BIOLOGICAL HAZARDS OF ATOMIC ENERGY

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Being the papers read at the
Conference convened by the
INSTITUTE OF BIOLOGY
and the
ATOMIC SCIENTISTS' ASSOCIATION
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FOREWORD

by SIR HENRY DALE

THE Conference, of which this volume reports the proceedings in detail, was organized for the open discussion of matters which are already raising urgent problems for the modern world; nor can it be doubted that they will continue to pose a succession of such problems, in a future which can be clearly foreseen. Few among those who are living in the midst of its changes have more than a vague apprehension of the manner and the speed with which the material framework of our civilization is now being transformed under the impact of scientific discoveries, as these are developed and applied in technical practice. There are many, it may be suspected, whose instinctive reaction to the mention of 'atomic energy' and its 'hazards' will be to turn away from the mere thought of such things with alarm, even with a feeling of resentment against the advance of scientific knowledge, because items of it can be abused by man's folly so as to threaten even the final destruction of all that the centuries of his civilization have achieved. There were, indeed, some contributors to the discussions at this Conference, and especially at its final session, who felt constrained to deal explicitly with moral issues involved in this aspect of its general subject; and they surely cannot be blamed for a feeling that no opportunity ought to be missed for giving the possibilities of such overwhelming disaster an urgent appeal to the general conscience, or for ensuring the continued alertness of scientists themselves to the dangers which threaten the true spirit of science through this lamentable involvement of knowledge, potentially so beneficent, in the secret planning of nations for competitive destruction.

Such dangers and tragedies, however, are by no means limited to the exploitation of atomic energy; and they were not the problems for the discussion of which this Conference was specially promoted and organized. Its object rather was to consider, at the high level of a purely scientific inquiry, all that is known about the actions upon living organisms of the different kinds and sources of radiant energy, many of which the spectacular progress of atomic physics has made newly available; and about the dangers to human life and health which are thus likely to arise in connexion with the industrial, medical, and biological applications of all this new knowledge, and even with the researches directed to the further advancement of atomic physics itself. The purpose and the value of such a discussion are readily apparent. The review of this varied and rapidly widening field by a body of chosen experts, each of them dealing with some aspect of the general subject which is a matter of his own special study and research, provides a comprehensive survey of what is already known, and reveals therewith the directions in which further investigations are required with a special urgency. It will be seen that the Conference had the great additional advantage of including among its contributors several scientists of high standing from other countries. And their presence and participation not only extended the range of expert experience on which the Conference could call; it had a further and symbolic value in emphasizing the need to maintain and to deepen all those international channels of scientific confidence and collaboration which present world conditions allow still to remain open.

Here, then, in a series of contributions to this important Conference, the available physical and biological data are set forth in detail, enabling estimates to be made of the hazards attendant upon the various proper and beneficent applications of atomic energy, and effective precautions to be proposed, by the conscientious application of which these dangers ought to be successfully prevented. The early records of the uses of the X-rays and radium, before the consequences of excessive or frequent exposure to them began to be recognized, had left a sad trail of human tragedies to give warning, if it were still needed, of the dire results of dealing with these potent but invisible agents in a spirit of careless confidence. Many of the articles here collected inevitably deal with their particular subjects at a level demanding, for a full understanding of their contents, a scientific equipment beyond the range of the general reader, or even of one whose special knowledge is limited to other departments of science. Any reader, however, with no more than the ordinary citizen's knowledge of scientific matters, will be able to form some idea of the range and complexity of the problems involved, on the biological as well as on the physical side. It will be clear to him, for example, that those concerned with the formulation of precautionary limits for the different kinds of radiation and the different radioactive elements cannot limit the objective of their calculations to the avoidance of immediately dangerous exposures; they are being urged to take account also of remoter possibilities, such as those of genetic effects imperceptible in the individual but involving some unmeasured danger of an ultimate racial impairment to whole populations. And, as a reassuring instance of the consequent tendency to make precautions stringent beyond proven necessity rather than prescribe them with an undue leniency, it may be noted that the limit of radioactivity imposed upon the water of the Thames, which receives the effluent from the Harwell Atomic Energy

Station, is only a fraction of that which occurs naturally in the very fine water-supply of New York City.

