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Chapter XII. RADIATION AND ITS BIOLOGICAL EFFECTS

Chapter Editor: E. O. Wollan

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A. Physical Aspects

SUPPLEMENT

By J. E. Rose
May, 1945

Page 3

Add to the list of references:

(4) Gray, L. H., Proc. Cam. Phil. Soc. 40 72(1944).

Page 4

Amend last two sentences to read:

A proper application of the Bragg-Gray principle permits this quantity to be estimated if such factors as W and ρ for the type of radiation are known. From such measurements the dose in roentgens can be approximated.

Page 7

Add this sentence at the end of 2.3:

Since the fraction of photon energy lost in air by photoelectric and Compton scattering varies by 20% from 0.05 to 4.0 Mev, the above is only approximate.

Amend the last sentence on the page to read:

Provided the energy and specific ionization are known at the particular point in the path, if N is the number of β particles per cm^2 and k is the specific ionization at a given point on the path, the dose is

$$kN \times 4.8 \times 10^{-10} \text{ r per } \beta \text{ particle per cm}^2.$$

Page 10

Amend the first sentence of the third paragraph under (d) to read:

A C_2H_4- filled chamber with a paraffin wall made conducting with a very thin coat of aquadag less than one micron thick should give readings (in r - equivalents) about 15% greater than the corresponding tissue dose.

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Page 12

Add to the list of references:

(6) Gray, L. H., Proc. Cam. Phil. Soc. 40 72(1944)

Page 15

Amend sub-section (c) to read:

There is probably no hazard for external irradiation. Little is known about "caustic" effects of large quantities, or of absorption through the skin.

Page 18

Add to the list of references:

(3) Failla, G, CH-1347, Feb. 15, 1944.

(4) Parker, H. M., CH-930, Sept. 10, 1943.

(5) Cantril, S. T. and H. M. Parker, CH-2812, Jan. 5, 1945.

A. PHYSICAL ASPECTS

1. Principles of Radiation Dosimetry

1.1 Introduction

The natural unit of dosage might be taken as the absolute amount of energy absorbed per unit volume of the absorbing medium as a result of irradiation. This however, cannot be conveniently measured, since it is only the ionization which is measurable, and this corresponds to only a fraction of the energy absorbed. It is ordinarily assumed that this fraction is constant in cases of biological interest.

The actual fraction appearing as ionization energy is approximately one-half in hydrogen, oxygen, and nitrogen, but is very different in rare gases. Some gases and many organic vapors show large variations relative to air in the fraction of absorbed energy which corresponds to ionization.

1.2 The Bragg-Gray Principle[1]

Consider a small air-filled cavity introduced into a solid or liquid medium in which electromagnetic radiation is being absorbed. If the cavity is sufficiently small, the ionization in it is almost entirely due to its traversal by secondary electrons generated in the surrounding medium. For this case:

$$E_V = \rho W J_V \qquad (1)$$

where E_V = kinetic energy of secondary electrons generated per unit volume of medium

ρ = ratio of stopping power of medium to that of air for electrons

W = average energy lost by a beta particle per ion pair formed in air. ($W \approx 32$ ev per ion pair)

J_V = number of ion pairs formed per unit volume in the small cavity

If the air and the surrounding medium have the same atomic number, then ρ is equal to the ratio of their electron densities. Otherwise, letting n represent the electron density of the medium and Z its atomic number, we have:

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1. Principles of Radiation Dosimetry (continued)

$$E_v = 2.55 \times 10^{-21} f_Z n W J_v \qquad (2)$$

where values of f_Z (variation of ρ with atomic number) are given in the following table, and

$$n = \text{sp. gr.} \times \text{Avogadro's number} \times \sum_i p_i Z_i / A_i \qquad (3)$$

where p_i is the fraction (by weight) of atoms in the medium having atomic number Z_i and atomic weight A_i.

Variation of ρ with Atomic Number

Z_i	4	6	(air) 7.3	8	12	16	24	32
f_Z	0.96	0.99	1.00	1.02	1.05	1.09	1.13	1.16

Although the Bragg-Gray principle was originally thought of in terms of x-rays or γ rays, it is applicable to any kind of radiation which produces ionizing secondaries. For fast neutrons, if a wall containing hydrogen is used, the recoil protons are responsible for the major part of the ionization. The cavity must be small compared to the range of these protons if it is to satisfy the conditions for the Bragg-Gray principle.

1.3 Thimble Chambers

a. A "thimble" ionization chamber may be used for biological purposes to measure the intensity of radiation within a medium. A thimble chamber constitutes a proper "cavity" in a medium when the wall thickness exceeds the maximum range in the wall of the secondary particles involved. Thus for gamma rays from radium and a graphite wall, a wall thickness of about 5 mm is required, while for 200 kev x-rays, a 0.2 mm wall is sufficient.

b. All dimensions of the thimble chamber must be such that a secondary particle crossing the chamber loses only a negligible fraction of its energy; for example, the dimensions should not exceed a few mm for gamma rays or 0.1 mm for 200 kev x-rays. The dimensions are correct when the ionization in the chamber is a linear function of the gas pressure. This condition of linearity is fulfilled either for a very small thimble chamber or for a chamber so large relative to the corpuscular ranges that the ionization in the pressure range used is at all times a gas effect and not a wall effect. (Although not a thimble chamber, the large chamber can be used

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under the conditions specified.)

c. In the special case in which wall and gas have the same average atomic number, there is no restriction on the dimensions.

d. Examples of errors due to finite cavity size, as determined by experiment, are:

Radiation	Wall Material	Chamber Volume (cc)	Error
Gamma rays	graphite	3	1%
	lead	0.1	6%
	lead	3×10^4	250%
X-rays (100 kev quantum)	graphite	0.1	1%
	copper	0.1	3%

e. Measurements in air: If a measurement is made with a small chamber of wall thickness t of "air equivalent" material (i.e., material equal to air in average atomic number), a small correction is required for absorption of radiation by the wall of the chamber. If the ionization per unit volume is J esu per sec, then

$$\text{Dose} = J(1 + \sigma_a t) \text{ roentgens} \qquad (4)$$

where σ_a = scattering absorption coefficient of the chamber wall, and t should be slightly greater than the maximum range of recoil electrons. In practice $\sigma_a t \sim 0.03$.

f. Measurements in other media:

$$\text{Dose} = J(1 + \sigma_a t - \sigma_a' t') \text{ roentgens} \qquad (5)$$

where σ_a' = scattering absorption coefficient of medium, and
t' = external radius of chamber considered as a sphere.

1.4 The Roentgen

The roentgen was first defined in 1928 at the International Radiological Congress in Stockholm; it was redefined with no essential change in meaning at the International Radiological Congress in Chicago in 1937. The later definition reads:

1 Principles of Radiation Dosimetry (continued)

"The roentgen shall be that quantity of x- or gamma-radiation such that the associated corpuscular emission per 0.001293 gram of air produces in air, ions carrying 1 esu of quantity of electricity of either sign."

The wording of this definition is unfortunately such that one cannot be exactly sure as to what the unit refers. If the roentgen were to be a measure of the incident radiation, then the term quantity should have been replaced by a more definite term.

In actual practice however, one is mainly interested in the energy absorbed per gram of a given medium when the medium is exposed to radiation. This quantity is referred to as the dose of radiation, which can be measured in roentgens. A small volume of a given medium receives a dose of one roentgen when it is exposed in an x-ray or gamma ray radiation field of such density and for such a duration that, if a similar volume of air should receive the same amount of radiation, ions carrying a total of 1/0.001293 esu of electric charge of either sign would be produced per gram of air. In actual practice rather large samples of material or tissue are irradiated. In this case the dose received by each portion of the medium is affected by the presence of neighboring parts. The above statement regarding dose in roentgens applies, however, to any small volume in the medium, but unfortunately a measurement exactly satisfying the definition cannot be made directly without some corrections.

If a small "air-wall" (see XII A,1.3e) thimble chamber can be inserted in the medium at the point where the dosage measurement is required, the dose can be directly measured either under such conditions that the effect of introducing the chamber need not be considered or else that satisfactory corrections for this effect can be made.

In many cases it is desirable to know the amount of the actual ionization in the medium rather than that which would be produced in air. A proper application of the Bragg-Gray principle permits this quantity to be measured accurately. From such measurements the dose in roentgens can be calculated with fair accuracy.

1. Principles of Radiation Dosimetry (continued)

REFERENCES

(1) Gray, L. H., "An Ionization Method for the Absolute Measurement of γ-Ray Energy," Proc. Roy. Soc. 156, 578 (1936).

(2) Quimby, Edith H., "Physical Methods of Dosage Determination in Radiation Therapy," J. Applied Phys. 13, 678 (1942).

(3) Kay, G. W. C., and Binks, W., Proc. Roy. Soc. A161, 564 (1937).

2. Practical Measurement of Dose

2.1 Ion Chambers

On the basis of the discussions on the principles of dosage measurements and the definition of the roentgen in XII A,1, it is seen that accurate results can be obtained if certain conditions are satisfied.

In the case of x-rays, the photoelectric type of absorption increases rapidly with atomic number and the choice of wall material for an ionization chamber is very critical. For soft x-rays, however, the range of the secondary beta rays in air is sufficiently short so that when the radiation is appropriately collimated a chamber with no wall other than a layer of air can be used and in this case a true measure of the radiation in roentgens can be made.

For hard gamma rays the choice of wall material is not so critical for approximate results. If bakelite (or other similar plastic) is used as wall, this material is sufficiently close to air in average atomic number so that, regardless of chamber size, a reasonably accurate measurement in terms of roentgens can be made. Small amounts of exposed metal will, however, cause a chamber to be too sensitive for radiation of 200 kev or less -- by as much as several hundred percent with small chambers.

2.2 Dosage Rate from Radium

An accurate measurement of the dosage rate from radium (in equilibrium) has been made by Gray.[1] At one cm distance from one mg Ra (filtered through 0.5 mm Pt),

$$J = 8.3 \pm 0.1 \text{ esu/hr per cm}^3 \text{ in graphite}$$

$$J = 8.4 \pm 0.1 \text{ r/hr}$$

For platinum wall of thickness t cm, provided t is not less than 0.03 cm,

$$J = (8.98 - 11.7t) \text{ r/hr} \qquad (1)$$

2.3 Dose per Photon

In some calculations it is convenient to express the dosage rate in terms of gamma ray flux. This can be given as

$$\text{r per gamma quantum per cm}^2 = (\sigma_a E \times 10^6 \times 4.8 \times 10^{-10})/32 \qquad (2)$$

2. Practical Measurement of Dose (continued)

where σ_a is the recoil absorption coefficient, equal approximately to 3.5×10^{-5} cm^{-1} in the range from 0.05 to 4 Mev, and E is the photon energy in Mev. Hence there are 5.3×10^{-10} E roentgens per gamma quantum per cm^2; or $2 \times 10^9/E$ gamma quanta per cm^2 equals 1 r.

2.4 Table of Roentgen Equivalents

Table 1

Energy Absorbed in Air for One Roentgen	Energy Absorbed in Tissue for One Roentgen
0.107 erg/cm^3 1.07×10^{-8} joule/cm^3 2.56×10^{-9} cal/cm^3 6.66×10^{10} ev/cm^3 2.08×10^9 ion pairs/cm^3	83 ergs/g 8.3×10^{-6} joule/g 1.98×10^{-6} cal/g 5.18×10^{13} ev/g 1.62×10^{12} ion pairs/g
Rate of Energy Absorption in Air for 0.1 r/24 hours or 1.16×10^{-6} r/sec	Rate of Energy Absorption in Tissue for 0.1 r/24 hours or 1.16×10^{-6} r/sec
1.24×10^{-7} erg/cm^3-sec 1.24×10^{-14} watt/cm^3 2.96×10^{-15} cal/cm^3-sec 7.75×10^4 ev/cm^3-sec 2.42×10^3 ion pairs/cm^3-sec	9.6×10^{-5} erg/g-sec 9.6×10^{-12} watt/g 2.29×10^{-12} cal/g-sec 6.00×10^7 ev/g-sec 1.88×10^6 ion pairs/g-sec

2.5 Measurement of Beta Rays

With β rays there is no need of a wall around the chamber for establishing equilibrium between the primaries and secondaries. Chambers with the thinnest possible wall should be used and a correction for absorption in the wall should be made.(2)

To express the dosage rate per β particle one must consider a particular point in the path of the β particle since the ionization varies rapidly along the path, becoming greater near the end of the path. If N is the number of β particles

per cm^2 and k is the specific ionization at a given point on the path, then the dose is

$$kN \times 4.8 \times 10^{-10} \text{ r per } \beta \text{ particle per cm}^2$$

2.6 Dose Measurement for Fast Neutrons

a. Elastic scattering of neutrons. Elastic scattering is the principal process by which fast neutrons produce ionization in the body. The contributions of inelastic scattering, (n,p), (n,α), and (n,γ) reactions [illegible]. The average amount of energy which is transferred [illegible] recoil nucleus in elastic scattering depends on the atomic weight of the nucleus and can be calculated to be

$$\bar{E} = 2AE_0/(A+1)^2 \qquad (3)$$

giving $\bar{E} = 0.5\ E_0$ for hydrogen
$= 0.151\ E_0$ for carbon
$= 0.125\ E_0$ for nitrogen
$= 0.111\ E_0$ for oxygen

It should be noticed that these are not the same values as would be obtained from the average logarithmic energy loss, which is

$$\left[\log E_0/E\right]_{av} = 1 \text{ for hydrogen, or } \bar{E} = 0.368E_0$$
$$= 0.158 \text{ for carbon, or } \bar{E} = 0.146E_0$$

b. Roentgen equivalent dose (r.e.d.). The tissue dose corresponding to a given neutron exposure will be referred to as one r-equivalent dose when the energy absorbed per gram of tissue is equal to that absorbed when the tissue has been exposed to one r of x-rays. One r-equivalent dose (r.e.d.) of any radiation will have been received when the energy absorbed per gram of wet tissue is 83 ergs. For fast neutrons the energy E_a in ergs absorbed per gram of tissue is

$$E_a = kEN\Sigma\sigma_i f_i Q_i \qquad (4)$$

where N is the number of incident neutrons per cm^2
E is the energy of the neutrons in Mev
$k = 1.602 \times 10^{-6}$, the factor to convert Mev to ergs

2. Practical Measurement of Dose (continued)

σ_i is the cross section for neutrons of energy E on atomic nuclei of type i
f_i is the fraction of the neutron's energy transferred to the nucleus per collision
Q_i is the number of atoms of type i per gram of tissue

The number N of neutrons of energy E per cm^2 giving a dose of 1 r.e.d. is then

$$N = 8/1.602 \times 10^{-6} \sum_i \sigma_i f_i Q_i \qquad (5)$$

The following table includes the values of the quantities necessary to calculate N for ordinary wet body tissue.

