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HEALTH CONSEQUENCES OF IONIZING RADIATION EXPOSURE

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The increasing use of ionizing radiations all over the world induces an ever- increasing interest of the professionals as well as of the whole society in health protection and the risk due to these practices. Shortly after its discovery, it was recognized that ionizing radiation can have adverse health effects and knowledge of its detrimental effects has accumulated. The fact that ionizing radiation produces biological damage has been known for many years.In this article we examine the types of health effects associated with large acute exposures and with low dose rate chronic exposure. The biological effects of ionizing radiation to cell, tissue, organ and systems in humans will be outlined.

INTRODUCTION

The interaction of ionizing radiation with human body, either from external sources (i.e. outside the body) or from internal contamination of the body by radioactive substances, leads to biological effects which may later show up as clinical symptoms. The nature and severity of these symptoms and the time at which they appear depend on the amount of radiation absorbed and the rate at which it is received.

Radiation Safety is concerned with cellular effects, which result in damage to crucial reproductive structures such as the chromosomes and their components (e.g., genes, DNA, etc.). Radiation interactions within the body produce microscopic subcellular-level effects that may result in cellular responses and, in the aggregate, may ultimately produce macroscopically observable effects on specific organs or tissues. Irradiation of biological tissue sets into motion a series of intracellular biochemical events that start with ionization of a molecule, and which may ultimately lead to cellular injury. Injury to a large number of cells may, in turn, lead to further injury to the organ and to the organism. Many factors may modify the response of a living organism to a given

dose of radiation. Factors related to the dose include the dose rate, the energy and type of radiation (Depending on the amount of ionization deposited along a unit length of track of radiation, LET), and the temporal pattern of the exposure. The DNA is considered to be the primary target molecule for radiation toxicity. Molecular damage, which includes damage to the DNA, can occur in one of two ways from an exposure to radiation. First, radiation can interact directly with the DNA, resulting in single or double-strand DNA breaks or bonding base pairs. Second, radiations can interact directly with other surrounding molecules within or outside of the cell, such as water, to produce free radicals and active oxygen species. These reactive molecules, in turn, interact with the DNA and/or other molecules within the cell (membranes, mitochondria, lipids, proteins, etc.) to produce a wide range of damage at the cellular and tissue levels of the organism[1,2,4].

Cellular/Organ Radiosensitivity: The health consequences of radiation exposure depend on also some biological factors which include species, age, sex, the portion of the body tissues exposed, different radiosensitivity, and repair mechanisms. According to the Law of Bergonie and Tribondeau, the sensitivity of cell lines is directly proportional to their mitotic rate and inversely proportional to the degree of differentiation[2,3]. Cellular changes in susceptible cell types may result in cell death; extensive cell death may produce irreversible damage to an organ or tissue, or may result in the death of the individual. If the cells are adequately repaired and relatively normal function is restored, the more subtle DNA alterations may also be expressed at a later time as mutations and/or tumors. [4]

ACUTE RADIATION SYNDROMES (ARS)

Acute Effects: High doses of ionizing radiation can lead to various detrimental effects. In the case of deterministic effects, a certain minimum dose, the threshold dose, must be exceed in order for the effect to be expressed. An increase in the size of the dose above the threshold dose will increase the severity of the effect.

The clinically observable results of acute overexposure are commonly referred to as **Acute Radiation Syndrome (ARS)**. This effect is seen only after whole-body exposures to relatively high doses (>1.0 Gy) such as might occur in a serious nuclear accident. The four stages of ARS are prodrome (or initial), latent stage, manifest illness stage and recovery or death. The prodromal phase is characterized by nausea, vomiting, malasia and fatique, increased temperature and blood changes. The latent stage is similar to an incubation period. The manifest illness stage gives rise to signs and symptoms specially associated with the radiation injury, hair loss, fever, infection, hemorrhage, severe diarrhea, prostration, disorientation, and cardiovascular collapse. The severity and time of onset of the signs and symptoms depend upon the radiation dose received, with the time of onset decreasing with increasing dose .

The clinical phase can be divided into four overlapping phases; A mild phase(0.5-1 Gy), Hematopoietic syndrome (1-8 Gy) characterized by deficiencies of White blood cells, lymphocytes and plateletes with immunodeficiency, increased infectious complications, bleeding, anemia and impaired wound healing. Gastrointestinal syndrome(8-30Gy), characterized by loss of cells lining intestinal crypts and loss of mucosal barrier, with alterations in intestinal motility, fluid and electrolyte loss with vomiting and diarrea, loss of normal intestinal bacteria, sepsis, and damage to the intestinal microcirculation, along with the hematopoietic syndrome. Central nervous system syndrome(>30 Gy) primarily associated with effects on the vasculature and resultant fluid shifts. Signs and symptoms include vomiting and diarrhea within minutes of exposure, confusion, disorientation, cerebral odeme, hypotension, and hyperpyrexia. Fatal in short time.

Without medical care, half of the people exposed to a whole body acute exposure of 3.5 Gy may die within 60 days (LD50/60). Exposed individuals who survive acute whole body exposures may also develop other delayed somatic effects such as epilation, cataracts, erythema, sterility and/or cancers[8].

