A. The Cell - Basic Unit of Structure

This section will be devoted to the effects of ionizing radiation on the human body. The structure of the body is quite complex, and it is often of value to deal with effects at certain levels of organization within the body. Thus, the human body contains many organs, each of which is composed of two or more types of tissue. In turn, a tissue is composed of similar cells, there being four types of tissues in the body: epithelial, connective, muscle, and nerves. The job of a tissue is to perform a special body function. The cell, which makes up the tissues of the body, is the basic unit of structure and function in the body. A cell contains many elements; hydrogen, oxygen, carbon and nitrogen are the main components. Human cells vary in size from approximately 3-100 μm.

A cell is normally composed of a nucleus surrounded by cytoplasm, both encased in membranes. Although highly complex in structure, the nucleus and cytoplasm contain about 70 percent water. The vital part of the cell is the nucleus, usually an oval body located near the center of the cell. From a chemical standpoint, the nucleus is quite active. The normal growth of the cell is controlled by the nucleus. Also, it initiates cell division and controls the repair of injured cells. The cytoplasm is a more or less colorless liquid substance. It secretes enzymes, and controls absorption and excretion in the cell.

Among the complex structures found in the cell are carbohydrates, fats, proteins and nucleic acids. Carbohydrates serve as food for the cell and as structural units. Fats store chemical energy. Proteins, which differ from each other by the number, sequence, length and arrangement of amino acid chains, are involved in all the metabolic activities (chemical reactions) which sustain cell life. Amino acids are composed of NH₂ groupings and about 20 amino acids are found in the proteins of mammals. The nucleic acids, DNA (deoxyribonucleic acid) and RNA (ribonucleic acid) function together to produce the cell's proteins. Most of the DNA is found in the nucleus. The DNA molecules are thought to carry the genetic code necessary for proper cell reproduction. The RNA is distributed throughout the cell and is thought to be the messenger which translates
the information contained in the DNA into instructions for protein production.

Many body cells have only a limited life span. In order that their functions be carried on, cells divide at a certain stage in their life (mitosis). The daughter cell then takes over the functions of the parent cell. As a cell divides, there appear in the nucleus threadlike structures called chromosomes. The chromosome number is fixed for a given species (23 pairs in human cells). Arranged linearly along the chromosomes are the genes which determine hereditary characteristics. Prior to cell division, the number of chromosomes is temporarily doubled. When a cell divides, the daughter cell receives a duplicate set of chromosomes from the parent as well as identical genes. If the process is normal, no alterations or changes occur. However, any changes which do occur in the chromosomes and/or genes are called mutations. These changes or mutations can then affect either the daughter cell or future cells.

The development of an organ then proceeds from mitosis, the term used to designate cell division. In a bisexual species, the union of two cells (gametes) - one from the male and the other from the female - produces an original cell from which the species will be reproduced.

This cell then undergoes a number of divisions which increase its number. In the embryonic state, all the cells look alike. However, changes in the structure of the cells begin to take place. The changes enable the cells to perform specialized functions. This process of change is referred to as differentiation. The result of this process is the development of differential cell types or lines. One of these lines is the germ line, the rest are called somatic. The germ line gives rise to either male or female gametes. The somatic lines develop into the tissues of the individual.

Since only the gametes can be transmitted to future generations of the species, damage to somatic cells is limited to the individual. Damage to the offspring of an individual may occur when there is damage to the cells of the germ line.

A great many agents can cause injuries to the cells. When such injury occurs, the effects are the same regardless of the agent which
caused the damage. Ionizing radiation produces damage to cells, but in a mostly nonspecific way; that is, other physical and chemical substances cause the same effects because the body responds the same to certain cell damage regardless of the cause.

Radiation passing through living cells will directly ionize or excite atoms and molecules in the cell structure. These changes affect the forces which bind the atoms together into molecules. If the molecule breaks up (dissociates), some of the parts will be charged. These fragments are called free radicals and ions, and are not chemically stable. Free radicals are electrically neutral structures with one unpaired electron. Because the cell has a higher water content, the most important free radicals are those formed from water molecules. For example, an excited \( \text{H}_2\text{O}^* \) molecule may dissociate into

\[ \text{H}_2\text{O}^* \rightarrow \text{H}^* + \text{OH}^* , \]

in which the hydrogen radical \( \text{H}^* \) has an unpaired \( e^- \) and the \( \text{OH}^* \) radical will have nine \( e^- \), one of which will be unpaired. The free radicals are very reactive chemically, and when combining can produce hydrogen peroxide (\( \text{H}_2\text{O}_2 \)), which is a chemical poison, and the \( \text{HO}^* \) radical which is more damaging than peroxide. Further effects are produced when the radicals and ions interact with other cell material. In this way, damage is caused in a direct and indirect manner. The role that each type of action plays in the total damage to the cell is still an unsolved problem. Of the damage which is done, the effects are greatest in the nucleus of the cell, but injury to the cytoplasm can also cause serious effects in the cell.

The total effect on cell processes is a function of the dose of radiation. The cell processes will be affected in varying degrees up to the ultimate result - cell death. Some damage to the cell may be repaired. This can be accomplished by action of the cell itself, or by replacement of badly injured cells in a given tissue through mitosis of healthy cells. On the other hand, if the extent of the damage to an organ is quite large,
the organ may not be able to repair itself. That is, damaged cells may show confused growth but eventually be unable to divide. Or the cells may begin to exhibit uncontrolled growth. Although many factors are important in assessing the total damage, it seems likely that most cell functions and structures are somewhat impaired by radiation.

B. Radiosensitivity

Since the cells which make up the tissues of the body differ both in appearance and function, one might suspect that their response to radiation would also differ. Such is the case, and this property is known as the radiosensitivity of the cell. The first statement about this property was given by Bergonie and Tribondeau. They found that the radiosensitivity of a tissue is directly proportional to the reproductive capacity and varies inversely with the degree of differentiation. Since then, other factors have been found which affect the radiosensitivity. Among these are the metabolic state of the cell, the state of cell division, and the state of nourishment. It turns out that to produce a given effect, the necessary radiation dose varies inversely as the relative sensitivity of the given tissue.