Table 2

Atom Type	% by Wt.	Atoms per Gram	f	$\sigma_i \times 10^{24}$ (cm^2)				
				E= 0.5	E= 1	E = 2	E = 3	E=4
H	10	6.02×10^{22}	0.5	5.5	4.2	2.85	2.2	1.7
C	12	6.02×10^{21}	0.151	3.5	2.5	1.7	1.5	1.6
N	4	1.71×10^{21}	0.124	3.5	2.5	1.4	1.3	1.6
O	73	2.74×10^{22}	0.111	3.5	2.0	1.2	1.3	1.8

c. Tolerance dose for fast neutrons. The biological effect resulting from ionization by fast neutrons has been shown by experiment to be from 2 to 10 times greater than that of the same amount of ionization produced by x-rays. For body tissue a factor of 5 is probably ample and 0.02 r.e.d. (or 0.01 n; see XII A,2.6 d) can be taken as the safe daily tolerance dose. Table 3 gives the number of neutrons per cm^2 for one r.e.d. and 0.02 r.e.d., and the number of neutrons per cm^2 per minute for 0.02 r.e.d. in 8 hours.

2. Practical Measurement of Dose (continued)

Table 3

E (Mev)	Neutrons/cm^2 for 1 r.e.d.	Neutrons/cm^2 for 0.02 r.e.d.	Neutrons/cm^2-min for 0.02 r.e.d./8 hr
0.5	5.7×10^8	11.50×10^6	24,000
1.0	3.83×10^8	7.66×10^6	15,960
2.0	2.84×10^8	5.68×10^6	11,840
3.0	2.40×10^8	4.80×10^6	10,000
4.0	2.22×10^8	4.44×10^6	9,240

d. Measurement of fast neutron ionization: the n unit. The dose for fast neutrons can be measured in the same way as for x-rays except that a true tissue-wall cavity must be used instead of an "air-wall" cavity. The Victoreen condenser r-meter with a 100 r chamber has been used for measuring fast neutrons. The bakelite wall contains hydrogen but since its percentage hydrogen content is less than that of body tissue the response of the chamber does not give a direct measure of tissue ionization.(3)

When a pure beam of fast neutrons is measured with the Victoreen r-meter (100 r chamber), and the scale is read as for γ rays, a reading of 1 r is called 1 n. One n unit as thus defined represents a tissue ionization equivalent to that produced by about 2.5 r of γ rays. (See XII C,3.)

A C_2H_4-filled chamber with a paraffin wall made conducting with a very thin coat of aquadag should give readings (in r-equivalents) about 15% greater than the corresponding tissue dose. When it is desired to measure fast neutrons in the presence of gamma rays, a pair of balanced chambers, one with a hydrogen-containing gas and one with argon, for example, can be used.(3)

2.7 Dose Measurement for Slow Neutrons

When slow neutrons enter the body they are practically completely absorbed in the first few centimeters. Most of the absorption arises from (n,γ) reactions in hydrogen and nitrogen. The necessary constants for H and N in body tissue are given in the following table:

2. Practical Measurement of Dose (continued)

Table 4

	Hydrogen	Nitrogen
Number of atoms/g	6.02×10^{22}	1.71×10^{21}
Capture cross sections (cm^2)	0.25×10^{-24}	1.4×10^{-24}
Gamma ray energy	2.2 Mev	10.8 Mev
Fraction of neutrons absorbed in the two elements	0.9	0.1
Absorption coefficient for the γ rays	$6.0 \times 10^{-5} cm^{-1}$	$2.5 \times 10^{-5} cm^{-1}$

It is difficult to specify accurately the dose per slow neutron due to neutron capture in tissue. It is, however, approximately true that the effect of a dose of slow neutrons is equal to that of the corresponding γ rays emitted upon neutron capture. From this, the dose in r.e.d. units corresponding to N_s slow neutrons per cm^2 incident on the body is seen to be:

$$N_s \left\{ 0.9\, \mu'_{air} E' + 0.1\, \mu''_{air} E'' \right\} \times 4.8 \times 10^{-10}/32 \qquad (6)$$

where μ'_{air} and μ''_{air}, respectively, refer to the absorption coefficients in air of the hydrogen and nitrogen gamma rays, and E' and E" to the respective energies in ev of these γ rays. Using 140 as the value of the quantity in brackets in equation (6), the dose corresponding to N_s slow neutrons per cm^2 is

$$\text{Dose} = 2.1 \times 10^{-9}\, N_s \text{ roentgens}$$
$$\text{or } N_s/cm^2 \text{ per r.e.d.} \cong 5 \times 10^8 \qquad (7)$$

An ordinary pocket chamber gives a good measure of the dose received from slow neutrons since the γ rays produced in the body are measured on leaving the body.

2. Practical Measurement of Dose (continued)

REFERENCES

(1) Gray, L. H., "The Rate of Emission of γ-Ray Energy by RaB and RaC and by Thorium B and Thorium C"," Proc. Roy. Soc. 159, 263 (1937).

(2) Parker, H. M., "Some physical aspects of the effects of beta radiation on tissue" - Report CH-930.

(3) Wollan, E. O., and [illegible] dosage meter" - [illegible]

(4) Wilson, H. A., "[illegible] chambers" - Report [illegible]

(5) Wilson, H. A., "[illegible] neutrons" - Report [illegible]

3. Dosage Rate as Related to Types and Distribution of Sources

3.1 Radium

a. Energy rate per curie

For α rays	=	124.8 cal/hr
β rays	=	6.3 cal/hr
γ rays	=	9.4 cal/hr
Total	=	140.1 cal/hr

b. Dosage rate for radium radiations filtered through 0.5 mm Pt

Dosage rate = 8.4 r/hr per millicurie at 1 cm
= 140 r/min per gram at 1 cm
= 0.014 r/min per gram at 1 meter
= 0.0023 r/sec per gram at 1 meter

c. Absorption of gamma rays from radium

A nomogram is given (Figure 1, XII A,3) for determining the relationship between radium quantity, lead protection, and safe distance, where safe distance is based on 0.1 r per 8 hours. A straight edge laid across the page relates these quantities.

3.2 Uranium (1)

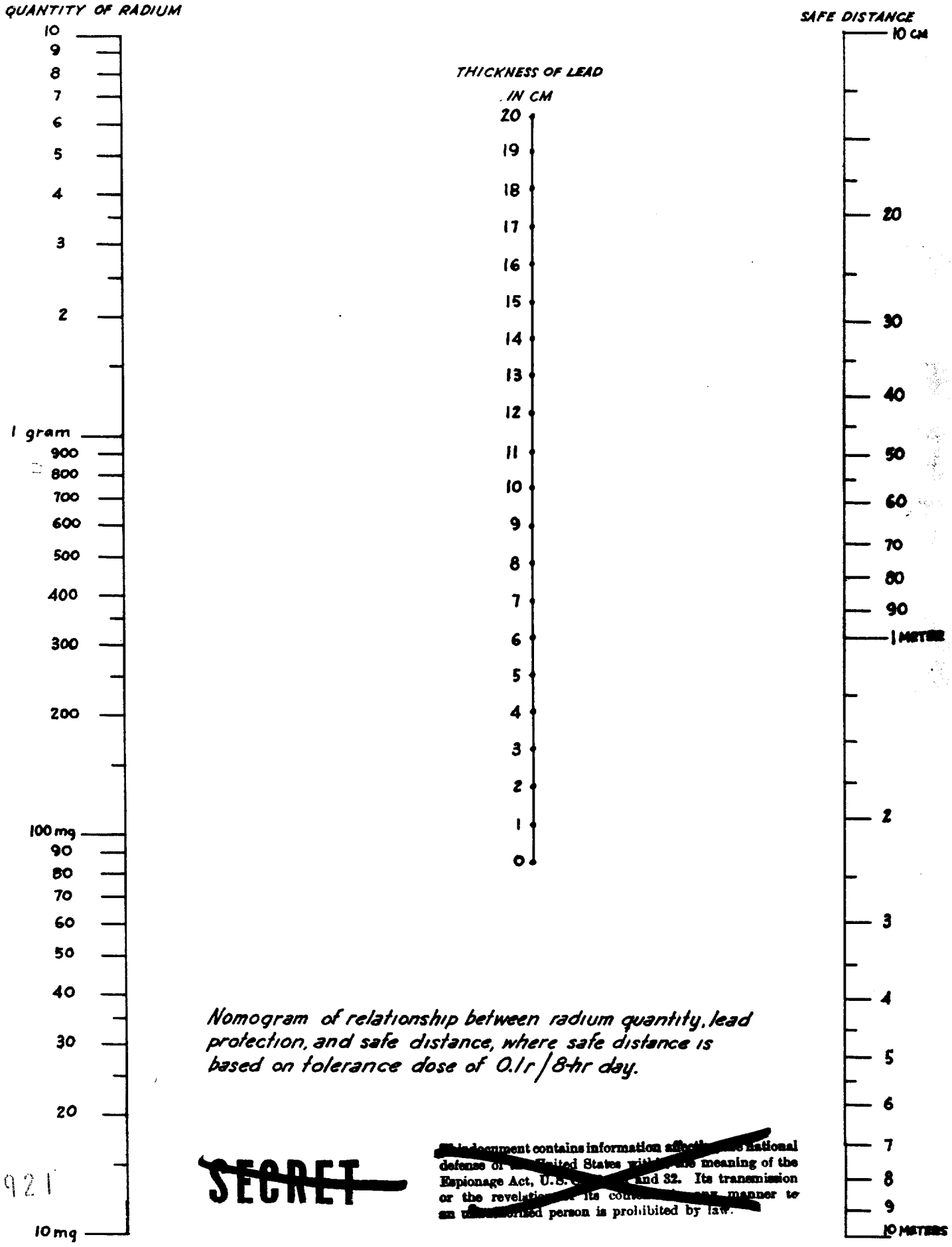
a. Gamma rays from uranium

Dosage rate = 0.005 r/hr from a surface of solid angle 2π. The absorption coefficient of the hard component equals 0.07 cm^{-1} for Pb.

b. Beta rays from uranium

These arise primarily from UX_2.
Dosage rate for contact with metal = 0.25 r/hr
Percent transmission by gloves:

Gloves	mg/cm^2	Remote Source	Contact
Canvas	24	90%	75%
Horsehide	90	69%	43%
Lead-leather	400	8%	2%



Nomogram of relationship between radium quantity, lead protection, and safe distance, where safe distance is based on tolerance dose of 0.1r/8-hr day.

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3. Dosage Rate as Related to Types and Distribution of Sources (continued)

c. Alpha rays

No hazard for external irradiation.

3.3 The Pile

For radiation from graphite pile refer to Chapter VIII and XI C,1.
For shielding of graphite pile refer to Chapter V F,2,5.

3.4 The Extraction Plant

For shielding refer to Chapter XI D.

A nomogram is given here (XII A,3, Figure 2) relating distance, thickness of concrete shield, and number of curies of 2 Mev gamma rays from fission products for 0.1 r/8 hr. A straight edge laid across the page gives the relation between these three quantities.

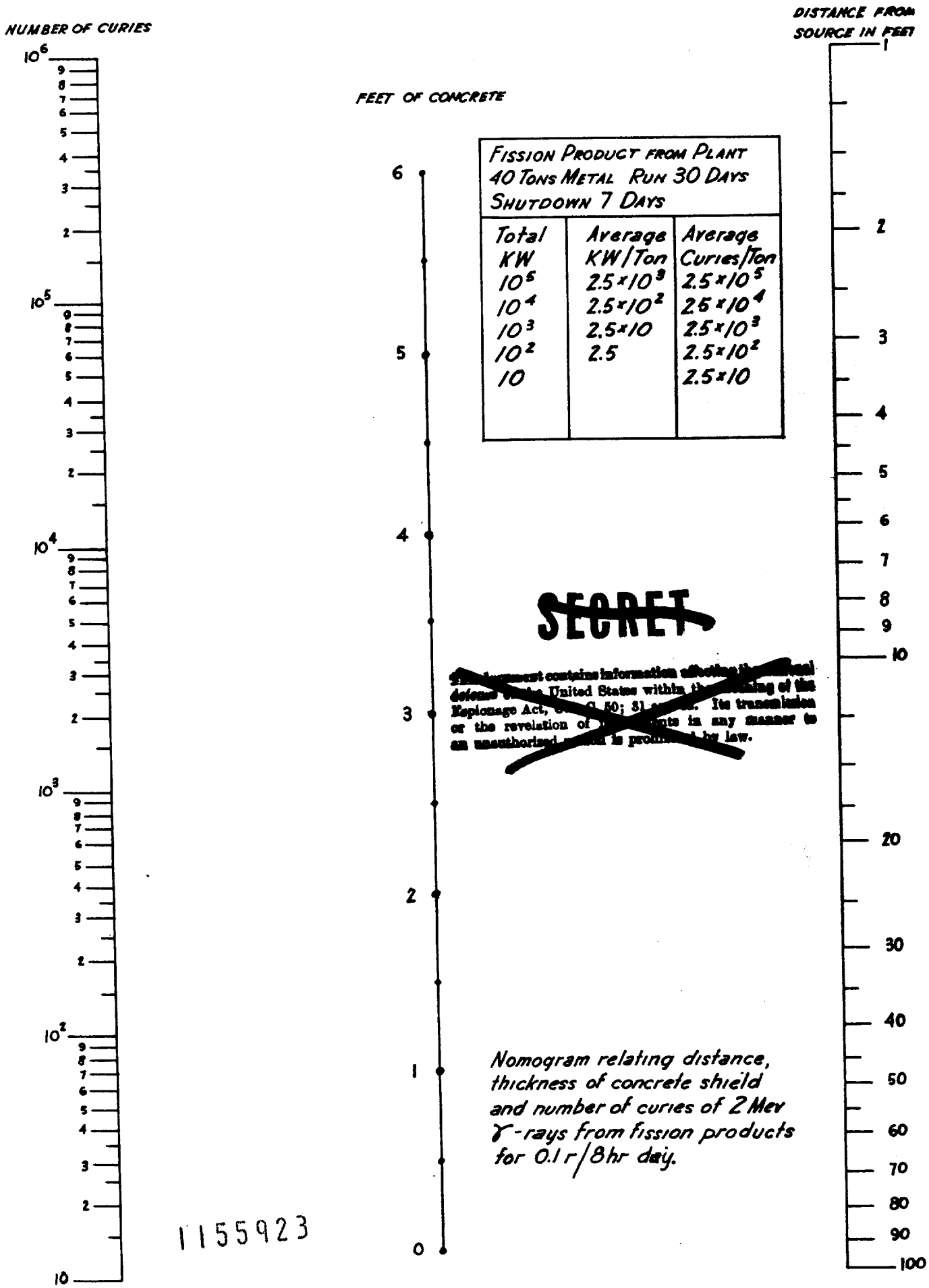
3.5 Fission Products

See Chapter III.

3.6 A Medium in which Radioactive Material is Uniformly Dispersed

A person or other living organism in a medium in which radioactive material is dispersed as gas, dust, or dissolved substances is subject to radiation hazard from (1) the radiation striking the outside of the body, and (2) radioactive material getting into the body via the lungs or gastro-intestinal tract.

For external irradiation, this problem involves only an expression of the safe amount of radioactive material per unit volume of the medium in terms of the tolerance dose. The internal effects which follow the breathing or ingestion of the material constitute a more complicated problem and involve a knowledge of the absorption and excretion rate for different substances in body organs.



