Like non-ionising electro-magnetic radiation, the ionising radiation is an essential part of our life. Not only is it present in our surroundings but its presence within our body makes it an inseparable component of living. An average person of about 60 kg body weight continuously emits around 24,000 gamma rays photons every minute which arise primarily from the radioisotope of potassium, $^{40}$K with natural abundance of 0.12% of natural potassium. From birth to death we are continuously getting exposed to gamma radiation from within and from all objects outside namely the building we live in, the earth, the cosmic radiations, radon in air and the food we eat – all contain measurable levels of radioisotopes of potassium, uranium, thorium and lead. The average radiation dose we get from natural sources of radiation is between 1 and 2 mSv/year. The exception is a few areas, notably, a coastal strip in Kerala where the thorium deposits in the earth enhance the level of exposure to the people living in the region. Areas of high background natural exposure are listed in Table I. On the other extreme is the nuclear holocaust in Hiroshima and Nagasaki instantly killing a large number of people and leaving many survivors with radiation effects. Within these two extremes lies the region of low level exposure where the benefits (primarily medical) exceed the probability of harm.

**Low level exposure**

The exposure for lethal effects is of the order of a few Gray (Gy) typically acute whole body exposure of more than 4 Gy. For practical purpose in this text Gray and Sievert (Sv) may be considered equal, that is, 1 Gy=1Sv which is true in many situations. While 1 to 2 mSv may be the annual dose from natural background exposure, the diagnostic medical procedures typically involve exposures of the order of 0.05 to 20 mSv and radiation therapy for cancer involves killing of tumour cells by 2-5 Gy. The low dose region may include people medically exposed for diagnostic or for therapy of non-malignant conditions, workers in radiation installations including medical, industrial and nuclear installations, people accidentally exposed to non-lethal doses i.e., exposure of a few mGy to a couple of Gy. This defines the region of interest discussed in this paper. The ionising radiations of interest are the X-rays and nuclear radiation namely gamma, beta and alpha in decreasing order of merit as alpha radiations are not much useful in biomedical practice. The focus of this article is the human data on radiation effects rather than the biological experiments on which large amount of information is available, difficult to be summarized in a small presentation such as this.

**Ionisation process**

Unlike non-ionising radiations which dissipate energy by thermal interactions, the ionizing radiations have sufficient energy to eject out an electron from the atoms of biomolecules in the body, be it carbon, nitrogen, hydrogen, oxygen, phosphorus, sulphur etc. The preponderance of water in the body makes hydrogen and oxygen atoms most abundant. The typical chain reaction passing through formation of active free radicals and leading to altered or damaged DNA is discussed below.

The ionising radiations deposit energy in the material concerned. Alpha and beta particles, being electrically charged, deposit energy through electrical interactions with electrons in the material. Gamma rays and X-rays lose energy in a variety of ways but each involves liberating atomic (orbital) electrons, which then deposit energy in interactions with other electrons. In some cases, an electron in the material may receive sufficient energy to escape from the atom (ionisation). The resulting positive atom is an ion.
Free radicals are highly reactive chemically, they can diffuse through cells and can alter important molecules in the cell by disrupting the bonds. We still do not fully understand the ways in which radiation damages cells but many involve changes to the DNA. There are two ways in which this can happen. Direct interaction of ionising radiation with DNA molecule may cause ionization and chemical alteration of DNA and secondly DNA may be changed indirectly when it interacts with a free radical produced in the water of the cell. Such chemical changes may lead to development of cancer or inherited genetic effects.

**Classification of radiation effects**

In the light of present knowledge, the biological effects of radiation are normally classified into two categories namely, the deterministic effects and stochastic effects.