Thus, cells which are most active in reproducing themselves, cells which have a high metabolic rate (rate of chemical changes) in the cell, and those cells which are more nourished than others are more sensitive to radiation. Also, there is evidence that cells are more susceptible to radiation at certain stages of division than at others. Moreover, cells not fully mature will also be more harmed by radiation than mature cells. In the body, bone marrow, lymphoid tissues, and the reproductive organs rank among the most radiosensitive. Muscle and bone cells are the least radiosensitive.

C. Radiation Damage

As has been pointed out, damage to somatic cells is limited to the individual whereas damage to germ cells may result in damage to the
offspring of an individual. One may broadly classify biological effects in man as somatic or hereditary. Somatic effects include any and all types of damage which affect only the individual; hereditary effects are those which can be transmitted to a future generation. Thus, damage to the genes of a somatic cell may produce damage to a daughter cell, but this would be a somatic effect, not hereditary. The term genetic damage refers to effects caused by chromosome and/or gene mutations. This may lead to hereditary effects only when the damage affects the germ line since only then can these effects be transmitted to a future generation.

D. Factors Influencing Radiation Effects

The radiation effects in man and animals are usually discussed in terms of total body and partial body irradiation, and with reference to damage to an organ. Because of the importance of some organs in the body, certain damage to these can induce effects in other organs. A number of physical factors are important in the determination of radiation effects:

1) sensitivity of the individual—for a select group, the effects may differ greatly from those in a heterogeneous group;

2) nature or type of radiation—some types of radiation are more effective in producing damage;

3) the absorbed dose—this is a function of the energy absorbed per gram of tissue;

4) time distribution or fractionation—a lethal dose given in a short time may not be lethal if protracted over a long time;

5) dose distribution—is the total body involved or only a specific organ?

6) age at irradiation—response is altered during growth in some systems.

The nature, severity and duration of biological effects depend upon the above and other factors. The combination of factors makes the effects on different organs differ for changes in the number of relevant parameters.
1. **Individual Sensitivity - Dose-Effect Curve**

Because a number of factors enter into the response of individuals to radiation, one might expect an effect to be seen in some at a lower dose than others. This may be due to certain host factors in the individual, such as general health, previous exposure to other agents, etc. Such a variation is seen, so that, if one studies the fraction of individuals which exhibit a given effect as the dose is varied, a dose-effect curve (Figure 5.1) is obtained. In the figure, for very low doses, no effects are seen. As dose is increased, the % affected increases with increased dose. Above 50% affected, the rate of increase slows, and larger doses are required to produce the effect in the remaining population. In the study of radiation effects, the dose \( D \) at which 50% of the population is affected is generally used as the reference dose. If the effect is death, the symbol \( LD_{50} \) called the median lethal dose (lethal

![Figure 5.1 Dose-effect relationship.](image-url)
dose to 50% of the exposed), is used. Moreover, since the time for an effect to show up may also vary, the symbol LD_{50/30} (lethal dose to 50% of the exposed within 30 days of irradiation) may be used.

Getting back to the dose-effect curve, we note that at D_{50}, half of the exposed would show the particular biological effect. This means that a single value of the dose cannot adequately describe the probability for all individuals. That is, almost half of those exposed show the effect for less than D_{50}. On the other hand, half have not yet shown the effect at D_{50}. This type of statistical behavior is typical of the response to radiation seen in mammals and implies a normal distribution of sensitivity with respect to dose.\textsuperscript{2}

2. Type of Radiation

As discussed in Section 4.B, the damage done by radiation depends upon the type of radiation. Not all radiation types are equally effective in producing biological damage. In radiobiology, the effectiveness is determined by the relative biological effectiveness (RBE). This quantity can be determined if one can establish the effect and control the conditions of the exposure. For this case,

\[
RBE = \frac{\text{Dose of 200-250 kV x rays to produce the effect of interest}}{\text{Dose of comparison radiation to produce the same effect}}
\]

In radiation protection work, one cannot control the conditions of exposure or concentrate on one effect. Thus, the quality factor, Q, an assigned value, is used to denote that the degree of response is modified for the type of radiation. Both the quality factor and the RBE are related to the LET. In general, for high values of LET one finds high values of RBE, and high LET radiation is more effective in producing damage than low LET.

For low LET radiation (electrons), the ion density is low so that recombination of ions and radicals is less likely. This allows ions and radicals to diffuse through the medium easily to form other products. This would increase the contribution of indirect effects. In addition, the
the small electrons colliding with large DNA macromolecules tend to produce only small bond breaks. This tends to lessen the effect of direct action.

In the case of high LET radiation (protons and other heavy recoils), the ion density is greater promoting more recombination and less diffusion. This would work to reduce indirect action. The much larger protons colliding with DNA would tend to produce many large fragments, and even damage the macromolecule beyond repair. This would enhance the effect of direct action.

If one looks at cells exposed to both low LET and high LET radiation, the survival curve will look something like Figure 5.2. In curve A, a similar set of cells are irradiated by high LET particles. The simple exponential implies that cells become inactivated following a hit. That is, single events are important. In curve B, cells of both high and low sensitivity are irradiated. The initial dropoff suggests the rapid

![Figure 5.2 Survival curves for low LET and high LET radiation.](image)
inactivation of the high sensitivity cells. The latter straight portion represents the removal of the low sensitivity cells. Curve C is typical of most types of similar cells irradiated by low LET radiation (\(^{60}\)Co).\(^7\) The initial shoulder portion implies that cells sustain non-lethal damage at first, followed by more damage which inactivates the cell.

Many models have been suggested to explain the shape of the survival curves.\(^8\) The simplest model explains curve A by assuming an exponential in which the slope of the line is a constant \(1/D\). This model is compatible with the assumption of direct action (or single hits) being the important reactions. Curve C is better explained by assuming a multi-target, single hit model.\(^7\) In this view, a number, \(n\), of targets must all be hit at least once to kill the cell. This is consistent with the shoulder portion of the curve C, which indicates more interactions are necessary to inactivate cells. That is, sublethal damage is followed by lethal damage.

