CHAPTER THREE: BIOLOGICAL EFFECTS OF RADIATION

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INTRODUCTION

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

In addition to the effects on the person receiving the dose, damage to the germ cells in the reproductive organs – the gonads – can result in heritable effects which arise in later generations.

THE INTERACTION OF RADIATION WITH CELLS

The basic difference between nuclear radiations and the more commonly encountered radiations such as heat and light is that the former have sufficient energy to cause ionization. In water, of which cells are largely composed, ionization can lead to molecular changes and to the formation of chemical species of a type that is damaging to the chromosome material.

The damage takes the form of changes in the construction and function of the cell. In the human body, these changes may manifest themselves as clinical symptoms such as radiation sickness, cataracts or, in the longer term, cancer. This overall process is usually considered to occur in four stages as follows:

1. The **initial physical stage**, lasting only an extremely small fraction (c. 10^{-16}) of a second in which energy is deposited in the cell and causes ionization. In water, the process may be written as:

$$H_2O \xrightarrow{\text{radiation}} H_2O^+ + e^-$$

where H_2O^+ is the positive ion and e^- is the negative ion.

2. The **physicochemical stage**, lasting about 10^{-6} s, in which the ions interact with other water molecules, resulting in a number of new products. For example, the positive ion dissociates:

$$H_2O^+ \longrightarrow H^+ + OH$$

The negative ion, that is the electron, attaches to a neutral water molecule, which then dissociates:

$$H_2O + e^- \longrightarrow H_2O^-$$

$$H_2O^- \longrightarrow H + OH^-$$

Thus, the products of the reactions are H^+, OH^-, H and OH. The first two ions, which are present to quite a large extent in ordinary water, take no part in subsequent reactions. The other two products, H and OH, are called free radicals, that is, they have an unpaired electron and are chemically highly reactive. Another reaction product is hydrogen peroxide, H_2O_2, which is a strong oxidizing agent formed by the reaction:

$$OH + OH \longrightarrow H_2O_2$$

3. The **chemical stage**, lasting a few seconds, in which the reaction products interact with the important organic molecules of the cell. The free radicals and oxidizing agents may attack the complex molecules which form the chromosomes. They may, for example, attach themselves to a molecule or cause links in long-chain molecules to be broken.

4. The **biological stage**, in which the timescale varies from tens of minutes to tens of years depending on the particular symptoms. The chemical changes discussed above can affect an individual cell in a number of ways. For example, they may result in:

(a) the early death of the cell or the prevention or delay of cell division; or

(b) a permanent modification which is passed on to daughter cells.

The effects of radiation on the human body as a whole arise from damage to individual cells, but the two types of change have quite different results. In the first case, the death or prevention of division of cells results in the depletion of the cell population within organs of the body. This type of effect was formerly referred to as deterministic, but the International Commission on Radiological Protection (ICRP) has now adopted the more descriptive term harmful tissue reaction.

In the second case, modification of even a single cell may result, after a latency period, in a cancer in the exposed individual or, if the modification is to a reproductive cell, the damage may be transmitted to later generations and give rise to heritable effects. In these cases, it is the likelihood of the effect occurring that depends on the dose. This type of effect is referred to as stochastic, meaning ‘of a random or statistical nature’.

To summarize, radiation-induced changes at the cellular level can lead to two distinct types of injury.

1. **Harmful tissue reactions** in which, above a certain threshold dose, the severity of the effects increase with increasing dose.
2. **Stochastic effects**, in which the probability of occurrence of the effect increases with dose. The effects include cancer induction and heritable effects in future generations.

HARMFUL TISSUE REACTIONS

Acute radiation effects

The harmful tissue reactions that arise from acute radiation exposure (a large dose over a relatively short period of time) are those that occur within a few weeks after the receipt of the dose. The effects result from a major depletion of cell populations in a number of body organs caused by the killing of cells and the prevention or delay of cell division. The main effects are attributable to bone marrow, gastrointestinal or neuromuscular damage depending on the dose received. Acute absorbed doses above about 1 Gy (gray) give rise to nausea and vomiting. This is known as radiation sickness and it occurs a few hours after exposure as a result of damage to cells lining the intestine. Absorbed doses above about 3 Gy can lead to death, probably 10–15 days after exposures. There is no well-defined threshold dose below which there is no risk of death from acute doses, although below about 1.5 Gy the risk of early death would be very low .Similarly, there is no well-defined point above which death is certain, but the chances of surviving an acute dose of about 8 Gy would be very low.

A reasonable estimate can be made of the dose which would be lethal for 50 per cent of the exposed subjects within 60 days of exposure. This is called LD560 and is thought to have a value of between 3 Gy and 5 Gy for man.

