RES MEDICA
Journal of the Royal Medical Society

Hazards of Radiation

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Abstract
Based upon a Dissertation given before the Society on Friday, 11th October 1957.
Radiations are of two types: Particulate and Electromagnetic. Particulate radiations are comprised of the sub-atomic particles, electrons, protons, neutrons and alpha particles which, when moving at high speed, possess the property of passing through matter, the depth of penetration being proportional to their kinetic energy and their electrical charge.
Alpha Rays which are rapidly moving nuclei of Helium atoms have mass 4 and charge 2 on the atomic scale and have little power of penetration in tissue, reaching to a depth of about 0.05 mm.
Beta Rays which are beams of fast moving electrons, can penetrate tissue up to a depth of 2 to 5 mm., and Protons with unit mass and electrical charge lie somewhere between these two.
Derived from an external source, these radiations are of little danger since they are obviously incapable of penetrating to the gonads and bone marrow, tissues in which the more sinister biological effects are manifest.
These radiations are particularly dangerous when derived from a source which may be ingested with food and perhaps selectively concentrated in body tissues, as, for example, Strontium 90 in bone.

ISSN: 2051-7580 (Online) ISSN: 0482-3206 (Print)
Res Medica is published by the Royal Medical Society, 5/5 Bristo Square, Edinburgh, EH8 9AL

Res Medica, Spring 1958, 1(2): 39-44
doi:10.2218/resmedica.v1i2.316

HAZARDS OF RADIATION

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By ANDREW GUNN

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Electro-magnetic radiations comprise a continuous spectrum extending from long electrical waves of several thousand metres wavelength, through infra-red, visible and ultra-violet light down to soft and hard X-rays and gamma rays of wavelength 10^{-7} mm. and less. Radiations of very short wavelength, namely X and gamma rays, have the property of high penetration in tissues and along with them ultra-violet light may be considered as a penetrating radiation in fair-skinned people. Particulate radiations, together with ultra-violet light, X and gamma rays are collectively known as *ionising radiations* because they possess the property of ejecting electrons from the outer shells of atoms in their paths, these being taken up by neighbouring atoms with the creation of pairs of ions. Because of their ionising property these radiations can effect chemical changes in any solution through which they pass.

It is the degree and not the nature of the hazard that is new, for man has always been subject to irradiation from cosmic rays and radio-active materials in the earth's crust and atmosphere, together with radio-active elements within his body in small amounts, such as Radium in bone, Potassium 40 and Carbon 14. The dose from these sources is in the order of 0·1 rontgen (r) per year, a dose believed to be of slight significance on any reckoning. The dose received from natural background radiation in the first 30 years of life, accepted as the period up to the upper limit of average reproductive capacity, is thus 3r. The dose received from an ordinary chest film is only a fraction of 1r, but a gastro-intestinal examination with apparatus commonly in use may amount to 15r per minute. It has been calculated that the dose to the foetus during X-ray pelvimetry is of the order of 3r, a dose equal to that received from natural background in the first 30 years of life, and this even before the child is born.

Medical diagnostic radiology in which only a few sites such as the hip, lumber spine, abdomen and pelvis are important, undoubtedly forms the most important source of man-made irradiation and its application is increasing steadily. While in Great Britain the genetic irradiation from this source has been estimated conservatively at 22 per cent.. of natural background radiation, figures for the U.S.A. and Sweden indicate that in these countries the dose from this source is equal to natural background.

Biological Effects

At the present time cellular damage from exposure to radiation is believed to be due to two causes:

1. Direct "hits" by the ionising particles or quanta striking and breaking the chromosomes—a purely mechanical process.
2. By the ionising of water contained in the cell very short lived oxidising radicals are produced which inactivate the cellular enzymes and may lead to cell death. This has been designated the "Poison Theory." Formation of these oxidising radicals is appreciably increased in the presence of molecular oxygen.

The proportion of cell damage to be ascribed to these two causes is unknown, but recent work suggests that the latter is just as important as the former, if not more so. It has been shown that the sensitivity of cells to irradiation is decreased if they are deprived of oxygen.

The desirability of protecting persons exposed to irradiation from military and civil sources has stimulated much research in radiobiology and this has been intensified since workers realised the importance of the "Poison Theory." It had formerly been thought that protection could be afforded only by shielding by physical means, but subsequently it was realised that chemicals might have a place to play in protection.