Some qualitative results which apply to high LET radiation are:

1) a smaller dose is required to achieve a given degree of effect,
2) the exponential survival curve implies little recovery from sublethal damage,
3) fractionation of dose seems to have little effect, and
4) the degree of damage is not affected greatly by dose rate.

For low LET, the following apply:

1) there is some recovery of sublethal damage,
2) fractionation of dose results in less effect, and
3) a dose rate dependence is seen, the effects of low dose rate are \(1/3\) to \(1/6\) those at high dose rate.

3. Absorbed Dose

The basic parameter, which can be associated with biological damage, is the energy absorbed per unit mass. However, we have seen that
the damage produced is also related to the type of radiation. But, in a given system, the absorbed dose for a given radiation type will acquire added significance in a small tissue mass. Moreover, for a very large energy deposition per unit mass, the absorbed dose will override the LET considerations.

4. **Time Distribution or Fractionation**

If a dose of some value is delivered in a number of smaller fractions, the effectiveness of the radiation is often reduced. This sparing effect is attributed to repair of sublethal damage and replacement of cells suffering lethal damage. For low LET damage, it is assumed that sublethal damage occurs before cell inactivation results. Since successive low LET doses, separated in time, are less effective than their sum delivered in a single, short dose, sublethal damage is somewhat repairable. When irradiation is given over many doses, repair occurs after each dose. In addition to repair, cell replacement is also able to offset cell death. Although little is known about the dose rate at which cell replacement counterbalances cell death, it is known that this effect acts to mitigate the effect of cell killing.

5. **Dose Distribution**

When the whole body is irradiated, the total effect is more severe for a given dose than if that dose were given to a specific organ. This indicates that when the tissue volume is reduced, the severity of the response is also reduced. The magnitude of this sparing effect has not been adequately measured.

6. **Age At Irradiation**

In addition to the fact that effects are more pronounced in the young, there is also an increased sensitivity in the unborn. Certain organs, such as bone and cartilage, show a definite response during growth.
but are relatively radioresistant when mature. Whereas, for the ovary, sensitivity for sterility decreases with age. Damage to the germ cells is of concern only during the period of child bearing. Some effects are irrelevant when the life expectancy of the individual is much less than the latent period required for the effect to show up.

E. Early Somatic Effects - Acute Radiation Syndrome

The somatic effects which are observed can be loosely divided into early and late effects. Although quite an arbitrary grouping, early effects are classed as those which appear within a few weeks after the exposure. The range of these effects as well as their duration depend upon the dose. For very high whole body doses, there are three basic forms of early or acute damage. In the range above about 20 Gy (2000 rad), the dose is fatal within a day or two. The same symptoms appear when the head suffers severe irradiation, which points to a breakdown of the central nervous system. This type of acute radiation syndrome is thus referred to as central nervous system death (CNS death).

For the range 5-20 Gy (500-2000 rad), symptoms may appear within hours. Death often occurs within a week or so. In this mode, the damage to the lining of the intestinal tract is the most severe. This form is called gastrointestinal tract death (GI death). At the lower end of this dose range, it is possible for one to survive this mode of death only to fall victim to the effects which prevail at lower doses.

At doses < 5 Gy (500 rad), the most important effect is damage to the blood forming organs. Since these centers are located in the bone marrow, this mode of death is often called bone-marrow death. The first signs may appear within a few days, depending upon the dose, and the total effect may not develop for a few weeks. Severe changes occur when the dose is > 2 Gy (200 rad). In the range above 3 Gy (300 rad), the damage is severe enough so that death becomes more and more probable.

In the preceding sections, the results are based on x and γ ray data. As such, the conversion to rem for other types of radiation is not justified in this instance.
The main clinical effects which follow acute exposure to total body doses of ionizing radiation are nausea, vomiting, loss of appetite and fatigue for doses > 1 Gy (100 rad) or so. As indicated above, the time of onset, the severity and the duration of the effects depend on the dose and the exposed organs. A summary of clinical effects for acute doses is given in Table 5.1 and may be used as a rough guide. Note the virtual absence of any symptoms in the dose range below 1 Sv (100 rem). Some people would be expected to have mild symptoms in the range 0.5-1 Sv (50-100 rem), because of differences among individuals. Below 0.5 Sv (50 rem), however, no symptoms at all are expected. In fact, special techniques are needed to detect doses this low.

Death occurs in a larger fraction of cases as the dose increases. If the dose becomes large enough, all cases of exposure result in death. In the range where survival is possible, the concept of the median lethal dose (LD50) is used. For man, the best estimate places the LD50 in the range of 3 to 5 Gy (300-500 rad). Of course, in this range all would have severe symptoms. Note that this dose refers to short-term total body radiation.

F. Late Somatic Effects

The problem in the study of late effects resulting from exposure to radiation is that the elapsed time may be rather long, thus making it hard to relate the cause to the effect. Since the late effects may be caused by many other agents besides radiation, there can be no positive assignment of the cause in most cases. At best, it can be shown that radiation increases the incidence of these nonspecific injuries.

The main late effects are discussed in the following.

