FUNDAMENTALS OF RADIOBIOLOGY

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FOREWORD

The story which the authors of this volume have to tell is a fascinating one. When it is complete it will be the story of how an almost incredibly small amount of energy can change the life of a cell, a tissue, or even an entire organism; but the story is as yet only fragmentary, and the key discoveries lie ahead. Herein lies its fascination to all those who have the good fortune to work in this field

The number of those engaged in the study of radiobiology is increasing apace, and not entirely, I believe, because of the big practical issues which depend on an extension of knowledge in this field —the improved use of radiation in the treatment of cancer and the avoidance of the hazards to the health of the community which arise from our having entered upon the age of nuclear fission. The subject can offer to a worker in almost any branch of science a definable problem and make almost unlimited demands on his knowledge and technical skill; and biologists in particular may find in radiation a means of disturbing the life of the cell in a controlled manner which may be of value in the study of fundamental processes.

Professor Bacq and Dr Alexander have undertaken the task of presenting a coherent account of the present status of research in this vast field. That the task is one of extraordinary difficulty anyone who has attempted it, on even a limited scale, will testify. This is so not only on account of the amount of material to be reviewed—the 960 original papers quoted in the bibliography represent a year's solid reading—but because of the variety of disciplines to be covered. Multiple authorship is one way of meeting this difficulty but it leaves the reader to build his own bridges. In this volume, Bacq and Alexander, partners in research and experienced teachers, have told us how they see the subject as a whole, and for this we owe them a great debt of gratitude, for the result is a most readable, stimulating and well documented book.

It is particularly valuable at this time to be able to look at radiobiology through the eyes of the physiologist and the chemist, and to compare their presentation with Lea's presentation of certain aspects of the same subject as it appeared to a physicist eight years ago. It is remarkable how few steps have to be retraced. During the intervening years radiation chemistry has been a focus of interest. It is a field in which Dr Alexander's own researches have already

broadened our outlook, and the reader of this book cannot fail to be impressed both by the present vitality of this branch of the subject and by its obvious relevance to radiobiology as a whole.

Professor Bacq's work on the protection afforded by chemical substances, and particularly his extensive studies with cysteamine and cystamine are well known to every radiobiologist. As a physiologist and pharmacologist he has long been specially interested in the reactions of the whole animal to irradiation, and I believe this volume will be welcomed not least for its critical survey of the domains which are at present obscure and tangled—endocrine intervention, the response of mammals to whole-body irradiation, and what the authors call the pathological biochemistry of irradiated tissues. These are domains in which we may confidently expect exciting discoveries in the next decade as we come to grips with the dynamic aspects of radiobiological damage.

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PREFACE

Much of the interest and fascination of the research in radiobiology is that it brings together scientists from many branches. This book is directed to all workers in this field in the hope that it may help to place their own contribution into perspective and to provide a background. Rapid progress can only come from a pooling of the results obtained by physicists, chemists, biologists and clinicians. Each group, immersed in its own problems and with an ever increasing literature appearing in a large number of journals, is finding it difficult to follow relevant developments in adjacent fields. We have not aimed to provide a review for the specialists of individual topics, but have tried to present the subject as a coherent whole. This treatment, will, we hope, also prove of value to radiotherapists, who have for many years used the powerful tool of ionizing radiation successfully in the therapy of cancer, in the absence of an adequate chemical and biological foundation. This position is now being remedied and a less empirical approach to radiotherapy may soon become possible.

This book is a survey and not a monograph. We have selected certain investigations from the enormous mass of published material, and have not attempted to present a complete review of the literature. Also we have deliberately chosen certain aspects of radiobiology for special emphasis since we feel that developments in these fields are most likely to advance the subject. A choice cannot be impartial; but if we have relied to a disproportionate extent on our own researches and on those best known to us we have made every effort to present fully opposing points of view. We have not hesitated to indicate which, in our opinion, are the most acceptable hypotheses at the present time; this has been done to introduce sense of coherence and does not imply a rigidity of viewpoint and we fully realize that new experimental data may alter the interpretations

Without the help given to us by colleagues and friends we could not have written this volume and it is a great pleasure to acknowledge our gratitude to them. In particular we should like to thank Professor P. C. Koller, and Dr L. H. Gray whose advice was constantly available to us and who gave us many hours of their time.

