AUSTRALIAN ATOMIC ENERGY COMMISSION

THE EFFECTS OF IONIZING RADIATION ON MAN

by

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ABSTRACT

This paper describes the major effects of ionizing radiation on man and the relationship between such effects and radiation dose, with the conclusion that standards of radiological safety must be based on the carcinogenetic and mutagenic properties of ionizing radiation. Man is exposed to radiation from natural sources and from man-made sources. Exposure from the latter should be regulated but, since there is little observational or experimental evidence for predicting the effects of the very small doses likely to be required for adequate standards of safety, it is necessary to infer them from what is seen at high doses. Because the formal relationship between dose and effect is not fully understood, simplifying assumptions are necessary to estimate the effects of low doses. Two such assumptions are conventionally used; that there is a linear relationship between dose and effect at all levels of dose, and that the rate at which a dose of radiation is given does not alter the magnitude of the effect. These assumptions are thought to be conservative, that is they will not lead to an underestimation of the effects of small radiation doses although they may give an overestimate.

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BIOLOGICAL RADIATION EFFECTS; CALIBRATION STANDARDS; CARCINOGENESIS; DOSE-RESPONSE RELATIONSHIPS; MAN; MUTAGENESIS; RADIATION DOSES; RADIATION HAZARDS; RADIATION PROTECTION; SAFETY STANDARDS

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INTRODUCTION AND SUMMARY

In large doses ionizing radiation is acutely injurious to biological tissue; this action, which is mediated through injury to the individual cells of the tissue, is made use of in the treatment of cancer by irradiation. Large doses of radiation may also produce delayed effects, of which much the most important are the induction of cancer, manifested in the exposed individual, and the induction of genetic mutation, manifested in his offspring. These effects are all readily demonstrated in animals, although the sensitivity of different species to radiation varies considerably.

There is ample direct evidence from various sources - atomic warfare, medical applications of radiation, occupational exposure to radiation - that ionizing radiation in large doses is an effective inducer of cancer in man, and the evidence is good enough to allow estimates of the actual risk that cancer will follow a large radiation dose to an individual. There is no direct evidence that radiation can induce genetic mutations in man, but experiments with animals leave us in no doubt that such is the case and can provide estimates of risk at high doses. Evidence that radiation in low doses is effective in the induction of cancer or mutation is scanty, and not easily reinforced by experiment because the effect after low doses, where it exists, can only be very small and is difficult to distinguish from the natural occurrence of cancer or mutation, whether in man or experimental animals.

Man's radiation exposure comes from several sources. The largest single contribution, on average about 100 millirem (units of dose) to an individual per year, comes from natural environmental sources and is unavoidable, though its magnitude varies considerably from one area to another. In most countries another substantial contribution, in some cases as much as half the dose from natural sources, comes from the medical uses of radiation, in particular diagnostic X-rays. Much smaller contributions to the overall dose to the population come from weapons test fallout, from various consumer uses of radiation, and from occupational exposure.

Since some exposure to ionizing radiation other than from environmental sources is useful and cannot be dispensed with, it is necessary to define standards of safety for this exposure. Standards of safety for

exposure to radiation and radioactive substances must be based on the ability of radiation to induce cancer or mutation, since standards adequate in these respects will be more than adequate to give protection against other harmful radiation effects. A practical difficulty in setting such standards comes from the absence of information on carcinogenic or mutagenic effects at the low doses where the degree of risk is likely to be acceptable. It is necessary to assess the risk at low doses by extrapolation from observations made at high doses. This could only be done with certainty if we knew the formal relationship between dose and effect for doses of all sizes and for all conditions of irradiation, but our knowledge of this relationship is necessarily defective.

In practice the difficulties are countered by two simplifying assumptions; these are that the effective response to a radiation dose is in simple proportion to the dose, for doses of all sizes, and that the magnitude of the response is unaffected by the rate at which a dose is given. It is believed that these assumptions are conservative, that is they will not lead to an underestimate of radiation effects at low doses, though in some instances they may well overestimate them. The assumptions imply that any radiation carries some risk, though for a small dose the risk may be very small, and that the risk associated with any radiation dose voluntarily incurred should be assessed as acceptable, or not, in the light of the benefits, if any, which flow from that dose. Standards based on this philosophy have proved satisfactory in practice.

RADIOACTIVITY AND RADIATION

A few of the elements which occur in nature are unstable; their constituent atoms change spontaneously, at rates characteristic for each such element, into atoms of a different element. Unstable elements are called radioactive because the change is accompanied by the release of rádiant energy. The radiation may be particulate (alpha- and beta-radiation) with low penetrating power, or electromagnetic (gamma-radiation) with high penetrating power. Many other radioactive elements can be created artificially. In either case the emitted radiations are able to produce ionization in the materials they penetrate, that is they can dislodge electrons from atoms and thereby create electrical disturbances great enough to break one or more of the chemical bonds which link atoms into molecules. If biological material is irradiated, this may, though not necessarily, lead to a drastic alteration of its integrity.

This alteration is expressed initially as an intracellular change whose consequences will be manifest only later, as cell death or as a delayed injury of some kind.

Radioactive materials are not the only source of ionizing radiation. Both particulate and electromagnetic radiations can be produced by electrical machines designed for that purpose, the best-known source of this nature being the X-ray generator used in medicine and industry. X-rays are penetrating electromagnetic radiations similar to gamma rays. Unlike light and heat, which are non-ionizing forms of electromagnetic radiation, ionizing radiations of any kind are not detectable by the senses but their intensity can be measured accurately by appropriate instruments.

