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BIOLOGICAL EFFECTS OF RADIATION

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ABSTRACT

Radiation biophysics is ordinarily concerned with the interaction of ionising radiations with matter and the effects on biological systems. All radiations of the electromagnetic spectrum have similar characteristics, but differ widely in their energies- from low energy radio and micro-waves to infrared, visible and ultraviolet light to high energy X-rays and γ- rays. All types of radiation, irrespective of their origin, can affect living organisms. Radiation in lower energy ranges interacts with matter by excitation process but high energy radiation can ionise atoms and the liberated primary electrons can further ionise or excite neighbouring atoms. Alpha and Beta rays interact directly with matter, while high energy photons and neutrons interact with matter indirectly by photoelectric, Compton and pair formation processes; any particular process may predominate depending on the energy of the incident radiation. Alpha rays are more harmful to skin tissues than hard X-rays. The effects are ordinarily due to radiation-induced chemical/biological changes. As water is the most common in biological systems, the chemical species produced during the radiolysis of water play a major role in the biological effects of radiation damage. Presence of oxygen enhances the harmful effects. Radioactive isotopes are becoming increasingly important in radiotherapy and are routinely used in nuclear medicine. Radiation protection and therapy are also part of radiation biophysics.

Key words: Radiation effects at molecular level, cellular level, organism level, protection & therapy

INTRODUCTION

Biological effects of radiation primarily result from radiation induced chemical/biological changes. Radiation can cause genetic mutation and cell damage. Charged particles such as alpha-rays and electrons damage living cells directly, whereas X-rays and γ -rays and neutrons damage indirectly .X-rays and r-rays have energies in excess of the ionisation threshold and, therefore, the ejected electrons are highly energetic and they in turn produce further ionisation due to secondary electron interaction processes with matter. Absorbed radiation is converted into a variety of chemical and biochemical reactions leading to biological damage in the living tissues, cells and organisms. The relative biological effectiveness (RBE) of various radiations depends on their linear energy transfer (LET) capabilities. The reference radiation is generally ^{60}Co γ - rays.RBE depends on the dose, dose rate, oxygen presence, post-irradiation recovery/damage and other parameters.

Radiolysis of Water: In biological systems, water is abundant and ubiquitous. Its high affinity for electrons, makes the radiolysis of water a primary event in the initiation of radiation damage in living cells. Absorption of radiation by water leads to ionised species which further react with neighbouring water molecules or other polar molecules, to form a variety of new reactive species and free-radicals. Free radicals are not the primary products of radiolysis of water, but secondary products from subsequent decomposition of ions and excited species produced initially. Free radicals and H_2O_2 can react with genetic material, proteins and other biological molecules and alter their functions, leadind to mutations, chemical lesions and biological complications like illness, cancer and ultimately death.

The role of oxygen: Oxygen is a highly reactive molecule. In the presence of oxygen the reactions produced by ionising radiation are different and are more harmful biologically. In the absence of oxygen, radicals can react with one another or dimerse(or polymerise). Presence of oxygen blocks restoration processes and enhances radiation damage. In the presence of oxygen, the formation of the peroxy-radical,is the predominant reaction. Peroxy radicals cannot dimerse or polymerise but give rise to hydroperoxide.Irradiated woater containing dissolved oxygen leads to the relatively large amounts of perhydroxy radicals. Therefore, all biological system are more radiosensitive in the presence of oxygen.A dose of radiation is more destructive to a biological system in the presence of oxygen than in its absence.

Effects of radiation on living systems: Radiation-induced biological effects can manifest at the (i) molecular, (ii) cellular and (iii) organism levels.

Effects at the Molecular level: Ionising radiations can break chemical bonds and radically alter the chemical structures of biological molecules. The principal reaction of amino acids in aqueous media is deamination with the release of water. Free radicals, produced on radiolysis of water, can react with macromolecules (proteins, enzymes, membranes and genetic material) an ddamage them. One of the primary biological/biochemical lesions is the alteration of intercellular relationships between enzymes and substrates.