No reader of this Report, I think, can fail to be impressed by the range and complexity of the knowledge required for the safe and sane handling of the problems with which it deals. Progress in this field of atomic physics was subjected, of course, to a wholly unnatural and forced development to meet the irresistible demands of war Knowledge and resources which under normal conditions might well have been the product of an ordered advance by successive stages and through many decades, have thus been thrust almost suddenly into the hands of a human community, which had but little opportunity in advance for preparation to deal with them. And thus physicists and biologists, physicians and engineers, have all been faced with a pressing need to use these newly won agents for the common good, and at the same time to prevent risk of their dangers. And here, in this Report, is abundant evidence that, if there should be delay in their safe and useful application, it will not be due to any lack of strenuous, enlightened, and courageous effort to deal with the problems which this situation has created, and to devise the precautions which it demands.

CONTENTS

THE BIOLOGICAL RESPONSE TO PENETRATING RADIATIONS

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SOME of the immediate physical changes which occur in living matter when radiation energy is absorbed are now comparatively well understood, but the complex sequence of events connecting these changes with the ultimate alteration in cellular behaviour to which they give rise is still largely unknown and remains a matter for speculation and discussion. The ultimate changes in cellular behaviour can, however, be observed qualitatively and many of the results recorded quantitatively. Penetrating rays affect living tissues, as distinct from isolated cells, by a direct action upon the individual cells composing the tissue; by an indirect action via the blood circulation; and by a constitutional effect upon the organism as a whole. According to circumstances these effects may be present together, or one may predominate to the actual or relative exclusion of the others.

DIRECT ACTION OF RADIATION

The direct effects of radiation upon living cells comprise two essentially different types of action. On the one hand there is the type of response which requires a certain threshold dose before any biological effect can be recognized, and on the other hand a type of response which is directly proportional to the amount of radiation given, however small (in theory) that amount may be. The difference is often expressed graphically by two superimposed curves (Fig. 1): one, a skewed S curve, represents the threshold type of reaction and the other, a straight line, that of the non-threshold type. In physical terms the latter suggests the probability that a single-event action, sometimes called a 'hit' or target action, is involved; the former that the response involves a two- or multiple-event action, or a reaction involving the idea of accumulation. In general terms, the 'hit' action is one in which there is no recovery factor and injury once done is permanent and unalterable; the threshold type of reaction is one in which recovery factors operate successfully until sufficient energy is accumulated to prevent the rate of repair keeping pace with the speed at which injury is inflicted, and a recognizable abnormality results.

Biological Hazards of Atomic Energy, pp. 1–6.

Classical examples of the non-threshold type of reaction are radiation-induced mutations and, under certain conditions, the production of chromosome aberrations. The diminution of mitotic activity, after exposure, in a proliferating tissue, radiation-produced erythema in the skin, and the occurrence of radiation anaemia may be given as examples of the threshold type of reaction. In practice, curves are frequently obtained which are intermediate between these two main types and it may be impossible to assign

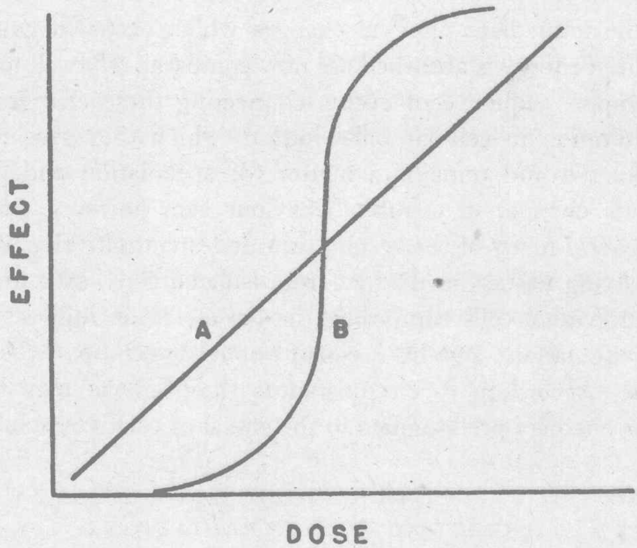

FIG. 1. Dose effect curves. Line *A* is a non-threshold type of response; line *B* a threshold type.

a given biological response definitely to one or another category until other tests have been applied.

