaneous nuclear transformations occur, accompanied by the emission of alpha rays or beta and gamma rays; in other cases, both artificial radioactivity and instantaneous transformations are produced.[7] The problems are to determine, for each element, what processes occur, what isotope is involved in each process, the kinds and energies of the particles and quanta emitted by the elements so disintegrated, and the influence of the velocities of the neutrons on these processes.

IV. Some Fields of Application of Neutrons to Biological and Medical Research

Some likely fields for biological and therapeutic research, involving the direct application of neutrons (apart from applications of neutron-induced artificially radioactive elements) have occurred to me, and may be mentioned here. Two general divisions of these applications may be conveniently set up, namely, "bulk-effects" produced by elastic collisions of neutrons with hydrogen and other nuclei in the irradiated matter, and "specific local effects," arising from the selective absorption of neutrons by atoms of high neutron-absorbing power, which process is followed by the liberation of nuclear energy by nuclear transformations. Within the latter of these divisions are included the interesting possibilities of introducing and localizing small concentrations of strong neutron absorbers in specific regions of the organism under investigation, followed by neutron irradiation, as pointed out earlier in this paper.

In the field of experimental biology there may be mentioned: (1) investigation of the bulk effects of neutrons in living tissue (animal and plant), as shown, for example, by their effects on the speeds of mitosis; (2) the destruction or enfeeblement of living bacteria by neutrons; (3) search for specific effects in organs or other special tissues of higher animals subjected to slow neutron bombardment; (4) investigation of the efficacy of neutrons in producing mutations in animals and plants. I regard (4) as one of the most interesting applications of neutrons to pure biology.

In the field of medical research there may be cited: (1) the possibility of destroying or weakening cancerous cells, by the general or selective absorption of neutrons by these cells. In particular, there exist the possibilities of introducing small quantities of strong neutron absorbers into the regions where it is desired to liberate ionization energy (a simple illustration would be the injection of a soluble, non-toxic compound of boron, lithium, gadolinium, or gold into a superficial cancer, followed by bombardment with slow neutrons); (2) the possibility of obtaining specific destructive action of slow neutrons on disease-producing bacteria. This seems to merit careful investigation, both from a medical and a purely biological standpoint. However unlikely, it is not inconceivable that, in some instances, a non-toxic compound of an element that absorbs neutrons strongly might be concentrated in infected regions and used to destroy the bacteria by subsequent neutron irradiation.

Researches covering these fields might well be expected to occupy the entire time of many workers for many years. Yet, if they led to the eradication of a single disease, or to a better understanding of biological processes involved in disease, so that the way to cure was made clearer, the effort would be justified.

V. Production of Neutron Beams

By "production of neutrons" is meant their liberation (ejection) from atomic nuclei. Like alpha particles, neutrons exist only in nuclei, and must be removed from them if they are to be used. The removal of a neutron from a nucleus involves nuclear disintegration, just as the spontaneous

[7] Artificial radioactivity produced by neutron bombardment.
Part I: Fermi, E., Amaldi, E., D'Agostino, O., Rasetti, F., and Segrè, E. *Proc. Roy. Soc. A 146*, 1934, 483.
Part II: Amaldi, E., D'Agostino, O., Fermi, E., Pontecorvo, B., Rasetti, F., and Segrè, E. *Ibid., 149*, 1935, 522.

emission of an alpha particle does. But, unlike alpha particles, which are spontaneously emitted by 23 radioactive elements and isotopes, neutrons are not spontaneously emitted by any known element,[8] and must be liberated by bombarding elements with particles or quanta of high energy. This fact makes the production of dense neutron beams difficult or expensive, by any method yet developed.

Neutrons have been obtained by disrupting nuclei with alpha particles (helium nuclei), protons (hydrogen nuclei), deuterons (nuclei of heavy hydrogen, or deuterium), and gamma rays. In each case, the disrupting agent must have sufficient energy to enter the nucleus and to overcome the binding energy which normally retains the neutron in the nucleus. In the case of gamma rays, no energy is required to penetrate the nucleus; hence only the binding energy is concerned.

The original method of obtaining neutrons, namely by bombarding beryllium with alpha particles from polonium, will not be considered here because of the low yield of neutrons, as compared with other sources, and because of the difficulty of getting large quantities of polonium. Three methods that are feasible for obtaining neutrons, at rates exceeding a million per second, will be considered, in probable inverse order of their potential neutron yields.