Fission Product from Plant 40 Tons Metal Run 30 Days Shutdown 7 Days		
Total KW	Average KW/Ton	Average Curies/Ton
10^5	2.5×10^3	2.5×10^5
10^4	2.5×10^2	2.5×10^4
10^3	2.5×10	2.5×10^3
10^2	2.5	2.5×10^2
10		2.5×10

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Nomogram relating distance, thickness of concrete shield and number of curies of 2 Mev γ-rays from fission products for 0.1 r/8hr day.

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3. Dosage Rate as Related to Types and Distribution of Sources (continued)

a. Tolerance concentration for external irradiation. If radioactive material is spread uniformly throughout a large volume of medium, then obviously, for a point within the medium, the energy E_a absorbed per unit volume equals the energy E_e emitted per unit volume: $E_a = E_e$.

b. Radioactive material in the atmosphere. For a person on the ground surrounded by a uniformly contaminated atmosphere, the relation becomes $E_a = 1/2E_e$.(2)

For a region contaminated with gamma-active material at an average distance R

$$E_a = \mu E_e \int_0^R \frac{2\pi r^2}{4\pi r^2} e^{-\mu r} = 1/2E_e(1-e^{-\mu r})$$

where μ is the absorption coefficient for the radiation. When $R \gg 1/\mu$ this reduces again to $E_a = 1/2E_e$.

In Table 1, XII A,2.4, there is listed in several different units the rate of energy absorption in air corresponding to 0.1 r per 24-hr day. These values, after multiplication by two (since $E_e = 2E_a$), represent in various units the radioactive material which when spread uniformly through a large air volume will give a tolerance dose for external irradiation. In this way the tolerance concentration is found to be 2.5×10^{-14} watts/cm^3 or 1.5×10^5 ev/cm^3-sec.

The tolerance concentration may also conveniently be expressed in terms of curies. Let E be the energy in ev of each gamma quantum or beta particle emitted. Then the energy emitted per second by the presence of M curies per cm^3 is 3.7×10^{10} ME. Equating this to 1.5×10^5 ev/cm^3-sec, one obtains the tolerance concentration in curies as

$$M = 4.15 \times 10^{-6}/E \text{ curies per cm}^3 \text{ of air} \qquad (2)$$

Values of M for radioactive gases are easily obtained from this formula when the energy of their radiations is known.

3. Dosage Rate as Related to Types and Distribution of Sources (continued)

c. Radioactive material in water. Here, for example, for fish in water, $E_a = E_e$. Since water and tissue are of approximately the same density, the figures in the fourth part of Table 1, XII A,2.4, give directly the tolerance concentration for water, so far as external radiation to an immersed body is concerned. The tolerance concentration for external radiation, corresponding to 0.1 r per [illegible] be obtained in the same way as for the atmosphere, [illegible] gives

$$M = 1.6 \times 10^{-3}/Z \text{ curies per gram of water}$$

d. Tolerance concentration for internal irradiation by breathing of radioactive gases. (See XII C,2.1 for [illegible]) gases such as Kr and Xe the absorption in the body is [illegible] and the hazard from breathing is mainly to the lungs. The lungs have an air volume of about 3000 cm^3 and a [illegible] about 1000 grams. For beta ray emitting substances all the energy is absorbed in the lungs, and since there are approximately 3 cm^3 of air per gram of lung tissue, the tolerance concentration is one third of the figures in the last column of Table 1, XII A,2.4. For the bronchi there is a somewhat larger effective volume to mass ratio. In general, however, for beta rays and gamma rays the external exposure is greater than the lung exposure since the effective volume of air from which radiation can come is greater for the former. For alpha particles (from radon, for example), the external effect is practically zero because of the protective skin layer, while for the lungs and bronchi there is no such protective layer.

On the basis of the incidence of lung cancer among workers in pitchblende mines a safe tolerance of from 10^{-13} to 10^{-14} curies of radon per cm^3 has been established.

REFERENCES

(1) Parker, H. M., "Radiation hazard from X metal" - Report CH-619.

(2) Wollan, E. O., "Tolerance concentration of radioactive gases in the atmosphere" - Report CH-504, Section B1, Appendix.

B. THE BIOLOGICAL EFFECTS OF RADIATION IN RELATION TO OCCUPATIONAL EXPOSURE

1. Relation Between Character of Radiation and Biological Effects

1.1 Specific Ionization

The relative biological effectiveness of various radiations in relation to specific ionization is discussed in XII C,3.1 and 3.2. The principle of specific ionization has practical application in radiation protection. The tolerance dose for fast neutrons must take into consideration the greater relative biological effect per unit of energy absorbed per gram of tissue as compared with x-rays or gamma rays (see XII A,2.6c). Shielding requirements for fast neutrons must therefore include this consideration. The tolerance dose for gamma radiation is established as 0.1 r per 24-hour day. For fast neutrons it is set as 0.01 r per day, or 0.02 roentgen equivalent dose per day (see XII A,2.6c. It will be noted that the "roentgen equivalent dose" is a measure of energy absorbed (1 r.e.d. = 83 ergs absorbed per gram of tissue), not of equivalent biological effect.

1.2 The Distribution and Penetration of Radiation

Whether or not a particular radiation will produce damaging effects, and also the nature of these effects, depends upon the ability of the radiation to reach the tissues in question. Although alpha particles are highly ionizing and destructive, their range of action in tissue is small, approximately 0.1 mm. But when material which is alpha-radioactive is deposited within the body in a vulnerable organ (e.g., bone marrow) the limited range of the alpha particle is no longer so great a factor. Similarly, low energy beta rays (as from Xe or I) cannot penetrate the skin to an effective depth, but the same beta emitter in the bone, lung, or thyroid in sufficient quantity may be most injurious. These are examples of <u>internal radiation</u>; the tolerance values for internal absorption of fission material based on existing knowledge are discussed in XII C,2.

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1. Relation Between Character of Radiation and Biological Effects (continued)

Even though the effectiveness of high energy gamma rays per unit density of ionization may be less than that of low energy gamma rays, their ability to penetrate into more vulnerable regions in the body may be a more deciding factor as a hazard than their lesser degree of specific ionization. This is illustrated in connection with the following comparison of the relative quantities of varying qualities of radiation required to produce erythema of the skin:

Quality of Rays	Exposure to Produce Erythema
Grenz rays	100 r
100 kv x-rays	350 r
200 kv x-rays	600 r
1000 kv x-rays	1000 r
Gamma rays (Ra)	2000 r

Thus a comparable erythema of the skin (due to ionization produced in and immediately below the skin) may be produced by 350 r exposure to 100 kv x-radiation or 2000 r of gamma radiation from Ra. But the effect on tissues underlying the skin can be far greater in the case of 2000 r of gamma radiation than in that of 350 r of soft x-rays.

The effect of distribution of the radiation (geometry) in altering the degree of ionization and biological effectiveness, and its dependence upon the quality of the incident radiation, are illustrated by the following tabulated results of calculations by H. M. Parker. For different qualities of radiation with varying geometries and for equal surface dose, he finds:

Type of Irradiation	Relative Total Body Ionization
Soft x-rays from large distance	Approx. 1.0
Gamma rays from large distance	2.5
Gamma rays from point source at 100 cm	1.9
Gamma rays from point source at 10 cm	0.6

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1. Relation Between Character of Radiation and Biological Effects (continued)

1.3 The Time Factor and Total Dose

Two aspects of the time factor in radiation exposure need consideration. These are (a) the dosage rate, and (b) the total duration of exposure.

(a) By dosage rate is meant the number of roentgens per unit of time. From clinical and experimental evidence it would seem that no restrictions need be placed on the dosage rate at which general body radiation is received at tolerance level under occupational conditions.

(b) The influence of the total duration of exposure upon biological effect is great and must be reckoned with when radiation is used in the treatment of disease, or when one attempts to establish limits of tolerance for exposure to radiation under working conditions.

The "total duration" factor can best be illustrated in connection with the "tolerance dose" - by which we mean the daily amount of radiation to which a normal person can be exposed day in and day out without sustaining permanent damage. For gamma radiation the tolerance dose is given as 0.1 r in any one 24-hour period, the dosage rate within that period being immaterial. Now suppose that an individual receives 0.1 r daily for 1000 days, the latter being the duration of the exposure. He is exposed then to a total of 100 r. His welfare depends greatly on whether he receives the 100 r in a total time of 1000 days or whether the duration for the same exposure is 100 or 10 days. The reasons for this are inherent in the regenerative properties of tissues (see XII B,2.1).

Apart from the time factors, the magnitude of the total dose - to which the total amount of tissue ionization is proportional - is obviously of outstanding importance for tissue damage.

1.4 Radiosensitivity of Tissues

a. Radiosensitivity. By radiosensitivity is meant the relative vulnerability to radiation of a tissue living in its normal physiological environment. Although we tend to think

1. Relation Between Character of Radiation and Biological Effects (continued)

of each tissue as having its own inherent radiosensitivity, advances in the application of radiation to medical uses have come about largely by learning to adapt the techniques of exposure to take advantage of the varying sensitivities of different tissues.

Not only may we think of different tissues as having differing radiosensitivities, but different organisms react differently to the same ionizing dose of radiation. There are also variations within strains of the same species. This is one of the obstacles in carrying over to man conclusions based on the biological effects of radiation found in the lower animals.

The problem is further complicated by various [illegible] events which can alter the radiosensitivity of a given tissue. A few examples will serve to bring out certain of these factors which are known.

b. Differentiation. Contrary to the more accepted principles of pharmacological action, the tissues which are less specialized in function tend to be the more vulnerable to radiation. The degree of specialization of a tissue is referred to as its differentiation. The highly complex cells of the nervous system are apparently little affected by ionizing rays. At the other extreme the primitive cells of the reproductive or lymphatic systems are extremely vulnerable.

c. Rate of growth. In general, the more rapidly growing and active cells tend to be the more radiosensitive ones in a given tissue.

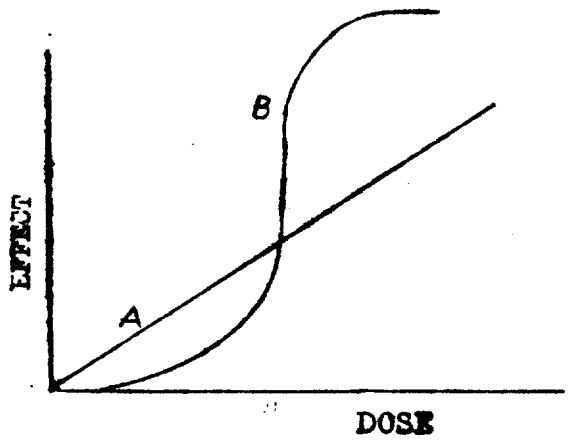
d. Cellular environment. The composition of the medium, or the environment of the cells comprising a tissue strongly affects the radiosensitivity. This is closely associated with the complex physio-chemical alterations which must ensue within the cell when it is subjected to unnatural ionization. Whether the effect of the ionization is a direct one, taking place within the cell, or an indirect one resulting from alterations in the environment, is still largely a matter of conjecture, although evidence is accumulating to show that both mechanisms may be active. As

[redacted]

1. Relation Between Character of Radiation and Biological Effects (continued)

an example of the effect of environment upon radiosensitivity one may cite the diminished effect of radiation upon otherwise extremely radiosensitive tissues when they are subjected to a reduced oxygen supply during the time of exposure. Likewise there is experimental evidence to show that a change in the acid-base relationship, affecting the permeability of cell membranes, can for certain tissues increase their radiosensitivity. Physical factors such as heat, cold or previous radiation may alter either the growth rate or environment of the cells, and thus produce a change in their vulnerability to ionization produced in them or in the medium in which they live.

e. Threshold and non-threshold effects. If one plots a dose-effect graph for various tissues subjected to radiation, there are in general two forms which the graph may take:



(A) Curve A illustrates the non-threshold case, where as the dose is increased there is a linear increase in the effect. There is no initial threshold of dose which must be exceeded before an effect is obtained. To recognize a non-threshold effect, it must be readily observable or measurable after exposure to minimal amounts of radiation. An example is the influence of radiation upon the germ plasm of lower organisms.

(B) Curve B illustrates a threshold effect. Here the effect is not measurable by present methods until a certain threshold of dose is exceeded. Thresh-

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1. Relation Between Character of Radiation and Biological Effects (continued)

old effects are not linear with dose but assume some form of S curve. The effects of radiation upon the skin and the blood-forming organs are examples Until the dose reaches or surpasses the threshold, the first signs of skin effect (erythema) or of effect upon the blood-forming organs (as reflected in the circulating blood) are not seen.

The majority of radiation effects are thought to be of the threshold type. It may be that as more delicate indicators are found to measure effects, more of them will be seen to be of the non-threshold type.

f. Reversibility of effects. The reversibility of radiation effects is important, particularly in occupational exposure. By reversibility is meant the return of a tissue to its previously normal state after exposure is discontinued. The reversibility of any specific effect is dependent upon the reparative or regenerative properties of the tissue. Some tissues, such as skin, the blood-forming elements, membranous linings of body cavities or glands, and peripheral nerves are endowed with a special mechanism for repair and regeneration. Other tissues, such as muscle, brain, and certain structures of the kidney or eye, have no provision for regeneration. In them repair is by the formation of a scar, which does not take over the function of the original tissue which it replaces. The effects in such cases are said to be irreversible.

In order for an effect to be reversible it must not produce injury beyond the limits of the normal capacity for regeneration. Otherwise the effect is permanent and may lead to complete destruction or exhaustion of the tissue.

Both the total dose and the total time over which it is given may affect the ability of the regenerative processes to function. If the total dose is excessive, irrespective of the time over which it is administered, regeneration and repair may be impossible. On the other hand, a total dose which will produce reversible effects if given at a rate slow enough to permit regeneration may instead result in irreversible damage to the tissues if given over a shorter period.

1. Relation Between Character of Radiation and Biological Effects (continued)

A tissue which has returned to apparent normal function following radiation damage may not, however, sustain repeated damage and may be unable to regenerate completely. Repeated radiation effect, initially followed by repair, will eventually exhaust the reserve for regeneration and end in death of the tissue. Hence previously sustained radiation injury (for example to skin) which has apparently been followed by regeneration and return to normal function must be carefully observed and a repetition of the injury avoided. Even bone marrow, in spite of its remarkable power of recovery from radiation injury, will eventually exhaust its regenerative reserve under too frequent or too heavy doses.

1.5 Summary

Before considering some of the biological effects of radiation in more detail, let us summarize certain general principles governing these.

(a) The nature of the radiation

(1) Different types of radiation produce varying degrees of ion density along their tracks through tissue.

(2) The ionization in a particular tissue is dependent upon the ability of the radiation to penetrate to a certain location or depth within the body. This is a function of both the energy of the radiations and the geometry of the exposure.

(3) The total duration over which a dose is given influences the effect produced.

(4) The total dose determines the total ionization which can be produced in the biological medium but the resultant biological effect is also influenced by the above factors.

1. Relation Between Character of Radiation and Biological Effects (continued)

(b) The biological system

(1) The radiosensitivity of a tissue or organism largely determines the form and degree of the effect produced.

(2) The radiosensitivity may in turn be influenced by such factors as rate of growth, [illegible] activity or function, and physical or chemical environment.

(3) Biological effects may or may not be threshold effects.