The illustrations of chromosomes were prepared for us by Professor Koller, Dr S. H. Revell and Mr L. F. La Cour, and we owe

a great debt to them for the efforts they made to obtain the illustrations we wanted.

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Chapter 1, *Figures 3–4*, LEA, D. E., *Actions of Radiations on Living Cells*, Cambridge University Press, 1946; *Figure 5*, HEITLER, W., *The Quantum Theory of Radiation*, Oxford University Press, 1954; *Figures 13–16*, CORMACK, A. and JOHNS, B., *Brit. J. Radiol.*, 1952, **25**, 369; *Figure 18*, TOBIAS, C. A. *et al.*, *Amer. J. Roentgenol.*, 1952, **67**, 1; *Table II*, LEA, D. E., *Actions of Radiations on Living Cells*, Cambridge University Press, 1946.

Chapter 2, *Figure 2*, DALE, W. M. *et al.*, *Phil. Trans.*, 1949, A **242**, 33; *Figure 6* and *Table II*, LEA, D. E., *loc. cit.*; *Figure 7*, TOBIAS, C. A., *Symposium on Radiobiology*, Wiley, New York, 1952, p. 357; *Figure 8*, SETLOW, R. and DOYLE, B., *Arch. Biochem. Biophys.*, 1953, **46**, 46; *Figure 10*, GRAY, L. H., *Brit. J. Radiol.*, 1953, **26**, 609; *Table I*, SETLOW, R. and DOYLE, B., *Arch. Biochem. Biophys.*, 1953, **42**, 83.

Chapter 3, *Table IV*, DAINTON, F. S. and COLLINSON, E., *Annu. Rev. phys. Chem.*, 1951, **2**, 99; *Tables VI–VII*, FRICKE, H. and HART, E. J., *J. chem. Phys.*, 1935, **3**, 60; *Figures 1–2*, BONET-MAURY, P., *Disc. Faraday Soc.*, 1952, **12**, 72; *Figure 3*, DAINTON, F. S. and SUTTON, H. C., *Trans. Faraday Soc.*, 1953, **49**, 1011; *Figure 4*, FRICKE, H. and HART, E. J., *J. chem. Phys.*, 1938, **6**, 229; *Figure 5*, GRAY, L. H., *loc. cit.*; *Figure 6*, LEA, D. E., *Brit. J. Radiol.*, Suppl. No. 1, 1947, p. 59; *Figure 8a*, GRAY, L. H., *Brit. J. Radiol.*, 1953, **26**, 638; *Figure 8b*, ALEXANDER, P. and FOX, M., *Trans. Faraday Soc.*, 1954, **50**, 605; *Figure 9*, FRICKE, H., *J. chem. Phys.*, 1934, **2**, 556; *Figure 10*, EBERT, M. and BOAG, J. W., *Disc. Faraday Soc.*, 1903, **12**, 189; *Figure 11*, FRICKE, H. and BROWNSCOMBE, E. R., *J. Amer. chem. Soc.*, 1933, **55**, 2358, and ALEXANDER, P. and BACQ, Z. M. *et al.*, *Radiation Res.*, 1955 (in the press); *Figure 12*, DALE, W. M. *et al.*, *Biochem. J.*, 1949, **45**, 93; *Figure 13*, DALE, W. M., *Biochem. J.*, 1951, **48**, 129; *Figure 14*, GRAY, L. H., *Brit. J. Radiol.*, 1941, **14**, 102.

Chapter 4, *Tables IV–V*, BARRON, E. S. G., *Symposium on Radiobiology*, Wiley, New York, 1952, p. 216; *Figure 2*, ALEXANDER, P. and FOX, M., *Nature, Lond.*, 1952, **169**, 572; *Figure 3*, ALEXANDER, P. and FOX, M., *J. Chim. phys.*, 1953, **50**, 415; *Figure 5*, BARRON, E. S. G. and FINKELSTEIN, P., *Arch. Biochem. Biophys.*, 1952, **38**, 105; *Figures 8* and *10*, TAYLOR, B. *et al.*, *Arch. Biochem. Biophys.*, 1948, **16**, 19; *Figure 9*, SPARROW, A. H. and ROSENFELD, F. M., *Science*, 1946, **104**, 245; *Figure 11*, ERRERA, M. C. R., *Bull. Soc. chim. biol.*, 1951, **33**, 555; *Figure 12*, SCHOENBERD, M. D. *et al.*, *U.S. Atom. Energy Comm. U.C.L.A.*, 11, 1949; 83, 1950; *Figure 13*, ERRERA, M. C. R., *Cold Spr. Harb. Symp. quant. Biol.*, 1947, **12**, 60.