Most of these direct effects occur at relatively low dosage and some show a quantitative equality whether observed *in vitro* or *in vivo*. Any part of the cell may be affected by radiation. The nuclear structure, however, particularly the chromosomes at division, shows such dramatic changes that the effects on cytoplasm and non-nuclear cell constituents are sometimes overshadowed or neglected, although they are often just as crucial for cell survival as nuclear structures and merit equally serious attention. Changes in the cytoplasm (Fig. 2, Pl. I) include, for example, vacuolation, lysis, and keratinization; changes in mitochondria, and in the Golgi apparatus; pigmentation, alteration in permeability, in UV absorption, in pH, and in viscosity; increase in cell size, alteration in secretory activity; effects on the mitotic spindle; surface changes affecting cytoplasmic cleavage (and therefore the distribution of nuclear material between daughter cells), metabolic disturbances, and effects on enzymes.

The nuclear changes (Fig. 3, Pl. I)—more familiar because more often figured both in the scientific and lay press—chiefly concern the chromosomes at division and include various structural abnormalities, breakage, fragmentation, lag in movement, bridges at anaphase, uneven division of nuclear material, clumping of chromosomes, abnormal precipitation of chromatic material, formation of micronuclei and vacuolation.

Thus there are very many different ways by which radiation may cause cell injury or death, and several may be operating simultaneously in any given tissue. The particular response selected may be the result of a direct or indirect action of radiation or of both, according to the conditions of experiment. The various changes produced by radiation are not specific. Other agents, physical and chemical, may produce similar changes.

If the biological response selected as a measure of radiological action is of the threshold type, recovery of actual cells affected or tissue repair by activity of other (unaffected) cells may eventually follow irradiation, and the histological picture presented at any moment becomes the resultant of initial damage plus reparative change (Fig. 4, Pl. I). The picture varies, however, with the type of tissue irradiated and also with such physical factors of irradiation as size of field and volume dose delivered. The observer needs also to be as skilled in selecting the optimum time for the examination of his material as he is in discriminating between true radiation effect and various artefacts which can lead the unwary astray.

INDIRECT ACTION OF RADIATION

When applied to higher animals, penetrating rays affect the blood-forming organs, the composition of the peripheral blood and the tissues of which the heart and blood-vessels are composed. Such a 'direct action' of radiation upon blood-vessels has, however, an obvious importance beyond any significance for the circulatory system itself, since interference with vascular supply produces destructive effects upon any tissue deriving nourishment from that supply, apart from any direct action of radiation upon the tissue itself (Fig. 5, Pl. I). By a long-standing custom among radiation biologists the term 'indirect effect' has come to be restricted to all those tissue changes which result from radiation-interference with blood-supply. Unfortunately, radiation chemists have adopted the same term for the process by which an atom or molecule is damaged by the irradiation of constituents of the surrounding medium, and thus the same term has come to carry two different meanings.

The amount of damage seen in a tissue after injury to its normal blood-supply will depend upon the suddenness with which the supply is cut off and the rapidity with which a collateral circulation (if any) can be established (Fig. 6). If the supply is completely cut off, then the resulting