THE HARMFUL EFFECTS OF RADIATION

Röntgen reported the discovery of X-rays in 1895 and it was recognized almost at once that X-rays could produce destructive injuries of the skin; a review published only two years later listed 69 such cases. The number was large because sources of X-rays, in the form of the Crookes high-vacuum tube, had already been used in research for 20 years and were not only available for experiment but, in many instances, were already generating X-rays unrecognized by their users. Becquerel's discovery of radioactivity was also in 1895 and, by 1900, research on the concentration of radioactivity from uranium ore had proceeded sufficiently far to allow observation of the first skin injury, resembling a thermal burn but with delayed onset, from exposure to radioactive materials. It also became known early in the century that radiation, in sufficiently large doses, could produce sterility and reduce the number of white cells in the circulating blood. It was realized, too, that irradiation of a sufficiently large fraction of the body would produce illness and sometimes death. These effects arose from cell destruction, and this property of radiation was used, from about 1900, in the treatment of cancer.

These acute destructive effects of radiation are not important from the viewpoint of radiological protection; they arise either from therapeutic applications, or from gross overexposure which should be readily avoidable. There are other, more insidious consequences of exposure to radiation, which are more difficult to counter. These are the induction of cancer and mutations.

In 1902 a skin cancer was attributed, for the first time, to X-ray exposure and, in the next decade, accounts of nearly a hundred similar cases were published. By then the risks associated with the use of X-rays were being taken seriously, but those risks associated with naturally occurring radioactive materials, while appreciated in some respects, were not fully recognized until about 1950, despite considerable development in standards of radiation hygiene well before that date. Other kinds of cancer besides skin cancer are induced by ionizing radiation; skin cancer gained early prominence because the low voltages available in early X-ray equipment did not allow production of very penetrating radiation, and the skin was likely to receive high doses in consequence.

Genetic mutations are heritable changes in organisms; some occur spontaneously and others may be induced by environmental agents. In 1927, experiments with the fruitfly, Drosophila, showed that ionizing radiation was effective in producing mutations. Similar observations have since been made with other species, including mammals, and it is clear that radiation must be regarded as a potential mutagen in man even though we have no direct observational evidence to that effect. In general, induced mutations are detrimental, and the production of mutations must be taken, along with the induction of cancers, as determining what standards of radiological protection are necessary. Standards adequate in these respects will be more than adequate with respect to other harmful effects of radiation. Radiation-caused cancer and mutations will be considered in more detail in subsequent sections.

THE UNITS OF RADIATION MEASUREMENT

The rad and the rem

In discussing the effects of ionizing radiation it is advisable to have some appreciation of the magnitude of the commonly employed units of radiation dose and their relation to everyday experience. The unit of absorbed radiation dose is the rad and it is defined in terms of radiant energy deposited per unit of mass. One rad represents the deposition of a very small amount of energy.* When used for heavy particles, in particular the neutral particles (neutrons) from certain nuclear reactions and the alpha particles from certain radioactive elements, the rad is an inadequate unit for biological purposes. This is because a given rad

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* In S.I. units, 10^{-2} joules per kilogram

dose of neutrons or alpha particles has more biological effect than its equivalent rad dose of X-rays or gamma rays. This difficulty is met by use of another unit, the rem or unit of dose equivalent, which is derived from the rad by multiplying by a quality factor appropriate to the radiation in question. Both units are commonly used but discussion of the biological effects of radiation in a quantitative sense should be in terms of the rem whenever possible. For most radiation the two units are roughly equivalent. These units are rather large for the purposes of radiological protection for which their one-thousandth submultiples, the millirad and the millirem, are generally more convenient. Table 1 illustrates some commonly encountered levels of dose, and should provide some perspective to statements about unsought exposure to radiation.

TABLE 1

DOSES IN PERSPECTIVE

Annual dose from natural background radiation	100 millirem
Recommended annual dose limit for members of the public +	500 millirem
Recommended annual dose limit for occupational exposure to radiation +	5 rem
Approximate mean lethal whole-body dose for man	500 rem
Localized, fractionated doses used in radiotherapy	500-5000 rem

+ Recommendation of the ICRP (see page 20)

The curie

Quantities of radioactive materials are expressed in terms of the curie, a unit defined simply as the rate at which unstable atoms disintegrate. The hazards associated with radioactive materials will sometimes depend on external radiation from them, but will more often arise from their ingestion or inhalation. In that case, quantities estimated in curie units (usually submultiples of the curie) cannot be translated directly into harmful effects. This is because the effective radiation dose from a radioactive element within the body depends not only on its

quantity, but on the nature and energy of its radiation, on its anatomical distribution within the body, and on its effective length of stay within the body. Sufficient information exists to allow reasonable estimates of dose to the whole body or specific organs from retained radioactivity in most instances, but relatively minor uncertainties remain.

SOURCES OF RADIATION EXPOSURE TO MAN

Natural sources

Man is obliged to live in a field of radiation from natural sources. This was given as 100 millirem per year in Table 1, and this is a reasonable estimate of the average figure, but the level is quite variable with location and 200 millirem is not very unusual, with occasional areas much higher. Table 2 shows a typical composition for natural environmental levels of radiation.