In considering methods of protection, the three important circumstances under which persons are likely to be exposed to irradiation must be distinguished:

1. Acute exposure to neutron and gamma radiation by persons in the vicinity of atomic explosions.
2. Exposure of patients to X-irradiation for therapeutic purposes.
3. Chronic exposure of persons in work carrying an occupational exposure, and to a lesser extent, of the general population who have been exposed to greater background radiation due to fall-out from nuclear tests and the increasing medical and industrial uses of X-rays.

Acute Exposure in War Time

Our knowledge is derived almost entirely from the reports following the explosion of atomic bombs over Hiroshima and Nagasaki in 1945. The majority of the 100,000 fatalities was due to blast injuries or severe burns, but in persons not so affected death was due to intense internal radiation following exposure to dense clouds of neutrons. The absorption of neutrons by the nuclei of certain elements, such as Sodium and Potassium, leads to the local emission by the now modified and unstable nuclei of more potent forms of radiation, and death results immediately from the intense chemical activity. In such circumstances protection is likely to be afforded only by screening by physical means. In persons farthest from the blast fatalities were due to severe radiation sickness like that often seen in a much milder form after radiotherapy. The severity of the illness varies according to the intensity of the exposure; when this was severe, death usually followed in a few days, but where the radiation was less intense the victims often survived several weeks. It is this last group that is most likely to benefit from chemical protective measures. The severity of the condition was much greater than that seen in civil practice; large numbers of the irradiated victims developed widespread areas of necrosis in the mucous membrane of the alimentary tract which were responsible for the pernicious vomiting and intractable diarrhoea frequently preceding death. The exceptional vulnerability of the lymphatic and haemopoetic systems leads to extensive haemorrhages and renders the victim very susceptible to infection both endogenous, through the weakened resistance of the alimentary tract, and exgenous as a complication of wounds and burns.

Protective Measures

These fall into two categories:

1. Factors designed to render the tissues less susceptible to radiations.
2. Factors to counter the leucopenia and thrombocytopenia.

As has been pointed out the irradiation of water within the tissue cells produces highly active oxidising radicals and organic peroxides. These radiotoxins react with substances of physiological importance within the cells in the process already described as the "Poison Theory." The presence of oxygen alters the radiation chemistry of water, increasing the poisonous action, and also alters the state of the enzyme systems rendering them more susceptible to radiations.

Reducing agents may afford protection by reducing the oxygen tension. Sodium hydrosulphite, for instance, protects *B. coli* against six times the lethal dose of X-rays by producing anoxic conditions. Cysteine, cysteinamine and glutathione, when injected into animals all quickly lead to conditions favouring reducing reactions and when injected immediately before irradiation have protected animals from doses which would otherwise have been lethal. While the immediate poisonous effects may be considerably reduced by such sulphydral compounds, there is every indication that the genetic and carcinogenic hazards remain unaffected.

Other treatment consists of correcting electrolyte imbalance and administering antibiotics since in the early days after irradiation the body is virtually defenceless and death from bacterial infection is otherwise inevitable.

Dr J. F. Loutit, a Fellow of the Royal Medical Society, and his colleagues at Harwell have made interesting contributions to knowledge by showing that splenic and marrow suspensions could be used to protect against fatal leucopenia in mice by recolonising the bone marrow. They have cured leukaemia in mice by whole-body X-irradiation followed by injection of splenic and marrow suspensions. Though of great interest, this work has no practical significance for man unless the immunological problems can be solved. However, a lead shield to an appreciable area of the bone marrow would appear to be a small but practical protective measure in reducing the number of deaths from fatal leucopenia.

Radiation and Malignant Disease

The first cases of radiation induced cancer were reported only a few years after the discovery of X-rays and since then further cases have provided considerable material for study. As examples of these may be cited the skin tumours reported in the pioneer radiologists, the high incidence of leukaemia in survivors amongst the atomic bomb casualties at Hiroshima and Nagasaki, the high incidence of lung cancer in the Austrian miners at Schneeberg and Jáchymow, following inhalation of radioactive particles and gases, and the bone tumours found in workers in the luminising industry in New Jersey who, because of inadequate precautions, ingested minute amounts of paint rendered radioactive by Radium and Mesothorium. These are well established facts but the radiation doses were all fairly high and whether these risks still hold when persons are continuously exposed to low dose rates will now be discussed.