(1) *Bombardment of Beryllium with Alpha Particles from Radium or Radon.* This method consists in intimately mixing powdered beryllium metal with radium or radon, in a sealed container. A Ra-Be source is, of course, constant, whereas a Rn-Be source decays at the same rate as the Rn gas. The introduction of beryllium into radon or radium in no wise injures the use of the gamma rays in the customary manners, since the neutrons are produced by the alpha particles which are otherwise unused, and the gamma-ray absorption of beryllium (at. wt. 9.02) is very small, indeed ($\mu = 0.074$ per cm. Be). The emission of neutrons is merely added to the emission of gamma rays by the source.

According to Fermi, Amaldi, D'Agostino, Rasetti and Segrè,[9] 1 curie of radon, mixed with beryllium gives, roughly, one million neutrons per second. On this basis, 1 gram of radium, mixed with beryllium, would give about 1.3 millions per second. The efficiency of this process is accordingly about 1 neutron per 100,000 alpha particles.[10] More recent estimates indicate a much higher yield of neutrons from Rn-Be. Jaeckel[11] estimates the yield to be 10 million neutrons per second per curie Rn; Paneth and Loleit[12] estimate the yield to be 3 million neutrons per second per curie; the corresponding efficiencies are: 1 neutron per 10,000 to 30,000 alpha-particles.

If desired, the gamma rays from a Ra-Be source of neutrons can be greatly reduced in intensity by filtering through a few centimeters of lead, without proportionate loss of neutron intensity, since the lead is quite transparent to neutrons (see Table 1). Conversely, the neutron intensity can be greatly reduced, without proportionate loss of gamma rays, by successive filtering through a few centimeters of paraffin (to slow down the neutrons) and a thin filter of boron or cadmium (to absorb the slow neutrons). Unless a paraffin filter is used (or some other material rich in hydrogen), the neutrons will not be appreciably absorbed; their initial velocities are very high, so they pass through matter with absorption that is less than that of the hardest gamma rays known. A Ra-Be or Rn-Be source may accordingly be used for the gamma rays without the necessity of filtering out the neutrons.

The strongest source of this type reported thus far is that of Paneth and Lo-

[8] If neutron-emitting radioactive elements ever existed in the earth's crust, they must have decayed, and had no long-lived progenitors.

[9] *Loc. cit.*

[10] For comparison 1 gram of radium emits about 7.26×10^{10} gamma rays per second, of which about 5.56×10^{10} are "hard" rays. See: Rutherford, Chadwick, and Ellis, "Radiations from Radioactive Substances," Cambridge University Press, 1930, p. 501.

[11] Jaeckel, R. *Ztschr. f. Phys.*, 1934, *91*, 493.

[12] Paneth, F. A., and Loleit, H. *Nature*, 1935, *136*, 950.

leit, who used 2,200 millicuries of Rn mixed with beryllium.[13]

(2) *Irradiation of Beryllium with Hard Gamma Rays.* Szilard and Chalmers[14] discovered, in 1934, that hard gamma rays from radium or radon disintegrated beryllium, accompanied by the emission of neutrons, as suggested by Chadwick and Goldhaber. Recently, Chadwick and Goldhaber[15] have further investigated this process; from their measurements it is possible to make an approximate calculation of the number of neutrons emitted per second by several kinds of sources. Taking the area of the beryllium nucleus as 10^{-28} cm.^{2}, for this "photo-disintegration" process, and the number of gamma rays from 1.0 gm. Ra, or 1.0 curie Rn, whose energies exceed 1.7×10^6 volts, as 1.14×10^{10} per sec., it is calculated that 1 gm. Ra or 1 curie Rn, surrounded by 10 cm. thickness of solid beryllium (7.8 kg. Be), would emit about 900,000 neutrons per second. This is of the same order as the strength of the source described under (1) above. Through the courtesy of the staff of the American Oncologic Hospital, Philadelphia, Dr. L. H. Rumbaugh and I are conducting a series of experiments with a neutron source of about 200,000 photoneutrons per second, obtained by allowing part of the gamma radiation from 4 grams of radium to pass through 500 grams of beryllium metal. Obviously, methods (1) and (2) can be combined.

The production of neutrons by photo-disintegration of beryllium and deuterium with hard gamma rays is of special interest because of a known but undeveloped possibility, namely, the production of intense beams of high energy gamma rays by high voltage machines. Thus a current of 1 microampere, in a tube operated at 1.7 to 3.5 millions of volts would, if converted into gamma rays (roentgen rays), be capable of producing some 500 millions of neutrons per second, by photo-disintegration of beryllium. This neutron flux would equal that from at least 200 grams of radium. Gamma rays used for generating photo-neutrons must be very hard rays; the binding energy of the neutron in beryllium, which is the most easily disintegrated element, is believed to be between 1.3 and 2.0 millions of volts. Consequently, only about 16 per cent of the gamma rays from radium or radon are hard enough to effect the disintegration.