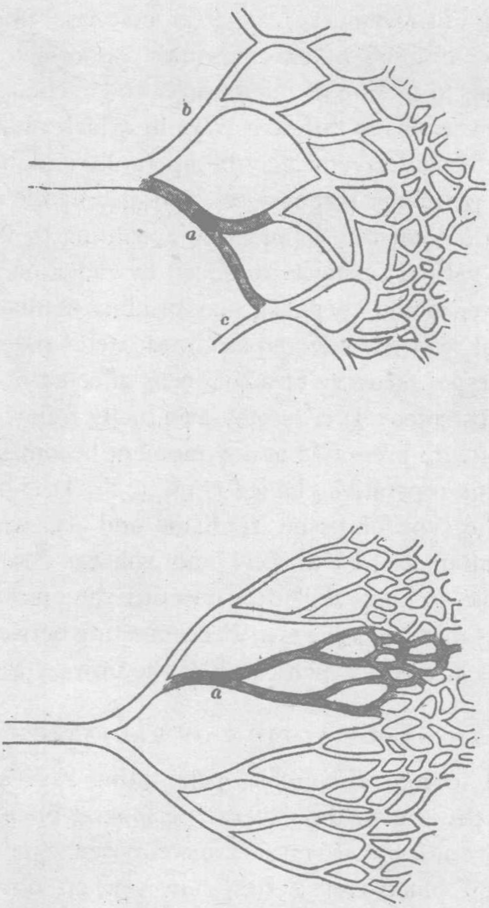

FIG. 6. Diagram of collateral circulation illustrating consequences of blockage at different points of the local vascular system (Adami and McCrae's *Pathology*).

destruction is indiscriminately distributed over the area supplied by the damaged vessels—a picture which is in marked contrast to the strictly regional distribution of degeneration effected by a direct action of radiation.

With single doses of radiation below 1,000 r the direct action of radiation on a tissue predominates, and while the circulation remains intact recovery from the direct effects of exposure is hastened. Above 1,000 r the effects of radiation are a combination of direct and indirect actions.

CONSTITUTIONAL EFFECTS OF RADIATION (RADIATION SHOCK)

The too-rapid discharge into the blood-stream of the débris of cell destruction after an exposure may produce toxic effects on any or every tissue of the body, and this may result in various degrees of radiation shock. Massive doses of radiation (~ 50,000 r), given experimentally to a single organ, produce within 3 hours a degree of devastation in a distant organ, protected from the original radiation, which is quite extraordinary. The larger the volume of living tissue irradiated, the greater the relative importance of this constitutional effect of radiation.

DOSIMETRY

When consideration is given to the question of biological response in a more general sense, one of the most striking results of radiation experiments to be seen is the enormous dose range involved (Table I), from reactions which are obtained after exposure to a few röntgens to those requiring

TABLE I. *Illustrative dose table*

	Dose in r	*Effect, &c.*
1.*	1	human toleration dose for one week (old style).
2.†	(up to) 70	received by diagnostician during examination of gut.
3.†	(up to) 120	received by customer viewing shoe fit.
4.†	170	produces temporary sterility in women.
5.*	500	(estimated) m.l.d. for man.
6.*	1,000	m.l.d. ascaris eggs.
7.†	1,000	human skin erythema (γ-rays).
8.*	5,000	sterilization dose for some *Drosophila* species.
9.†	20,000	inhibits regeneration in worm segments.
10.*	200,000	m.l.d. *B. mesentericus* spores.
11.*	1,000,000	inactivation dose for some viruses.

* Total body irradiation.
† Localized irradiation.

many millions. There is a ten-thousandfold difference, for example, between the extremes of sensitivity among different types of living cells when measured by the lethal effect, and the same organism may vary greatly in radiosensitivity at different stages of development. Again, cell division may be temporarily inhibited in one tissue by exposure to a few hundred röntgens and in another tissue it may survive an exposure to twenty thousand röntgens. The reasons for such great differences in sensitivity to radiation are still quite unknown. Where an appreciable volume of complex tissue is being irradiated, e.g. with multiple fields, the greatest biological change is not necessarily found at the points of highest dosage. On the other hand, no tissue is entirely invulnerable and all organisms are killed if sufficiently large doses of radiation are given.

All this makes radiosensitivity a difficult term to define precisely. A body cell whose behaviour is capable of being altered by a given dose of radiation may be regarded as a radiosensitive cell under the given conditions, irrespective of whether the change in behaviour is advantageous or otherwise to the organism as a whole. A particular form of behaviour can sometimes be elicited when the right handling of radiation as a tool has been learned.