TABLE 2

NATURAL BACKGROUND RADIATION

(in millirem per year)

External Sources	
Cosmic radiation	28
Terrestrial radiation	51
Radioactive sources within the body	
Potassium-40	19
Other naturally-occurring radioactive elements	2
Total	100

The contribution of the cosmic component increases with both altitude and latitude, and the terrestrial component is very dependent on local soil composition. Differences in the dose rates from terrestrial gamma sources account for most of the variation in background radiation from one geographical area to another. The extent of variation in terrestrial gamma radiation can be exemplified by the mean annual outdoor doses for Dunedin, N.Z. and Rome, which are 37 and 181 millirem respectively. Considerably higher radiation levels are found in a few areas, the best-known being in Brazil and India, in localities where soil concentrations of uranium or thorium are high. Another source of variation in human environmental exposure stems from the different radioactivities of

traditional building materials, which will partly reflect local mineral variation.

The existence of such substantial natural variations prompts the question: can any harmful effect be identified in populations naturally exposed to higher levels of environmental radiation, whether arising from terrestrial gamma sources or from the presence of radioactive elements in traces in water supplies? Do, for example, the children of cities at high altitudes and with granitic soils rich in the uranium series of radioactive elements show a higher incidence of genetically determined illness, or of leukaemia, than those of the alluvial plains below? The answer is simply, no, they don't, as far as can be determined from any investigations yet carried out. This answer needs some qualification. It really means that either there are no such effects or, if there are such effects, they cannot be measured in a population of any size that might reasonably be sampled. A further matter for reflection emerges here: if radiation dose increments of the order of 50 millirem per year do not, or can not, produce any measurable effect and, if in fact the potential hazard of such doses is largely ignored (there has been no observable exodus from Rome to Dunedin), how seriously should we take individual dose increments, of one millirem or so, which come from man-made sources of radiation other than those used in medicine.

Occupational exposure and consumer uses

In any developed country there are currently various occupational sources of exposure to ionizing radiation. No reliable figures for mean population dose from occupational exposure in Australia are available, but there are reasonable estimates for the United Kingdom and the United States; the Australian figure will certainly be less, in view of a lesser degree of technological advancement and the absence of nuclear power reactors and their associated infrastructure. The expression 'population dose', expressed in man-rem, means the sum of the doses to exposed individuals in the whole population at risk, and the expression 'mean population dose' is the average dose received by an individual in that population. Individuals who are occupationally exposed may well receive substantially larger radiation doses than the population average, and carry a proportionately greater risk, but the population dose is the appropriate measure of detriment to the whole population. In addition to the occupational contribution to population dose, there will be a

contribution from exposure to the public from various kinds of nuclear plant, at present insignificantly small, and a rather more substantial contribution from various consumer products - luminous wrist watches, television sets, air travel are amongst these.

Fallout

A further contribution to population dose comes from the fallout from nuclear weapons. This is declining and will continue to decline if atmospheric testing is not resumed; the total projected dose from this source to individuals in the southern hemisphere is in the region of 70 millirem, varying with the organ considered.

Medical sources

The major man-made contribution to population dose remains to be mentioned. This is the diagnostic use of radiation in medicine, in particular the use of X-rays. Diagnostic radiology is the largest artificial source of radiation exposure in all developed countries though the reported annual doses vary considerably from one to another. No reliable data are available for Australia but the Australian dose levels may reasonably be supposed to lie somewhere between the U.K. and U.S. figures given below. Radiation dose from medical applications of radiation is not subject to regulatory control and while some such exposure is necessary and inevitable, it is clear from the existence of a four-fold range in countries with comparable health care that techniques can be improved or unnecessary exposures eliminated.

The various sources of radiation dose to man are compared in Table 3.

TABLE 3

SOURCES OF POPULATION DOSE

(annual per capita dose in millirem)

Source	United Kingdom	United States
Natural environmental radiation	100	130
Medical exposure	20	72
Fallout	2	4
Occupational exposure, consumer uses etc.	1	3
Totals	123	209

Notes on Table 3

Note 1 These figures are approximations and have been rounded off.

Note 2 Medical exposure is usually reported as the 'genetically significant dose', that is the dose to the gonads of people who are potential parents. It is not certain that this is the best measure of total detriment; this may be the bone marrow or whole-body dose, which would be substantially larger.

Note 3 A U.S. estimate of mean population dose from occupational exposure in 1970 was 0.79 millirem, from the nuclear power industry, 0.0028 millirem, and from miscellaneous consumer sources, 2.0 millirem. These make up the figure of 3 in the table.

SOURCES OF DATA ON RADIATION EFFECTS IN MAN

This paper is concerned almost exclusively with the two major delayed effects of radiation on man, mutagenesis and carcinogenesis, since only these are of real consequence to the practice of radiological protection. Doses large enough to cause early death have been received in a few radiation accidents, and the acute lethal dose in man is known well enough to permit rational treatment of major radiation exposure or to allow prediction of the immediate effects of hypothetical accidents; this aspect of radiation injury need not be considered further here.

There are no positive data with direct relevance to radiation mutagenesis in man. It is not possible to do more than set upper limits to the magnitude of genetic effects from radiation in man by argument from the existence of natural environmental radiation, or from the apparent absence of genetic effects in the survivors of Hiroshima and Nagasaki.

Carcinogenesis, unfortunately, is another matter; there are many sources of human experience although few of them are suitable for the quantitative treatment needed to help establish the formal dose-response relationship which is required for the proper regulation and control of man-made radiation exposure. The principal sources of data are listed in Table 4. The predominance of medical experience is apparent.