Most, but not all irradiation-induced cancers occur in severely damaged regions; skin cancer is preceded by severe dermatitis and bone tumours by radiation osteitis. The tumours arise in the regenerating tissue which replaces the damaged, directly irradiated cells.

Tumours may be induced by three distinct mechanisms:

1. The induction of tumours in a localised normal region of the body by large doses of radiation may be described as the "Direct carcinogenic effect."
2. Radiations may act as carcinogenic agents and induce carcinogenesis in combination with other predisposing factors. Irradiation of tuberculous skin lesions may speed up the appearance of lupus cancers and irradiation of osteomyelitic lesions may result in osteogenic sarcoma.
3. An indirect or remote carcinogenic effect.

While the first two carcinogenic effects of radiation are local phenomena, the third is a systemic effect. In mice the incidence of ovarian tumours is significantly increased by small daily doses of gamma rays for over a year, or by a single large dose. If, however, one ovary is shielded from radiation and retains its normal function while the other is irradiated, the latter does not produce a tumour. If the experiment is varied and one ovary is excised while the other is irradiated, a tumour will be produced. Hormonal changes rather than a direct action of irradiation on the ovaries is implicated and this interpretation finds support in the observation that the grafting of an ovary from a speyed mouse into the spleen is followed by tumour formation in the grafted ovary. Under these conditions ovarian hormones are discharged directly into the portal circulation and are metabolised by the liver before they reach the systemic circulation. To compensate for the low level of ovarian hormones in the blood the pituitary increases its secretion of ovarian stimulating hormones which stimulate the ovary to hyperplasia and finally to neoplasia.

In medical practice the remote risk of inducing a new tumour by radiation therapy has to be accepted when this form a therapy constitutes the only hope of eliminating an existing tumour or at least of prolonging life.

Leukaemogenic Effects of X-rays

Animal experiments show that the incidence of leukaemia is increased by irradiation and this has been confirmed in man by evidence from the following sources:

Studies by the Atomic Bomb Casualty Commission show that the incidence of leukaemia amongst persons exposed to irradiation in Hiroshima and Nagasaki, and still resident there, is four times higher than that expected in a non-irradiated population, and further that the incidence is highest in those nearest to the site of the explosion.

In a recent survey under the auspices of the Medical Research Council, Court-Brown and Doll found that the incidence of leukaemia in persons irradiated for ankylosing spondylitis was ten times greater than in non-irradiated spondylitics, and there is obvious correlation between the dose received and the incidence of leukaemia. However, the total incidence of leukaemia in irradiated spondylitics is only one per thousand, so that it would appear justifiable to continue with this form of therapy which is the only one known to bring relief from pain and increased mobility to a large percentage of sufferers. It is pointed out that the mortality for interval partial gastrectomy is 13 per thousand in the best hands.

Conditions of exposure to radiation in Japan and in the treatment of ankylosing spondylitis are not comparable with radiation in small doses over long periods which might be received by persons engaged in work carrying a radiation hazard. There is some evidence to show that there is an increased death rate from leukaemia in radiologists, but knowledge of the occurrence of leukaemia under conditions of chronic exposure is too scanty to allow any reliable conclusions to be drawn. Most workers have found the life expectancy for radiologists to be no shorter than that for other medical specialists.

The potentially leukaemogenic nature of X-rays is emphasised by Dr Alice Stewart and her colleagues, whose findings suggest that exposure of children to X-rays during pre-natal life may be an aetiological factor in the development of leukaemia in infancy and childhood. It is probable that the foetus is more susceptible to the leukaemogenic effects of radiations than either children or adults.

In the belief that the incidence of chronic lymphatic leukaemia is not increased by exposure to X-rays (and this was also a finding amongst the atomic bomb casualties) workers studied the differences in the frequency of a history of exposure to X-rays for therapeutic or diagnostic purposes amongst patients with this form of leukaemia and amongst those suffering from acute leukaemia and chronic myeloid leukaemia. It was found that a history of exposure to X-rays was given in significantly greater frequency by patients with acute leukaemia and chronic leukaemia than by those with chronic lymphatic leukaemia. These studies suggest for the first time that the comparatively low dosages of X-rays received in diagnostic procedures may induce leukaemia.