For doses up to about 10 Gy, death is usually caused by secondary infections that result from the depletion of white blood cells, which normally provide protection against infection. The range of doses from 3 to 10 Gy is often called the region of infection death. In this range, the chances of survival can be increased by special medical treatments ,which include isolating the subject in a sterile (i.e. infection-free) environment and giving a bone marrow transfusion to stimulate white blood cell production.

For doses above about 10 Gy, survival time drops abruptly to between 3 and 5 days .It remains at about this figure until much higher doses are reached. In this region, the radiation dose causes severe depletion of the cells lining the intestine. Gross damage occurs in the lining of the intestine, followed by severe bacterial invasion. This is called the region of gastrointestinal death .At much higher doses, survival times become progressively shorter. There are very few human data in this region, but from animal experiments the symptoms indicate some damage to the central nervous system and hence the region is called the region of central nervous system death. However, it is found that death is not instantaneous even in animals irradiated with doses in excess of 500 Gy.

Another effect which shows up soon after an acute overexposure to radiation is erythema that is, reddening of the skin. In many situations the skin is subject to more radiation exposure than most other tissues. This is especially true for b-rays and low energy X-rays. A dose of about 3 Gy of low-energy X-rays will result in erythema, and larger exposures may lead to other symptoms such as changes in pigmentation, blistering and ulceration.

The levels of exposure of workers and members of the public arising from normal operations in the nuclear energy industry, or from industrial and medical applications of radiation, are far below the levels that would induce early effects. Such high doses could be received only in the unlikely event of an accident. However, the low doses received in normal operations may cause harmful effects in the long term, and these are discussed below.

It will have been noted that, in this discussion, early effects have been considered in terms of the absorbed dose, expressed in grays, rather than as equivalent dose in sieverts (Sv). This is really a question of definition; the radiation weighting factor, w_R, discussed in the previous chapter, and hence the concept of equivalent dose, is intended to apply only to exposures within the normal recommended limits and should not be applied to doses at levels that could lead to early effects.

2-Late tissue reactions

Another radiation effect which may be described as a tissue reaction but which may not occur for many years is damage to the lens of the eye. This takes the form of observable opacities in the lens or, in extreme cases, visual impairment as the result of a cataract. Again, there is a threshold dose and so, by setting a dose limit for the lens of the eye, the occurrence of these effects can be prevented.

There is some evidence from animal experiments that exposure to radiation may slightly reduce the life expectation of individuals who do not exhibit any specific radiation induced symptoms. Observations of human populations exposed at relatively high levels indicate that, if shortening of life occurs at all, it is very slight, almost certainly less than 1 year per sievert.

STOCHASTIC EFFECTS – CANCER INDUCTION

It became apparent in the early part of the twentieth century that groups of people, such as radiologists and their patients, who were exposed to relatively high levels of radiation showed a higher incidence of certain types of cancer than groups not exposed to radiation. More recently, detailed studies of the populations exposed to radiation from atomic bombs, of patients exposed to radiation therapy and of groups exposed occupationally, particularly uranium miners, have confirmed the ability of radiation to induce cancer. Cancer is an over proliferation of cells in a body organ. It is thought that cancer may result from damage to the control system of a single cell, causing it to divide more rapidly than a normal cell. The defect is transmitted to the daughter cells, so the population of abnormal cells builds up to the detriment of the normal cells in the organ. The estimation of the increased risk of cancer is complicated by the long and variable latency period, from about 5 to 30 years or more, between exposure and the appearance of the cancer and by the fact that radiation-induced cancers are not normally distinguishable from those that arise spontaneously or as a result of other carcinogens such as tobacco smoke. The incidence of cancer in a normal population is high, with about one person in three expected to die eventually from some form of cancer. This high background makes it very difficult to establish whether any additional cases of a particular type of cancer are the result of radiation exposure, even in populations that have been exposed to relatively high levels. At the high doses and dose rates experienced by the groups mentioned earlier, the ICRP has estimated that, averaged over a typical population of all ages, a dose of 1 Sv to each individual would result in a radiation-induced fatal cancer in about 10 per cent of the persons exposed.