Presence of oxygen enhances the damage. Almost all proteins are denatured by ionisation which results in the loss of enzyme activity. The dose – response curve indicates that one reaction by a radical is sufficient to produce enzyme inactivation. Nucleic acids are the most radiosensitive molecules in the cell. Nucleic acid bases are readily reduced by electrons and react rapidly with hydroxyl radicals to produce addition products.

Effects at the cellular level: Radiation damage to the genetic material can be hereditary or somatic. Hereditary effects of radiation are mainly due to radiation induced mutations in the ova and sperm cells. Ionising radiations increase the normal process of decay. Radiation can damage chromosome, considered to be the root-cause of cell damage.Radiation may cause cell division not to occur properly or not at the proper time. In complex organisms certain cells never divide(central nervous system), some devide occasionally (kidney, liver etc.,) and other cells divide continuously (bone marrow cells). Therefore, acute damage is most likely to occur in those cells which are undergoing rapid cell division (Ex: lymphoid cells). Consequently, infants are more susceptible to radiation damage than adults.

Radiation damage of cell membranes with abnormal changes in their permeabilities leads to cell death.Lesions in cell membranes lead to spatial disorganisation of enzymes, nucleus and cytoplasm, proteolytic and nucleic acid-attacking enzymes can then destroy the macro molecules (by phagocytosis).This enzyme-release hypothesis can explain many cellular phenomena of radiation damage. Higher doses of radiation lead to cell liquefaction and death. Shortening of life-span, cancer induction and damage to the long-term effects of radiation damage.

High doses to the gastro-intestinal tract lead to damage of submucosal, vascular and connective tissues. In skin the effects are dermal necrosis, loss of hair and disfunctions of sweat glands. The spinal chord is highly radiosensitive. Radiation damage leads to demyclination and loss of glial cells. Opaqueness and contract in the eyelens are the result of radiation.

Radiation Carcinogenesis: Radiation carcinogenesis is a stochastic process(no dose threshold). The development of cancer appears to be dependent on many parameters.Ingeneral terms, carcinogenesis takes place in two steps: - initiation (irreversible) and promotion. Ionising radiation acts as initiator as well as promoter. Estimation of the risk can be expressed in terms of a linear- quadratic function.

$I_d = I_n + I_n \alpha_1 D + \alpha_2 \alpha_2 D$

Where I_d is the observed incidence of cancer for dose, D, I_n is the normal incidence of cancer without the radiation dose and α_1 and α_2 are linear and quadratic risk coefficients, respectively.

Effects at the Organism level: All forms of ionising radiation are harmful above certain minimum dose levels. There is no clear-cut criterion for threshold dose levels. Exposure to ionising radiations cannot be completely avoided as human beings are exposed to these from natural as well as man-made sources of radiation. Compared to other risks (smoking, chemical, and biological pollutants), the biological effects of low-level ionising radiations are slight.

The most important, ubiquitous and harmful natural radiation sources are the decay products of radon, ^{222}Rn. ^{222}Rn is the gaseous daughter product of the decay of radium ^{226}Ra, and ^{222}Rn once released into the atmosphere due to uranium building construction etc., pervades and being dense settled in enclosed spaces of building. Accumulation of radon also depends on the type of construction, the type of ventilation and the geographical location.Randon radiation damage is due to the decay products of radon and α-rays (not due to radon gas directly).On inhalation of radon gas, the decay products are absorbed as aerosol particles by the bronchial tissues, leading to lung tissue damage and lung cancer.

Other naturally occurring nuclides of importance to humans are ^{42}K, ^{90}Sr , and ^{31}I being gaseous can spread over a large area and is absorbed by living organisms through the food chain. It causes minimal damage due to its very short half-life. Of all machine-produced sources, medical X-rays, γ-rays in nuclear medicine and nuclear reactors constitute by far the greatest health hazards.