Chapter 5, *Figures 7–8, 12, 19*, KOLLER, P. C., *Progr. Biophys.*, 1953, **4**, 195;

Symposium on Chromosome Breakage, 1953; and *Figure 13*, LANE, G. R., *Heredity*, 1951, **5**, 1, Oliver and Boyd, Edinburgh; *Figure 18*, GRAY, L. H., *Brit. J. Radiol.*, 1953, **26**, 609.

Chapter 6, *Figure 1*, BACQ, Z. M. *et al.*, *Arch. int. Physiol.*, 1949, **67**, 142.

Chapter 7, *Figure 3*, BACQ, Z. M., *Enzymologia*, 1941, **10**, 48; *Figures 4–5*, KOLLER, P. C. and CASARINI, A., *Brit. J. Cancer*, 1952, **6**, 173; *Figure 6*, REVELL, S. H., *Heredity*, Suppl. 1953, **6**, 107; *Figure 8*, BUTLER, J. A. V., *Nature, Lond.*, 1950, **165**, 714; *Figure 10*, ALEXANDER, P., *Nature, Lond.*, 1952, **169**, 226; *Table IV*, AUERBACH, C., *Cold Spr. Harb. Symp. quant. Biol.*, 1951, **17**, 199

Chapter 8, *Figure 2*, ANDERSON, E. H., *Proc. nat. Acad. Sci.*, 1951, **37**, 340; *Table I*, GILES, N. H. and RILEY, H. P., *Proc. nat. Acad. Sci.*, 1950, **36**, 337.

Chapter 9, *Figure 1*, TOBIAS, C. A., *Symp. Radiobiol.* (ed. J. J. Nickson), Wiley, New York, 1952, p. 241; *Table I*, RUGH, R., *J. exp. Zool.*, 1949, **110**, 357; *Table III*, BACQ, Z. M., *Acta Radiol.*, 1952, **38**, 489.

Chapter 10, *Table I*, FISCHER, P., *Arch. int. Physiol.*, 1954, **62**, 134; *Table II*, DUBOIS, K. P. *et al.*, *Proc. Soc. exp. Biol. Med.*, 1951, **76**, 38; *Table III*, RICHMOND, J. E. *et al.*, *J. biol. Chem.*, 1951, **190**, 817; *Table V*, NIZET, A., *Arch. int. Physiol.*, 1954, **62**, 129; *Table VI*, NIZET, A., *Symp. Radiobiol.*, Liège, 1954, Butterworths, London, 1955; *Figure 1*, BACQ, Z. M., *J. Physiol., Paris*, 1951, **43**, 640; *Figure 3*, THOMSON, J. F. and MIKUTA, E. T., *Argonne nat. Lab.*, 1952, ANK-4794, p. 140; *Figure 4*, BACK, A. and BLOCH-FRANKENTHAL, L., *Proc. Soc. exp. Biol. Med.*, 1947, **66**, 366; *Figure 5*, KUNCKEL, H. O. and PHILLIPS, P. H. *Arch. Biochem.*, 1952, **37**, 366; *Figure 6*, SUSSMAN, A. S., *J. cell. comp. Physiol.*, 1953, **42**, 273; *Figure 7*, SHERMAN, F. G. and FORSSBERG, A., *Arch. Biochem.*, 1954, **48**, 293; *Figure 8*, KLEIN, G. and FORSSBERG, A., *Exp. Cell Res.*, 1954, **6**, 211.

Chapter 11, *Figure 1*, STAPLETON, G. E. *et al.*, *J. cell. comp. Physiol.*, 1953, **41**, 345.