STOCHASTIC EFFECTS

Acute exposures may lead to early or late effects which may be either stochastic or deterministic. The immediate or acute effects described above are largely the result of the killing of cells in some crucial population. Delayed or late effects are due to damage to cells that survive but retain some legacy of the radiation damage. Hereditary (genetic) effects and cancer are called stochastic effects. If this cell is a germ cell, it may result in a genetic mutation expressed in a future generation. Hereditary effects from exposure to ionizing radiation have not been identified in humans. If the cell damaged is a somatic cell, the consequence may be cancer in the individual exposed. Increasing the radiation dose does not increase the severity of the effect in individual, it simply increases the frequency or incidence of the effect in a population.[5,6]. The risk of stochastic effects is the primary reason for limiting doses to both the public and radiation workers. For the purposes of radiation protection, it is assumed that the probability of a stochastic effect increases linearly as the dose increases and that there is no threshold dose. For this reason, a stochastic effect is called a Linear or Zero-Threshold Dose-Response Effect. If there is no threshold dose then it is considered that even small doses of radiation might cause cancer. It may be concluded that the currently available epidemiological data (Hiroshima, Nagasaki, Chernobyl, the registries of nuclear workers) provide no evidence of proven radiation carcinogenesis in the region of low doses (0-100 mSv). Although it is not yet possible to determine clinically whether a specific malignancy was caused by radiation, radiation-induced tumours and leukemia have been detected and statistically quantified by epidemiological studies of populations exposed to relatively high radiation doses The induction of cancer is a chance ("stochastic") event unlike the induction of radiation sickness which is completely predictable. Epidemiological evidence has consistently linked exposure to ionizing radiation with increased rates of carcinogenesis in any organ in which cancer can occur. It is now accepted that ionizing radiation can cause cancer in any organ which cancer occurs naturally. The risk of cancer induction is assumed to be broadly proportional to the number of irradiated cells at risk in a given organ or tissue, even though between species the evidence indicates that there is no correlation with body size. Organs vary significantly in their susceptibility to cancer and in their latent period before the onset of malignant transformation.

Stochastic effects can also be caused by many other factors, not only by radiation. Since everybody is exposed to natural radiation, and to other factors, stochastic effects can arise in all of us regardless of the type of work (working with radiation or not). Since there is no evidence of a lower threshold for the appearance of Stochastic Effects, the prudent course is to ensure that all radiation exposures follow a principle known as **ALARA (As Low As Reasonable Achievable)**. Probability of Stochastic Effects are for fatal cancer 5.0 % per Sv, non-fatal cancer1.0 % per Sv. Radiation-induced, solid cancers have a long latency period, generally >10 years [5,6,7] Leukaemia and thyroid cancer in children can appear as soon as a few years after exposure.

RADIATION ACCIDENT AND EARLY DIAGNOSIS

Radiation accidents may be viewed as unusual exposure events which provide possible high exposure to a few people and, in the case of nuclear plant events, low exposures to large populations.Our understanding of the acute effects of total-body radiation is derived from analysis of the clinical course of individuals exposed to radiation after the detonation of atomic bombs over Japan and radiation accidents that have occurred throughout the world.

Most radiation injuries are "local" injuries, frequently involving the hands. These local injuries seldom cause the classical signs and symptoms of the acute radiation syndrome.

Evaluation of specific signs and symptoms is required for triage of victims, selection of therapy and determination of prognosis. Clinical observations, laboratory examinations and cytogenetics are the main diagnostic methods used in cases of whole body exposure[8,9].

CONCLUSIONS

The health effects related to ionizing radiation exposure can be result in immediate effects, mainly to organs with rapidly dividing cells, which include the hematopoietic system, gastrointestinal tract, and skin, or delayed effects such as cataracts and embryo/fetal development problems. Carcinogenic effects also may occur in any number of organ systems. This end point may not be expressed for several years after the initial exposure. Besides with epidemiologic studies, the most fruitful approach to further understanding risk from exposure to ionizing radiation is through molecular studies, including the identification of unique biomarkers and pathogenic pathways at the cellular and tissue levels.

Table 1. Estimated threshold absorbed doses for deterministic effects after acute exposure

Exposure Health Effect	Organ	Absorbed Dose (Gy)
Temporary sterility	Testis	0.15
Nausea		0.35
Depression of blood cell forming process	Bone marrow	0.5
Reversible skin effects	Skin	2
Permanent sterility	Ovaries	2.5-6
Vomiting		3
Temporary hair loss	Skin	3-5
Permanent sterility	Testis	3.5
Skin erythema	Skin	5-6

Table2. Biological Effects of Short Term Radiation on Humans

Dose (Gy)	Effect
0-0.25	No detectable injury or symptoms
0.25-1.00	Measurable transient blood changes Temporary decrease in white blood cell count
1.00-2.00	Acute radiation sickness-nausea, vomiting, decrease in white blood cells
2.00-3.00	Vomiting, diarrhea, loss of appetite, listlessness, death in some cases.
3.00-6.00	Vomiting, diarrhea, hemorrhaging,deaths occurring in 50% of cases at 3.5 or above without medical treatment
Above 6.00	Eventual death in almost all cases

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