Chapter 13

Biological Effects of Exposure to Radiation

Current radiation protection guidelines are predicated on the assumption that any radiation exposure carries some risk of a detrimental effect. In this chapter the biological effects of exposure to various levels of ionizing radiation and the principles that are used to support current guidelines will be presented.

13.1 Categorization of Effects \(^{i, ii}\)

Radiation effects can be broadly categorized as stochastic or non-stochastic. Stochastic effects have the following properties:

1. The probability that the effect will occur increases with increased absorbed dose.
2. There is no relationship between the magnitude of the absorbed dose and the severity of the effect. For an individual this is an all or none response, either the effect is seen or it isn't.
3. The same effect can be seen in unexposed individuals.

Stochastic effects caused by radiation exposure include cancer and hereditary defects.

Non-stochastic effects have the following properties;

4. There is a threshold of dose below which no effect is seen.
5. The effect can be directly attributed to radiation exposure.
6. The magnitude of the effect increases with increasing radiation dose.

Non-stochastic effects include many of the acute effects described in the following section, including non-malignant damage to the skin, cell depletion in the bone marrow causing hematological deficiencies, gonadal cell damage leading to impairment of fertility, and cataract formation.

13.2 Dose Response Relationships

There is much debate regarding the shape of the dose response curve at low doses for long term stochastic effects. A number of models have been used or advocated including a linear model, a linear quadratic model, and a quadratic model. Some models advocate a threshold below which no effects are seen and some do not. Some investigators purport that there is a beneficial effect associated with low level exposures (radiation hormesis). For radiation protection purposes, the International Commission on Radiological Protection (ICRP) has made certain simplifying assumptions as follows: \(^{iii}\)

- Within the range of exposure conditions usually encountered in radiation work, there is a linear relationship without a threshold between dose and the probability of effect;
- The total risk to a tissue or organ is a simple summation of the doses received;
- The collective dose equivalent is an index of the total detriment to a population; and
The severity of effect is independent of dose.

13.3 Acute Radiation Exposure and Short Term Effects\textsuperscript{iv}, \textsuperscript{v}

Large radiation doses received over a relatively short time interval can cause acute or prompt effects. Characteristic of non-stochastic effects, most acute radiation effects have thresholds and, once caused, increase in severity with increased radiation dose.

Since individuals are not equally sensitive to radiation, the dose necessary to cause a given effect will not be the same in all individuals. Also, the organs affected by the syndrome are not equally sensitive to radiation, and as a result, each has its own threshold above which effects are caused.

One of the most sensitive biological indicators of radiation damage is a change in the numbers of peripheral blood cells, usually beginning at whole body doses between about 25 and 50 rads. The degree and magnitude of these changes increase with higher doses. The primary symptoms can be summarized as follows:

**Leukocytes (White Blood Cells)**

*Total White Cell Count* - A transitory increase in number is seen during the first two days or so after exposure followed by a decrease to below normal levels. A minimum is reached in the seventh or eighth week following exposure. Recovery may require several months.

*Neutrophils* - The neutrophil count parallels the total white blood cell count. The initial increase in the white blood cell count is apparently caused by mobilization of neutrophils.

*Lymphocytes* - A sharp drop in number is seen within hours of exposure. The count remains depressed for several months. Recovery may take months or even years.

The total white cell and neutrophil counts are of limited usefulness as an index of severity of radiation exposure because of the wide fluctuations and the delay before the minimum levels are observed. The lymphocyte count is more useful since depression occurs within a few hours of exposure; however, there is little relative difference in fluctuation with small or large doses.

**Erythrocytes (Red Blood Cells)**
A slow drop in number begins several days after exposure. A minimum in the red cell count is reached within several weeks after exposure. A slow recovery occurs over a period of weeks. The change in the red cell count is much less striking than the change in the white blood cells and platelets, especially in the sub-lethal range.

**THROMBOCYTES (PLATELETS)**

A steady decrease in number occurs reaching a minimum in about one month. Recovery is very slow, lasting several months or even years. The platelet count appears to be the most useful indicator of the severity of exposure because the degree of depression from the normal value is roughly proportional to the estimated whole-body dose. The main disadvantage in its use is the delay seen in the depression.