Chapter 12, *Table 1*, FISCHER, P. *et al.*, *Bull. Acad. Méd. Belg.*, 1954 (in the press).

Chapter 13, *Figures 1–2*, *Atomic Medicine*, publ. C. F. Behrens, Williams and Wilkins, Baltimore, 1953, 2nd edn.; *Figure 3*, The Effects of atomic weapons, p. 348 (*U.S. Atom. Energy Comm.*), McGraw Hill Book Co., New York, 1950.

Chapter 14, *Table I*, ALEXANDER, P., BACQ, Z. M. *et al.*, *Radiation Res.*, 1955 (in press); *Table II*, VERLY, W. *et al.*, *Acta Bioch. Biophys.*, 1954 (in press); *Figures 1–2*, BACQ, Z. M. and HERVE, A., *Brit. J. Radiol.*, 1951, **24**, 617; *Figure 3*, STRAUBE, R. L. and PATT, H. M., *Proc. Soc. exp. Biol. Med.*, 1953, **84**, 702; *Figure 4*, BACQ, Z. M. *et al.*, *Science*, 1953, **117**, 633; *Figure 5*, BACQ, Z. M., *Bull. Acad. Méd. Belg.*, 1953 (6) **18**, 426; *Figure 6*, DOHERTY, G. D., 1952, *Fed. Proc.*, **11**, 35; *Figure 7*, FISCHER, P. and GOUTIER-PIROTTE, M., *Arch. int. Physiol.*, 1954, **62**, 76; *Figures 8–9*, BACQ, Z. M. *et al.*, *Bull. Acad. Méd. Belg.*, 1953 (6), **18**, 226; *Figure 10*, BACQ, Z. M. *et al.*, *Science*, 1951, **111**, 356; *Figure 11*, BACQ, Z. M. and HERVE, A., *Arch. int. Physiol.*, 1951, **59**, 348; *Figure 13*, FORSSBERG, A. and NYBOM, N., *Plant Physiol.*, 1953, **6**, 78; *Figures*

14–15, BACQ, Z. M., HERVE, A. and SCHERBER, F., *Arch. int. Pharmacol. Thér.*, 1953, **94**, 93; *Table V*, HOLLAENDER, A. and STAPLETON, G. E., *Physiol. Rev.*, 1953, **33**, 85; *Table VI* and *Figures 16–17*, GEREBTZOFF, M. A. and BACQ, Z. M., *Experientia*, 1954, **10**, 341.

Chapter 15, *Figure 1*, JOLLES, B., *Brit. J. Radiol.*, 1950, **23**, 18; *Table I*, KAPLAN, H. S. and PAULL, J., *Proc. Soc. exp. Biol. Med.*, 1952, **79**, 670; *Tables II–III*, JACOBSON, L. O., SIMMONS, E. L., MARKS, E. K. and ELDREDGE, J. H., *Science*, 1951, **113**, 510.

Chapter 16, *Table I*, COLE, L. J. *et al.*, *Proc. nat. Acad. Sci.*, 1953, **39**, No. 8, 759; *Figure 1*, KAPLAN, H. S. *et al.*, *J. nat. Cancer Inst.*, 1953, **14**, 303.

Chapter 17, *Tables I–II*, BACQ, Z. M. and HERVE, A., *Abstr. 7th int. Congr. Radiol.*, Copenhagen, p. 133; *Table III*, The Effects of atomic weapons, *U.S. Dep. Defense and U.S. Atom. Energy Comm.*, McGraw Hill, New York, 1950.

CONTENTS

1

EFFECTS OF IONIZING RADIATIONS ON MATTER

COMPARISON OF THE DIFFERENT RADIATIONS

In this book we are concerned with the very short wavelength electromagnetic radiations, x- and γ-rays, and the corpuscular radiations made up of electrons (β-rays), helium nuclei (α-rays), protons and neutrons. The former are radiations of the same character as ultra-violet (u.v.) or visible light, but since they are of much shorter wavelength, the energy of their quanta * is of the order of 10^4 higher than those of u.v. light, so that in practice there is little similarity. The absorption of light waves (infra-red, visible and u.v.) depends in general on the molecular structure of the absorbent and only indirectly on the atomic composition.