**Deterministic effects**

Under this category are effects which have a threshold. Although some people do not subscribe to the view that threshold exists, ICRP (International Commission on Radiological Protection) so far has accepted the view that threshold exists for some effects. No effects can be observed below the threshold level and after the threshold is crossed the severity of the effect is a function of dose. Cataract, loss of fertility, erythema, mental retardation are some examples of deterministic effects. These effects were previously called as non-stochastic effects but ICRP in its Report No. 60 preferred to assign the name “deterministic effects”. Another way of classifying the radiation effects is based on whether there is cell kill or cell modification. If the dose is large enough, it results in killing of sufficient number of cells to impair the function of the tissue. With low dose the probability for such effect is zero. The threshold values for deterministic effects are high in practical sense. For example a dose of 0.15 Sv (150 mSv) is required for temporary sterility as a single dose or 0.4 Sv (400 mSv) per year for many years. Similarly the threshold value for detectable opacity of eye is fairly high (0.5 to 2.0 Sv). Such radiation doses are normally not received by radiation workers in occupational practice. The average radiation dose for radiation worker in medical set-up, be it radiology, nuclear medicine or radiotherapy, on a global basis does not exceed 3 mSv/year with few exceptions. Since there exists threshold, it is possible to “prevent” such effects.

**Stochastic effects**

At doses below the threshold for deterministic effects, stochastic effects are possible. Stochastic implies “random or statistical in nature”. The probability of the effect, rather than severity, is a function of dose, probably with no threshold. The effects included in this category are carcinogenic and genetic effects. Of the various forms of damage that radiation can cause in cells, the most important is that in the DNA. Damage in the DNA may prevent the survival or reproduction of the cell but frequently the damage is repaired by the cell. If repair is not perfect,
it may result in a viable modified cell. These modified cells may lead to cancer as a result of exposure to other carcinogens or mutants either before or after the exposure to radiation. When a modified cell retains reproductive capacity it may give rise to a clone of modified cells that eventually results in cancer. A modified germ cell in the gonads, with the function of transmitting genetic information to descendants of an exposed individual, may transmit incorrect hereditary information and may cause severe harm to some of these descendants. These somatic and hereditary effects, which may start from a single modified cell, are called stochastic effects. The lack of threshold for such effects poses difficulty in radiation protection.

**Sources of human data on radiation induced cancer**

The risk of cancer following radiation exposure is evaluated from epidemiological studies. Of particular value is the follow-up of the survivors of the atomic bombings of Hiroshima and Nagasaki in 1945 for which a pattern of increasing risks with increasing dose has been demonstrated for leukemia and many solid cancers. Shimizu et al. has reported on cancer mortality among 76000 atomic bomb survivors followed from 1950 to 1985. This is the only study which includes both sexes and all ages and is most meaningful in determining risk estimates.

Information is also available from a wide range of studies of patients irradiated for medical reasons, such as women with tuberculosis (TB) who received multiple chest fluoroscopies, and children irradiated for benign conditions such as *Tinea capitis* (ringworm of the scalp). UNSCEAR Report of 1994 reviews the relevant studies. Table 2 gives summary of 5 sources of epidemiological studies on radiation induced cancer risks. Effects of low dose chronic exposure of radiation workers in UK and elsewhere have been reported recently. It must be remembered that the risk at low level is quite small which demands very large sample data for statistical power. The statistical