13.3.1 The Acute Radiation Syndrome

Acute exposure of the whole body at doses above about 200 rads severely depletes radiosensitive cells in many organs simultaneously. The combined effects cause the acute radiation syndrome, otherwise known as radiation sickness. The acute radiation syndrome can be subdivided into the hematopoietic syndrome, the gastrointestinal syndrome, and the central nervous system syndrome. Nausea and vomiting, malaise and fatigue, increased body temperature, and blood changes are symptoms that are common to all subdivisions of the acute radiation syndrome.

13.3.1.1 Hematopoietic Syndrome

A dose of about 200 rads causes depression of blood cell formation. At a dose of about 400 rads, complete ablation of the bone marrow occurs. At these doses, spontaneous regrowth of the bone marrow is possible if the individual survives the initial physiological effects of destruction of the marrow. A dose of about 700 rads causes irreversible destruction of marrow. The symptoms seen as a result of these changes include hemorrhage due to platelet deficiency, infection due to granulocyte deficiency, and anemia due to hemorrhage and red cell deficiency.

In addition, onset of nausea, vomiting, malaise, and fatigue may occur within several hours and epilation (loss of hair) may occur within 2 to 3 weeks. If the dose is sufficient to cause death, it will almost always occur within 1 to 2 months following exposure.

13.3.1.2 Gastrointestinal Syndrome

A dose of about 600 rads causes desquamation of the intestinal epithelium. In addition to the symptoms of the hematopoietic syndrome, severe nausea, vomiting, diarrhea, and dehydration begin soon after exposure. Death within 1 to 2 weeks is likely.

13.3.1.3 Central Nervous System Syndrome

At doses at and above 2000 rads the predominant symptomatology is related to central nervous system damage including ataxia, convulsions, and coma. Unconsciousness occurs within minutes of exposure followed by death within days to weeks, depending on the magnitude of the dose.
13.3.2 Mortality

Current estimates of the lethal dose for acute radiation exposure are based on animal studies, Japanese atomic bomb casualties, radiation accidents, and medical radiation therapy experience. Energy of radiation, fractionation of dose, geometry of exposure, type of radiation, method of exposure, and rate of exposure all have influence over human effects. While the setting of precise mortality values for man is not possible, many estimates have been made. The National Council on Radiation Protection and Measurement (NCRP) estimates that a mid-line absorbed dose in man of 260-325 rads is sufficient to cause death in 50% of exposed individuals within 30 days (LD-50/30) vii.

Cronkite viii estimates that, assuming no medical treatment is provided, the low lethal dose at which the most sensitive healthy individual would not survive is about 250 rads, the dose at which no individual would survive is about 500 rads, and the LD-50/60 to be about 350 rads. The most recent UNSCEAR report viii states that the LD-50/60 for acute irradiation is likely to be around 300 rad bone marrow dose in the case of humans receiving no or little medical treatment. This report also estimates that for healthy humans receiving good supportive medical treatment after irradiation (e.g., barrier nursing, antibiotics symptomatically and blood cell infusions), the LD-50/60 is likely to approach or equal 500 rad, and states that a dose of 700 rad would probably kill about 95% of healthy people.

13.4 Secondary or Delayed Effects ix

Delayed effects are usually manifested with doses of many hundreds or even thousands of rads. Because it is unlikely that an individual will survive whole body doses of this magnitude, delayed effects are usually observed with partial body doses such as with radiation therapies, accidents with large sealed sources, or accidents with x-ray diffraction equipment. A chronic change is often seen in the skin which includes telangiectasia, atrophy, and ulceration. Other examples include: lymphopenia, agranulocytosis, and anemia when exposure is to the hematopoietic system; suppression of thyroid secretion resulting from destruction of the normal bronchial and vascular tissues; histological sterility, complete absence of gametes, artificial menopause, and temporary sterility with high doses to the gonads.

13.5 Late Effects

Late effects may be caused by acute or chronic exposure to external or internal radiation sources. Most late effects are stochastic in nature, primarily cancers, but some are non-stochastic. Many of these effects will be discussed below. Delayed effects may not be manifested until 5 to 30 years after exposure.