The energy of x- and γ-rays on the other hand is almost entirely absorbed by ejecting electrons from the atoms through which they pass, and this process is entirely independent of the manner in which these atoms are combined into molecules. Moreover, the amount of energy absorbed from a beam of hard x- or γ-rays by a given weight of material is almost independent even of its elementary composition, although this is not so for soft x-rays.

It is clear, therefore, that the action of x-rays is much less selective than that of light: *e.g.* if u.v. light of 2600 Å is passed through an equal mixture of nucleic acid and a serum protein more than 90 per cent of the energy is taken up by the nucleic acid and less than 10 per cent by the protein. Using γ-rays the same amount of energy would be absorbed by the protein as by the nucleic acid. On absorbing a quantum of light the whole of its energy is stored in the molecule which becomes excited and can then undergo one of a number of different reactions or lose the energy as heat or light (fluorescence).

An atom on absorbing a quantum of x- or γ-rays loses an electron. With the exception of extremely soft x-rays, with which we are not concerned, the energy of the quantum taken up is greatly in excess

* The energy of each quantum of an electromagnetic radiation in electron volts (eV) is given by $12{,}400/\lambda$ (where λ is the wavelength in Å). The quantum is the smallest step in which radiation can be absorbed, *i.e.* a molecule has to absorb a whole quantum of u.v. light or none at all.

of that required to produce an ionization (*i.e.* to eject an electron from an atom) and this surplus is stored as kinetic energy in the ejected electron. The latter is then sufficiently energetic to produce ionization in the atoms through which it passes. For the x-rays used in radiobiology almost all the ionizations are produced by the ejected electrons and the effect of initial absorption of the quantum of x-rays is usually neglected. Consequently the ions produced are not distributed at random throughout the solution but are concentrated along the track of the ejected electron. This represents another fundamental difference between u.v. light and ionizing radiation.

If there are no chemical changes all the energy of x-rays as well as of light waves eventually appears as heat in the absorbing material. With the dose rates used in radiobiology a significant change in temperature would not be produced and the heating effect can in general be neglected except perhaps for very densely ionizing radiations or in 'hot spots' where a disproportionate amount of energy is dissipated. In these cases any heating would be accompanied by a high concentration of reactive radicals which would be more damaging than the heat produced.

The distinction between x-rays which are produced in generators and γ-rays which are given off by some radioactive elements has disappeared. Until comparatively recently the most energetic x-rays produced were obtained from 400 kV therapy tubes giving a spectrum ranging in wavelength from 0·03 Å and having an average wavelength of 0·06 Å*, while γ-rays were obtained from radium with a wavelength of 0·01 Å corresponding to x-rays of $1{\cdot}2 \times 10^6$ V. With the development of new machines such as the van de Graaff generator, powerful linear accelerators, betatrons, synchrotrons and microtrons, x-rays corresponding to many million volts can now be generated and these fall within and beyond the wavelength range of γ-rays. The ready availability from atomic piles of the radioactive isotope cobalt-60 (^{60}Co) has provided a useful source of pure γ-rays of high energy, 1·1 to 1·3 MeV†.

β-*rays*—Since the chemical and biological effects of x- and γ-rays are produced by the ejected high-speed electron and not by the primary ionization it follows that similar results can be obtained by direct bombardment with electrons of comparable energies. Such

* In the spectrum of x-rays given out by therapy-type machines the most energetic radiations (*i.e.* those of shortest wavelength) have an energy equivalent to the peak voltage [*i.e.* their wavelength is $\lambda = 12{\cdot}4/(\text{kV of set})$]. However, the average energy of all radiations is according to LEA[1] half this value.

† The electron volt (eV) is a unit of energy corresponding to $1{\cdot}60 \times 10^{-12}$ ergs. 1 MeV = 10^6 eV, 1 keV = 10^3 eV.

electron beams are called β-rays and can either be obtained from special generators or from radioactive isotopes of which a large choice is now available (see *Table I*). The distance of penetration of β-rays depends on their energy (see *Figure 1*), but even with 2 MeV electrons the range in water (or in biological tissue) is only 5–7 mm. However the disadvantage of the short range of the β-rays can be overcome by dissolving radioisotopes in the solution or system which is to be irradiated when the whole volume will be uniformly exposed. In biological systems the isotope may become localized in certain regions and the resultant irradiation will then not be uniform.