1. Cancers

In its 1980 report, the Committee on the Biological Effects of Ionizing Radiation (BEIR) indicated that cancer was considered to be the most important somatic effect of low-dose ionizing radiation. Cancer
Therapeutic Range - 1 to 10 Sv
Lethal Range - Over 10 Sv

<table>
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<tr>
<th>Range:</th>
<th>Subclinical 0 to 1 Sv</th>
<th>1 to 2 Sv</th>
<th>2 to 6 Sv</th>
<th>6 to 10 Sv</th>
<th>10 to 50 Sv</th>
<th>Over 50 Sv</th>
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</thead>
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<tr>
<td>Incidence of Vomiting:</td>
<td>None</td>
<td>1 Sv: 5%</td>
<td>3 Sv: 100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Delay Time:</td>
<td>-</td>
<td>3 Hours</td>
<td>2 Hours</td>
<td>1 Hour</td>
<td>30 min</td>
<td>30 min</td>
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<tr>
<td>Leading Organ:</td>
<td>None</td>
<td>Hematopoietic Tissue</td>
<td>GI Tract</td>
<td>Central Nervous System</td>
<td></td>
<td></td>
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<tr>
<td>Characteristic Signs:</td>
<td>None</td>
<td>Moderate Leukopenia</td>
<td>Severe Leukopenia, Hemorrhage, Infection, Purpura, Epilation Above 3 Sv</td>
<td>Diarrhea, Fever, Disturbance of Electrolyte Balance</td>
<td>Convulsions, Tremor, Ataxia, Lethargy</td>
<td></td>
</tr>
<tr>
<td>Critical Period Post-Exposure:</td>
<td>-</td>
<td>-</td>
<td>4-6 weeks</td>
<td>5 to 14 Days</td>
<td>1 to 48 Hours</td>
<td></td>
</tr>
<tr>
<td>Therapy:</td>
<td>Reassurance</td>
<td>Reassurance, Hematologic Surveillance</td>
<td>Blood Transfusions, Antibiotics</td>
<td>Consider Bone-Marrow Transplantation</td>
<td>Maintenance of Electrolytic Balance</td>
<td>Sedatives</td>
</tr>
<tr>
<td>Prognosis:</td>
<td>Excellent</td>
<td>Excellent</td>
<td>Good Therapy Effective</td>
<td>Guarded Therapy Promising</td>
<td>Hopeless Therapy Palliative</td>
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<tr>
<td>Convalescent Period:</td>
<td>-</td>
<td>Several Weeks</td>
<td>1 to 12 Months</td>
<td>Long</td>
<td>-</td>
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<tr>
<td>Incidence of Death:</td>
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<td>None</td>
<td>0 to 80% (Variable)</td>
<td>80 to 100% (Variable)</td>
<td>90 to 100%</td>
<td></td>
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<tr>
<td>Death Occurs Within:</td>
<td>-</td>
<td>-</td>
<td>2 Months</td>
<td>2 Weeks</td>
<td>2 Days</td>
<td></td>
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<tr>
<td>Cause of Death:</td>
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<td>-</td>
<td>Hemorrhage, Infection</td>
<td>Circulatory Failure</td>
<td>Respiratory Failure, Brain Edema</td>
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</table>

Table 5.1 Summary of Clinical Effects of Acute Ionizing Radiation Doses.
may be induced by radiation in nearly all human tissue. The main sites of solid tumors are the breast in women, thyroid, lung and some digestive organs. These tumors have long latent periods (approximately 10 to > 30 years) and occur in larger numbers than leukemia.\textsuperscript{6} Leukemia (abnormal increase in white blood cells) has a much shorter latent period. The incidence peaks within a few years of exposure and returns to normal levels after about 25 years.\textsuperscript{10} Reference 6 contains an extensive discussion on radiation induced cancers and presents data on the incidence in specific organs. The ICRP\textsuperscript{10} has estimated that the fraction of all cancers, for both sexes and all ages, is $1.25 \times 10^{-2} \text{ Sv}^{-1}$ ($1.25 \times 10^{-4} \text{ rem}^{-1}$).

2. Tissue Effects

Among the more prominent late effects in tissues are cataracts (see 5.1.7) and sterility (see 5.1.4). Radiation-induced cataracts are slowly progressive over a period of time, but may stop or even regress.\textsuperscript{1} Sterility is a late effect which may be either permanent or temporary. In some cases, fertility will return in a few years.\textsuperscript{6}

3. Life-span

Information on life-shortening effects in man is still inadequate. The effects of long-term, low-level irradiation on longevity cannot be predicted. With the exception of tumor induction, there is no evidence of life shortening.\textsuperscript{6,10}

4. Growth and Development

Effects on the embryo depend upon the dose as well as the age of the embryo. The younger the embryo, the more it is affected.\textsuperscript{1} Here, as in the case of other late effects, the results of damage are the same as those caused by other agents. The effects on the fetus are so much more important since minor damage may be amplified during growth into a major anomaly. Relatively high doses can cause death, malformation, growth
retardation and impairment of function. Susceptibility to certain cancers appears to be higher during prenatal and childhood periods.

The incomplete status of these problems at the present time reflects the lack of needed information. Such data are very hard to obtain, and require careful work and analysis. In each case of late effects, extensive data are needed before any real firm conclusions may be drawn. As the dose rate is reduced, one approaches background levels and any effects produced by the applied dose rates may be masked by effects produced by other agents or background radiation.

G. Hereditary Effects

The study of hereditary effects attempts to discover the traits which can be transmitted from generation to generation in a given species. The genes are the determinants of the inherited traits. Any change or mutation of a gene, which is usually quite stable, can result in an altered trait. Such changes can be produced by radiation, as well as other agents. The study of radiation-induced mutations is thus hampered by the fact that other substances also act to produce the same effects. Since the change is not unique, radiation only serves to increase the frequency of the effect. Increases in the rate are small even for high doses. Thus, the study requires the use of large numbers of subjects studied over many generations. In the case of man, the study is very difficult, since large numbers are seldom available and the time between generations is so long. To date, there has been no demonstration of radiation induced mutations in man.

For this reason, much of the present knowledge is based on work with animals. At all doses and dose rates used up to the present, radiation is known to induce mutations in all species studied. Because of this, any increase of radiation to humans should bring about an increase in the mutation rate. Sometimes the application of animal data to man can result in error. However, in this case, the effects on some other species are similar enough to those in man.

Studies have shown that some hereditary effects in man are caused by chromosome damage. Up to the present time, the lack of knowledge about
the harmful traits has made estimates of the magnitude of these effects uncertain. When more diseases and effects can be related to certain types of mutations, then better estimates can be made.

Genes may be dominant or recessive. When genes differ, the trait which results may be determined by either gene, or some intermediate trait may occur. If the trait is determined by one or the other of the genes, this gene is then a dominant gene. The other is a recessive gene. Mutations in dominant genes give rise to damage in the offspring of the first generation. Damage to offspring caused by recessive genes occurs only if the same altered gene is received from each parent. Unless these changes occur frequently, recessive damage won't show up for many generations.