(4) Certain biological effects are reversible following irradiation, to a degree dependent upon the regenerative capacity of the tissue. The reparative processes may, however, be exhausted by either an excessive total dose or one received too rapidly to permit repair or regeneration to be accomplished.

(5) The repetition of radiation injury, following regeneration, eventually leads to death of the tissue.

2. Occupational Disease or Pathological States Resulting from Overexposure

2.1 The Tolerance Dose

The tolerance dose for total body exposure to gamma radiation of 0.1 r per 24-hour day and the tolerance dose for fast neutrons of 0.02 r.e.d. have been discussed in previous sections (see XII A,2.6c, XII B,1.3a and b).

A brief review of the history of the tolerance dose brings out the difficulties in precisely establishing the permissible working level for long continued exposure. The evidence on which the tolerance dose for external total body irradiation has been established has been gained almost

2. Occupational Disease or Pathological States Resulting from Overexposure (continued)

entirely from medical experience in using x-rays and gamma rays as therapeutic or diagnostic agents. Attempts were made to determine a safe level as early as 1902 only six years after it was demonstrated (1896) that x-rays could produce severe skin damage. The early radiation injuries were largely those to skin, but the demonstration of the marked radiosensitivity of the blood-forming organs ([illegible]-1905) and of the reproductive organs of animals ([illegible]) carried some warning that more serious damage [illegible] the skin could be anticipated. The first organized [illegible] to insure protection from x-rays was made in [illegible] 1915 by the British Roentgen Society. Definite acti[illegible] however, was delayed. To quote from Henshaw,[1] "[illegible] of the war activity which existed then, this plan failed to bring forth important advancement. As a result of war de-mands, caution gave way to action and protective measures were again forgotten. The taking of increased risks [illegible] this time probably was a factor which contributed to an un-fortunate development in 1919 and 1921, both in this country (U.S.A.) and in Europe, when a number of prominent radiation workers died of apparent radiation injuries, particularly aplastic anemia. Unfavorable publicity developed, and def-inite action resulted." This analysis by Henshaw states our problem concisely, and serves as a warning that we should insure adequate protection for the far more formidable tasks of the present war.

Individuals in various countries attempted to establish safe working levels. Since the roentgen was not yet adopted as a quantitative unit of radiation, the tolerance dose was originally expressed in "erythema dose." The erythema dose was that amount of radiation which produced a perceptible reddening of the skin. The radiations evaluated originally were largely soft x-rays, and the tolerance level was variously determined as 0.01 erythema dose per month. For 200 kv x-radiation this is equivalent to ~0.2 r per day. This figure was finally adopted by the International Com-mittee on X-ray and Radium Protection in its report in 1924,[2] which was the first agreement on any definite level of tolerance. As an outgrowth of the International Com-mittee there was formed in the United States an Advisory Committee on X-ray and Radium Protection which published its first report in 1931 in the Bureau of Standards Hand-book No. 15. Here the tolerance dose was set at 0.2 r per

2. Occupational Disease or Pathological States Resulting from Overexposure (continued)

day. This was later revised to 0.1 r per day (Bureau of Standards Handbook No. 20) for x-rays and gamma rays. Although the reason for this change is not given, it was presumably made to allow for the greater penetration and potential damage by gamma rays as compared to x-rays, and to reduce the likelihood of genetic damage - a matter which was then gaining recognition as a potential radiation hazard.

The safety factor inherent in the present tolerance dose is a debatable one. For those not acquainted with radiation effects at first hand the safety factor may seem exaggerated. Increased experience, however, tends in the direction of questioning the adequacy of the safety factor. Early tolerance dose values (based on soft x-rays) were arbitrarily weighted by a safety factor of ~25-40. With increasingly energetic radiation (x-ray and gamma) the safety factor becomes all the more important. A factor of 25 times the present tolerance dose would give a permissible exposure of 2.5 r per day. Animal experimentation has shown[5] that continuous gamma ray exposure of 1.9 r per 24 hours will significantly reduce the life span in mice. From known experience with radium workers receiving something less than 1 r per day we can judge that the safety factor is not more than 10. This is not as wide a margin of safety as some workers feel is imposed upon them by the 0.1 r per day level. For this reason we need to emphasize continually that although 0.1 r per day is the tolerance dose, less than 0.1 r per day is desirable and should be striven for when practicable.

Observable damage to the blood-forming and reproductive organs first prompted the establishing of a tolerance value for total body radiation. Although the skin was the first and remains the most common site of damage, no tolerance dose has ever been set for permissible localized exposure of the skin of those working with radiation. The possibility of genetic damage was seen from experimental results in lower organisms. The problem of a tolerance value for radioactive gases was encountered in dealing with radon, and limits of atmospheric concentration under working conditions have been established. The occurrence of fatal blood disorders and malignant bone tumors in radium dial painters has

2. Occupational Disease or Pathological States Resulting from Overexposure (continued)

only recently led to the establishing of a maximum tolerance amount of radium which can be deposited within the body without apparent harmful effects.

In order to clarify the hazards of radiation exposure, the more important effects as observed in occupational exposure will be reviewed.

2.2 The Blood

It is fortunate for our purposes that the circulating blood is in man a relatively early and available index of overexposure to radiation. Certain aspects of this problem are not, however, commonly appreciated.

Radiation affects the tissues which form blood. These are located in the bone marrow and lymphatic system scattered over the body. Alteration in the blood count thus reflects injury not to the blood directly, but to the blood-forming tissues.

The effect is rapid; an alteration in blood count may be observed within an hour after total body overexposure. The rapidity and magnitude of the observable effect and the recuperation time depend upon the dose and upon the regenerative powers of the blood-forming tissues.

Anemia is a late, not an early, sign of overexposure. When the production of red blood cells has been affected and is reflected in the circulating blood, the condition of the bone marrow is precarious.

The white blood cells are the earliest index of overexposure. The following table indicates the nature of the alterations which may appear.

[redacted]

2. Occupational Disease or Pathological States Resulting from Overexposure (continued)

The Normal Circulating Blood Elements in the Adult (Wintrobe)

Type of Cell	Average Normal	Minimum	Maximum	Effect of Radiation on the Blood Producing Centers to Produce Changes in Circulating Blood
RED BLOOD CELLS	(millions per mm³)			Decrease in red blood cells (anemia) is a late sign of overexposure.
Male	5.4	±0.8		
Female	4.8	±0.8		Radiation-induced anemia is extremely serious and often fatal.
HEMOGLOBIN Content of red blood cells	(g per 100 cc)			
Male	16	±2.0		
Female	14	±2.0		
	(thousands per mm³)			
WHITE BLOOD CELLS	7000	5000	10,000	White blood cell decrease (leukopenia), or alterations in the normal ratio of the two principal elements (neutrophils and lymphocytes) are the earliest objective signs of overexposure.
Segmented neutrophils	4000 (54-62%)	3000	5800	
Juvenile neutrophils	300 (3-5%)	150	400	The effect may be: 1. Diminution of total white blood cells (leukopenia)
Lymphocytes	2100 (25-35%)	1500	3000	2. Inversion of normal neutrophil-lymphocyte ratio without leukopenia.
Monocytes	375 (3-7%)	285	500	
Eosinophils	200 (1-3%)	50	250	
Basophils	25 (0-0.75%)	15	50	

[redacted]

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2. Occupational Disease or Pathological States Resulting from Overexposure (continued)

A white blood cell level falling below 5000 should be looked upon with concern in one working under radiation exposure. Men who show unusual sensitivity may have to be given work not involving any radiation hazard.

We have no means as yet for permanently reviving a blood count which has been lowered by radiation. It is entirely up to the individual's blood-forming organs to do it for him. Avoiding all further radiation and observing the rules of healthful living will aid but not guarantee a recovery.

2.3 The Reproductive Organs and Germ Plasm

The elements of the reproductive organs which may be injured are (a) the progenitors of the sperm or ova, and (b) the genes which make up the chromosomes and transmit hereditary factors.

a. Reproductive organs. Sterility can readily be produced by radiation but the dose necessary for the male is ~ 800-1000 r to the testes; in the female (depending upon the age) a dose of about 600 r in the ovaries will cause permanent sterilization. Animal experiments in progress[4] indicate that continuous exposure to gamma radiation on levels of 4 and 8 r per day will produce damage to the ovaries and testes. This was previously shown by Russ and Scott,[3] who exposed mice to continuous gamma radiation (11.7 r per 24 hours) for a period of 4 months, and observed a markedly decreased fertility as well as diminished viability of the young. Gross negligence in protection could produce, over a period of years, alterations in the fertility of the individual. There is no evidence to indicate that exposure to our present tolerance level will do so.

b. Genetic injury. In 1927 Muller[5] demonstrated that the mutation* rate of the fruit fly could be accelerated by exposure to x-rays. Bagg and Little[6] and Snell[7] have produced radiation-induced mutations in mice. Radiation increases the rate of appearance of the common mutations which are known to occur spontaneously; it produces the uncommon ones only rarely. Single exposures of 30-40 r will double the mutation rate in the fruit fly. Single doses of ~ 500 r are required to produce mutations in mice, but these are produced in far lower incidence than in the fruit fly.

** A mutation is an hereditarily transmissible abrupt alteration in germ plasm.

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2. Occupational Disease or Pathological States Resulting from Overexposure (continued)

Radiation-induced mutations have been found to have characteristics which bear on the practical consideration of radiogenetic changes due to occupational exposure. The most important of these is that there is a linear relationship between dose and increase in mutation rate. There is no threshold effect (see XII B,1.4e). The cumulation of exposure is thus additive. Furthermore, the magnitude of the effect is independent of the wave length and dosage rate of the exposure.(8)

Mutations, whether spontaneous or [illegible], are about 90% lethal or sublethal. This means [illegible] offspring does not survive the gestation or [illegible] dies shortly thereafter. The lethal mutations [illegible] dominant or recessive. By dominant is meant that, [illegible] the exposed parent organism, the lethal effect appears [illegible] of its direct offspring. By recessive is meant that the effect might appear only in some succeeding generation of the radiated subject. In man it would appear in [illegible] descendants only should cousins or near relatives intermarry. It has been calculated from the laws of genetics that some 5000 years would be required for a mutated gene to meet another mutated gene descended from the original mutation. This would indicate that we need not be too concerned about the recessive deleterious effects of mutations.

The viable mutations (about 5% of all mutations, whether spontaneous or produced by radiation) are about 95% deleterious ones. Of these the majority (about 96%) pertain to other than the sex chromosomes. The remaining are sex-linked mutations,* appearing in the sons of the daughters of the sperm carrying the mutated gene. The spontaneous rate of appearance of these dominant deleterious yet viable mutations (which constitute about 4% of all mutations) is about 1:2700. It has been calculated that an accumulated dose of 300 r will raise this probability to 1:230.(8)

Knowledge of genetics, and particularly the entire radiogenetic knowledge, have been gained from experimental

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*Based on the number of chromosomes in the female (48) and male (47) the chance is further reduced by a factor of 1:24 in the female and 1:47 in the male.

2. Occupational Disease or Pathological States Resulting from Overexposure (continued)

studies in the fruit fly and to a far lesser extent in mice. Actually very little is known about genetics in man. Such information as we have is derived from extrapolation through many unknowns. The validity of findings in the fruit fly cannot be taken at face value for man, but these findings do show the problem and form the basis for practical considerations in radiation protection.

As yet no evidence is at hand to prove that the offspring of the present generations of radiation [illegible] abnormal. It can be argued, however, that [illegible] erations or intermarrying may produce abnormalities.

The linear relationship between dose and mutation percentage is important. If experimental work in [illegible] organisms is valid for man, then one can only escape this effect by complete protection from or avoidance of all radiation exposure including natural radiation (cosmic, etc.). Complete avoidance of all radiation exposure is not possible; it therefore behooves us to keep protection within practicable limits of safety and avoid all unnecessary exposure.

2.4 The Skin

The effect of radiation on the human skin was the first indication of any biological effect of x-rays and radium. Becquerel, who carried a tube of radium in his vest pocket, developed a burn of the underlying skin. X-ray dermatitis was in evidence within a few months after the discovery of x-rays. The greatest number of radiation injuries in occupational exposure is still to the skin of x-ray and radium workers. Our concern for the skin of hands of physicists and chemists on the Project is based on the lamentable past history of x-ray and radium development. It would seem needless to make the same mistakes in handling artificially produced radioactivity.

The characteristic effect of large doses of x-ray or radium gamma rays upon the skin is the production of an erythema. In this respect such radiations are comparable to ultraviolet radiation except that the period between exposure and erythema extends to about four weeks with a single radiation exposure. As was previously noted, the dose required to produce erythema is larger for shorter wave lengths

2. Occupational Disease or Pathological States Resulting from Overexposure (continued)

and also increases with increase in the length of time over which the radiation is administered. Except for gross negligence, we do not expect to see erythema as a result of occupational exposure on the Project. Rather we fear the daily overexposure of the hands to small amounts of radiation, which, if continued over a period of years, may lead to irreversible changes. These late changes are a dryness, cracking, brittleness or ridging of the nails, a loss of the normal sensitivity of the fingertips with a flattening of the normal skin ridges, atrophy of the skin and its appendages, fine blood vessel dilatation producing areas skin like the port-wine stain of a birth mark, localized thickening forming wart-like growths, and lastly ulceration from minor abrasions which fail to heal and progress to cancer of the skin, some 25% of which end fatally. In one series the average time between the onset of radiation exposure to the recognition of skin cancer was 9 years. The age of these victims ranged from 28 to 60 years.(9)

The Project abounds in opportunities for overexposure to the skin - particularly that of the hands. The beta rays from uranium itself are not without potential hazard when the metal or the salts are handled.(10) Neutrons produce skin damage with an effect about six times that of a comparable energy absorption of 200 kv x-rays.(11) Gamma and beta rays are ever present in pile operation, chemical and physical research, and extractions of the product and by-products. It is sufficient to emphasize that beta particles of an average energy associated with the long-lived fission products will penetrate well below the skin. A more detailed discussion of the penetration of beta radiation in tissue will be found in a report by H. M. Parker.(12)

As was previously noted, no tolerance dose for skin exposure has ever been established. Past experience with fluoroscopy and radium handling leads one to assume, however, that for long-continued exposure over a period of years a limit of 0.1 r per day exposure of the skin to a radiation which will effectively penetrate below the outer horny layer (0.1 mm) is a safe limit.

2. Occupational Disease or Pathological States Resulting from Overexposure (continued)

Protection from overexposure of the skin is in general far more difficult on the Project than protection from total body exposure. Since safety is necessary, certain principles pertaining to skin protection are enumerated below. These can be derived by expanding a statement contained in the report of the American Advisory Committee cautioning radium workers: "All manipulations shall be carried out as rapidly as possible and with the hands and body as far from the radium as practicable. The radium preparations must not be allowed to come in contact with any part of the technician's body (especially the hands) at any time." Applying this admonition to our tasks:

Don't pick up any presumably active material until you have ascertained its activity and hazard.

Use distance or mechanical remote control in handling radioactive substances where practicable.

Use protective gloves (leaded-leather) when they are indicated. But use caution in handling substances of mixed beta and gamma activity. The gloves do not protect from gamma activity - they rather contribute to the exposure of the hand by the secondary scattering from the lead.