This is the same as saying that the average risk to an individual from a dose of 1 Sv is about 1 in 10 or 0.1. The extrapolation of this estimate to the much lower doses and dose rates normally encountered as a result of operations in the nuclear industry and elsewhere introduces further uncertainty. A very conservative approach would be to make a linear extrapolation from high to low doses. Since a dose of 1 Sv carries a risk of fatal cancer of 10 per cent, the risk from a dose of 1 mSv would be 1000 times lower, or 0.01 per 34 Biological effects of radiation cent. However, on the basis of theoretical considerations, experiments on animals and other organisms, and limited human data, ICRP concluded that this probably overestimates the risk of radiation exposure at low doses and dose rates by a factor of between 2 and 10. This factor is referred to as the **dose and dose rate effectiveness factor (DDREF)** and, to err on the safe side, ICRP recommends using only the factor of 2. This means that the additional risk of fatal cancer imposed on an average individual by exposure to radiation at low doses and dose rates can be estimated using a risk coefficient of 0.05 per sievert (this is usually written as $5 * 10^{-2}$/Sv). Using this coefficient, the risk of fatal cancer due to a given dose can be estimated using the relationship:

Risk = dose (Sv) * risk coefficient (Sv^{-1}), For a dose of 10 mSv (0.01 Sv), the risk of fatal cancer would be:

$$\text{Risk} = 0.01\ \text{Sv} * 5 * 10^{-2}\ \text{Sv}^{-1} = 5 * 10^{-4}$$

In addition to fatal cancers, exposure to radiation also gives rise to cancers which are non-fatal or curable. These need to be taken into account, but clearly it would be inappropriate to give them the same weight as fatal cancers.

STOCHASTIC EFFECTS – HERITABLE

The heritable effects of radiation result from damage to the reproductive cells. This damage takes the form of alterations, known as **genetic mutations**, in the hereditary material of the cell. It has already been mentioned that reproduction occurs when the ovum is fertilized by a sperm. As a result, the offspring receives a complete set of genetic material from each parent. Thus the child receives two complementary sets of genes, one from each of its parents. In general, it is found that one gene is ‘dominant’ and the other is ‘recessive’.

The dominant gene determines the particular characteristic with which it is associated. Recessive genes are only recognized when, by chance, two of the recessive-type genes come together. A considerable number of diseases are associated with recessive genes and will therefore manifest themselves only when both parents have the same recessive genes. Spontaneous mutation accounts for the fact that an appreciable fraction of the world’s population suffers from 1 of the 500 or more defects or diseases attributable to heritable effects. Radiation can induce gene mutations which are indistinguishable from naturally occurring mutations. It should be noted in passing that heat and chemicals can also cause mutations.

Mutated genes can be either dominant, in which case their effects would manifest themselves in the first generation of offspring, or recessive, when the effect would not occur in the first generation. A recessive mutation will result in an effect only if the same mutation is inherited from both parents.
It is generally assumed that all mutations are harmful, although this cannot be strictly true since man has attained his present advanced state via a series of mutations. However, this has occurred over an immense time span and the number of harmful mutations which have had to be eliminated from the species over this time is incalculably large.

Since ionizing radiation can cause an increase in the mutation rate, its use will increase the number of genetically abnormal people present in future generations. Clearly, the consequences of excessive genetic damage would be very serious indeed and strict control must be exercised over the radiation exposure of the general population. The risks of heritable effects due to exposure of the gonads are very uncertain. Clearly, only that exposure which occurs up to the time of conception can affect the genetic characteristics of the offspring and, since the mean age of childbearing is about 30 years, only a proportion of the dose received by a typical population will be genetically harmful. As such, the ICRP estimates (ICRP *Publication 103*) that the total risk of heritable disease, up to the second generation, averaged over both sexes and all ages is about $0.2 * 10^{-2}$/Sv.

In a population of working age, because of the different age distribution, the risk is about $0.1 * 10^{-2}$/Sv.

DETRIMENT

To assist in quantifying and combining the consequences of exposure of different organs and tissues of the body, the ICRP has developed the concept of **detriment**. This takes into account the relative risks and the average latency period of fatal cancers in different organs, an allowance for the ill health resulting from non-fatal cancers and for the risk of serious heritable effects in all future generations descended from an exposed individual. On this basis, the ICRP has provided estimates of what are termed **detriment-adjusted nominal risk coefficients** for exposure at low-dose rates. It should be appreciated that these values are the result of calculations using data that have significant uncertainties and that, for most purposes, the use of a nominal risk coefficient of $5 * 10^{-2}$/Sv is appropriate.

In situations in which the exposure is not uniform over the body, it is necessary to know the relative contributions that individual organs make to this overall estimate of detriment.
The second column shows the probability of fatal cancer in each organ for an equivalent dose to that organ of 1 Sv. The third column gives the probability of severe heritable effects in future generations from an equivalent dose of 1 Sv to the gonads. The final column shows the relative contribution of each organ to the overall detriment, taking account of the factors discussed above.

These estimates of the relative contributions to the overall detriment from radiation exposure provide the basis for definition of the tissue weighting factors, w_T, used to calculate the quantity effective dose.