Heavy ionizing particles—α-rays are the nuclei of helium atoms (*i.e.* double charged positive particles of atomic weight 4). They are given off by a few radioactive substances, notably radon—obtained

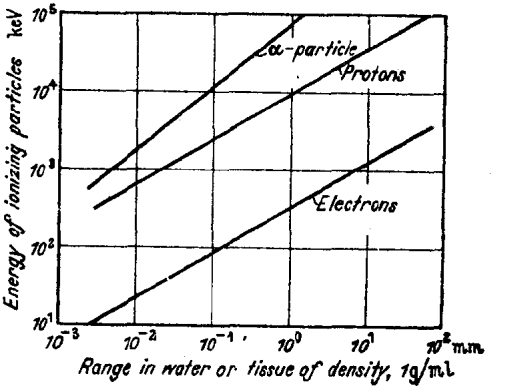

Figure 1. Relationship between the range of an ionizing particle in water (mm) *and its energy* (keV)

as a decay product from radium—and polonium*. The latter is a pure α-emitter while radon also gives off β-rays. Because of their high charge and low velocities the particles are readily stopped by matter and in water or tissue the range of a particle from radium C^1 is only 7·0 μ (see *Figure 1*), and many ions are formed along its track (*i.e.* the ionization density is very high, see p. 20).

Protons are hydrogen nuclei having mass 1 and carrying one charge; they can be obtained artificially from the cyclotron, proton-synchrotron or a van de Graaff generator. Their properties such as ion density and penetration are intermediate between those of the α-particle (mass 4) and the electrons (mass $5{\cdot}5 \times 10^{-4}$).

* α-rays of very low energy and consequently giving an extremely high ion density can be obtained by the artificial disintegration of boron or lithium by slow neutrons. For example when the nucleus of a lithium atom captures a neutron it immediately dissociates to give an α-particle. Tritium ($_3H$) remains and this decays slowly by giving off β-rays.

Table I. List of Some β-ray Emitting Isotopes

Element	$\mathcal{Z}$	A	*Half-life, hour, day or year*	*Radiation*	%	E_{max} MeV	*Formation in the pile*
H	1	3	11·8 y	β^-	—	0·018	$^{2}H(n\gamma)^{3}H$, $Li(n\alpha)^{3}H$
Be	4	10	$2{\cdot}5 \times 10^6$ y	β^-	—	0·555	$^{9}Be(n\gamma)^{10}Be$
C	6	14	5568 y	β^-	—	0·155	$^{13}C(n\gamma)^{14}C$
Na	11	22	2·7 y	β^+	—	0·557	—
				γ	—	1·30	—
P	15	32	14·3 d	β^-	—	1·701	$^{31}P(n\gamma)^{32}P$
	15	33	25 d	β^-	—	0·26	—
S	16	35	88 d	β^-	—	0·167	$^{34}S(n\gamma)^{35}S$
Cl	17	36	4×10^5 y	β^-	—	0·714	$^{35}Cl(n\gamma)^{36}Cl$
K	19	40	$1{\cdot}3 \times 10^9$ y	β^-	89	1·33	Naturally occurring
			$1{\cdot}3 \times 10^9$ y	γ	11	1·46	—
Ca	20	45	152 d	β^-	—	0·255	$^{44}Ca(n\gamma)^{45}Ca$
Fe	26	59	47 d	β^-	50	0·46	$^{58}Fe(n\gamma)^{59}Fe$
				γ		1·1	—
				β^-	50	0·26	—
				γ		1·30	—
As	33	77	40 h	β^-	—	0·80	$^{76}Ge(n\gamma)^{77}Ge \xrightarrow{\beta^-} {}^{77}As$
Br	35	82	34 h	β^-	—	0·447	$^{81}Br(n\gamma)^{82}Br$
						0·323	—
						0·181	—
—	—	—	—	γ	16	1·321	—
					18	1·036	—
					65	0·769 etc.	—
Rb	37	86	19·5 d	β^-	80	1·822	$^{85}Rb(n\gamma)^{86}Rb$
				β^-	20	0·716	—
				γ		1·081	—
Sr	38	89	53 d	β^-	—	1·463	$^{88}Sr(n\gamma)^{89}Sr$
Ag	47	110	270 d	β^-	58	0·087	$^{109}Ag(n\gamma)^{110}Ag$
					35	0·570	—
					5	2·90	—
—	—	—	—	γ	—	1·48	—
						0·9	—
						0·66 etc.	—
Ag	47	111	7·5 d	β^-	91	1·04	$^{110}Pd(n\gamma)^{111}Pd \xrightarrow{\beta^-} {}^{111}Ag$
				β^-	8	0·70	—
				γ		0·34	—
				β^-	1	0·80	—
				γ		0·24	—
I	53	131	8 d	β^-	86	0·605	—
				γ		0·364 etc.	$^{130}Te(n\gamma)^{131}Te \xrightarrow{\beta^-} {}^{131}I$
				β^-	14	0·25	—
				γ		0·637	—
Au	79	198	2·69 d	β^-	—	0·96	$^{197}Au(n\gamma)^{198}Au$
				γ	—	0·441	—
Hg	80	203	43·5 d	β^-	—	0·208	$^{202}Hg(n\gamma)^{203}Hg$
				γ	—	0·279	—
Tl	81	204	2·7 y	β^-	—	0·775	$^{203}Tl(n\gamma)^{204}Tl$
RaE(Bi)	83	210	5·02 d	β^-	—	1·17	Naturally occurring