Keep the hands uncontaminated by fission products. This means the wearing of clean gloves where indicated. The frequent monitoring of hands and gloves is desirable as a check both on techniques and on hazard.

Keep the clothing free from contamination.

Careful attention to the details of techniques and orderliness is the only way to minimize the hazard of skin injury.

2.5 Radioactive Poisons

A long discussion on internal poisoning by fission products is given in XII C,2. In the case of radium and radon as radioactive poisons, tolerance values were established over a period of four decades, largely by experience from

2. Occupational Disease or Pathological States Resulting from Overexposure (continued)

human misfortune, and animal experimentation only confirmed the observed effects. It is to be hoped that this order will be reversed in our case.

Radioactive poisons may be either solid or gaseous. Solid radioactive particles may be a hazard either through ingestion or inhalation, gaseous products only through inhalation (see XII A,3.6d).

The earliest experience with radioactive poisons was in studies of inhaled radon in man. The blood of workers concerned with the separation of radium showed an eventual effect upon the blood-forming organs. The magnitude of the exposure can be correlated with the level of the radioactivity in the exhaled air.(13) Similar studies have been made upon workers concerned with the preparation of mesothorium.(14) The high incidence of lung cancer in the uranium mines of Bohemia has been directly attributed by some investigators to the high radon concentration of the mine atmosphere (average concentration 3×10^{-12} curies/cc). The permissible concentration under working conditions is established by law in several states; 1×10^{-14} curies/cc of air is the tolerance value specified by the Bureau of Standards.

Internal radiation from ingestion and internal deposit of radioactive materials was first encountered by Martland(15) among the radium dial painters. As little as one to two micrograms deposited in the bones has proved to be lethal. The continued bombardment of bone marrow by alpha particles results either in a fatal anemia or in malignant bone tumors. Signs of poisoning may appear only years after ingestion. Experience with human beings has led the Bureau of Standards to establish 0.1 micrograms of radium as the limit which can be deposited in the body without risking eventual damage.(16)

There is a similar hazard of internal radiation resulting from absorption and deposition of the various fission products in the body, but the tolerance concentrations can only be estimated until experiment establishes them. Protective measures must proceed on the basis of complete elimination of this hazard. For example, the handling of the product

2. Occupational Disease or Pathological States Resulting from Overexposure (continued)

will require utmost caution until absorption, deposition, and elimination studies have been made. Even then one cannot extrapolate too freely from animal studies. The product emits an exceedingly energetic alpha particle, and its half life is only some 15 times that of radium. If the metabolism of the product proved to be similar to that of radium, the deposition of some 50 micrograms of the substance would become an important hazard.

2.6 General Effects

The foregoing discussion has covered only specific foci of damage resulting from occupational overexposure to radiation. These are the more important examples of damage which workers in radiation have sustained thus far. That other organs and tissues of the body may participate in these effects is evident from accumulating experimental data. Clinical and experimental observation must be closely pursued to bring out important and as yet undetermined effects for which protection will be needed.

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C. BIOLOGICAL ASPECTS*

1. Tracer Studies (1) (2) (3) (4) (5) (6) (7) (8) (9)

Revised Edition: By J. G. Hamilton, October, 1944

1.1 Introduction

Radioactive isotopes, free from inert carrier, of Sr, Y, Zr, Cb, Ru, Te, Cs, Ba, La, Pr, Ce, and Np were administered to rats as chlorides in isotonic solutions of NaCl at pH ranging from 2.3 to 3.5. Iodine was given as NaI,(1) and Xe was given by inhalation in an oxygen-gas mixture.(1) Unseparated fission products, free from inert carrier and uranium, after 90 days cooling were administered in an isotonic solution of NaCl at pH 2.5.

Adult rats received the various radioactive preparations in solution by oral, parenteral, and intrapulmonary administration. In the earlier experiments the parenteral administration was by way of the intraperitoneal route. Due to the difficulty of absorption of some of the radioactive isotopes, considerable retention of activity on the surfaces of the intra-abdominal organs took place. In order to gain a more accurate picture of the true deposition of these radioactive isotopes in the intra-abdominal organs it became necessary to employ the intramuscular route of administration.

The animals were sacrificed in groups of three for each route of administration and at varying intervals ranging from one to sixty-four days. Sixteen to eighteen representative tissues were removed from each animal and their activities individually measured. The results are summarized in Table 1.

1.2 Parenteral Administration

Figures 1, 2, and 3 summarize the present status of knowledge concerning the metabolism of the individual fission products, and of an assayed sample of the unseparated fission mixture free from uranium, following parenteral administration. The deposition per organ is presented. Only those structures which show a high deposition of the radioactive material are listed. Some of the parenteral studies, e.g., on Zr^{89}, I^{131}, Ba^{133}, La^{140}, could not be continued for the full 64 day period due to the short half lives of these radioactive materials.

The "per cent uptake" as shown by the curves is equal to the amount

* The material on tracer preparation discussed in C.1.1 of the first edition will be discussed in III D.7, 8 and 9.

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TABLE 1

A SUMMARY OF THE METABOLIC PROPERTIES OF THE PRINCIPAL LONG-LIVED RADIO-ELEMENTS PRODUCED IN URANIUM BY FISSION TOGETHER WITH VALENCE STATES USED FOR THESE STUDIES, HALF-LIVES, AND RELATIVE CONTRIBUTION TO THE TOTAL RADIATION ENERGY OF THE RADIOACTIVE MIXTURE.*

Element	Valence	Half-life	Oral Absorption	Distribution of Absorbed Element at 16 Days	Half-time of Excretion of Absorbed Element	Lung Retention at 16 Days	% of Total Energy of Radiation at 60 days cooling after 100 days Operation
Sr^{89}	(+2)	55 d	15%	Bone 50%	~200 d	< 1%	10.6%
Sr^{90}	**(+2)	~ 5 yrs	15%	Bone 50%	~200 d	< 1%	0.43%
Ba^{140}	**(+2)	12.5 d	10%	Bone 60%	~200 d	< 1%	7.7%
Y^{91}	(+3)	57 d	< 0.2%	Bone 70%	~500 d	20%	9.6%
La^{140}	(+3)	40 hrs	< 0.3%	Bone 35%	> 16 d	20% (est)	< 0.05%
Ce^{141}	(+3)	28 d	< 0.05%	Bone 35%	~ 50 d	35%	5.7%
Ce^{140}	**(+3)	340 d	< 0.05%	Bone 35%	~ 50 d	35%	11.5%
Pr^{143}	(+3)	13.5 d	< 0.5%	Bone 40%	~ 40 d	20%	1.0%
Zr^{93}	(+4)	65 d	< 0.01%	Bone 50%	~ 80 d	75%	19.7%
Cb^{93}	(+5)	35 d	< 1.0%	Bone 20%	~ 50 d	50%	27.1%
Ru^{103}	(+4)	42 d	< 0.01%	Kidney 1.5%	~ 20 d	60%	4.4%
Ru^{105}	**(+4)	330 d	< 0.01%	Kidney 1.5%	~ 20 d	60%	1.3%
Cs^{135}	(+1)	36 yrs	100%	Muscle 30%	~ 10 d	< 1%	0.27%
I^{131}	(-1)	8 d	100%	Thyroid 20%	~ 30 d from thyroid	< 1%	0.05%
Xe^{135}	(0)	5.4 d	Tissue content at equilibrium ranges from 2 to 0.1 times concentration in air		~1 hr	< 1%	< 0.1%
Te^{127}	(+4)	30 d	25%	Kidney 6%	~15 d		0.47%
Np	(+3)		< 0.1%	Bone 50%	>15 d	10% (est)	< 0.1%

* Report by J. G. Hamilton, Sept. 5, 1944 (Secret - 5892), - (Army - MD7293).
** Values for per cent of total radiation include short-lived daughter activities.

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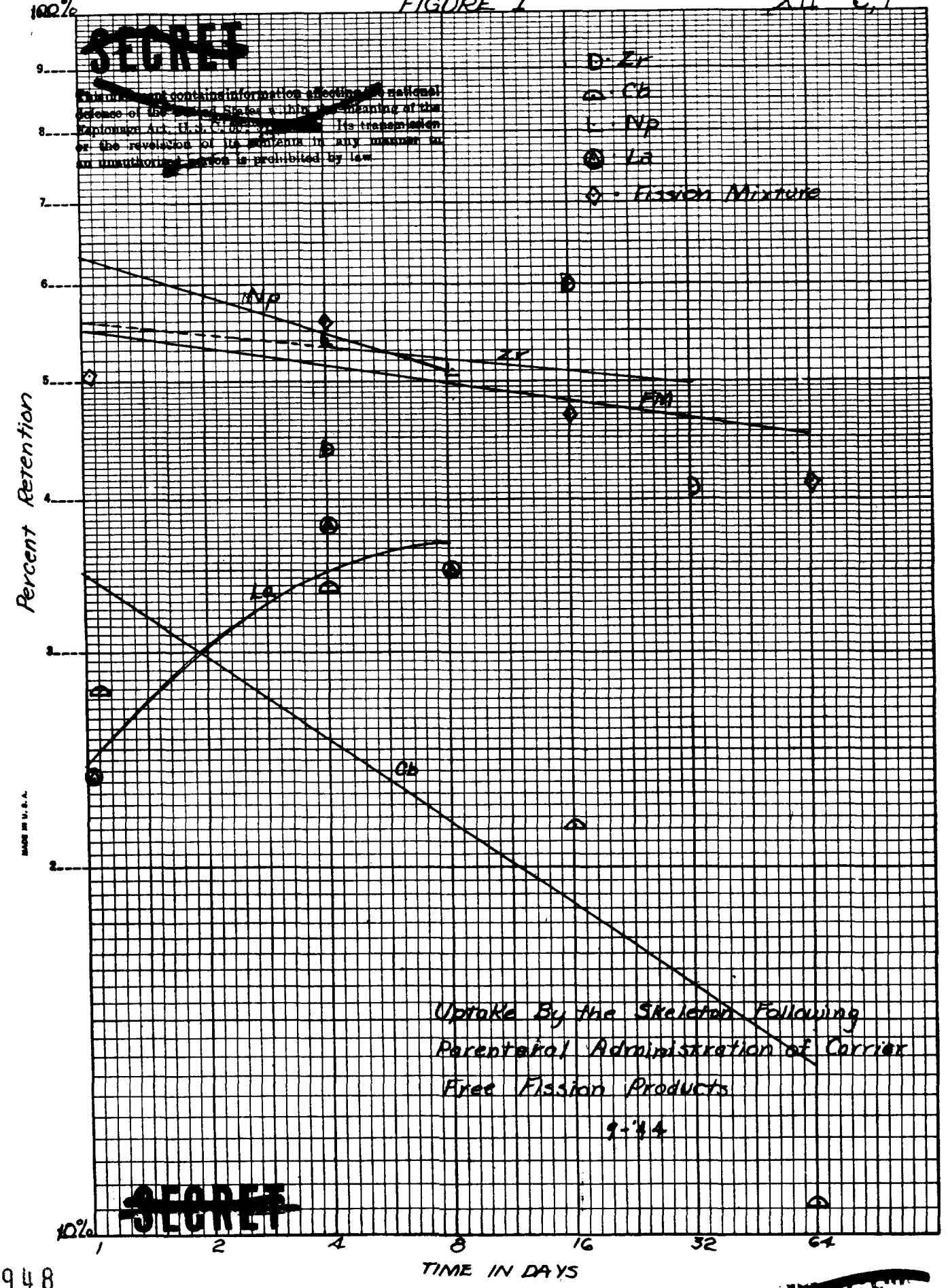
FIGURE I

XII C, 1



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XII C.1

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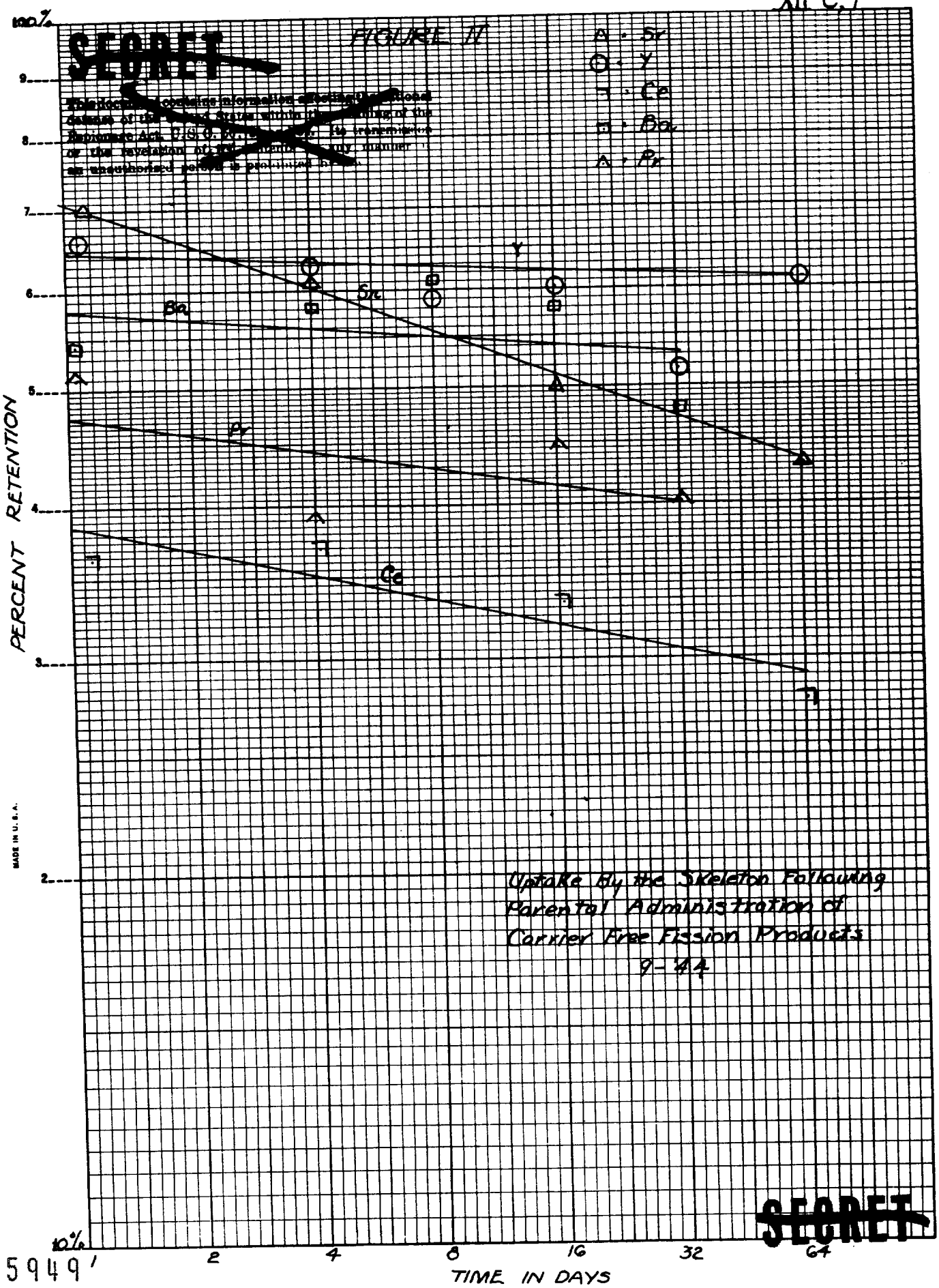
FIGURE II



