



Member's Paper

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Possible Health Effects of Low Level Exposures to Ionising Radiation

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1. Introduction

The United Nations Scientific Committee on the Effects of Ionising Radiations (UNSCEAR), in its 1993 report to the General Assembly states that 'The Committee's interest in the biological effects of radiation is mainly concentrated on the effects of low doses'(1). This highlights the fact that today probably no other topic in radiation sciences has been drawing so much attention as the likely health effects of exposure to ionising radiation at low levels. This is so for several valid reasons. In occupations dealing with radioactivity and ionising radiations, while one can bring down the radiation fields and exposures to very low levels by proper practices and control, they can not be totally eliminated. This will be over and above the background radiation which is ubiquitous with wide spatial variation depending on the geochemical and other features of the area. Further, the health effects associated with these low level exposures are, if at all, likely to be a small fraction of natural incidence of such maladies. An obvious question would be, why not extrapolate backwards from the high exposure risk data which is more or less well established. This is not always possible since such extrapolations are wrought with severe uncertainties due to dose-rate effect, repair mechanism, adaptive response etc. Thus the exact determination of the health risk at low exposures continues to be a challenging task. Various aspects of this problem are presented in the paper.

2. Low Level Exposures

The global average dose due to natural background radiation is about 2 mSv/yr. This corresponds to an average life-time dose of 140 mSv. However the natural background radiation and consequent life-time dose vary from place to place ranging up to two orders of magnitude. The internationally accepted limit for occupational exposure is 20 mSv per year averaged over 5 years. But the globally averaged exposures for radiation workers in different fields are in the range of 2 to 8 mSv/yr (2) . Further, there is a declining trend in this due to improved technology and practices.

When we say low level exposure, it generally refers to dose rates of fraction of a mSv per minute and/or integrated dose in the range of 200 to 400 mSv.

3. Biological Effects

It is well established that biological effects are of two types; deterministic and probabilistic. The deterministic effects, such as depression of red blood

cells, skin reddening and blistering, induction of sterility etc., arise out of massive cell damage or cell-killing due to the exposure of the biological system to ionising radiation. These effects are characterised by their appearance within a few hours to a few weeks after the exposure. A very important feature of the deterministic effects is that they occur only above a particular level of exposure called 'Threshold Dose'. The threshold doses are different for high dose rate (acute) and low dose rate exposures. For human species, about 200 mSv of acute exposure is needed for any discernible deterministic effect. Such exposures can occur only in serious radiation accidents or from unwanted but inevitable exposure of healthy tissues in radiation therapy. For more commonly encountered low dose rate exposures the threshold is significantly higher, of the order of a few Sieverts.

Probabilistic effects, also known as 'Stochastic Effects' result from the 'Mutagenic' action of ionising radiation, a simplified picture of which is as follows:

In a living cell the Deoxyribonucleic acid (DNA), present in the chromosomes residing inside the nucleus, is the repository of all the information required for governing the cell-functioning and its replication. The DNA is a double-stranded helical macro molecule. The backbone of each strand is a string of sugar and phosphate residues and the two strands are linked by a pair of 'Nucleotide' bases. Four different types of nucleotide bases namely Adenine, Guanine, Cytosine and Thymine occur in the DNA molecule. The cardinal feature of the DNA is that while the occurrence of a particular nucleotide base along the strand of the molecule is not influenced by the neighboring ones, the base pairing is highly specific. That is, Adenine on one strand can pair only with Thymine on the other strand with a similar matching between Cytosine and Guanine. Thus, the sequence of nucleotide bases on one of the strands of DNA completely determines the sequence on the other. (This plays a paramount role in cell replication but we need not go into its details here.) The sequence of such base pairs in the DNA molecule is the 'Text' of information required for all cell activities. If the DNA molecule is affected either by affecting the individual base pair or its sequence, the information content gets altered and such a change is called Mutation. If the cell happens to be a somatic (non-germinal) cell in the body, the mutagenic disturbance can lead to loss of control over the cell division which may eventually result in cancer induction. Or if it happens to be a germ cell, the mutated information can get passed on to the