TABLE 4

SOURCES OF HUMAN DATA ON RADIATION CARCINOGENESIS

Military Uses of Radiation	Occupational Exposure
Survivors of Hiroshima and Nagasaki[1]	Radiologists[2]
Fallout exposure from H-bomb test at Bikini	Luminous dial painters (radium)
	Uranium miners[4]
Medical Uses of Radiation	
Radium injections and patent medicine nostrums[3]	X-ray treatment for enlarged thymus glands[6], ring worm, inflammation of the breast, and some gynaecological disorders
Thorium-X treatment[5]	
Thorium use as an X-ray contrast material ('Thorotrast')	
Phosphorus-32 treatment of polycythaemia	X-ray fluoroscopy for pulmonary tuberculosis
X-ray treatment for ankylosing spondylitis[1]	X-ray diagnostic procedures in pregnant women[7]

Notes on Table 4

1. The bomb survivors provide the most reliable quantitative data, followed by the ankylosing spondylitis patients. The other sources are either too few or possess large uncertainties in dose estimates.

2. This refers to American observations on the incidence of leukaemia in radiologists, as well as the early victims of skin cancer.

3. This was primarily an American fad of the 1920s and 1930s, although radioactive spas and even 'radon galleries' were fashionable in Europe. One U.S. clinic alone is reported to have administered some 14,000 intravenous injections of radium, in 10 microcurie doses, and radium water nostrums, containing one or two microcuries per dose, were widely sold. The maximum allowable body burden of radium is now set at one-tenth of one microcurie. The intake of radium often led to bone cancer from its deposition in bones, or to cancers of the sinus cavities in the skull bones from the accumulation within them of radon, the gaseous daughter product of radium, and radioactive daughter products of radon. About 40 deaths from

radiogenic cancer have been identified in dial painters and people treated with radium, and probably other such deaths went unrecognized. Studies of former dial painters and other people with residual body-burdens of radium, including fatal and non-fatal cases, have allowed recommendation of safe limits for radium and their subsequent extension to other radioactive elements.

4. Lung cancer was recognized as the major cause of excessive mortality in the miners of the Erz Gebirge ('ore mountains') in central Europe in 1879, but its association with radioactivity in the mine atmospheres was not recognized until the 1920s, and not fully accepted even then. The development of American uranium mines in the 1940s was undertaken initially without adequate appreciation of the carcinogenic properties of the mine atmospheres which contained high concentrations of radon and its daughter products. In consequence, there has been a considerable excess of lung cancer in U.S. uranium miners who worked underground, an epidemic whose consequences are still being felt, even though adequate control measures are now required.

5. Thorium-X is a short-lived form of radium which was used in at least 2000 cases, mainly in Europe, for treating spinal tuberculosis and ankylosing spondylitis (a form of spinal arthritis). It has produced some 60 cases of bone cancer.

6. Thymus enlargement, a fashionable medical diagnosis 50 years ago, was often treated by radiotherapy. The thyroid gland was usually included in the radiation field, and the consequence was sometimes thyroid cancer.

7. In 1956 an epidemiological study of the incidence of leukaemia and other forms of childhood cancer in the United Kingdom indicated that diagnostic irradiation of pregnant women might increase the frequency of cancer in the first ten years of life of children who had received intra-uterine exposure. Such an effect is hard to detect unless very large numbers of children are observed. The original suggestion has been supported by some studies but not by others; most notably it does not appear to be borne out by observations on Japanese children who were irradiated in utero at Hiroshima or Nagasaki. There are two elements to the suggestion,

firstly that there is an association between foetal irradiation and the subsequent incidence of cancer in children, and secondly that the association indicates a causal relationship between exposure and effect. The reservation is necessary because mothers are generally X-rayed for some medical reason, not randomly, and this may select foetuses more likely to develop cancer than is the normal expectation. At present the question is unresolved but any risk is minimized by avoiding unnecessary radiation exposure of pregnant women. If the existence of a causal association were confirmed, it would provide, for the first time, direct evidence of carcinogenic effects from small doses of radiation; the dose to the foetus is in the region of one rem. However, the risk associated with this low dose is still small.

Data from the Japanese survivors continue to be collected and will provide further information because some forms of cancer are still appearing in excess in the irradiated population. This may allow continued refinement of our ideas on the quantitative relation between radiation dose and the incidence of cancer, to be discussed in a later section, but a point to note is that the sources listed in Table 4 refer only to radiation given at high doses or high dose rates. There is necessarily some uncertainty in inferring the effects of the low doses, which may be important in radiological protection, from observations at high doses. Lung cancer is one of the forms of radiogenic cancer which may not appear until 20 years or more after exposure, therefore some further cases are expected to appear in uranium miners who worked underground before the introduction of adequate standards of protection. A few of the other sources of radiation exposure may still yield small numbers of cases, but it can be hoped that the incidence of radiogenic cancer will decline within the next few years.