Uptake By the Skeleton Following Parenteral Administration of Carrier Free Fission Products
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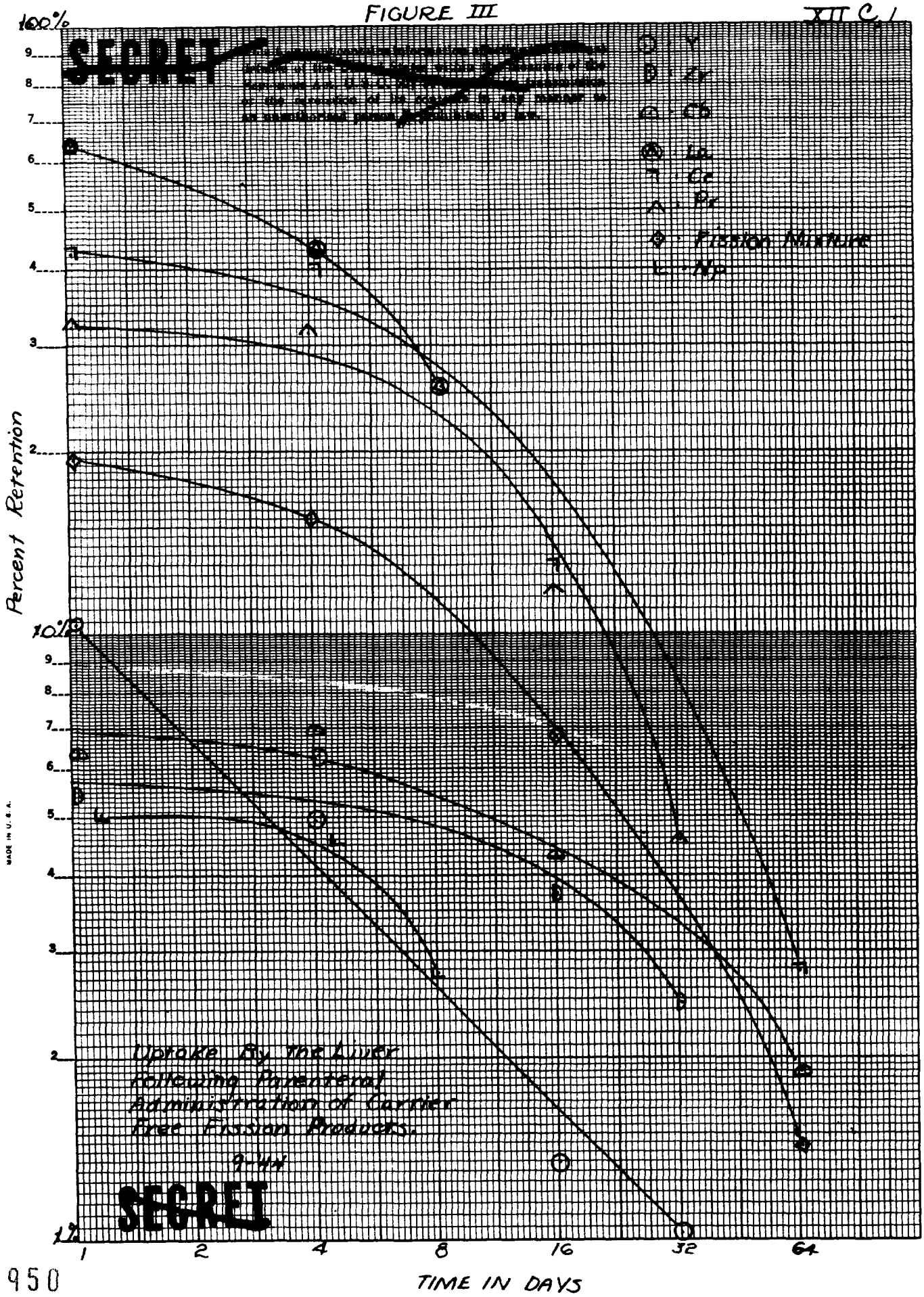
FIGURE III

XII C, 1



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of the given material present in the given organ at the time indicated, divided by the total amount absorbed by the animal. In the cases of Y, Zr, Cb, Ru, Te, La, Ce, Pr, Np, and the unseparated fission products, corrections were applied to the observed values of deposition to compensate for the material left unabsorbed at the site of injection. This type of correction is not entirely satisfactory but does give a clearer picture of the distribution of the absorbed material.

1.3 Intrapulmonary Administration

In addition to the parenteral and oral studies, the absorption of these substances into the lungs has been investigated. The solutions of the individual radioactive isotopes and of the fission mixture were directly introduced into the lungs. The values given in Figure 4 indicate the distribution of the retained activities on the basis of retention in the lungs. By "per cent retention" in Figure 4 is meant the amount of the given material present in the lung at the time indicated, divided by the total amount retained by the animal. This method of presentation is made necessary by the fact that it is impossible to introduce an exactly known dose directly into the lungs. However, in most instances from one-third to one-half of the injected sample is retained in the lungs or absorbed through the pulmonary tissue and deposited elsewhere in the body. Moreover, the total activities in the animals for the longer experiments indicate that the over-all excretion rates are comparable to the values observed for the parenteral studies. The pulmonary retention of Sr, Te, I, Cs, and Ba is insignificant and can be ignored. The metabolic pattern of the fission products when inhaled as a dust, smoke, or the like, is, of course, going to be modified by the behavior of the particles upon which the active material may be deposited.

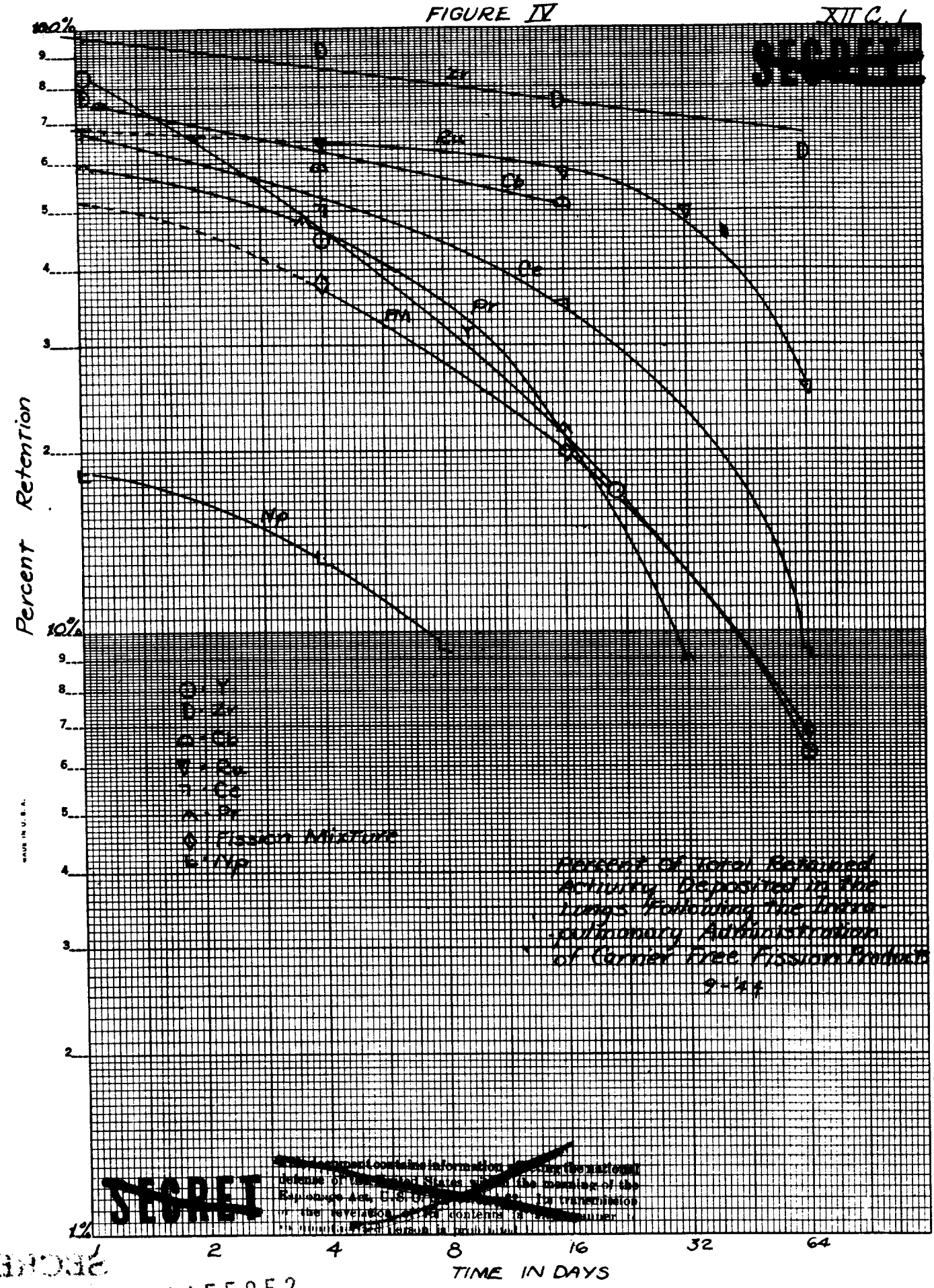
It should be pointed out that the metabolism of the radioactive isotopes absorbed through the lungs is very similar to their metabolic behavior following parenteral administration.

Radio-autographic studies of the pulmonary distribution of these radioactive isotopes after introduction directly into the lungs have been carried out for the following elements: Y, Zr, Cb, Ru, Ce, Pr, fission mixture and Np. These experiments include intervals up to 64 days for those long-life fission products listed above which possess half-lives of sufficient value to permit the extension of the studies over this period of time. The distribution pattern for Ru shows rather a uniform localization in the air sacs and alveolar ducts, while in the cases of Zr and Cb the pattern was completely random in character. Y, Ce, Pr, the fission mixture, and Np gave results of an intermediate character between these two extremes. No significant localization in the lymph nodes, blood vessels, the bronchial tree, or the trachea was observed in any of these studies.

Xenon tracer studies(1) were done by exposing a group of animals to a mixture of Xe^{127} and O_2 over a period of 18 hours. The Xe^{127} concentration per gram of tissues was found to be 0.1 to 2 times the Xe^{127} concentration per cc of the inhaled gas mixture. The highest values were in fat and the lowest in the blood; the average value for the entire animal was 0.25.

FIGURE IV

XII C.1



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1.4 Excretion

Prior to the time of sacrifice the urine and feces were collected, separated, and their activities determined daily for each group of three animals.

In general it may be stated that with the exception of Ru, Xe, Te, Cs, the 340d Ce, and possibly Sn^{90}, the rates of elimination of the retained fractions of the listed isotopes either approximate or are less than their rates of radioactive decay.

1.5 Summary of Results

The most significant conclusions that can be derived in the survey of all of the work done with the long life fission products can be summarized in the following manner: the alkaline earths, rare earths, Zr, Np, and Cb when introduced into the body are deposited primarily in the skeleton, where the average degree of retention of the absorbed radio-elements is approximately 50 per cent of the initial absorbed quantity. The retained fractions of these radio-elements are eliminated at rates which are less than their rates of radioactive decay with the exception of the 340 day Ce and possibly Sn^{90}. The remaining five long-lived radio-elements, Ru, Te, Xe, I, Cs do not show any significant degree of localization in the skeleton and in addition there is no very striking deposition in any other of the tissues with the exception of deposition of I in the thyroid. The rates of elimination for all of these four radio-elements are much greater than their rates of radioactive decay, with the exception of I accumulated in the thyroid. In this particular case the release of accumulated I in the thyroid is many times slower than its rate of radioactive decay.

The members of the long-lived fission product group which are absorbed by way of the digestive tract include the alkaline earths, tellurium, iodine, and cesium. A high degree of retention by the lungs has been observed following direct intrapulmonary administration of the rare earths, Zr, Cb, Ru and Np. The pulmonary retention observed for the alkaline earths, Te, I, and Cs is negligible under the conditions of the experiment.

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2. Tolerances for Fission Products

2.1 Derivation of Equations

The toxic effect of internally deposited fission products is due practically exclusively to their beta radiation. Since the ranges of beta rays in tissue are small we may consider as an approximation that all the radiation emitted within a tissue is absorbed within that tissue. This leads to the following formula for converting curies of deposited radioactive material into roentgens per day. In equation (1) I_i is the internal dosage rate in r/day.

In general, r/day = curies x (disintegrations/second) x (sec/day) x (ev/disintegration) x (ergs/ev) x (g-r/erg) x (1/g)

$$\text{Hence, } I_i = Q_d \times 3.7 \times 10^{10} \times 86{,}400 \times E \times 1.6 \times 10^{-12} \times 1/64 \times 1/W$$
$$= 61\ E\ Q_d/W \qquad (1)$$

where W = grams of tissue absorbing radiation from Q_d
Q_d = curies deposited
E = average energy, in ev

The total dose D given to a tissue by the complete decay of such a source <u>in situ</u> (assuming no excretion) is

$$D = 61E \frac{Q_d}{W} \frac{1}{\lambda} \qquad (2)$$

where λ = decay constant, in days^{-1}.

The extent to which a swallowed or inhaled fission product will deposit in a given tissue depends upon its chemical properties and physical form, which regulate the degree of absorption into the blood from gut or lung and the degree of deposition from the blood into the tissue in question. Thus we have, for ingested material:

$$Q_d = Q_o ad \qquad (3)$$

where Q_o = ingested activity, in curies
a = fraction absorbed from gut into blood
d = fraction deposited from blood into tissue

For inhaled material we have:

$$Q_d = Q_o fbd \qquad (4)$$

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2. Tolerances for Fission Products (continued)

where f = fraction retained by lung from inhaled air
b = fraction absorbed from lung into blood

Thus equations (1) and (2) become, in terms of the material presented to the gut and lung, respectively,

$$Q_o = I_1 \frac{W}{61\ Ead} \text{ (gut)} = I_1 \frac{W}{61\ Efbd} \text{ (lung)} \qquad (5a,5b)$$

$$Q = D \frac{W}{61\ Ead} \lambda \text{(gut)} = D \frac{W}{61\ Efbd} \lambda \text{(lung)} \qquad (6a,6b)$$

If the radioactive product in question is suspended in water or in air with which contact occurs continuously [illegible] the day, we have

$$Q_o = C_o V \qquad (7)$$

where C_o = curies/liter
V = liters administered
$V_1 \approx 3$ liters water ingested per 24 hours
$V_2 \approx 5 \times 10^3$ liters air inhaled per 8 hours

Substituting in equations (5) and (6), we get

$$C_o = I_1 \frac{W}{61\ V_1 Ead} \text{ (gut)} = I_1 \frac{W}{61\ V_2 Efbd} \text{ (lung)} \qquad (8a,8b)$$

$$C_o = D \frac{W}{61\ V_1 Ead} \lambda \text{ (gut)} = D \frac{W}{61\ V_2 Efbd} \lambda \text{ (lung)} \qquad (9a,9b)$$

If the exposure to such a "maintained" atmosphere is long (compared to the period of the emitter) the maximum intensity (I_m) that can be achieved from such exposure is related to C_o by

$$C_o = I_m \frac{W}{61\ V_1 Ead} \lambda \text{ (gut)} = I_m \frac{W}{61\ V_2 Efbd} \lambda \text{ (lung)} \qquad (10a,10b)$$

Equations (8), (9), and (10), which define the radiation received by a tissue as a result of ingestion or inhalation of active material, can easily be modified to take account of the radiation received by the gut or lung due to incomplete absorption of retained material by substituting (1 - a) and (1 - b) for bd in these equations. In the case of the gut, since the

2. Tolerances for Fission Products (continued)

passage through is of the order of one day, I = D for the unabsorbed material and equation (8a), with the substitution of (1 - a) for ad, applies in place of (9a) or (10a).