progeny leading to genetic effects. Ionising radiations are known to bring about such mutations either by directly affecting the DNA or by producing active chemical species in its vicinity which can affect the DNA. Both direct and indirect modes of damage are probabilistic in nature and the probability increases with radiation dose. Some common types of damage to DNA are; (i) base damage, (ii) single strand break, (iii) double strand break and (iv) cross linkage of the molecule. The damage to DNA is subject to very efficient repair mechanisms mediated by enzyme actions. If the damage is confined to a single strand, the repair mechanism uses the information provided by the other strand. The repair is then highly efficient and error free. Misrepairs are frequent in the case of double strand breaks. Such instances result in the loss of biological information which may lead to carcinogenic or genetic effects. It must be mentioned here that the mutations are nothing new nor specific to ionising radiations; they are also introduced by other agents such as excessive heat, certain type of chemicals and viruses etc. The mutagenic phenomenon has always existed in nature and it is part of our evolutionary system. The frequency of natural mutations is about a million times more compared to the number introduced by the radiation at the levels we are interested in, as can be seen from Table 1.

Table 1. DNA damage in Mammalian cells(3)

Type of Event	Spontaneous events/yr	Events/10 mSv
Single strand breaks	$\sim 4.4 \times 10^7$	10
Double strand break		0.4
Depurination and/or base legions	$\sim 1.4 \times 10^7$	
	$\sim 1.1 \times 10^7$	9.5
Total	$\sim 7 \times 10^7$	20

4. Risk Evaluation

It is the mutagenic effect of radiation which has given rise to maximum concern amongst the public. Unlike the deterministic effects, these effects are supposed to have no threshold levels of exposure. Though there are arguments against this no-threshold model, it is generally accepted as a safe hypothesis in the absence of firm data to disprove it. According to this, however small the radiation dose is and whether it incurred in one shot or over an extended period, the effect, or more appropriately the probability of its occurrence, is proportional to the integrated dose. Furthermore, irrespective of the number of persons exposed in the population and the levels of their exposure, the probability of the manifestation of these effects in the population is proportional to the sum

total of all the individual exposures called cumulative dose expressed in Person-Sieverts (PY).

The biological information system has been built with a large redundancy which provides a degree of resilience to the system. Besides, cancer is a multifactorial disease which needs more than just an initiator. It is in this context that these effects are called stochastic and dealt with in terms of probabilities. For quantitative assessment, the biological detriment of these effects are expressed in terms of Risk coefficients. Simply put, the risk coefficient is the frequency of undesirable events introduced in the population due to unit collective dose(there are several variants of this definition, each one having its own advantages).

Understandably, there has been an enormous scientific effort in terms of laboratory studies on animals, *in-vitro* experiments on mammalian cells and epidemiological studies towards determining the risk coefficients. While the laboratory experiments have significantly contributed to our understanding of radiobiological basis for risk determination, the risk coefficients themselves have been obtained basically from epidemiological studies. The data base currently available from such studies fall under two categories; High Dose Rate Exposures (HDR) and the Low dose or Low Dose Rate Exposures (LD/LDR). The HDR data base consists of more than 3×10^5 Person-Years (PY) of Life Span Studies (LSS) of the Atomic bomb survivors in Hiroshima and Nagasaki and more than 10^6 PY each from radiation treatment and diagnostic cases. Of them, the LSS is the most thoroughly planned one and it is essentially based on this study that the risk coefficient for cancer is estimated to be about 5×10^{-2} per Sievert.

For the genetic effects, the UNSCEAR specifies a risk factor of 1×10^{-2} per Sievert. This figure has been derived essentially from animal studies involving higher levels of exposure. None of the epidemiological studies conducted so far, including the LSS, have shown any evidence of genetic effects.