It is estimated that already about 10% of human liveborn offspring suffer from serious disorders of genetic origin. In evaluating radiation induced genetic effects in humans, mouse data must be used. The estimates of the increased serious genetic disorders in humans due to radiation exposure are small relative to the natural incidence cited above. That is, the ICRP\textsuperscript{10} has estimated that the fraction of effects to be expected, in the first two generations, can be taken as about $4 \times 10^{-3}$ Sv$^{-1}$ ($4 \times 10^{-8}$ rem$^{-1}$).

H. Stochastic and Nonstochastic Effects-Risk

For some of the effects that have been mentioned, the relative damage or severity of the effect increases with increased dose. Higher doses produce a greater degree of that type of damage. On the other hand, for some effects, increasing the dose increases the chance, or probability of the effect occurring. The terms "nonstochastic" and "stochastic" effects have been employed by the ICRP\textsuperscript{10} to distinguish between these. Nonstochastic effects are those in which the severity of the effect varies with the dose. For these types of effects, a threshold dose may exist. That is, if the dose is kept below the threshold dose, the effect will not be observed. Nonstochastic effects are considered to result from the collective injury of a substantial number of cells in the tissue.\textsuperscript{7}
Examples of such effects are cataracts, skin ulcerations or burns, depletion of blood-forming cells in bone marrow, and impairment of fertility.

Stochastic effects are those in which the probability of the effect occurring increases with dose, without threshold. Any dose, therefore, has a certain probability, however low, of causing the effect. Stochastic effects may result from injury to a single cell or a small number of cells. Carcinogenic (cancer) and heritable effects are examples of stochastic effects. In those, once the effect is induced, the severity is already determined by the nature of the effect.

From a protection standpoint, preventing nonstochastic effects may be achieved if the dose limit is set low enough so that the threshold dose is not exceeded. In this case, the risk of producing nonstochastic effects could be reduced to zero. The ICRP has recommended dose limits intended to prevent detrimental nonstochastic effects. However, since stochastic effects have some chance of occurring no matter how low the dose, the ICRP limits intend to limit the probability of stochastic effects occurring to an acceptable level. That is, any exposure to radiation involves a risk, and no risk should be undertaken without the expectation of a net benefit. Since the setting of limits involves judgments that cannot wholly be based on scientific knowledge, the concept "acceptable risk" has evolved. The basis for an acceptable level of risk in radiation work is comparison to the risks in other occupations considered to have high safety standards. The average annual mortality in these occupations is $10^{-4}$. The risk factor of $10^{-4}$ represents 1 chance in 10,000 that an accidental death due to occupational hazards will occur during the year. The risk factors used by the ICRP are the estimated probability of occurrence of stochastic effects per unit dose, that is, the sum of the risk factor for all radiation induced cancers ($1.25\times10^{-2}\text{ Sv}^{-1}$) and the average risk factor for hereditary effects ($4\times10^{-3}\text{ Sv}^{-1}$). The average annual dose equivalent in cases of occupational exposure is about 5 mSv (.5 rem). So, the average annual risk would be $(1.65 \times 10^{-2}\text{ Sv}^{-1}) (5\times10^{-3}\text{ Sv}) = 8.25\times10^{-5}$, approximately $1\times10^{-4}$ or comparable to other safe industries.
For more discussions on risk and risk factors, for both radiation workers as well as risks in everyday living, one may consult References 11 and 12, respectively.

The ICRP makes a further point in their recommendations. They recommend that all necessary exposures be kept as low as reasonably achievable, taking into account economic and social factors.\textsuperscript{10} This part of the recommendations is referred to as optimization. That is, achieving the optimum net benefit such that the increased protection cost to reduce exposures is balanced by the reduction in the expected harm (detriment).

I. Biological Responses of Specific Organs

With respect to specific damage in various organs of the body, some effects may be stochastic or nonstochastic. For the stochastic effects, the risk factors from Reference 10 will be given. For nonstochastic effects, the threshold doses from Reference 7 are quoted. The sensitivity of the method for detecting damage is an important factor. For this reason, the threshold dose is defined as the amount of radiation required to cause a particular effect in at least 1-5\% of those exposed.\textsuperscript{7} With the exception of tissues such as skin, which respond for short-term irradiation, data is lacking for reactions to long-term protracted exposures in all organs. Knowledge of the radiosensitivity of different tissues regarding nonstochastic effects is based mainly on therapy experience. The thresholds are based on therapy irradiation conditions; typically, 20-35 exposures to x or \( \gamma \) rays over a 4-7 week period, not occupational exposure conditions. The following summary points out some of the specific aspects of biological response in specific tissues and organs of the body:

1. Blood and Bone Marrow

The blood is composed of three major types of cells, namely, the erythrocytes (red cells), the leukocytes (white cells), and platelets, suspended in a fluid called plasma. The red cells supply other body cells
with food and oxygen, and remove waste products. White cells help to combat infections, and the platelets aid in blood-clotting action. Plasma is a viscid liquid which contains water, proteins, salts, and free ions. Blood contains about 45% red cells, approximately 1% white cells and platelets, and 54% plasma.

Bone centers are filled with marrow, either red or yellow. Red marrow is found in the skull, breastbone, ribs, pelvis, and spine of adults. The red marrow provides the blood-forming function. Yellow marrow provides fat storage.

White cells are the first to be affected by radiation. Although there are subtypes of white cells which differ in their sensitivity, the net effect of irradiation is to reduce the number of white cells. This lack of white cells is known as leukopenia. For acute whole body doses > 1 Gy (100 rad), the maximum drop in the leukocytes is seen within 2-5 weeks. The platelets drop in number somewhat more slowly. A few weeks later, a loss of red cells (anemia) occurs.