BIOLOGICAL DAMAGE INDUCED BY DIFFERENT TYPES OF IONIZING RADIATION

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DR. SPEAR has surveyed the manifold ways in which living cells may respond to exposure to ionizing radiations. The diversity of response clearly raises difficult problems in relation to the assessment of radiation hazards. These difficulties are increased by the fact that the damage resulting from a given total dissipation of energy in the cell is not fixed but depends on many factors. Among other things, it depends on the physiological condition of the cell at the time of irradiation, on the duration of the exposure, and on the type or quality of the ionizing radiation, which determines whether the energy is delivered to the cell by a few densely ionizing particles, as when tissues are exposed to neutrons or α-radiation, or by a large number of less densely ionizing particles, as in exposures to X- or γ-radiation. This paper is primarily concerned with the influence of radiation quality, but as we shall see, the physiological factor, the time factor, and radiation quality are not three independent factors but are interrelated in the extent to which they modify biological response to a given dose of radiation. This is well illustrated by considering growth inhibition in roots exposed, on the one hand, to γ- or X-radiation—two of the low ion density group of radiations—or, on the other, to α-radiation, a typical high ion density radiation (Gray and Scholes).

Roots of *Vicia faba*, which have been exposed to a dose of radiation which is insufficient to kill them—say, 150 röntgens—pass through a period in which their growth rate relative to that of control roots falls to a minimum at about the sixth day after irradiation, and then returns to normal. We know that the growth inhibition is conditioned almost entirely by the damage sustained by the cells in the extreme tip, whose function it is to maintain a continued supply of new tissue by repeated division. Without inquiring more closely at this stage into the nature of the primary damage to these meristematic cells, we may use the minimum value of the growth rate of irradiated roots compared with their controls as an arbitrary measure of radiation damage. Fig. 1 shows the relation between minimum growth rate and dose for α-, X-, and γ-radiation.

Biological Hazards of Atomic Energy, pp. 7–18.

The results obtained with α-radiation lend themselves to the simplest type of formulation, since the relation between the logarithm of the growth rate—relative to that of control roots—and the dose is rather accurately linear, and independent of the duration of the exposure. We have used exposure times as short as 10 minutes and as long as 24 hours without detecting any systematic influence of the time factor on response to α-radiation.

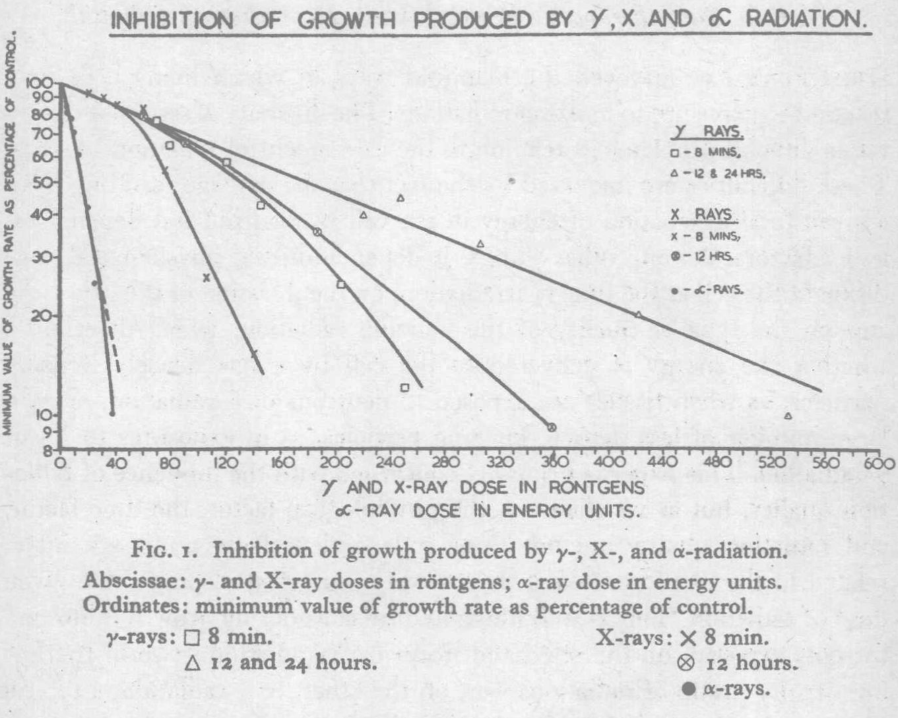

Fig. 1. Inhibition of growth produced by γ-, X-, and α-radiation.
Abscissae: γ- and X-ray doses in röntgens; α-ray dose in energy units.
Ordinates: minimum value of growth rate as percentage of control.