Most cases of overexposure do not involve the whole body. Partial exposures may occur for many reasons; penetration to deep tissues may not be possible due to the type or energy of the radiation, the radiation field may be localized, portions of the body may be shielded, etc.

The organs that are most susceptible to radiation induced effects are the gonads, red bone marrow, bone surface, lung, thyroid, and breast. With the exception of the gonads, the primary somatic effect to these organs is induction of cancer. The primary stochastic and/or non-stochastic effects due to radiation injury are summarized below.
**GONADS**

*Stochastic* - The stochastic effects of primary concern are induction of hereditary defects and tumor induction. It is believed that the frequency of dominant, sex-linked, and certain chromosomal diseases would increase in direct proportion to dose. However, the hereditary detriment is likely to be less than the detriment due to somatic injury in the irradiated individual. The risk of serious hereditary ill health within the first two generations following irradiation of either parent is thought to be about $10^{-3}$ (1 in 10,000) per rem. Human gonads appear to have a relatively low sensitivity to induction of cancer by irradiation since no carcinogenic effects in these organs have yet been conclusively documented.

*Non-stochastic* - The primary non-stochastic effect is impairment of fertility. An acute dose of 30 rads to the testes or 300 rads to the ovaries may cause temporary sterility. Significantly higher doses can cause permanent sterility.

**RED BONE MARROW**

*Stochastic* - The primary stochastic effect is induction of leukemia. The incidence of leukemia appears to reach its peak within a few years after acute irradiation and returns to pre-irradiation levels after about 25 years. The risk factor for leukemogenesis is taken to be about $2 \times 10^{-5}$ (2 in 100,000) per rem.

**BONE SURFACE**

*Stochastic* - Irradiation of the endosteal cells and epithelial cells on bone surfaces carries a risk of about $5 \times 10^{-6}$ (5 in 1,000,000) per rem for induction of bone cancer.

**LUNG**

*Stochastic* - Cancer of the lung has been observed in miners exposed to radon and its decay products. It appears that the risk due to material distributed uniformly in the lung is greater than from material distributed non-uniformly. It is also likely that external irradiation of the lung can also induce cancer. The risk factor for lung cancer is taken to be $2 \times 10^{-5}$ (2 in 100,000) per rem.

**THYROID**

*Stochastic* - The epithelial cells of the thyroid follicles appear to be the cells at risk. The risk of cancer induction in the thyroid appears to be higher than $2 \times 10^{-5}$ (2 in 100,000) per rem. Because of man's success in treating thyroid cancer and the slow progress of this type of tumor, the overall mortality risk factor is taken as $5 \times 10^{-6}$ (5 in 1,000,000) per rem.

**BREAST**

*Stochastic* - During reproductive life, the female breast tissue may be one of the more...
radiosensitive tissues of the human body. For radiation protection purposes the risk factor is taken to be about $2.5 \times 10^{-5}$ (2.5 in 100,000) per rem.

**SKIN**

*Stochastic* - The risk that skin will develop a fatal cancer is very low compared with other tissues discussed here.

*Non-stochastic* - An acute dose of 200 to 300 rads of low energy x-rays causes erythema, a reddening of the skin similar to a sunburn or first degree thermal burn. A transient wave of mild erythema may occur within hours of exposure accompanied by a sensation of warmth or itching. More severe reddening occurs within two to three weeks following exposure, the interval decreasing with increased dose. Higher doses may cause changes in pigmentation, epilation, blistering, necrosis, and ulceration.

**EYE**

*Non-stochastic* - The lens of the eye is among the most radiosensitive tissues of the body. An acute dose of several hundred rads to the eye can cause acute conjunctivitis and keratitis. Doses on the order of 1500 rads can cause damage to the retina, cornea, conjunctiva, and optic nerve. Radiation induced cataracts form on the equatorial portion of the anterior epithelium of the lens. At high doses, cataracts develop within months and progress rapidly, clouding the lens completely. At lower doses the opacities may take years to develop and may remain small enough so that no significant vision impairment is caused. An acute dose as low as 100 rads can cause microscopic changes in the lens within minutes of exposure. The threshold of x ray induced cataracts appears to be about 200 rad from a single dose to 550 rad for doses fractionated over a period of 3-13 weeks. The BEIR V report states that the threshold for a vision-impairing cataract under conditions of highly fractionated or protracted exposure is thought to be no less than 800 rads.