THE SIGNIFICANCE OF SMALL DOSES OF RADIATION

The experiences listed in Table 4 provide unequivocal evidence that large doses of radiation, particularly if given at high dose rates, are carcinogenic in man. Observations on animals leave us in no doubt that large doses will also be mutagenic in man. For both carcinogenesis and mutagenesis it is possible to make a reasonable estimate of the actual risk incurred from the receipt of large radiation doses, doses that is of

100 rem or more to the whole body or to a sensitive organ. Difficulties appear when we try to assess the effects of small man-made increases in radiation exposure. What practical significance should be attached to a fallout dose of a millirem or so or an occupationally-received dose of a few hundred millirem? And, in particular, what is the real significance of a population dose when it is the sum of very small individual doses? An answer to these questions demands knowledge of the formal relationship between radiation dose and its effect; is it a matter of simple proportion or does some more complex relationship apply? And does it matter how quickly or slowly the dose is given? Since man and other species have evolved and become stable in the presence of an appreciable level of environmental radiation, it might even be the case that small radiation doses have no effect at all. The following sections will review briefly the available evidence on dose-response relationships and indicate the philosophy which has been adopted in setting standards of radiological protection.

RADIATION CARCINOGENESIS

Dose-response relationships, for either carcinogenesis or mutagenesis, can conceivably be of several kinds. Figure 1 illustrates some of these.

Curve A is a threshold response where no effect is seen until a certain level of dose is exceeded. Responses of this sort are common with chemically toxic agents. Acute radiation injury displays a threshold response, but evidence for the presence or absence of threshold doses for carcinogenesis and mutagenesis is almost impossible to obtain. Curve B is a linear response where the incidence of the effect is in simple proportion to dose, and curve C is a curvilinear response where incidence is some other function of dose; there is, for example, reason to think that the incidence of some kinds of radiation effect may be in proportion to the square of the dose. It will usually be impossible to differentiate between different types of response at very low levels of dose, either by observation in man or by experiments with animals. Nor is the theoretical basis of carcinogenesis sufficiently well understood to allow responses to be predicted from first principles.

Human experience is limited. At present there have been reported some 200 cases of leukaemia and other forms of cancer, above normal expectation, in the study group of about 100,000 people, including

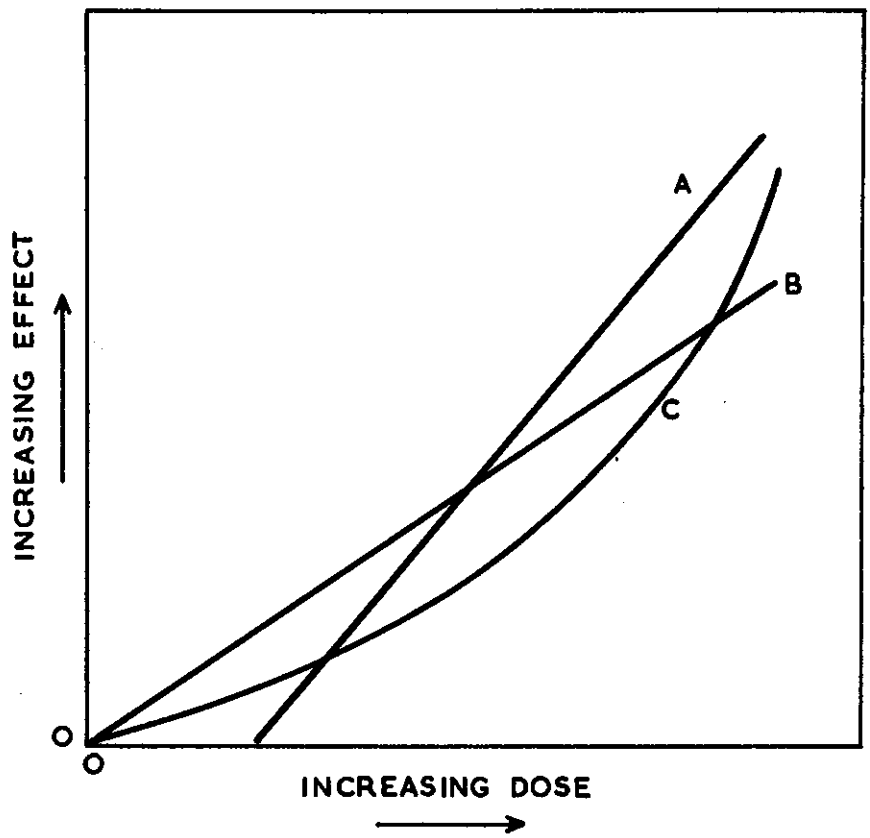

FIGURE 1. DOSE-RESPONSE RELATIONSHIPS

unirradiated controls, of the Atomic Bomb Casualty Commission. Over 4000 people in the study group have died of cancer during the period of observation and, since the number attributable to irradiation is a small fraction of the total and the radiation doses received by the group are not known very accurately, it is not possible to make very precise statements on the dose-response relationship. Leukaemia appears much sooner after radiation exposure than other forms of cancer, reaching a maximum incidence at 5 or 6 years and then declining, and is in consequence the form about which most is known. If the incidence of leukaemia is compared with radiation dose separately for the two cities, the incidence at Hiroshima appears linear, as in curve B of Figure 1, but at Nagasaki there appears to be a threshold, since leukaemia was not seen after doses less than 100 rads. Unfortunately the actual numbers of cases are too few to allow a firm conclusion about either, and the actual form of the dose-response remains uncertain. If there is in fact a difference between the two cities it may be attributable to a substantial difference

in the quality of radiation. Exposure at Nagasaki was almost entirely from gamma radiation, but that at Hiroshima included a large neutron component, and there are theoretical reasons for expecting a different response with heavy particles.