Equation (10) applies to an atmosphere maintained at a constant radioactivity, such as may be the case in the vicinity of a continuously operating extraction plant. Exposure to a radioactive atmosphere which is decaying (such as would result from accident or enemy action) results in a [illegible] intensity which rises to a maximum and then falls. The [illegible] intensity and total dose are related to the initial activity [illegible] air by

$$C_o = I_m \frac{We}{61\ V_1 Ead} \lambda\ (\text{gut}) = I_m \frac{We}{61\ V_2 Erbd} \lambda\ (\text{lung}) \quad (11a, 11b)$$

$$(e = 2.72)$$

$$C_o = D \frac{W}{61\ V_1 Ead} \lambda^2\ (\text{gut}) = D \frac{W}{61\ V_2 Erbd} \lambda^2\ (\text{lung}) \quad (12a, 12b)$$

(since $D = I_m \frac{e}{\lambda}$)

2.2 Interpretation of Equations

The use of equations (5) through (12) is complicated by the difficulty of evaluating some of the constants. The values for f, a, and b are not difficult to measure experimentally; these are being determined for each fission product separately, and for every state in which each occurs, since no two products, nor the same products in two different states, can be expected to behave, either chemically or biochemically, in an identical fashion. However, d -- which, in conjunction with W, sets the concentration factor for each tissue -- is difficult to determine, particularly for small organs or for tissues which are diffused throughout the organism (e.g., bone marrow). The values to be used for I_i, I_m, and D, in order to set tolerance limits on inhaled or ingested radioactive materials, are taken from clinical and experimental results with x-rays, particularly those derived from whole body irradiation. While not a valid source of data for the calculations in hand, these are the only results available on radiation toxicity.

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2. Tolerances for Fission Products (continued)

Other things being equal, the tolerance amounts or concentrations (Q_o and C_o) derived from equations (5) through (12) will depend mostly upon the quotients $\frac{I}{d/W}$ and $\frac{D}{d/W}$ -- the ratio of radiosensitivity of the tissue to its ability to concentrate the isotope in question -- and upon a and b, the absorptions. For each isotope the tolerance concentration or amount of activity may be set as that amount which causes I or D in the gut or lung or any internal tissue to rise to the maximum safe amount.

2.3 Application of the Equational Assumptions

A simplification of the procedure is afforded by the experiments to date which show that most of the fission products, if absorbed, are deposited in bone. Thus we need to consider (except for a few elements, such as iodine) only the tolerance for gut, lung, and bone. In addition, the bone marrow is among the most radiosensitive and most essential of tissues and we may, with some justification, apply to this tissue the tolerances found for whole body irradiation.

The value of a depends upon two factors: (1) the chemical properties of the element involved -- since the intestinal juices are near neutrality and contain both bicarbonate and phosphate ions, many of the fission products will form insoluble compounds and be poorly absorbed; (2) the presence or absence of food, which can hinder absorption by precipitation of the emitter and also screen the intestinal walls from radiation during passage. The second of these factors introduces a large and uncontrollable variable, and the values of a and W used are therefore those expected in the absence of food.

The chemical properties of the element in question also critically influence f, b and d. The value of f is also dependent upon the physical state of the element; particle size has much to do with the extent of lung deposition of inhaled material. Because of the uncertainties in evaluating f, the maximum value of 1.0 (applicable to small particles and to certain compounds) has been chosen. The deposition factor, d, for the radiosensitive bone marrow has been set at 0.25 on the assumption that half the activity deposited in the skeleton (about 50% of that absorbed for most of the fission products) is in the marrow.

2. Tolerances for Fission Products (continued)

Excretion has been set at zero (except where stated) on the basis of the evidence to date, which shows that it is sufficiently slow to be neglected for all except the very long-lived products.

2.4 Application of the Equations: Basic Data on Metabolism

The data in Table 1 are taken from Hamilton's reports[1] to illustrate the metabolism (absorption, distribution, and excretion) of the fission products as far as they are known at this date.

REFERENCE

(1) Hamilton, J. G. -- Reports CH-379, CH-498, CH-554, CH-630, CH-708, CH-769, CH-775, CH-843, CH-848, CH-908.

2. Tolerances for Fission Products (continued)

TABLE 1

PERCENT OF AMOUNT ABSORBED FOUND IN

				Total Tissue of						One Gram of						Excreta (Time after Absorption)		
Element	% Absorbed when Ingested	% Absorbed when Inhaled	Time after Administration (Days)	Liver	Kidney	Spleen	Nodes	Whole Bone[3]	Muscle	Liver	Kidney	Spleen	Nodes	Whole Bone[3]	Muscle	Urine	Feces	% per day
La	0.3	---	1	65	1.8	0.2	---	26	2.0	6.6	1.0	0.5	0.05	1.5	0.02	0.12	1.6	---
	---	35	4	40	1.2	0.1	---	34	2.4	3.7	0.5	0.1	0.06	2.1	0.02	0.4	7.4	3.0
	---	---	8	30(33)[2]	1	0.1	---	34(30)[2]	2.0	3.0	0.4	0.15	0.13	2.1	0.02	2.3	27	0.5
Sr	8-16	---	1	0.08	0.04	0.03	0.006	70	1.0	0.08	0.03	0.03	0.1	4.4	0.01	10	13	---
	---	---	16	0.006	0.008	0.001	---	50	0.09	0.0005	0.004	0.0006	---	3.1	0.0008	11	26	0.15
	---	---	64	---	---	---	---	45-25	---	---	---	---	---	2.7-1.5	---	12	37	---
Y	---	40	2	(8)[2]	1.5	1.0	0.04	(65)[2]	2.5	---	0.7	---	0.42	---	0.02	5.3	6.4	---
	---	70	4	(9)[2]	1.4	0.5	0.013	(70)[2]	1.3	---	0.6	0.5	0.11	---	0.01	5.8	12	1.5
	---	97	15	---	0.9	0.5	0.013	---	---	---	0.4	0.6	0.12	---	0.03	7.0	24	0.4
	<0.1	---	64	0.5	0.6	0.3	---	60	1.0	0.04	0.2	0.2	0.005	3.7	0.005	---	27	0.05
Ce	---	27	4	(22)[2]	---	---	---	50(30)[2]	---	---	---	---	---	3.1	---	---	---	3.0
	---	41	8	32(32)[2]	---	---	---	28(36)[2]	---	---	---	---	---	1.7	---	3.3	12	2.0
	<0.02	64	16	15(27)[2]	---	---	---	24(47)[2]	---	---	---	---	---	1.5	---	---	---	1.0
	---	---	64	4	0.25	1.0	---	23	---	---	---	---	0.2	1.4	---	3.4	52	0.5
Zr	< 0.01	2	4	(5)[2]	(10 in blood)		---	40(50)[2]	---	---	---	---	---	---	---	5	9	2.0[4]
	---	7	16	(10)[2]	---	---	---	(30)[2]	---	---	---	---	---	---	---	---	---	---
Cb (see Zr)	< 0.01	<20	4	---	---	---	---	27	---	---	---	---	---	---	---	20	13	---
Ru	< 0.05	35	4	2	2.4(14)[2]	---	---	7(5.7)[2]	---	---	---	---	---	0.44	---	33	12	4.0
	---	42	16	1.5	1.4(16)[2]	---	---	5(16)[2]	---	---	---	---	---	0.31	---	38	35	0.8
I	100	(100)[5]	1-30	(20, in thyroid only)			---	---	---	---	---	---	---	---	---	60-80	---	---
Ba (see Sr)	10	---	4	---	---	---	---	70	---	---	---	---	---	4.4	---	Ca. 20[5]		---
Mixture[1]	4.7	60	4	(9.5)[2]	1.7	1.6	---	41(58)[2]	6	(1)[2]	0.8	3.1	0.04	2.6	0.05	---	11	3.0
	5.5	75	16	10(9)[2]	1.3	0.5	---	44(77)[2]	2	(0.8)[2]	0.5	1.0	0.10	2.7	0.017	7	27	1.0
	6.0	93	64	(4)[2]	---	---	---	(80)[2]	---	(0.4)[2]	---	---	---	---	---	---	---	---

[1] Sr is 20% of the mixture used.
[2] Given by lung; % of the amount remaining in body exclusive of lung, gastrointestinal tract, and feces.
[3] Marrow plus cortex (calculated as 8% of body weight for the rat).
[4] Of % absorbed after parenteral administration (15% of amount injected).
[5] Estimate.

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2. Tolerances for Fission Products (continued)

2.5 Application of the Equations: Final Results -- Tolerances

The values taken for the other constants in the equations involved are:

Constant	Gut	Lung	Bone Marrow	Thyroid
W	1.0	1.2	1.8	0.03[illegible]
I_i (once, or 1 day only)	200	1.0	1.0	10[illegible]
I_m (maintained atmosphere)	1.0	0.1	0.1	1.0[illegible]
I_m (decaying atmosphere)	10	1.0	1.0	10
D (once only)	200	400	400	10,000
D (decaying atmosphere)	1000	400	400	10,000

Using the values and data given in the above table, and in XII C,2.4, in the equations of XII C,2.1, tolerance concentrations for ingestion and inhalation for various fission species have been calculated. The results appear in Tables 2 and 3.

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2. Tolerances for Fission Products (continued)

TABLE 2. TOLERANCE DOSES FOR INGESTION

			a	d	Once Only			Continuous Intakes; Concentration Maintained			Continuous Intake; Concentration Decaying		
Isotope	Average Energy (Mev)	Half Life (Days)	Absorption %	Marrow Deposition %	Tolerable Amount mc	Tissue Setting Tolerance*	Tolerance Set by Equation	Tolerable Concentration μc/liter H_2O	Tissue Setting Tolerance*	Tolerance Set by Equation	Tolerable Concentration μc/liter H_2O	Tissue Setting Tolerance	Tolerance Set by Equation
I	0.15	8	100	20[1]	1.37	T	5a	0.39	T	10a	10.7	T	11a
Te	0.2												
	0.2												
Ba (+La)	0.7	12.5	10	25	1.7	BM	5a	3.1	BM	10a	84	BM	11a
La	0.45	1.7	0.3	20	7.3	G	5a	12	G	8a	121	G	8a
Ce (+Pr)	0.15	28	0.1	14	7.8-4.6[2]	G	5a	13-7.6[2]	G	8a	27-16[2]	G	10a
	0.72	70[5]											
Pr	0.24	13	0.1	14	14	G	5a	23	G	8a	230	G	8a
Sr (+Y)[3]	0.43	55	10	40	1.6-0.9[2]	BM	6a	0.3-0.07[2]	BM	10a	2.2-0.5[2]	BM	12a
	0.63	380[6]											
Y	0.35	58	0.1	30	9.4	G	5a	15.5	G	8a	155	G	8a
Zr (+Cb)	0.15	20	0.1	2.5	22	G	5a	36	G	8a	364	G	8a
	0.15	60											
Cb	0.04	35	0.1	2.5	83	G	5a	136	G	8a	1360	G	8a
Ru (+Rh)	0.05	30	10	2.5	33-5.7[2]	G	5a	31-3.4[2]	BM	10a	480-50[2]	G	10a
	1.0	80[7]											
Mo (+43)	0.33	2.8	1.0	2.5	10	G	5a	16.5	G	8a	166	G	8a
Mixed	---	---	---	---	14.6[4]	BM	---	1.20[4]	BM	---	8.6[4]	BM	---
Assumed	1.0	15	10	25	1.18	BM	5a	1.8	BM	10a	49	BM	11a
"	"	30	"	"	"	"	"	0.90	"	"	24	"	"
"	"	60	"	"	"	"	"	0.45	"	"	12	"	"
"	"	120	"	"	"	"	"	0.23	"	"	5.2	"	12a
"	"	240	"	"	"	"	"	0.11	"	"	1.3	"	"
"	"	480	"	"	0.68	"	6a	0.056	"	"	0.32	"	"
Assumed	"	60	100	25	0.118	"	5a	0.045	BM	10a	1.2	BM	11a
"	"	"	50	"	0.235	"	"	0.090	"	"	2.4	"	"
"	"	"	10	"	1.18	"	"	0.45	"	"	12	"	"
"	"	"	5	"	2.36	"	"	0.90	"	"	24	"	"
"	"	"	1	"	5.30	G	"	4.5	"	"	56	G	8a
"	"	"	0.1	"	3.30	"	"	5.5	G	8a	55	"	"
Assumed	0.01	60	10	25	118	BM	5a	45	BM	10a	1220	BM	11a
"	0.1	"	"	"	11.8	"	"	4.5	"	"	122	"	"
"	0.2	"	"	"	5.90	"	"	2.25	"	"	61	"	"
"	0.5	"	"	"	2.36	"	"	0.90	"	"	24	"	"
"	1.0	"	"	"	1.18	"	"	0.45	"	"	12	"	"

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1 Thyroid deposition only.
2 First figure is for zero cooling time; second is after decay of accompanying shorter-lived isotope.

3 60 hour Y.
4 30 days old, "effective β" measurement. Long-lived Sr, Zn, and Sb are principal hazards from this time on.

* T = Thyroid; BM = bone marrow; G = gut

5 Includes excretion rate of 1% per day.
6 Includes excretion rate of 0.15% per day.
7 Includes excretion rate of 0.8% per day.