(3) *Bombardment of Various Elements with High Velocity Deuterons Generated in High Voltage Machines.* The development of apparatus for generating high voltages, by means of which charged nuclear particles can be accelerated to great velocities, holds out the greatest promise for the production of intense neutron beams. There is every reason to believe that these machines will presently be able to generate neutrons more rapidly than the combined output of all the Ra-Be and Rn-Be sources that could be prepared from all the radium that has ever been mined. At present, high voltage machines are in an experimental and developmental stage. But they have already made possible the performance of many valuable physical experiments that involve neutrons, directly or indirectly, and have shown the lines along which future developments of high voltage apparatus may be expected to proceed.

Neutrons have been generated in high voltage machines by bombarding various elements with ions of hydrogen, helium, and deuterium; by far the greatest efficiency is obtained with deuterium ions (deuterons) so only this method will be considered here.

For the generation of neutrons, voltages exceeding 2 million are very desirable, because the efficiency of neutron production rises rapidly with the voltage of the ions. The considerable difficulties attendant on the generation of such voltages are being overcome by various means. Six types of generators will be listed here. The potentialities of none of these have been exhausted, so it is impossible to describe one

[13] Paneth and Loleit, *loc. cit.*
[14] Szilard and Chalmers. *Nature*, 1934, *134*, 494.
[15] Chadwick, J., and Goldhaber, M. *Proc. Roy. Soc. A 151*, 1935, 479.

method as "best." Some of the methods have been further developed than others, as regards the magnitude of the voltages and ion currents attained, and some are better than others in regard to constancy and homogeneity of output.

For convenience, high voltage generators may be divided into two classes: (A) those which generate the full voltage in a single step, and (B) those in which the "output voltage," used in accelerating the ions, is reached by recurrent application of lower accelerating voltages along the paths of the ions. In the first group there may be listed:

(1) Electrostatic generators, particularly those invented by Van de Graaff, and used by Van de Graaff and Bramhall, by Tuve, Dahl, and Hafstad, and others.

(2) High voltage transformers, particularly arrangements using a group of transformers in cascade, as used by Crane and Lauritsen.

(3) Series-parallel condenser generators, developed by Cockroft and Walton, in which a set of high voltage condensers are charged in parallel and discharged in series. (This was the first method by which ions were artifically accelerated to sufficiently high velocities to produce nuclear disintegrations in the laboratory.)

The second group includes:

(4) Successive acceleration of ions through hollow cylinders connected to a high frequency vacuum tube oscillator. This method, developed by Lawrence and Sloan, gives "output voltages" which are, roughly, the products of the peak voltages of the numbers of pairs of accelerating tubes.

(5) The "cyclotron," invented by E. O. Lawrence. This ingenious and singularly successful apparatus employs only two electrodes and a strong magnetic field at right angles to the electric field. As in (4), the electrodes are connected to a high frequency oscillator. With a peak voltage of only 25,000 volts, deuterons of energies exceeding 6 million volts have been produced. This machine has probably yielded more information about nuclear transformations and has been used for inducing artificial radioactivity in more elements than has any other high voltage machine, at the present time.

(6) Beams' apparatus for successive accelerations. This machine is similar in principle to that mentioned in (4), but employs the transmission of an electric pulse along "trolleys," instead of an oscillating circuit. The apparatus is of more recent design than the others, and is still in an experimental state.

Space does not permit a detailed discussion of these apparatus. The advantage of high voltage machine generation of neutrons, over generation by radium or mesothorium sources, lies in the great output that is potentially available. This is because deuterons are used instead of alpha particles, because very large numbers of ions can be used, and because the voltages to which they can be artificially accelerated greatly exceed the equivalent voltages accelerating natural alpha particles. The disadvantages of high voltage sources are that the machines are costly to construct, require the most careful design, based on considerations of the intended use, and must be constantly maintained by skilled operators.

VI. THE HANDLING OF NEUTRONS

(a) *Protection.* The protection of personnel against harmful physiological effects of neutrons (which one might call "neutron burns") is analogous to protection against gamma and roentgen-ray burns. As with confined sources of gamma type radiation, the simplest form of protection against neutrons is distance from the source. Protective absorbers of neutrons must necessarily be thicker than those used for the same degree of protection against gamma radiation of radioactive origin, because of the low absorption coefficients of all elements for fast neutrons.

Absorption of neutrons must be in two successive steps: first, diminution of their

velocities by scattering, and second, removal of the slow neutrons by nuclear absorption. The former process is best accomplished by passing the neutrons through hydrogen-bearing materials such as paraffin, water, or oil; for the latter process, boron, cadmium, lithium or their compounds are most efficient and convenient. A good filter that performs both of these functions is a water solution of boric acid, 2 or 3 feet thick.