### 13.6 Risks Associated with Radiation Exposure

For doses within the range of the occupational exposure limits, the relation between the dose received by any individual and any particular biological effect induced by irradiation has not been determined. Statistical limitations on all studies that have been conducted prevented extrapolation to low doses. For radiation protection purposes the ICRP has made simplifying assumptions regarding stochastic effects in the range of exposure conditions usually encountered in radiation work. The primary assumption is that there is a linear relationship without a threshold between dose and the probability of an effect.

The ICRP estimates of the risks of inducing a fatal malignant disease, non-stochastic changes, or substantial genetic defects expressed in liveborn descendants are shown in Table 13.1. The current NCRP risk estimates are in agreement with these values. The NCRP believes that risk estimates are likely to undergo substantial re-evaluation in the near future. This statement is supported by the Executive Summary of the National Research Council's BEIR V report which states the following:

"On the basis of the available evidence, the population-weighted average lifetime excess..."
risk of death from cancer following an acute dose equivalent to all body organs of 0.1 Sv (0.1 Gy of low-LET radiation) is estimated to be 0.8%, although the lifetime risk varies considerably with age at the time of exposure. For low LET radiation, accumulation of the same dose over weeks of months, however, is expected to reduce the lifetime risk appreciably, possibly by a factor of 2 or more. The Committee's estimated risks for males and females are similar. The risk from exposure during childhood is estimated to be about twice as large as the risk for adults, but such estimates of lifetime risk are still highly uncertain due to the limited follow-up of this age group.

<table>
<thead>
<tr>
<th>ORGAN</th>
<th>RISK PER REM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonads (genetic)</td>
<td>$4 \times 10^{-4}$</td>
</tr>
<tr>
<td>Whole Body</td>
<td>$4 \times 10^{-5}$</td>
</tr>
<tr>
<td>Breast</td>
<td>$2.5 \times 10^{-5}$</td>
</tr>
<tr>
<td>Red Bone Marrow (leukemia)</td>
<td>$2 \times 10^{-5}$</td>
</tr>
<tr>
<td>Lung</td>
<td>$2 \times 10^{-5}$</td>
</tr>
<tr>
<td>Thyroid</td>
<td>$5 \times 10^{-6}$</td>
</tr>
<tr>
<td>Bone Surface</td>
<td>$5 \times 10^{-6}$</td>
</tr>
<tr>
<td>All Other Tissues Combined</td>
<td>$5 \times 10^{-5}$</td>
</tr>
<tr>
<td>Total Somatic Risk (Cancer Mortality)</td>
<td>$1 \times 10^{-4}$</td>
</tr>
<tr>
<td>Total Genetic Risk</td>
<td>$4 \times 10^{-5}$</td>
</tr>
</tbody>
</table>

The National Research Council's cancer mortality risk estimate of 0.8% per 0.1 Sv (8 x 10^{-4} per rem or 8 in 10,000) is in fact substantially higher than the ICRP risk estimate of 1 x 10^{-4} per rem (1 in 10,000).

Furthermore, on June 22, 1990, the ICRP released a statement xvi in which it said:

"New data and new interpretation of earlier information now indicate with reasonable certainty that the risks associated with ionizing radiation are about three times higher than they were estimated to be a decade ago . . . . This increase calls for some quantitative changes in the Commission's recommendations. One such change to be recommended by the Commission is a reduction of the dose limits for occupational exposure. The current figure of 50 millisievert (5 rem) in a year will be reduced to 20 millisievert (2 rem) in a year, with some provision to allow year-to-year flexibility."
13.7 Considerations for Women of Reproductive Age

The NRC has established a regulatory guide suggesting that women of reproductive age be provided with information regarding effects of radiation on the fetus and embryo. The portion of this document intended to be provided to female radiation workers of reproductive age can be obtained from the Radiation Safety Section (RSS) upon request.

References