The loss of white cells affects resistance to infection. The drop in the platelet number affects clotting action, so that open wounds may not heal. Anemia causes a general weakness in the individual. Recovery will take place if the damage to the bone marrow is not too great. The marrow will regenerate and produce new blood cells to replace the cells which were lost. When the damage to the red marrow is too great, the effects are likely to be permanent. The LD_{50/60} is not known precisely, but is estimated to lie in the range 2.5-5 Gy (250-500 rad).

For fractionated or protracted doses, the effects are not as severe due mainly to replacement and some repair. Although dose rate influence on damage is not well known for humans, it is believed that the blood forming system can withstand 3-10 Gy (300-1000 rad) if protracted over several months. The threshold dose for nonstochastic effects is 2 Gy (200 rad).

With respect to leukemia, the red bone marrow is believed to be the main tissue involved. The risk factor is taken as 2x10^{-3} Sv^{-1} (2x10^{-5} rem^{-1}).
2. **Lymphatic System**

The lymphatic system is a network of small tubes which permeate the body tissues. A fluid called lymph, somewhat like plasma but with less proteins, drains from tissues into the lymphatic system. The lymph picks up waste products from the tissues. Along the course of a lymph vessel are oval-shaped glands (lymph nodes) which filter out foreign substances from the lymph. Thus purified, the lymph is passed back into the blood stream.

The spleen contains the largest mass of lymphatic tissue in the body. The spleen filters dead blood cells from the blood and is a source of white blood cells. Also, the spleen stores red blood cells.

The lymph nodes show the first signs of hemorrhaging and infection after acute irradiation. The spleen may exhibit weight loss and damage to lymphocytes (a subtype of white blood cells). A complication in the function of lymphoid tissues is a drop off in the body's immune response to infection.

3. **Digestive Tract (GI Tract)**

The digestive tract, or alimentary canal, consists of the mouth, pharynx, esophagus, stomach, and the small and large intestines. This system is often called the GI tract. In an adult man, the canal may be as much as 9 m in length. The cells which line the walls of the intestines secrete substances which act on food to make absorption into the blood stream possible. The stomach is the reservoir in which the major chemical phases of digestion occur. The radiosensitivities of the many sections of the canal vary greatly. The small intestine is quite radiosensitive, whereas the stomach and esophagus are much less radiosensitive.

The symptoms of damage to the canal are nausea and vomiting. The initial effects are impaired secretion and discontinued cell production. When cell breakdown occurs, the dead cells are released from the walls of the tract. This debris clutters up the intestine. The exposure of tissues under the surface layer may lead to ulcers. The threshold dose for ulceration is estimated as 45 Gy (4500 rad). In fatal
cases, infection, failure of food absorption, and dehydration from diarrhea are the causes. As indicated earlier, the LD$_{50}$ for acute whole body exposures is in the range 5-20 Gy (500-2000 rad).

4. Reproductive Organs

Since the reproductive organs are the source of germ cells, damage to these cells can result both in somatic and hereditary effects. For the present, our concern is only with the somatic effects. The response of germ cells to radiation differs slightly in the male and female. These cells are highly radiosensitive, while other cells of the reproductive system are relatively radioresistant. Radiation can produce sterility in both sexes, but the degree depends upon the dose delivered. In man, partial sterility can be induced at doses as low as 0.15 Gy (15 rad). Based on dog experiments, it is inferred that the human testes can tolerate 1 mGy d$^{-1}$ (0.1 rad/d) for an indefinite period of time without fertility impairment. It requires a larger dose to produce permanent sterility in the male than in the female. Acute exposure of the ovaries to 0.65-1.5 Gy (65-150 rad) may cause prompt impairment of fertility and acute doses > 3 Gy (300 rad) will cause permanent sterility. Threshold doses for testes of 5-15 Gy (500-1500 rad), and for ovaries of 2-3 Gy (200-300) have been estimated.

Germ cells which survive damage can transmit any genetic changes caused by the radiation. For this reason, the total effect of radiation on the gonads may not be seen for several generations. The estimated risk factor for the first two generations is 4x10$^{-3}$ Sv$^{-1}$ (4x10$^{-5}$ rem$^{-1}$).

5. Nervous System

The nervous system, composed of the brain, spinal cord, and the peripheral nerves, acts to coordinate body activity. The spinal cord and peripheral nerves are highly radioresistant, but the brain is more sensitive than often supposed. Lesions and functional impairment have been
observed for brain doses above 10 Gy (1000 rad) in adults. In children, doses from 1-6 Gy (100-600 rad) have produced detectable physical and functional changes.\textsuperscript{8} Necrosis of the brain has an estimated threshold dose of 50 Gy (5000 rad), the damage occurring directly or through lack of blood supply due to blood vessel damage. Inflammation of the spinal cord producing numbness, tingling, weakness or paralysis can be caused by radiation damage depending on dose, irradiated tissue volume and nerve location. The estimated threshold dose is 50 Gy (5000 rad). Peripheral nerves have been damaged at doses > 60 Gy (6000 rad) during conventional radiotherapy.

6. Thyroid Gland

The thyroid, a gland located at the base of the throat, secretes a hormone known as thyroxine, which helps to control basal metabolism. The action of the thyroid seems to be closely connected with the functions of the pituitary and adrenal glands. Thyroxine contains about 65 percent iodine, and is essential for growth and development. Damage to the thyroid, or to the other two glands, have marked effects in the body.

The thyroid is radioreistant from the standpoint of external radiation. It can be severely damaged if radioiodine is inhaled, since iodine will concentrate in the thyroid. Damage causes a decrease in production of thyroxine (hypothyroidism) which produces a lower metabolism rate. Muscle tissue may then fail to absorb enough oxygen and health can be badly impaired. The threshold dose is estimated to be 45 Gy (4500 rad).

The sensitivity of the thyroid to cancer induction appears to be higher than that for leukemia induction. However, the tumors are slowly progressive so that treatment is generally successful. So, the mortality (death rate) for thyroid cancers is much lower than that for leukemia. The mortality risk factor is taken as $5 \times 10^{-4} \text{ Sv}^{-1}$ ($5 \times 10^{-6} \text{ rem}^{-1}$).
7. **Eyes**

The lens of the eye is highly susceptible to irreversible damage by radiation. The lens cells of the eye are not replaced by regrowth. The retina is much less sensitive than the lens.