When the production and filtering of neutrons are accompanied by gamma rays, or other penetrating emissions, protection must be provided against such emissions. For example, in the use of Ra-Be or Rn-Be sources, one must provide the customary protection against the gamma rays of the Ra or Rn. In addition to this, there is a (relatively weak) emission of very penetrating gamma radiation associated with the *production* of the neutrons by these sources. (Its mean energy is estimated to be of the order of 6 million volts, as compared with the maximum energy of 2.19 million, for Ra C.) High voltage machine sources of neutrons usually emit penetrating gamma radiation. Thus Crane, Delsasso, Fowler, and Lauritsen[16] find that gamma rays of 11 wave lengths are emitted by lithium, when bombarded by fast protons of energy less than 1 million volts. The hardest of these gamma-ray lines corresponds to an energy of 16 million volts. The *absorption* of neutrons by some elements is also accompanied by gamma-ray emission. For example, slow neutrons, when absorbed in cadmium, cause the emission of quanta whose energies are estimated to be as high as 10 million volts.[17] The number of absorption-emission quanta is probably exactly the same as the number of neutrons absorbed in the quantum-emitting absorption process involved. Their high energies tend to minimize the danger of physiological effects.

Frequent blood counts of persons exposed to strong neutron sources will serve to detect excessive dosages of gamma rays, and *probably* of neutrons; the latter has not yet been settled by experiment. According to recent reports, persons working in the vicinity of the cyclotron (in California) become very noticeably *radioactive*, as a result of artificial radioactivity produced in their body tissues by absorption of slow neutrons. Measurement of the extent of such radioactivity should provide an immediate and simple means of determining the order of magnitude of the exposure to slow neutrons (but not to fast ones). An obvious variation of this method would be to carry in a pocket an element such as silver, rhodium, vanadium, bromine, or iodine (i.e., an element in which artificial radioactivity is strongly induced by exposure to slow neutrons), and to measure its radioactivity at some definite time after the exposure to slow neutrons. The amount of exposure to fast neutrons is not so easily determinable.

(b) *Measurement and Filtration.* The intrinsic characteristics of a beam of neutrons are: first, the number traversing unit area in unit time; second, the velocities of the neutrons; and third, the directions of their paths. The first and second of these determine the energy flux in the beam; the third is important for calculating effects of the beam when the source is of extended area, or when the beam has been passed through a scatterer of extended area.

Unfortunately, the measurement of these characteristics is not very easy, at the present time. The number of neutrons emitted, per second, by any source is probably not known to better accuracy than a factor of two; the distributions of their velocities are probably even more uncertain than the number emitted; and scattering experiments that are free from errors of performance and interpretation are not easy to devise, especially when the neutrons used are heterogeneous in energy. These difficulties arise mainly from the fact that the efficiencies of detection and measurement of neutrons vary through

[16] Crane, H. R., Delsasso, L. A., Fowler, W. A., and Lauritsen, C. C. *Phys. Rev.*, 1935, *48*, 125.

[17] Herszfinkiel, H., and Wertenstein, L. *Nature*, 1936, *137*, 106.

wide limits with the velocities of the particles being measured, and the limits of these variations are unequal for different means of measurement. In general, it is necessary to use more than one method of measurement to make even an approximate determination of the energy flux in a neutron beam.

Six methods of measuring neutron beams may be listed here:

(*a*) *Paraffin-lined ionization chambers.* Here, the integrated ionization produced of H-particles ejected from the paraffin by neutrons is measured. This method is fairly suitable for neutrons of high energy, but is open to the errors attendant on the measurement of the ionization of any nuclear particles, and the additional uncertainty of how the probability of ejection of an H-particle depends on the velocity of the neutron. The method is not suitable for slow neutrons.

(*b*) *Thin ionization chambers, arranged with very sensitive linear amplifiers.* These record the passage of individual ionizing nuclear particles, and measure the ionization per cm. path of each particle, from which the energy of the particle can be deduced. They have been a very valuable help in the study of neutrons, but are subject to the uncertainty of efficiency for detecting neutrons of various velocities. When the ionization chambers are lined with lithium or boron, they are adaptable for measurement of slow neutrons; when lined with paraffin, they may be used for fast neutrons, but with different efficiencies.

(*c*) *Methods using artificial radioactivity induced by neutrons.* These involve the exposure of suitable "detector" elements to the neutron beam, followed by measurement of the ionization produced by the decay of the radioactivity of the detector, by means of Geiger-Müller counters or ionization chambers. The detector element usually has very selective response to neutrons of different velocities; neutrons of low, or relatively low, energies give the greatest response.