The other major source of useful information, the 14,000 patients with ankylosing spondylitis who were treated in the United Kingdom with X-radiation in the 20 years from 1935, have shown an excess of about 130 cases of leukaemia and other cancers. As with the Japanese survivors, information is most precise for leukaemia. The dose-response is clearly curvilinear, resembling curve C of Figure 1, although it is possible to argue that it is linear at the lower (but still high) levels of dose recorded. Although there are considerable uncertainties in both sets of data, it can be inferred from them, with some confidence, that a population dose of 1,000,000 man-rem, given in individual whole-body doses of 100 or more rem at high dose rates, will give rise to 15 or 20 cases of leukaemia and perhaps 100 cases of all forms of cancer within the first 20 or 25 years. An excessive incidence of some forms of cancer, in particular cancers of the lung and of the breast, is still apparent in the Japanese survivors. Since it is not known how long this will continue, the figure given above may be an underestimate, and an overall figure of 200 per 1,000,000 man-rem is commonly used. Some of the Japanese were exposed as children and it may well be another 20 years before a final estimate can be given. Estimates, such as those given above, are referred to as risk coefficients, and may be used to calculate the upper limit of the possible effects of hypothetical exposures to radiation, but their limitations should be remembered - they may not be reliable at low doses and low dose rates.

The bone cancers seen in people exposed to or treated with radium, and the lung cancers seen in underground uranium miners, are caused by irradiation with alpha particles over long periods. Because the radiation is of different quality and the exposure is so protracted, it is difficult to make any simple comparison between the effectiveness of radiation doses in these categories and those from X- or gamma-radiation, with respect to carcinogenesis. However, it does appear that bone is relatively insensitive to the induction of cancer by radiation and that the lung is fairly sensitive, with a risk per rem which is broadly similar for all types of radiation.

There is little prospect that further observations on man will resolve all difficulty over the form of the dose-response relationship for carcinogenesis. It might be hoped that experiments with animals would remedy the situation but the problem is not simple. In order to get significant results without using excessive numbers of animals, experimenters commonly use inbred strains of mice which are sensitive to the induction of one kind of cancer or another. The net result has been the accumulation of information about animal tumours which often have no close human equivalent. This information cannot be used to argue safe dose limits in man, but it may provide the basis of valid generalizations on dose-response relationships. In particular, it may throw light on the general validity of two simplifying assumptions which are used in the determination of acceptable limits of dose: that the dose-response relationship is linear and that the rate at which a dose is given has no bearing on its effect.

A study of the results of animal experiments shows that in fact few, if any, responses are linear except over a restricted range of dose; some tumours appear to require threshold doses to be exceeded while others do not, and there is frequently a maximum incidence beyond which increasing doses become less effective. In certain instances, notably the induction of bone cancer in various species by strontium-90, use of the assumption of linearity appears substantially to overestimate the effects of small doses. There is also some suggestion that X- and gamma-, but not heavy particle radiations, are less effective at low dose rates, but evidence on this point is insufficient for certainty. It can be said that animal experiments provide good evidence that the two simplifying assumptions referred to above are conservative; that is, their use may lead to overestimation of the true effects of small radiation doses, but not to underestimation.

Another point, applicable to both human and experimental radiation carcinogenesis, should be noted. A radiation dose will kill some of the cells of an organ in which it may induce cancer. A cell which is killed, or rendered incapable of division, cannot initiate cancer. At small doses, cell killing is trivial but with increasing dose the number of surviving cells, in which cancer may be induced, will decrease exponentially. Therefore, even if the induction of cancer in susceptible cells is proportional to dose, the observed incidence of cancer will be

less than expectation as dose increases and may eventually decrease with increasing dose, as is in fact sometimes observed.

RADIATION MUTAGENESIS

The mutagenicity of ionizing radiation is well established but, as with carcinogenesis, we have insufficient knowledge of the quantitative relationships between dose and effect to allow very precise estimation of the consequences of small doses from the observable effects of large ones. The incidence of radiogenic cancer or mutation can be expressed in absolute terms, without reference to the spontaneous frequency of cancer or mutation, or in relative terms by taking the spontaneous frequency as the basis of measurement. Estimates of carcinogenesis are usually given in absolute terms, as was done in the previous section, because the spontaneous rates of cancers are subject to large environmental variations which are imperfectly understood. For radiation mutagenesis however, a relative measure is probably more appropriate. This is for two reasons; an absolute system requires information on the number of genes at risk, which we do not have, and, secondly, each species has evolved a spontaneous mutation rate appropriate to its needs. In consequence, the effect of a change in mutation rate depends on the value of the spontaneous rate, the effect being greater where the spontaneous mutation rate is low. The relative risk per rem is defined as the fraction by which one rem per generation will increase the natural rate of mutation. A commonly used alternative is the reciprocal of this fraction, the doubling dose.

The assumption that response is proportional to dose at low doses has been used for mutagenesis, as for carcinogenesis, in deriving standards of radiation protection. In the fruitfly, Drosophila, this assumption is supported by observations down to the lowest doses that it is practicable to test using point mutations, that is changes in individual genes, as the criterion of effect. Mice may well be a more appropriate model for man than fruitflies, and corresponding experiments with mice show substantial departures from linearity if a wide range of doses is considered; an apparent reduction of the effectiveness of radiation at very high doses and again at low doses. The first observation can be constrained into the hypothesis of linearity with the assumption that certain types of sex cells possess increased sensitivity

to both cell killing and mutagenesis by radiation. The second is explicable by the occurrence of mutational repair processes in cells, which are effective at small doses or at low dose rates, but are swamped by high doses. There is other evidence that such repair does occur in genetic material. There is no evidence of an actual threshold dose in male mice, but there does appear to be one for female mice when tested at very low dose rates. At 9 millirem per minute their mutation frequencies do not differ significantly from those of controls, even at high total doses.