<table>
<thead>
<tr>
<th>Table 2: Features of some epidemiological studies of radiation-induced cancer risks</th>
<th>Parameter</th>
<th>Life span study (LSS) of Japanese atomic bomb survivors (Shimizu et al)</th>
<th>Ankylosing Spondylitis study (ASS) (Weiss et al)</th>
<th>Massachusetts tuberculosis patients given chest fluoroscopies (Boice et al)</th>
<th>Children in Israel irradiated for ringworm of the scalp (Ron et al)</th>
<th>UK National registry for radiation workers (Kendall et al)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Population size</td>
<td>75991 (with DS86 doses)</td>
<td>14109</td>
<td>2573</td>
<td>1084</td>
<td>95247</td>
<td></td>
</tr>
<tr>
<td>2. Period of follow-up</td>
<td>5-40 years following exposure</td>
<td>Up to over 50 years (mean 25.2 yrs)</td>
<td>Up to over 50 years (mean 30 years)</td>
<td>Up to over 50 years (mean 26 years)</td>
<td>Up to over 50 years (mean 30 years)</td>
<td>Up to over 50 years (mean 26 years)</td>
</tr>
<tr>
<td>3. Ranges of:</td>
<td>(a) ages at exposure</td>
<td>All</td>
<td>Virtually all</td>
<td>Under 15 to over 40</td>
<td>Up to 5 years</td>
<td>Up to 15 years</td>
</tr>
<tr>
<td></td>
<td>(b) sexes</td>
<td>Female</td>
<td>Female</td>
<td>Male &amp; Female</td>
<td>Male</td>
<td>Male &amp; Female</td>
</tr>
<tr>
<td></td>
<td>(c) ethnic groups</td>
<td>Japanese Western (UK)</td>
<td>Western (N. American)</td>
<td>Medical/therapy for non-malignant disease</td>
<td>Medical/therapy for non-malignant disease</td>
<td>Medical/therapy for non-malignant disease</td>
</tr>
<tr>
<td>4. Setting in which exposure was received</td>
<td>War</td>
<td>Medical/therapy for non-malignant disease</td>
<td>Occupational</td>
<td>Occupational</td>
<td>Occupational</td>
<td></td>
</tr>
<tr>
<td>5. Range organs irradiated</td>
<td>All</td>
<td>All (but mainly those in proximity to spine)</td>
<td>Mainly breast &amp; lung</td>
<td>Mainly brain</td>
<td>Mainly breast</td>
<td></td>
</tr>
<tr>
<td>6. Availability of dose estimates</td>
<td>Individual basis</td>
<td>Mean organ doses: indiv. only for red bone marrow at present</td>
<td>Organ doses: Individual basis</td>
<td>Brain, thyroid &amp; skin doses: individual basis</td>
<td>Individuals whole-body external doses</td>
<td></td>
</tr>
<tr>
<td>7. Range of doses</td>
<td>Mainly 0-4 Gy</td>
<td>Mainly 0-4 Gy</td>
<td>Mainly 0-3 Gy</td>
<td>Brain: 0-6 Gy (mean 1.5 Gy) Thyroid: 0-0.5 Gy (mean 0.09 Gy)</td>
<td>Mainly 0-0.5 Gy (mean 0.03 Gy)</td>
<td></td>
</tr>
<tr>
<td>8. Dose rate</td>
<td>High</td>
<td>High</td>
<td>High, but highly fractionated</td>
<td>Low</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>9. Radiation Quality</td>
<td>Mainly low-LET</td>
<td>Low-LET</td>
<td>Low-LET</td>
<td>Low-LET</td>
<td>Mainly low-LET</td>
<td></td>
</tr>
</tbody>
</table>
power of an epidemiological study to detect an excess risk associated with ionising radiation exposure depends upon many factors. These include the number of people in the study and the period over which they are followed, the underlying level of cancer risk in the population, the distribution of dose in the study group, the magnitude of the increase in the risk per unit dose, and the consequent distribution of expected excess cancer risk in the population.

**Dose-response analysis**

At higher doses, linear response with dose is accepted universally. However, there are controversies on the dose response at low-level exposure, the response being not linear throughout. One of the main epidemiological sources of information of the shape of the dose response relationship for radiation-induced cancer is the study of the atomic bomb survivors of Japan. Pierce and Vaeth examined mortality data up to 1985, based on the DS86 dosimetry. In their analyses, those with shielded kerma estimates in excess of 4 Gy were excluded, in view of an apparent leveling-off in the dose-response beyond 4 Gy that may be associated with errors in the estimates of such high doses or with cell killing. Pierce and Vaeth estimated a linear extrapolation overestimation factor (LEOF), i.e., the ratio of the slope from the fit of a linear dose-response model to the slope at low doses from fitting a linear-quadratic model (comparable to the DDREF of ICRP).