$\mathcal{Z}$ is the atomic number; A is the atomic weight.

With the newer generators many heavy ionizing particles can now be produced. Any atom stripped of one or more of its electrons if accelerated will become an ionizing particle. Deuterons are frequently used; they have mass 2, charge 1 and consequently their penetration and ionization density is intermediate between that of protons and α-particles. Carbon atoms which have lost six electrons, C^{6+}, are probably the most densely ionizing particles used in radiobiology. With a mass of 12 and charge of 6 they are almost as different from α-particles as electrons are from protons.

Neutrons—Fast neutrons (particles having mass of 1 but carrying no charge) are usually obtained either from a cyclotron, atomic pile or indirectly from a van de Graaff generator, but can also be obtained more simply by the bombardment of beryllium with α-particles. A simple low-power source is the complex salt $RaBeF_4$. Neutrons do not produce ionization directly but knock out protons from the nucleus of the atom they traverse. The biological effects of fast neutrons are, therefore, almost wholly due to protons in exactly the same way as the effects of x-rays are produced by the ejected electrons. Unlike the other ionizing radiations, however, the number of ionizations produced depends largely on the nature of the elementary composition of the material through which the neutrons pass. The reason for this is that the transfer of energy between neutrons and protons does not depend on the atomic number but on other factors, and the number of ionizations produced by a given dose of neutrons in 1 g of water will be about 2·5 times that produced in 1 g of air; this makes neutron dosimetry very difficult (see p. 15). Neutrons, like x-rays, can penetrate large amounts of matter since the protons are ejected at random within the irradiated material. The ionizations are, therefore, concentrated along short tracks inside the irradiated body.

Slow neutrons do not eject a proton but are captured by the nuclei through which they pass, thereby producing a new nucleus which is radioactive and will emit β- or γ-rays. During the process of neutron capture the nucleus emits a γ-ray. Many of the radioactive substances listed in *Table 1* are produced in this way in atomic piles. The reactions of slow neutrons, although of much chemical interest, are unlikely to be of great biological importance since the effects produced by the ionizing radiations emitted are much more far-reaching than those resulting from the transmutation of relatively few atoms. In this connection it should be pointed out that very high energy electromagnetic or β-radiations (*i.e.* greater than 8 MeV), produced for example by a synchrotron or betatron, will also produce nuclear transformations in some of the elements

through which they pass. An animal irradiated from one of these generators becomes detectably radioactive. In x-ray therapy with a 25 MeV betatron 5 per cent of the total dose received by the patient is emitted by the carbon isotope ^{11}C which is produced *in situ* from the ordinary ^{12}C atoms in the body by the x-rays. A case is recorded where the gold tooth of a man accidentally exposed to slow neutrons became so radioactive as to produce ulceration of the gum.