Dose rates (accumulated doses) are of crucial importance in understanding the biological effects of radiation. Accumulated low doses can start off chain reactions leading to genetic damage and cancer. As a rule of thumb, a dose of 0.25 Gy is considered the limited dose. Doses in the range below 1Gy affect sensitive organs and tissues, such as reproductive organs and bone marrow tissues, and cause sterility and lower production of lymphocytes. Radiation doses of ≈ 1Gy damage eyes leading to blindness, causes deficiencies in the immune system and lead to anaemia due to non-formation of new erythrocytes by the bone marrow. The central nervous system and some tissues such as cartilage are fairly radio resistant to small or medium doses of ionising radiations. Doses in the range of 3-5 Gy lead to death within months due to bone marrow damage, haemorrhages, anaemia, infection and malnutrition. Doses of 10 – 40 Gy lead to death within weeks due to severe damage to the gastro-intestinal and other organs. Very high doses, > 100Gy, cause death within hours or days, the due to damage to the central nervous system.

RADIATION PROTECTION AND THERAPY: Protection from, or neutralisation of, ordinary effects of radiation is not possible in biological systems, but protection from secondary effects at low and moderate doses of radiation is feasible.

Hormesis: Hormesis is positive stimulation by low doses of any potentially harmful agent. The hormesis hypothesis states that at sub-harmful doses (below zero equivalent point, ZEP, which is the maximum quantity of an agent that can be administered with no discernible effect), ionising radiation is beneficial to living organisms instead of being hazardous; and low levels of ionising radiation may infact be essential to well being of life by influencing increased life span, disease resistance and resistance to larger doses of radiation. The effect of any radiation at harmful doses is diametrically different from those of hormesis doses. The basis for this assumption is radiation stimulation. Examples are photo-reactivation of radiation, induced sporulation in bacteria, accelerated growth and reproduction in moulds and drought resistance in seeds etc..

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Radiation Protection: As radiolysis of water produces free radicals, addition of substances that compete for these free-radicals (free-radical scavengers) could minimise the random effect. Some of these molecules rendering chemical protection against radiation are cysteine and molecules containing free sulphydryl(-SH) groups and chelating agents such as EDTA. Protecting of sensitive organs and sites from irradiation is another method of protection. As longer-wavelength X-rays are absorbed by the skin surface, leading to skin damage,filtering of such radiations can be achieved by shields(Al, Cu etc.,)

Radiation Therapy: Inspite of the hazardous nature of ionising radiations, living organisms have to live with them and they are very much a part of nuclear medicine for diagnostics as well therapeutic treatments. X-rays are routinely used in Rontgenography and CAT-scan radiography. Radioactive isotopes (radionuclides) are employed as tracers in many biological processes. Labelled-radionuclides can easily be monitored due to their radioactivity and high sensitivity. Various functions of organs and their abnormalities can be monitored due to their radioactivity and high sensitivity. Various functions of organs and their abnormalities can be monitored by such methods.Some of these are: diagnosis of the function of the thyroid gland by radioiodine; the function of kidneys by renography and the uptake, distribution and elimination process of metabolites and drugs by pharmacokinetic methods.Labelled proteins are used in clinical investigations – in the metabolic process of plasma proteins and the gastro-intestinal tract. By such investigations any abnormalities due to the effects of radiation or chemicals can be evaluated.

Rapidly dividing cells with undifferentiated structure(tumours) are more sensitive to radiation than strongly differentiated cells undergoing slow division. Use of ionising radiation in cancer therapy is based on the sensitivity of different types of cells to these radiations. Cancer cells react like ordinary cells in their response to oxygen. Whether the presence of oxygen should enhance the destruction of tumours is very difficult to evaluate due to various complex reactions. The role of re oxygenation in radiotherapy of human tumours is not properly explained.

Present day radiation therapy relies on the administration of radiation dose not in a single shot, but in fractions separated over a time period. This procedure is to allow the recovery of normal cells from the effects of radiation. The cell repair and repopulation factors are taken into account in models to explain the effects of radiation.The effects of irradiation by the dose-fracctionation procedure can also be expressed in terms of a linear-quadratic model $\log S = - n (\alpha D + \beta D^2)$

Where S is the survival fraction of the species and n is the number of fractions of the total dose. The ratio of single-hit and multi-hit coefficients, α/β is a useful measure of dose specification in terms of the flexure dose (the minimum dose per fraction below which protection of normal tissues is not realised).The linear quadratic dose-fractionation model is supposed to give a better understanding of the clinical radiotherapy so that effective tumour control can be realised with minimal damage to normal cells.

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