For leukemia mortality the maximum likelihood estimate for the LEOF from the Japanese data was 2.0 (90% CI 1.1 to at least 3.1) with adjustment for random dosimetry errors; the corresponding values for leukemia incidence were 2.5 (90% CI 1.3 to 8.4). Thus these data suggest that a linear dose-response model does not provide a good fit and that linear-quadratic model with an LEOF of about 2 is to be preferred, i.e., the slope of the dose-response at low doses is approximately half of that based on a linear dose-response. Dose-response analyses have also been performed for some groups with medical exposures. Boice et al. studied the relationship between the risk of breast cancer and dose for women in Massachusetts (USA) given multiple chest X-ray fluoroscopies. For this study, the doses were mostly in the range 0-3 Gy. A linear dose-response model is found to provide as good a fit to these data as a linear-quadratic model, whereas a purely quadratic model did not fit well. In a study of Canadian tuberculosis patients given fluoroscopies, Miller et al. showed that linear dose-response model fitted well with the data on the breast cancer among patients in Canadian provinces other than those in Nova Scotia. (In Nova Scotia patients, who generally received higher doses, the dose-response relationship was also linear, but with a steeper slope than that for other Canadian patients). Among the women given radiotherapy for cervical cancer, the risk of leukemia increased with dose up to 4 Gy in a linear manner, although the data were also consistent with a quadratic dose-response; beyond 4 Gy the risk decreased, probably as a result of cell death.

The relative risk of mortality for leukemia and for all other cancers in Japanese atomic bomb survivors is given in Table 3. Mortality rates for both cancer groups are high among those who received 0.20-0.49 Gy, compared to those with doses under 0.01 Gy. Within the range 0-0.49 Gy, the estimated trend in

<table>
<thead>
<tr>
<th>Absorbed dose (Gy)</th>
<th>Site of cancer</th>
<th>0.01 - 0.05</th>
<th>0.06 - 0.09</th>
<th>0.10 - 0.19</th>
<th>0.20 - 0.49</th>
<th>0.50 - 0.99</th>
<th>1.00 - 1.99</th>
<th>≥2.00</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cancers</td>
<td>1.06</td>
<td>1.08</td>
<td>1.12</td>
<td>1.36</td>
<td>1.66</td>
<td>2.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>except leukemia</td>
<td>(1.00-1.12)</td>
<td>(0.98-1.19)</td>
<td>(0.97-1.15)</td>
<td>(1.03-1.21)</td>
<td>(1.23-1.31)</td>
<td>(1.43-1.90)</td>
<td>(1.66-2.50)</td>
<td></td>
</tr>
<tr>
<td>Leukaemia</td>
<td>0.99</td>
<td>1.08</td>
<td>1.79</td>
<td>4.15</td>
<td>8.01</td>
<td>18.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.68-1.40)</td>
<td>(0.87-1.22)</td>
<td>(1.18-2.68)</td>
<td>(2.76-6.19)</td>
<td>(5.34-11.90)</td>
<td>(12.1-28.2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Estimated relative risk of mortality for ranges of absorbed dose above and below 2.0 Gy in the life span study cohort of Japanese atomic bomb survivors (Shimizu et al.)

- DS86 dosimetry, both cities, both sexes, all ages at exposure, 1950-1985: comparison is with the control (0 Gy) group.
- 90% CI given in parentheses.
relative risk per gray was 2.40 for leukemia ($p<0.05$) and 0.38 for all cancers other than leukemia ($p<0.05$). The latter estimate is similar to the value for the whole dose range, in linear dose-response mentioned earlier. However, the estimated slope for leukemia under 0.5 Gy is about half of that of whole dose range, in consistence with the linear-quadratic dose-response described above.