MECHANISM OF ENERGY LOSS BY IONIZING RADIATIONS

Interactions between beams of electromagnetic or particulate radiation and matter can only be described quantitatively in the language of quantum mechanics. The problem, although very difficult, has been solved by contemporary physics and detailed treatments are given in advanced modern textbooks[2]. It is not possible here to do more than give a list of some of the more important processes. Excitation of atoms and molecules by the absorption of a quantum of visible or u.v. light will not be considered.

As we have seen, virtually all the ionizations which result from the absorption of x- or γ-rays are produced by the ejected electrons. The first problem is, therefore, to determine the number and energy of the electrons produced when these rays are absorbed. For all radiations the energy (or intensity) of the beam before absorption (I_0) is related to that after absorption (I) by the equation $I = I_0 e^{-\mu x}$ where μ is the absorption coefficient and x the amount of material. The thickness x may be expressed variously as cm, g/cm^2, atoms/cm^2, or electrons/cm^2. Since the product μx must be dimensionless, μ is correspondingly expressed as cm^{-1}, cm^2/g, cm^2/atom, or cm^2/electron. To indicate which unit is being used the following symbols are conventionally employed :

μ_e for cm^2/electron, μ/ρ for cm^2/g (mass coefficient),
μ_a for cm^2/atom, μ for cm^{-1}.

All these coefficients can be interconverted if the atomic weight (A) and the atomic number ($\mathcal{Z}$) are known ; *e.g.* in terms of μ_e,

$$\mu_a = \mathcal{Z}\mu_e$$
$$\mu/\rho = \mathcal{N}(\mathcal{Z}/A)\mu_e$$
$$\mu = \rho\mathcal{N}(\mathcal{Z}/A)\mu_e$$

where $\mathcal{N}$ is Avogadro's number and ρ the density.

There are essentially three mechanisms by which energy can be transferred from the radiations to the material through which they pass and, when scattering can be neglected as is normally the case,

μ_a is made up of three components, τ_a, σ_a and π_a, corresponding to energy absorption by the photoelectric effect, Compton effect and pair formation.

The photoelectric effect—By this mechanism a quantum gives up all its energy (*i.e.* is completely absorbed) to an atomically bound electron which it ejects. The kinetic energy of this electron is the energy of the quantum less the energy required to remove the electron from the atom (the binding energy). Since electrons at different levels have different binding energies the energy of the photoelectron will vary, but for the atoms making up organic materials and water a maximum value for the binding energy of 500 eV may be taken*. Compared with the high quantum energy of the radiations used in radiobiology the binding energy is comparatively so small that virtually all the energy is retained by the photoelectron which then produces further ionizations.

The absorption coefficient per atom μ_a of the material varies with the wavelength, λ, of the radiation and the atomic number, Z, of the elements of which it is composed. The atomic absorption coefficient for photoelectric absorption (τ_a) is given by

$$\tau_a = c.\lambda^m.Z^n$$

where c is a constant, m is of the order of 3 and n varies from 3·5 to 5. Consequently the photoelectric absorption falls off very rapidly as the radiations become more energetic (*i.e.* harder), and for x-rays of energy greater than 1 MeV the contribution of photoelectrons to the total energy absorption can be neglected (see *Figure 2*). Also since the absorption varies as a high power of Z the photoelectric absorption is much greater for heavy elements than for light elements.

The Compton effect—The elementary view is that this process is a 'billiards ball' like collision between the quanta of radiation† and the outer shell electrons of the atoms through which they pass. The amount of energy transferred to the electron which is ejected varies and can be calculated from the theoretically derived equation

* When an inner electron has been ejected an outer or free electron can fall into its place. In this process energy is set free since the gross change is the removal of an outer electron which requires only about 10 eV compared with the value of about 500 eV for inner electrons. This energy is liberated as a quantum of radiation —corresponding to very soft x-rays—which is usually absorbed by the same atom to give an electron of extremely low energy having a high specific ionization (see p. 19). This gives rise to a highly localized release of about 500 eV and is referred to as the Auger effect.

† The scattered quantum after it has given up a fraction of its energy to the ejected electron will behave normally and can undergo all the processes for energy loss (*e.g.* another 'Compton collision').