When the cells of the lens become damaged, the cells lose their transparency. The opacities which may occur will appear after a latent period. The term cataract is applied to these lens opacities. The formation of cataracts is generally a late somatic effect. Acute effects in other eye structures occur only after high doses. At high doses, cataracts may develop within months, while at low doses, the latent period may be years.

In the early stages of development, radiation induced cataract may be distinguished from that due to other causes. The initial opacity appears as almost a dot near the center of the lens, whereas spontaneous cataracts tend to begin at the periphery of the lens. The central opacity grows larger, developing a clear center, so that it resembles a doughnut. As it continues to progress it becomes similar in appearance to other types of cataracts, and therefore can no longer be distinguished. It is possible for the lesion to grow for a time and then remain stationary. The lowest dose observed to cause a progressive cataract in radiotherapy patients was 5 Gy (500 rads). For the case of occupational exposure, extrapolation suggests that > 8 Gy (800 rads) of low LET radiation would be necessary to produce a vision impairing opacity.

For high energy neutrons (7.5 MeV) in fractionated doses, the threshold for visual impairment appeared to be 3-5 Gy (300-500 rad). On this basis, the ICRP has recommended that no change is required for the neutron quality factor relative to cataract formation. In relation to the lens, other parts of the eye are radioresistant. In terms of the threshold dose, the estimate is 5 Gy (500 rad) with respect to cataract production.
8. **Lungs**

The lungs are cone-shaped organs made up of very small air sacs called alveoli. When a person breathes, the air is directed down the trachea (wind pipe). From there, two large tubes (bronchi) direct the air toward each lung section. Many small tubes (bronchioles) branch out from the bronchi to connect with the alveoli in the lungs.

During breathing, each air sac is expanded and compressed by lung muscles, and is thus filled and emptied. Air passes through the walls of the alveoli into tiny blood vessels (capillaries).

The effects produced in the lung by radiation are the result of damage to the air sacs. The lungs are not normally affected by external radiation. As in the case of the thyroid, the greater hazard occurs from internal radiation from inhaled dust and vapors. However, when a major portion of the lungs are irradiated at high dose, a fatal pneumonia may result. The \( \text{LD}_{50} \) in man for acute exposure is about 8-10 Gy (800-1000 rad) for gamma rays. The damage which occurs is to the alveoli and the lung blood vessels. The tissues of the upper respiratory tract are relatively less radiosensitive. The threshold dose for nonstochastic damage in the lung is 40 Gy (4000 rad).

Cancer of the lung has been observed in miners exposed to high radon concentrations. There is also evidence that external irradiation can induce lung cancer in man. The risk factor for lung cancer is \( 2 \times 10^{-3} \text{ Sv}^{-1} \) (2x10^{-5} rem^{-1}).

9. **Liver and Gall Bladder**

The liver is radioresistant as compared with other organs. The liver, the largest gland in the body, secretes bile for digestion. The gall bladder stores and concentrates the bile secreted by the liver. When bile is needed, it passes from the gall bladder to the intestine.

External radiation is not too effective in causing damage to these organs. Most damage is caused by internal exposure from radionuclides which concentrate in the liver. Impairment of liver function occurs
for exposure of the entire liver to 30 Gy (3000 rad) of conventional therapeutic irradiation. The damage is indicated by decreased liver function and fluid accumulation (ascites). The threshold dose for nonstochastic effects in liver is 35 Gy (3500 rad).

10. **Kidneys**

The kidneys help to control the concentration and content of the blood by excreting water and waste products. The waste products pass from the kidneys through small tubes (ureters) into the bladder (this system is called the urinary tract). Impairment of renal functions does not add to mortality in the case of total body radiation. Damage to the kidney is indicated by an increase in amino acids in the urine. These effects occur mostly from internal radiation. The appearance of blood in the urine is an indication of severe renal damage. The dose to cause injury in the system, is lowest for the kidneys, highest for the ureters. The threshold dose for a fatal kidney infection (nephritis) is estimated to be approximately 23 Gy (2300 rad) when delivered in fractionated doses. The tolerance of the bladder is higher than that of the kidney, with a threshold of 55-60 Gy (5500-6000 rad) when fractionated over 4 weeks.

11. **Circulatory System**

The heart and blood vessel system are damaged seriously only for very high doses of radiation. The heart is not highly radiosensitive, but can be damaged by doses in the range 40-60 Gy (4000-6000 rad). The threshold for inducing inflammation of the lining surrounding the heart (pericarditis) is 40 Gy (4000 rad). Blood vessels show damage after 40-60 Gy (4000-6000 rad). In many cases, vascular damage in advance of tissue effects suggests that this is an important factor in tissue injury.

12. **Skin**

The degree of skin damage varies with the dose and the species
of animal. Skin is easily damaged but has a tremendous capacity for repair. Various structures of the skin show quite different sensitivities. The damage seems to be greater for less penetrating radiations.

Slight damage to the skin may result in an erythema (reddening). With increasing dose, loss of hair (epilation), dry, scaly skin and death of tissue in the epidermis (outermost skin layer) may occur. For increased damage, ulceration may result. The threshold dose for skin ulceration is estimated to be 55 Gy (5500 rad).

Skin cancer is a late effect of chronic irradiation at very high dose rates. However, skin is less likely to develop fatal cancer. The ICRP feels that the nonstochastic limit for skin will prevent the occurrence of skin cancer.

13. Hair

Irradiation can lead to temporary baldness (epilation). This condition may last for a few weeks. The hair begins to return, but the new hair may have different characteristics, such as a new color.

With respect to hair follicles, an acute dose of low LET of 3-5 Gy (300-500 rad) can cause temporary epilation. The threshold for permanent epilation for acute exposure is about 7 Gy (700 rad).

14. Bones

Bone is composed of living cells which are distributed in a matrix of fibers and bone salts. Although the marrow of the bone is very radiosensitive, the bone cells, fibers, and salts are relatively radioresistant.