**Thyroid cancer**

Studies of thyroid cancer incidence following radiation exposure have been reviewed by Shore and a combined analysis of seven studies has recently been performed by Ron et al. Among these people with external low-LET exposures, including the Japanese atomic bomb survivors, the excess relative risk per gray (ERR Gy$^{-1}$) tends to be higher than that for most solid cancers. Furthermore, this measure of risk is high for those irradiated at young ages. For example, the ERR Gy$^{-1}$ among atomic bomb survivors irradiated at young ages was 5.1 whereas it was 0.8 for those irradiated as adults. Data on thyroid cancer risk are available from Chernobyl accident of 1986. A highly significant increase in the incidence of thyroid cancer among those persons in the affected areas who were children in 1986 is the only clear evidence to date of a public health impact of accidental radiation exposure. It is reported that incidence of childhood thyroid cancer (0-14 y) prior to the accident in Belarus was between 0 and 0.14/100,000/y and it jumped to 2.5/100,000/y in 1991, about a 20-fold increase. About 800 cases in children under 15 years have been reported till the end of 1995. Thyroid cancer is usually non-fatal with early diagnosis, treatment and attention. Only three of the affected children have died of thyroid cancer so far. These aggressive papillary thyroid cancers in children respond favourably to standard therapeutic procedures.

**Childhood cancer after in utero exposure**

The main sources of information on cancer risks following radiation exposure in utero are studies of those with prenatal diagnostic X-ray exposures, as well as those irradiated as a consequence of the atomic bombings of Hiroshima and Nagasaki. Among the former category, the most powerful study is a national case-control study of childhood cancer mortality in UK, namely the Oxford Survey of Childhood Cancer (OSCC). Bithell has shown that the OSCC contains 73% of the total statistical information (reflecting the precision of risk estimates) among the prenatal X-ray studies presented in Table 4. Consequently, the width of the 95% confidence interval for the relative risk, as given in this table, is smallest for the OSCC. The OSCC was started in the mid-1950s and, up to 1979, mothers of 14759 cases and the same number of matched controls had been interviewed. During the late 1950s they reported a doubling in the risk of childhood cancer associated with prenatal X-ray exposure. Later analyses covering a longer period indicated a falling risk with time and an average raised risk of about 40% (95% CI 31.5-50), i.e., an ERR of 0.4. Some of the other studies listed in Table 4 did not show a statistically significant increase in risk (at the 5% level), owing to the smaller number of cases and controls involved. This is reflected by the wider confidence intervals for the relative risk quoted in Table 4 some of which include the value 1 (consistent with no excess). However, studies of prenatal X-rays other than the OSCC have yielded values for the relative risk of childhood cancer similar to or consistent with that from the OSCC. Based on the OSCC and other studies, the combined estimate of the raised risk is 39% (95% CI 31.5-37), i.e., an ERR of 0.39 which is a statistically significant increase in risk.

These studies, together with data from the long-term follow-up of those exposed to atomic bomb radiation, suggest strongly that irradiation in utero increases the risk of cancer. Furthermore, the statistically significant increase in childhood cancer risk seen in the OSCC arises from doses of about 10-20 mGy (low-LET), reflecting the high excess relative risk.

**Low dose rates occupational exposures**

Studies on radiologists in the UK and USA and on medical X-ray workers in China have shown raised risks for leukemia and other cancers. Although the dose information is not particularly good, it is thought that some of the early radiologists and the Chinese workers received doses in excess of 1 Gy, possibly at high dose rates. The first analysis of the UK National Registry for Radiation Workers (NRRW) examined cancer mortality in relation to radiation dose. Table 5 provides data covering over 950000 workers. The mean lifetime dose received was 33.6 mSv; however, over 8000 workers
had a lifetime dose in excess of 100 mSv. For all malignant neoplasms, the trend in the relative risk with dose shown in Fig 1 was positive but was not statistically significant \((p=0.10)\). Based on a relative risk protection model, the central estimate of the lifetime risk of these data was 10% \(Sv^{-1}\), which is 2.5 times the value of 4% \(Sv^{-1}\) cited by ICRP\(^{39}\) for risks associated with exposure of workers (based on applying a DDREF of 2 to the Japanese data). The 90% confidence interval for the NRRW-derived risk ranged from a negative value up to about six times the ICRP value. There was also an indication of an increasing trend with dose in the risk of multiple myeloma \((p=0.06)\): the estimated trend in the relative risk was about three times that obtained from the Japanese survivor mortality data under a linear dose-response model, with a 90% confidence interval ranging from just under zero to twenty times the Japanese value.