(*d*) *Nuclear disintegrations in photographic plates.* By special technique, the paths of alpha and H-particles emitted by the disintegration of light elements can be recorded in certain photographic plates. This method has the disadvantages of slowness (because of the time required to make microscopic examination of relatively large areas), and of selective response to relatively slow neutrons. The records are, of course, permanent. This method will doubtless be further developed.

(*e*) *Wilson cloud chambers.* With these apparatus, the paths of disintegration products of nuclear disintegrations can be photographed, and the kinds and energies of the particles determined. They must be used with relatively weak sources, and must be protected against (strong) gamma radiation, which renders them inoperative.

(*f*) *Chemical measurement.* Hopwood and Phillips[18] recently reported the results of attempts to measure the integrated effects of neutron irradiation by means of the chemical action on colloids, and by the promotion of simple chemical reactions. They found the effects of neutrons to resemble those of gamma radiation, in both cases. It is expected that this, or a similar method, will be further developed.

A beam of heterogeneous neutrons may be subjected to strong filtration, which removes the low energy particles. A filter consisting of a few millimeters of cadmium, boron, or lithium will remove a very large percentage of the slow neutrons without removing significant percentages of the fast ones. However, much remains to be learned about filtration processes. For example it has been lately found that cadmium, whose absorption of slow neutrons is known to be extremely high, nevertheless transmits a band of slow neutrons which are capable of inducing radioactivity in gold.[19] This, and similar phenomena found in silver and indium, suggest that the neutrons which are strongly absorbed

[18] Hopwood, F. L., and Phillips, J. T. *Nature*, 1935, *136*, 1026.
[19] Frisch, O. R., Hevesy, G., and McKay, H. A. C. *Nature*, 1936, *137*, 149.

in any element have a *minimum* energy of magnitude depending on the element, as well as a maximum energy; in other words, the neutrons may move too slowly to be captured by a nucleus, as well as too fast for capture. More complete information on this subject will probably lead to a modification of filtering technique.

The optimum thickness of paraffin for slowing down neutrons from a Rn-Be source is about 10 cm., where the disintegration of lithium is used for detection of the slow neutrons.[2] For neutrons of lower initial energies, I find that the optimum thickness of paraffin is less than 10 cm.; for neutrons of higher energy, it would doubtless be greater than 10 cm. The most appropriate scatterers for neutron sources of various energy maxima and energy distributions are yet to be determined. The process of slowing down neutrons by hydrogen collisions is somewhat complicated by the fact that hydrogen also *absorbs* part of the slow neutrons, which process is accompanied by the emission of gamma radiation. (The absorption is caused by the direct combination of the neutron with a hydrogen nucleus, forming an atom of deuterium.) The amount of the absorption and the energies at which the neutrons are most apt to be absorbed by hydrogen have not yet been accurately determined.

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Additional Note. Since the foregoing paper was written, two important papers describing experiments on the biological action of fast neutrons have appeared. In one of these. Lawrence and Lawrence[20] compared the action of measured dosages of fast neutrons from the cyclotron (California) on the blood of live rats with the effects of measured dosages of very hard roentgen rays (900,000 volts). The effects were similar in character, as regards the diminution of the number of lymphocytes per cubic centimeter in the blood, but the dosage of neutrons required to produce a given effect was only about one-tenth the roentgen-ray dosage which gave the same effect, indicating that *the fast neutrons were about 10 times as efficacious as hard roentgen rays in producing this action.* The other paper, by Zirkle and Aebersold[21] describes experiments on the relative retardation of the growth of roots of wheat seedlings that had been irradiated with measured dosages of fast neutrons and hard roentgen rays. They find that *one roentgen of fast neutrons is as effective as 20 roentgens of the x-rays* in this action. It is significant that the apparatus and methods of measurement of dosages used by these authors were the same as those of Lawrence and Lawrence, making the results of the two kinds of experiments directly comparable. This fact allows the significant conclusion to be drawn that the biological effects of equal amounts of fast neutron irradiation of different organisms may depend considerably on the nature of the organism and/or the biological process thereby affected.

[20] Lawrence, J. H., and Lawrence, E. O. The biological action of neutron rays. *Proc. Nat. Acad. Sc.*, Feb., 1936, *22*, 124.

[21] Zirkle, R. E., and Aebersold, P. E. Relative effectiveness of x-rays and fast neutrons in retarding growth. *Proc. Nat. Acad. Sc.*, Feb., 1936, *22*, 134.