When radionuclides, such as strontium or plutonium, are internally deposited in the bone marrow or bone tissue, then great damage can be done. These effects again are late effects since the damage may take years to show up.

In children, the developing bone cells and cartilage show a greater response. For doses as low as 1 Gy (100 rad), some retardation of
growth may be seen. Mature bone in adults can withstand fractionated doses of 65 Gy (6500 rad) in a 6-8 week period.

In adults, the developing bone cells lining the bone cavity are the radiosensitive cells at risk with respect to cancer. The risk factor is taken as $5 \times 10^{-4}$ Sv$^{-1}$ ($5 \times 10^{-6}$ rem$^{-1}$).

15. Muscle

Mature muscle is relatively radioresistant, but in children when muscle is growing, the radiation response is greater. Contraction and delayed healing show up for doses of approximately 60 Gy (6000 rad) fractionated. The threshold dose is estimated to be $> 100$ Gy (10,000 rad).

16. Breast

The breast in females is one of the more radiosensitive organs with respect to cancer induction. The latent period seems to be related strongly to age at exposure. An estimate of the latent period is 5 years for women 25 years or older. The risk factor is taken as $2.5 \times 10^{-3}$ Sv$^{-2}$ ($2.5 \times 10^{-5}$ rem$^{-1}$).

REFERENCES


BIBLIOGRAPHY


QUESTIONS

5.1 What is the basic unit of structure in the body?

5.2 What are main component elements of the basic unit of structure in the body?

5.3 What are the two principal parts of a cell? What does each part do?
5.4 What tiny parts in the nucleus of a cell determine the hereditary traits of a daughter cell? To what are they attached?

5.5 What term is given to changes in the chromosomes or genes of cell?

5.6 Correlate the items in list A. with those in list B.

<table>
<thead>
<tr>
<th>List A</th>
<th>List B</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. cell division</td>
<td>differentiation, gametes,</td>
</tr>
<tr>
<td>b. bisexual cells</td>
<td>somatic cells, hereditary</td>
</tr>
<tr>
<td>c. process of cell change</td>
<td>cells, mitosis</td>
</tr>
<tr>
<td>d. cell damage limited to</td>
<td></td>
</tr>
<tr>
<td>e. germ line</td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

5.7 Name two changes to atoms or molecules that will occur when radiation passes through living cells.

5.8 What terms are given to the fragments of molecules that result from radiation?

5.9 In what part of a cell is radiation damage most likely to be serious?

5.10 What term indicates that dose of radiation below which no effects are observed?

5.11 What term is used to indicate the different response of cells to radiation?

5.12 List some of the factors affecting or determining the radiosensitivity of cells.

5.13 Compare genetic damage with somatic damage to cells.

5.14 Define the term "median lethal dose" and indicate its symbol. What level of dose does this term represent in man?

5.15 Explain the term RBE.

5.16 How is LET of the radiation related to the biological damage?

5.17 What are survival curves?

5.18 List some of the qualitative results that apply to high LET and low LET radiation.

5.19 Under what conditions is sublethal damage of a cell repairable?
5.20 Explain the terms
   a) CNS death
   b) GI death
   c) Bone-marrow death

5.21 List the late somatic effects.

5.22 Explain
   a) stochastic effects
   b) nonstochastic effects

5.23 What is the basis for an acceptable level of risk?

5.24 List the three types of blood cells and the fluid that transports them through the body. Indicate the principal function of each.

5.25 Indicate the effects that occur upon loss of
   a) white cells,
   b) platelets and
   c) red cells

5.26 Indicate three functions of the spleen.

5.27 Which part of the digestive tract is highly radiosensitive?

5.28 What is the result of a high radiation dose to the reproductive organs?

5.29 Which organ of the nervous system is the most radiosensitive?

5.30 What radionuclide presents the greatest internal hazard to the thyroid gland?

5.31 What hazard do neutrons and x ray present to the eye?

5.32 From what does the greater radiation hazard to the lungs occur?

5.33 To what does the term "epilation" refer?

5.34 What organ of the body is easily damaged by radiation, but has a tremendous capacity for repair?

5.35 Which part of the bone is the most radiosensitive?

5.36 Explain why the study of hereditary effects resulting from radiation is difficult.
5.1 The following table is adapted from the National Safety Council, Accident Facts, 1979. Calculate the risk (the probability of death per person/year) for each profession. How do these compare with cancer risk due to radiation?

**PROBABILITY OF ACCIDENTAL DEATH BY TYPE OF OCCUPATION**

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Number of Accidental Deaths for 10,000 Workers for 40 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Mining</td>
<td>252</td>
</tr>
<tr>
<td>b. Construction</td>
<td>228</td>
</tr>
<tr>
<td>c. Agriculture</td>
<td>216</td>
</tr>
<tr>
<td>d. Transportation and Public Utilities</td>
<td>116</td>
</tr>
<tr>
<td>e. Government</td>
<td>44</td>
</tr>
</tbody>
</table>

Answers:  
- a. $6.3 \times 10^{-4}$/person-year  
- b. $5.7 \times 10^{-4}$/person-year  
- c. $5.4 \times 10^{-4}$/person-year  
- d. $2.9 \times 10^{-4}$/person-year  
- e. $1.1 \times 10^{-4}$/person-year

5.2 According to the "absolute-risk projection model" of the 1980 BEIR Report, if 1,000,000 people, representative of the U.S. population, receive a single exposure of 0.1 Gy due to low LET radiation, there would be 766 eventual cancer deaths as a result of the radiation. Calculate the risk estimator. How does this compare with the risk factor suggested by ICRP?

Answer: $7.66 \times 10^{-3}$ cancer deaths/person-Gy

5.3 A town's population of 60,000 is exposed to radiation due to passage of a radioactive cloud after an accident. The average gamma dose is estimated to be 0.04 Gy. What are the predicted cancer deaths?

a) by BEIR model above, and  
b) by ICRP risk factor?

Answer: a) ~ 18  
b) ~ 30