γ-rays: □ 8 min.
Δ 12 and 24 hours.

X-rays: × 8 min.
⊗ 12 hours.
● α-rays.

Growth inhibition induced by both X- and γ-radiation, on the other hand, is markedly dependent on the duration of exposure. The two curves depicted for each radiation show the results of very short and very long exposures—8 minutes and 12 hours in the case of X-rays, and 8 minutes and 24 hours in the case of γ-rays. Intermediate times have also been investigated and, in fact, the results for each radiation can only be represented by a family of curves (Figs. 2 and 3) whose form suggests that, by contrast with the damage induced by α-radiation, that induced by X- or γ-radiation is of at least two kinds, one kind being independent of the duration of exposure and the other a type of damage from which the cell may recover, even while being irradiated, so that the net damage sustained is less the slower the radiation is delivered.

For the purpose of formulating protection recommendations it has been necessary, as a first step, to decide upon a maximum permissible rate of exposure to X- or γ-radiation and to relate all other radiations to these by the assignment of a factor representing their relative biological efficiency. What value would we assign to α-radiation in respect of growth inhibition in roots of *Vicia faba*?

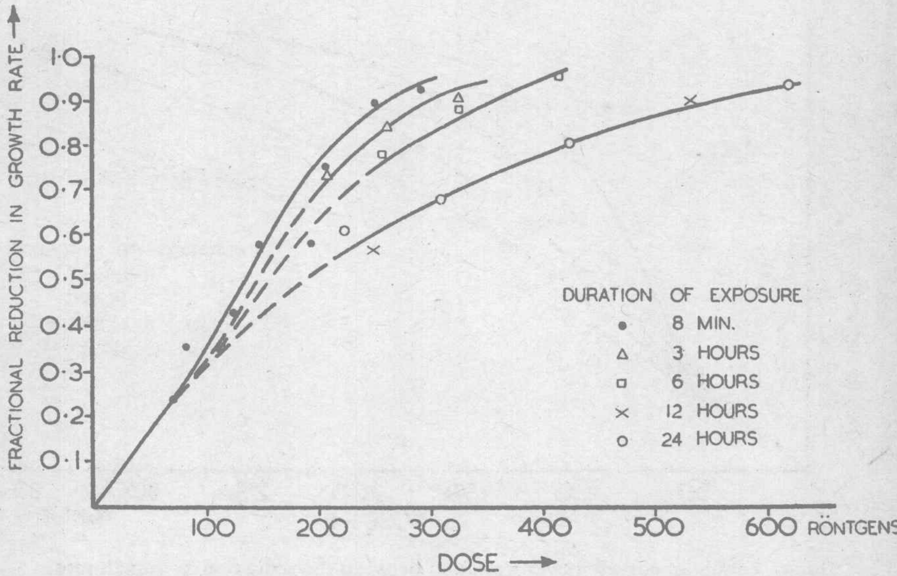

FIG. 2. Family of curves showing relation between the reduction in growth rate and the dose for different durations of exposure to γ-radiation.

Abscissae: dose in röntgens.

Ordinates: fractional reduction in growth rate.

● 8 min. △ 3 hrs. □ 6 hrs.

× 12 hrs. ○ 24 hrs.

At the level of heavy damage (85 per cent. growth inhibition) and short exposure times, the α-ray dose required to produce a given degree of damage is only about a quarter of the X-ray dose, so that the relative biological efficiency of α-radiation relative to X-radiation is about 4; relative to γ-radiation it is about 7. In the case of prolonged exposures at the same level of damage, the values would be about 8 and 12 respectively, and these same figures would apply to slight damage given either slowly or rapidly. It will be seen, also, that whereas X-radiation is some 1·5 times as effective as γ-radiation when delivered in a short time and in such a manner as to inflict heavy damage, it is doubtful whether there is any difference at the level of minimal damage.

In practice, faced with such a complex situation, prudence obviously