5. Low Level Exposures

It is well established that for rays, which is of primary concern in the population exposure, the biological risk has a strong dose and dose rate dependence. Firstly, the dose response curve is observed to be non-linear and the effects at low doses estimated by the backward interpolation of high exposure data tend to be over estimates. Second and more important observation is that for the same total dose, the lower dose rate exposure results in a significantly lower detriment. Based on extensive experimental and epidemiological studies the Dose and Dose-Rate Effective Factor (DDREF) has been observed to be in the range of 2-13. It may be mentioned here that the basis for presently used risk coefficients is the LSS of Atomic Bomb Survivors which is essentially a high dose rate category. Of course, to extend its application to low level exposures,

a DDREF of 2 has been used. However the actual DDREF applicable could be significantly lower resulting in much lower risk coefficients as observed in the low dose low dose-rate (LDR) epidemiological studies discussed below.

The presently available LDR data consists of about 2×10^6 PY of occupational workers and more than 10^6 PY of environmental exposure in High Background Radiation Areas (HBRA). This data does not provide a clear support to the presently adopted risk coefficients. It is even consistent with a 'No-Risk' model. Amongst the LDR, the epidemiological investigations in China happen to be the largest. It has about 10^6 PY of observation for people living in HBRA with a mean radiation dose of 5.4 mSv/yr and a similar number in control areas with a mean dose of 2 mSv/yr. The study shows no increase in the cancer mortality for the HBRA population (4). As a matter of fact, the frequency of observed cancers in the HBRA population is marginally less compared to that of control population (but not significant enough to firmly support any negative correlation of cancer with radiation exposure). Large scale LDR epidemiological studies have also been conducted amongst the radiation workers in USA, Japan, France, Canada and Sweden. None of them show any significant association of cancer with low level exposure. Recently, the International Agency for Research on Cancer conducted a study on the data pooled for radiation workers from three countries (5). The combined data clearly indicate that the presently used risk factors for cancer are significant over estimates at least up to 300 mSv.

There have also been other reports of occurrence of health effects due to low level exposure. In general, they have not been able to stand the rigorous scientific analysis and have been discredited by subsequent large scale studies. Some time back Kochu Pillai et al (6) reported higher prevalence of mentally retarded children (12 in the surveyed population of 12918) in the monazite belt of Kerala as compared to zero prevalence (none in 6000) in the control population. The difference was attributed to the higher background radiation, 15-30 mGy/yr, in the monazite belt as compared to 1 mGy/yr in the control area. However, later analyses faulted this report on several counts including the anomalous observation of zero incidence in the control population (7). Similarly in UK, Knox et al, reported correlation of cancer (leukemia) with high background radiation (8). But a subsequent large scale study on the same did not provide any confirmation for the conclusions of Knox (9). It was noted that the statistical methods employed by Knox were obscure and the results were difficult to interpret.

Gardner et al (10) reported clusters of childhood leukemia amongst the population living in the vicinity of UK Sellafield Nuclear facilities. A possible linkage of these clusters to the radiation exposure of the fathers was suggested. This was in total contradiction of the LSS data; no excess cancer has been observed amongst the children of atomic bomb survivors who

had significantly higher exposure. Still, the report created quite a sensation and prompted several large scale and systematic surveys. These studies did not provide any support to the suggestion that fathers' radiation exposure increases the cancer risk for the children¹¹. Studies have also been conducted amongst the children in the vicinity of nuclear facilities in France, USA, Germany and Canada. None of them gave any evidence for the excess cancer as reported by Gardner.

6. Adaptive Response

Over the years, there has been a large number of studies which provide support for the hypothesis that an initial low level exposure to ionising radiation can mitigate the severity of deleterious effects of subsequent high exposures. There have also been reports that such low exposures can even be beneficial by preparing the cell to face the deleterious agents other than ionising radiation. However the evidences for such effects are still not unequivocal. If firmly established, they can lead to substantial reduction of risk coefficients at low level exposures.

7. Conclusion

Detrimental effects of exposure to the ionising radiations is one of the most widely studied subjects. Based on extensive laboratory studies and epidemiological surveys, the risk coefficients have been arrived at on a conservative basis. They have been derived from high exposure data. Quite small as they are, there are strong reasons to believe that they are over estimates for low level exposures and can be considered only as upper limits. How small they are or whether they exist at all at low exposures are the issues of interest at present.

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