Point mutations do not constitute the only kind of genetic damage induced by radiation. Other kinds of mutation are associated with the presence of microscopically visible aberrations of chromosomes, the intracellular structures that carry the genetic material; the relation of these to dose is usually better represented by mathematical relationships which suggest that, as with carcinogenesis, the assumption of linearity is conservative. Since experiments with mice have shown clearly that radiation is a much less effective mutagen at low dose rates than at high dose rates, the further assumption, that there is no dose-rate effect, is not made. In fact, estimates made at high dose rates are reduced by a factor of 3 to allow for this, when transferred to low dose rates. With this proviso, the observation that the children of parents irradiated at Hiroshima or Nagasaki do not have death rates differing from controls implies that the doubling dose in man is not less than 150 rem, if the average parental dose was 100 rem. If this estimated parental dose is too high and a lower value is taken, the estimate of minimum doubling dose is correspondingly reduced.

There is an alternative approach to estimates of the doubling dose in the experimental data on the frequency of induced mutations in mice. These data are not ideal since the genes selected for study are probably biased in the direction of increased sensitivity - there is certainly a considerable range of sensitivity in the sets of genes usually tested - but this bias will lead to a more conservative result. Mouse-based estimates also lead to a doubling dose estimate in the region of 100 rem, and this is a reasonable figure to take as a basis for estimating the genetic effects of radiation at low dose rates.

It is not possible to apply this estimate to all forms of genetic disease, but it is applicable to the one per cent, or so, of all children

who are born with disease deriving from dominant or sex-linked mutations. About one fifth of these are new spontaneous mutations, that is 2000 per million live births. If 100 rem will double this number of spontaneous mutations, one rem may then induce 20 extra mutations of this sort in the first generation. If exposure at this rate is continued, the incidence of mutations could rise to an equilibrium with an excess of about 100 per million live births. Other categories of genetic disease present more difficulty. Diseases related to visible chromosome changes will be increased but the numbers will be much less. Many cytogenetic abnormalities of this sort will be unobserved - they will be expressed by failure of the egg to implant in the uterus or by its death soon after implantation. These events have no bearing on human well-being. Recessive mutations will also be induced but their contribution will certainly be negligible in the first generation and, if indeed there is any continued effect, its incidence will be spread slowly over very many generations. There is some experimental evidence bearing on this point. Several experimental populations of mice have been irradiated repeatedly over many generations; in one case 200 rem per generation to the males over 45 generations. It is remarkable that in these circumstances there is no evident difference between the mice of irradiated and unirradiated lines in growth rates or lifetime survival.

There are other categories of disease which may have a genetic basis, including various degenerative diseases, and it is generally uncertain just what importance should be attached to the genetic component; but the total genetic impact of a population dose of radiation, in terms of real or potential casualties, is unlikely to exceed that of carcinogenesis from the same dose and may be considerably less. It might be noticed that of 1,000,000 infants, some 50,000 are born with a disease wholly or partly attributable to a genetic component, and that some 150,000 will eventually die from cancer. Therefore any excess in either category from small doses of radiation will be quite undetectable. It is also the case that if the background environmental radiation everywhere present does in fact contribute to the normal incidence of cancer and mutation, the contribution is very small.

STANDARDS OF RADIOLOGICAL PROTECTION

Practising radiologists soon became aware of the need for some standards of protection for themselves and their assistants but were

handicapped initially by the lack of a physical unit of dose. The maximum allowable daily dose was originally defined as 1/1000 of the amount of radiation that would produce reddening of the skin - the 'erythema dose'. This was a rather elastic unit and sometimes reached 2 rem per day, in contemporary units of dose. In 1928 the International Society of Radiology sponsored formation of the International Commission on Radiological Protection (ICRP), an independent organization which still exists and has continued to make recommendations in the field of radiological protection. The introduction of a physical unit of radiation exposure in 1928, the röntgen, (R), made its task easier. This unit, which was the basis of X - radiation measurements, is not very different numerically, for X-rays and gamma radiation, from the rem units of dose which are now used to specify standards of protection. Originally maximum levels were set at 0.1 R per day and in 1949 this was reduced to 0.05 R per day or 0.3 R per week. This reduction was not because ill effects had been seen at the higher level but because more penetrating radiations had come into use, which would increase the effective dose to deeper parts of the body.

In 1956 the ICRP and various national organizations concerned with radiological protection reviewed their position. It had been assumed, and this assumption had been borne out in practice, that if the average dose rate were low enough, that is, not more than the allowed 0.3 rem per week, no injury would be seen in the lifetime of exposed individuals, although it was conceivable that some might accumulate as much as 750 rem in a working life of 50 years. Some new factors suggested that a reduction might be desirable even though the previous limits had appeared to be adequate. It was already believed that the incidence of genetic mutation was proportional to dose; this was of little consequence when the only people exposed were a small number of radiation workers, but the advent of nuclear power meant not only more occupational exposure, but also some exposure of the general population. It was also thought possible that carcinogenesis was linearly related to dose, and this has the implication that there is no absolutely safe dose of radiation, even though the risk associated with a very small dose may be infinitesimal.