The nature of the relationship between the incidence of leukaemia and the dose of X-rays, and consequently an understanding of the scale of risks involved, remains to be discovered. It is of great importance to determine with some degree of confidence whether a threshold exists below which exposure is not associated with an increased incidence of leukaemia. Many consider that the possibility of very small doses of X-rays being able to induce leukaemia cannot be ruled out. Research is needed to diminish the risks still further but not at the expense of effective treatment and accurate diagnosis.

Strontium 90

There is also much concern on account of the potential somatic dangers from internal radiation from the radioactive isotope, Strontium 90. This is a particularly dangerous fall-out product from nuclear tests because:

1. It has a high yield.
2. It is chemically similar to Calcium and finds its way into the Soil—Plant—Animal cycle of Calcium.
3. It is largely retained in the skeleton.
4. It has a long biological half-life (7½ years).

It has been known for many years that ingestion of Radium and Thorium by the workers in the luminising industry is followed in a large proportion of cases by bone lesions including osteogenic sarcoma. Like Radium, Strontium is selectively concentrated in bone and the beta rays emitted may produce bone tumours, or leukaemia by marrow irradiation. The hazard has long been recognised but too little is known to assess it quantitatively. American work indicates that the doses which produce sarcomatous change are extremely small. The fundamentally important question is: "How does tumour formation vary with dose?" If a threshold exists below which tumours do not develop then the small doses resulting from test explosions are probably harmless. If, however, there is no threshold and tumour formation is a linear function of dose, even the smallest dose will impart a small but definite probability of a bone tumour being formed.

It is the genetic effects, however, that have caused the greatest concern. The hazard to the human species from the genetic point of view arises from the fact that radiations have the property of inducing mutations. Some workers have suggested that the production of mutations in somatic cells accounts for carcinogenic and leukaemogenic effects of radiations. As far as is known, radiation induced mutations are in every way comparable to natural mutations, but it is unlikely that natural background radiation contributes more than between 2 and 22 per cent. of spontaneous mutations.

One of the most outstanding features of a mutation is its complete irreversibility. There can be no question of repairing the damage done since each gene is the jig upon which its progeny is constructed. Genetic mutation is thus cumulative, and long continued exposure to radiation of low intensity induces as much gene mutation as an equal dose of radiation of higher intensity. There is no going back in heredity; damage once done cannot be undone. As Muller has pointed out we are but the trustees of our own germplasm; it is the property of our offspring, and, indeed, of the whole human race.

In considering radiation hazards particular interest has been focused on the low range of doses and on the delivery of radiations at very low intensity. Before one can assess the hazards quantitatively one must know whether there exists a threshold below which radiations do not have deleterious effects. I have tried to show that when considering genetic damage the idea of a threshold does not apply since mutations, once induced, are irreversible, and since the minimum amount of incident radiation is capable of inducing genetic mutation.

The theory that radiation induced cancer, or indeed all cancer, is due to somatic mutation, brings into the same focus the two most important harmful effects or radiation, namely carcinogenesis and genetic damage. If this theory is correct, very serious consequences may be expected from nuclear tests already carried out.

Using *Drosophila*, workers have shown that there is no departure from a linear relationship in experiments with acute doses down to 25r. Moreover, the regression line through their experimental points cuts the axis at zero dose at a value not inconsistent with the observed rate of mutation in non-irradiated controls. Even if this work is substantiated it would not be justifiable to assume that the same conditions hold for man; but it should serve as a solemn warning to all that great hazards may attend the use of X-rays and even the relatively small contributions made to natural background radiation by fall-out from nuclear tests. It is probable that there is no dose below which radiations are harmless, and even with very small dose rates ill effects will be seen if a sufficient number of people are observed. The genetic effects of atomic radiation would be wholly bad because they would increase slightly the sum of misery and wastage against which the race has to battle, but, longterm though some of the consequences are, they are unlikely to hamper the course of human progress in the widest sense of that expression.

All references quoted in the Dissertations may be consulted in the original papers on the Society's premises.