### Summary

1. The data from survivors of bombing of Hiroshima and Nagasaki in 1945 indicate a dose-dependent pattern of increasing risk of leukemia and most solid cancers. The increase is significant at acute doses in the range 200-500 mGy and above. 2. The data from patients irradiated for medical reasons suggest a statistically significant increase in the risk of the thyroid cancer at doses 100-300 mSv received in childhood. 3. Risk of childhood cancer following obstetric radiography is indicated in several studies.
Table 5—NRRW study population by lifetime dose and employer (Kendall et al.)

<table>
<thead>
<tr>
<th>Employer</th>
<th>&lt;10.0</th>
<th>10.0-50.0</th>
<th>50.0-100.0</th>
<th>100+</th>
<th>Total workers</th>
<th>Collective dose (man Sv)</th>
<th>Mean dose (mSv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>British Nuclear Fuels</td>
<td>10223</td>
<td>7464</td>
<td>3083</td>
<td>4847</td>
<td>25617</td>
<td>1805</td>
<td>70.4</td>
</tr>
<tr>
<td>Ministry of Defence Atomic Weapons Establishment</td>
<td>8599</td>
<td>1249</td>
<td>239</td>
<td>154</td>
<td>10241</td>
<td>85</td>
<td>8.3</td>
</tr>
<tr>
<td>Defence Radiological Protection Service</td>
<td>20717</td>
<td>4635</td>
<td>1018</td>
<td>876</td>
<td>27246</td>
<td>381</td>
<td>14.0</td>
</tr>
<tr>
<td>Nuclear Electric</td>
<td>4490</td>
<td>2533</td>
<td>696</td>
<td>480</td>
<td>8199</td>
<td>198</td>
<td>24.1</td>
</tr>
<tr>
<td>United Kingdom Atomic Energy Authority</td>
<td>14916</td>
<td>5455</td>
<td>1631</td>
<td>1912</td>
<td>23914</td>
<td>730</td>
<td>30.5</td>
</tr>
<tr>
<td>Total</td>
<td>58945</td>
<td>21336</td>
<td>6667</td>
<td>8269</td>
<td>95217</td>
<td>3198</td>
<td>33.6</td>
</tr>
</tbody>
</table>

Fig. 1—Relationship between dose of radiation and presence of malignant neoplasms as reported in the National Registry for Radiation Workers (NRRW), UK*. (C.I = Confidence Interval)
These studies, together with data from the long-term follow-up of those exposed to atomic bomb radiation, suggest strongly that irradiation in utero increases the risk of cancer. The Oxford Survey of Childhood Cancers reported 40% increase in the childhood cancer rate (up to 15 years of age) following radiation doses 10-20 mGy (low-LET). Data on workers occupationally exposed to low-LET radiation at low dose rates indicate excess cancer risks, notably for leukemia. The statistical uncertainties are, however, sufficiently large for the risk estimates to be consistent with those derived by extrapolation from high dose rate studies based on a DDREF of 2, as well as with values differing by at least a factor of two. Although these low dose rate studies are not, therefore, strong enough to allow the derivation of quantitative risk estimates they are generally consistent with the estimates derived by ICRP in Publication 60 and with the assumption of a raised risk of cancer even at low doses.

Acknowledgement
The permission granted by the National Radiological Protection Board, UK to use the data included in the Tables is gratefully acknowledged.

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