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2. Tolerances for Fission Products (continued)

TABLE 3. TOLERANCE DOSES FOR INHALATION

			f	b	d	8 Hours/Day, One Day Only			8 Hours/Day, Continuous; Concentration Maintained			8 Hours/Day, Continuous; Concentration Decaying		
Isotope	Average Energy (Mev)	Half Life (Days)	Lung Retention %	Absorption %	Marrow Deposition %	Tolerable Concentration μc/liter (x 10^{-3})	Tissue Setting Tolerance	Tolerance Set by Equation	Tolerable Concentration μc/liter (x 10^{-3})	Tissue Setting Tolerance	Tolerance Set by Equation	Tolerable Concentration μc/liter (x 10^{-3})	Tissue Setting Tolerance	Tolerance Set by Equation
I	0.15	8	100	100	20[1]	280	T	8b	260	T	10b	6.4	T	11b
Te	0.2		"	?	?									
	0.2		"	?	?									
Ba (+La)	0.7	12.5	"	50	25	11	L	8b	61	L	"	1.65	L	11b
La	0.45	1.7	"	"	"	18	"	"	700	"	"	19	"	"
Ce (+Pr)	0.15	28	"	"	"	19--11[2]	"	9b	19--11[2]	"	"	0.50--0.30[2]	"	"
	0.72	69[5]	"											
Pr	0.24	13	"	"	"	33	"	8b	170	"	"	4.7	"	11b
Sr (+Y)[3]	0.43	55	"	"	"	18--8.8[2]	"	9b	10.5--2.2[2]	"	"	0.76-0.015[2]	"	12b
	0.63	380[6]	"											
Y	0.35	58	"	"	"	22	"	8b	27	"	"	0.74	"	11b
Zr (+Cb)	0.15	20	"	"	"	52	"	"	60	"	"	1.6	"	"
	0.15	60	"											
Cb	0.04	35	"	"	"	200	"	"	390	"	"	10.6	"	"
Ru (+Rh)	0.05	30	"	"	"	70--7.8[2]	"	"	61--6.8[2]	"	"	1.6--0.18[2]	"	"
	1.0	80[7]	"											
Mo (+43)	0.33	2.8	"	"	"	24	"	"	600	"	"	16	"	"
Mixed[4]	---	---	---	---	---	94[4]	"	---	36[4]	"	---	0.26[4]	"	---
Assumed	1.0	15	100	50	25	7.9	L	8b	36	L	10b	0.97	L	11b
"	"	30	"	"	"	"	"	"	18	"	"	0.49	"	"
"	"	60	"	"	"	"	"	"	9	"	"	0.24	"	"
"	"	120	"	"	"	"	"	"	4.5	"	"	0.10	"	12b
"	"	240	"	"	"	"	"	"	2.2	"	"	0.026	"	"
"	"	480	"	"	"	4.5	"	9b	1.1	"	"	0.006	"	"
Assumed	"	60	"	100	"	24	BM	8b	27	BM	"	0.73	BM	11b
"	"	"	"	50	"	7.9	L	"	9	L	"	0.24	L	"
"	"	"	"	20	"	5.0	"	"	5.6	"	"	0.15	"	"
"	"	"	"	10	"	4.4	"	"	5.0	"	"	0.14	"	"
"	"	"	"	5	"	4.2	"	"	4.8	"	"	0.13	"	"
"	"	"	"	1	"	4.0	"	"	4.5	"	"	0.12	"	"
Assumed	0.1	"	"	50	"	79	L	"	89	L	"	2.4	L	11b
"	0.2	"	"	"	"	39	"	"	45	"	"	1.2	"	"
"	0.5	"	"	"	"	16	"	"	18	"	"	0.48	"	"
"	1.0	"	"	"	"	7.9	"	"	8.9	"	"	0.24	"	"

1 Thyroid deposition.
2 First figure is for zero cooling time; second is after decay of shorter-lived isotope.
3 60-hour Y.
4 30 days cooling; "effective β" measurement. Long-lived Sr, Rn, and Sr are principal hazards from this time on.
5 Includes excretion rate of 1% per day.
6 Included excretion rate of 0.18% per day.
7 Includes excretion rate of 0.5% per day.

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3. Relative Biological Effectiveness of Various Radiations

The subject of the relative biological effectiveness of various radiations has been reviewed in detail in a recent report,[1] to which the reader is referred.

3.1 Qualitative Effects

In practically all cases it has been observed that the various ionizing radiations produce qualitative effects which are indistinguishable from each other.

3.2 Relative Quantitative Effects

For a great variety of radiobiological effects, investigated upon widely diverse organisms, different radiations are not quantitatively equivalent.

The common physical basis upon which comparisons of quantitative effects are made is the energy absorbed per gram of tissue from the swift ionizing particles which spend their tracks in the tissue. To illustrate by an actual example: hatching of Drosophila eggs is reduced to 50 percent by an x-ray exposure during which one gram of eggs absorbs 13,300 ergs from the electrons ejected by the x-rays.[2] Other experiments with fast neutrons show that the same amount of damage is done by an exposure to fast atomic nuclei (chiefly hydrogen) ejected by neutrons when one gram of eggs absorbs only 5,500 ergs. The relative biological effectiveness (RBE) of these two radiations is then for this case 13,300/5,500 or 2.4:1.0, the fast neutrons in this case being the more effective. It should be remembered that the term relative biological effectiveness as here used is based on equal amounts of energy absorbed in the tissue or, in other words, equal doses in <u>roentgen equivalent</u> dose.

When not two but several radiations are thus compared with respect to their effectiveness in producing a given biological effect, it is found that their RBE values vary progressively with their <u>specific ionization</u> values (SI). The specific ionization is the number of ion pairs produced by an ionizing particle (electron or fast nucleus) per unit length of its track. If a primary radiation does not consist of ionizing particles but ionizes indirectly by ejection of such particles -- as is the case for x-rays, gamma rays, and fast neutrons -- the specific ionization ascribed to the primary radiation is that produced along the tracks of the secondary particles.

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3. Relative Biological Effectiveness of Various Radiations (continued)

Along the track of an individual particle, the specific ionization varies directly with the square of the particle's charge and inversely with its speed. Thus, an alpha particle produces a greater specific ionization than a proton or an electron of the same speed. Also, since even a relatively slow electron is faster than most "fast" nuclei, electrons usually produce lower specific ionization than nuclei.

In most experiments, entire ionization tracks are located in the biological material. Because of the variation of SI along individual tracks (due to progressively decreasing speed), it is convenient to characterize a radiation by its average SI, which is simply the total number of ion pairs produced in all the tracks divided by the total length of all the tracks. For radiation consisting of or producing the same type of ionizing particle -- e.g., electrons -- the average SI is less the greater the initial speeds of the ionizing particles. For example, the fast beta rays from [redacted] (RaB plus RaC) produce about 6×10^4 ion pairs per cm [redacted]k in tissue, while the slow electrons ejected by very soft x-rays (8.3 A) produce about 7×10^6 ion pairs per cm (cf. Figures 1 and 2, XII C,3).

In Figures 1 and 2 are summarized the results of some of the more extensive investigations reported in the literature. The abscissas are values of specific ionization, and below the axis are indicated the actual radiations used in various experiments to produce the different specific ionizations. The ordinates are arbitrary values of RBE per unit energy absorbed per gram of tissue.

It will be noticed that various types of curves are obtained, depending upon the nature of the organism. In some cases RBE decreases with increase in SI, but in the majority of cases it increases.

In the literature are many more reports, the results of which are not charted because only two radiations were used. In many of these investigations the two radiations were fast neutrons and x- or gamma rays, the former producing high and the latter low SI. In all of these investigations, if the biological object was a higher plant or animal (including mammals), the fast neutrons have been found to have higher

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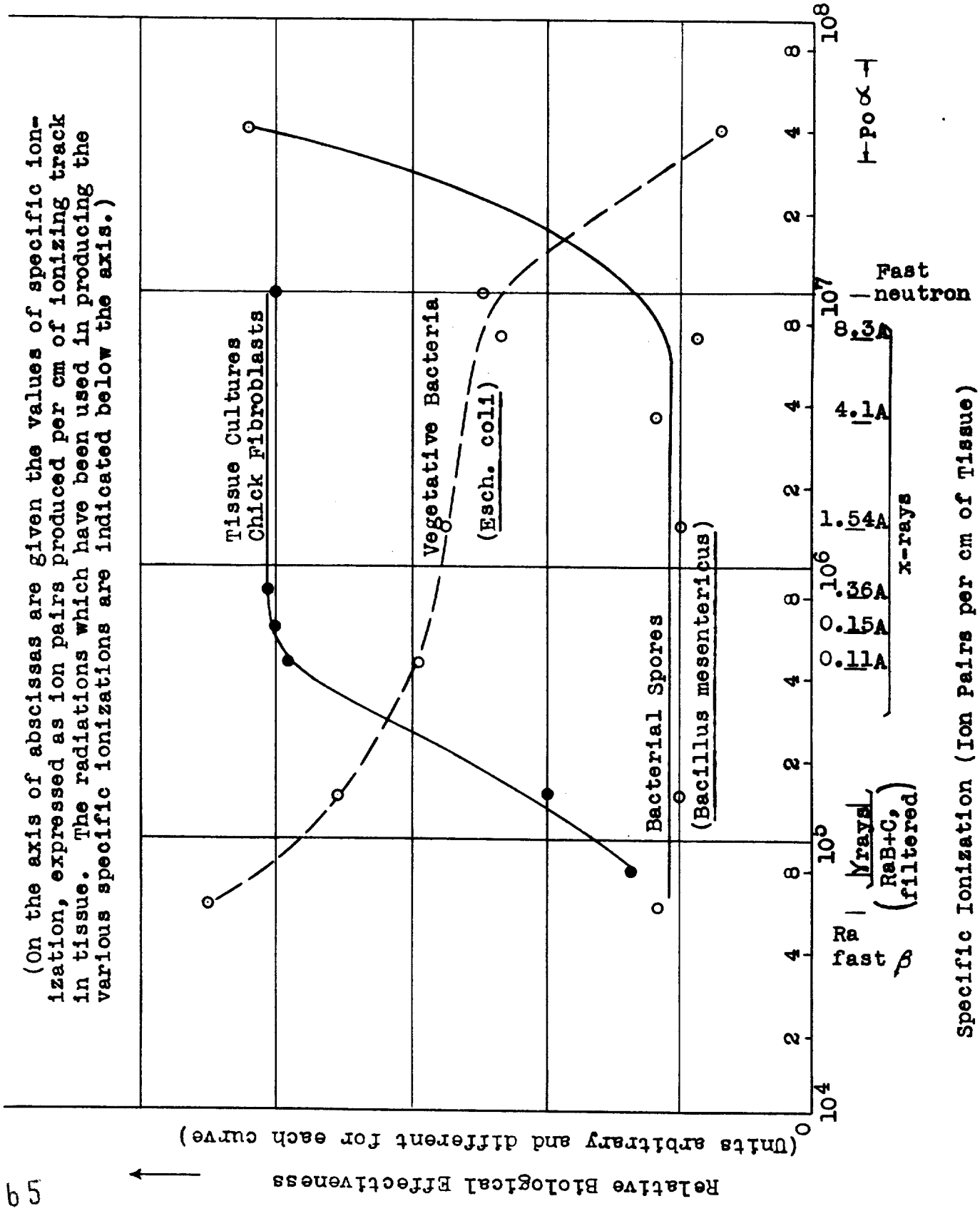

VARIATION OF BIOLOGICAL EFFECTIVENESS WITH SPECIFIC IONIZATION

(On the axis of abscissas are given the values of specific ionization, expressed as ion pairs produced per cm of ionizing track in tissue. The radiations which have been used in producing the various specific ionizations are indicated below the axis.)

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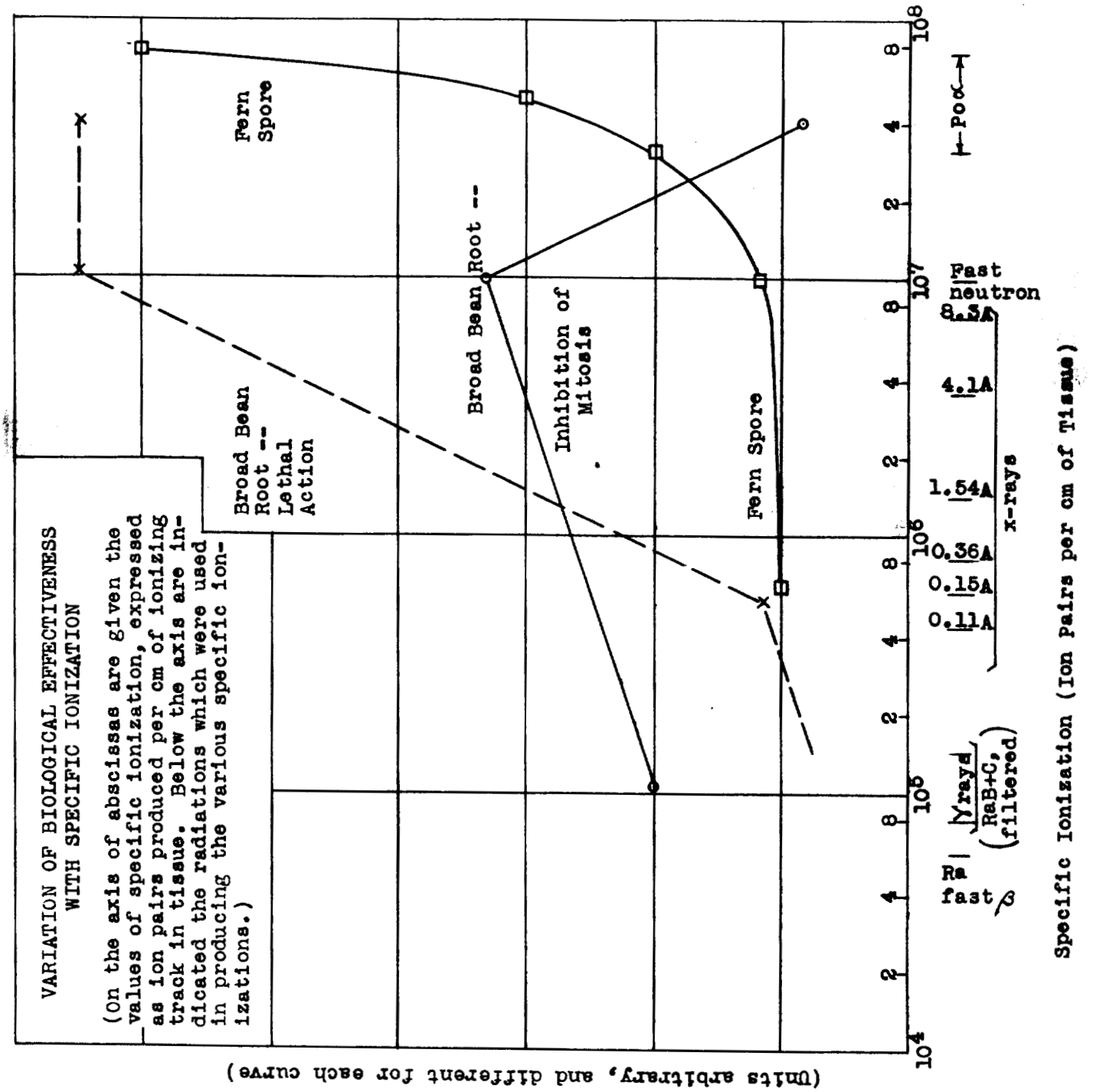

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3. Relative Biological Effectiveness of Various Radiations (continued)

RBE than x- or gamma rays.* For various effects on mammals the ratios of effectiveness vary from 2:1 to as high as 20:1.

On the basis of these various investigations it seems indicated that fast neutrons, producing high SI, are to be regarded as more dangerous, per unit energy absorbed, than x- or gamma rays producing low SI.

Further details will be found in reference (1).

REFERENCES

(1) Zirkle, R. E. - Report CH-946.
(2) Stone, R. S., Cole, K. S., Cantril, S. T., Wollan, E. O., and Hamilton, J. G. - Report CH-708.

*One exception is to be noted: In producing gene mutations, fast neutrons are reported to be less effective than x-rays.

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