For these reasons the ICRP, and analogous national bodies, reduced the occupationally allowed dose to 5 rem per year (equivalent to 0.1 rem per week) and introduced the concept of a dose limit for members of the

public, set at 0.5 rem per year. The ICRP recommendations are explicitly based on the assumption of a simple proportional response to dose, at all levels of dose. This philosophy implied that all radiation exposure should be regulated on a cost-benefit basis and replaced the former concept of a dose which is tolerated because it does not cause evident harm. The ICRP also made the assumption that the incidence of effects is independent of the rate at which a dose is given, although its recommendations do set limits to the rates at which dose may be accumulated. Acceptance of the ICRP philosophy of protection requires a belief that the assumptions of linearity and absence of dose-rate effects are conservative - that extrapolation from data obtained at high doses will not lead to underestimates of effects at low doses or low dose rates. These assumptions have been questioned from time to time but there are no observations, in man or in the laboratory, which throw serious doubt on their conservatism. There are observations which suggest they lead to overestimates of low dose effects, which may sometimes even be zero. It is possible to derive further standards and working limits to ensure that releases of radioactivity do not cause recommended dose limits to be exceeded. Such derived limits are used to ensure that occupational and public exposure is adequately controlled.

A final comment

In spite of occasional allegations to the contrary, the record of safety in major nuclear establishments has been good. In both the United States and United Kingdom, atomic energy workers have shown reduced death rates, from cancer or from other causes, when compared to their counterparts in other industries. This does not mean radiation was positively beneficial to these workers; it simply reflects the higher standards of selection and care practised in the nuclear industry and is an indication that the protection standards are adequate. The epidemic of cancer in underground uranium miners does not negate this assertion but it does show that the hazards of radioactivity in underground uranium mines were not adequately recognized at the time of their development, nor were the responsibilities for their control recognized and accepted until much damage had already been done. Existing standards, if properly enforced, will ensure that uranium miners are not subjected to enhanced risk of lung cancer from exposure to radioactive materials. Alarmist statements have been made on occasion relating to the alleged occurrence of

harmful consequences from trivial discharges of radioactivity from nuclear establishments. None of these claims can be substantiated and most have been convincingly refuted.

The application of ionizing radiation to man's purposes is not claimed to be absolutely safe. No human activity is absolutely safe, and all carry some risk. The merit of the philosophy underlying radiation protection is that the upper limit of this risk is defined, and it can be accepted or rejected on the logical basis of weighing the expected benefits against the possible cost in injury. Other activities of man do not always allow us this choice.

GLOSSARY

The following definitions are provided for the reader not familiar with some nuclear and other terms used in this paper. The explanations are drawn from standard glossaries.*

alpha-particle	A helium 4 nucleus emitted during a nuclear transformation. *Alpha-decay* is radioactive decay in which an alpha-particle is emitted; whence *alpha-radioactivity, alpha-activity, alpha-emitter, alpha-radiation.*
beta-particle	An electron of either sign which has been emitted by an atomic nucleus or *neutron* in the process of a transformation; whence *beta-emitter, beta-gamma activity, beta-radiation.*
carcinoma	A form of cancer. A disorderly growth of cells which invade adjacent tissue; whence *carcinogen,* a substance which induces cancer in a living organism, *carcinogenesis, carcinogenic, carcinogenetic.*
chromosome	The microscopically visible intracellular structure which contains the molecules carrying genetic information.
curie(s)	A unit of activity defining the number of spontaneous nuclear disintegrations occurring per unit time; 1 curie = 3.7×10^{10} disintegrations per second; whence *picocurie, microcurie* and similar submultiples.
dose-response relationship	The biological effect of absorption of radiation or energy as a function of dose.
gamma radiation	Electromagnetic radiation emitted by the nuclei of radioactive substances during decay; whence *gamma activity, gamma emitter. Gamma rays* are similar to X-rays.
gonad	A sex-gland; ovary or testis.
ionizing radiation	Radiation which knocks electrons from atoms during its passage, thereby leaving electrically charged particles (ions) in its path; whence *ionization.*

irradiation	Exposure to ionizing radiation.
man-rem	The unit of population dose, obtained by summing the radiation doses to all individuals in that population.
mutation	A change in the characteristics of an organism produced by an alteration of the hereditary material; whence *mutational, mutagen, mutagenesis, mutagenic, mutagenicity.*
neutron	A nuclear particle having no electric charge and the approximate mass of a hydrogen nucleus; whence *neutron absorption, neutron activation, neutron capture.*
particulate	Having particle form. Can be used to describe matter (in powder form) or radioactive particles.
rad	A unit of *absorbed ionizing radiation dose,* whence *millirad, megarad,* etc.
radiogenic	Caused by radioactive decay.
radiology	The application of penetrating *ionizing radiation* in medicine; whence *radiologist, radiological.*
radiotherapy	Treatment of disease by use of *ionizing radiation.*
radon	A gaseous product of the disintegration of radium.
rem	A unit of radiation dose equivalent, the product of absorbed dose, quality factor and other modifying factors necessary to obtain an evaluation of the effects of irradiation received by exposed persons, so that the different characteristics of the exposure are taken into account; whence *millirem* etc.
threshold dose	The smallest dose of a harmful agent that will produce a specified result.

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* Sources :

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