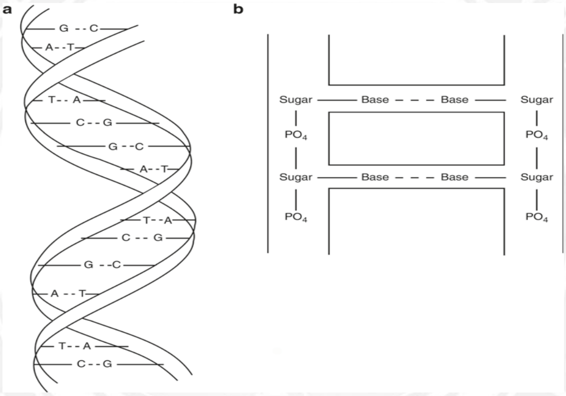
4.3Effects of Radiation

DNA Molecule

The nucleus of the cell is the most sensitive part to radiation and this sensitivity has been attributed to the DNA molecule. To



understand the effect of radiation on the DNA molecule, a knowledge of its structure is essential. It has a double- helical structure consisting of two strands, which are like the two rails of a ladder The strands are composed of sugars interlinked by phosphate bonds. The two strands are connected to each other by rungs made of four bases: thy- mine (T), adenine (A), guanine (G), and cytosine (C).The bases are bonded to the sugar molecule on the strands on both sides, and are paired to each other by hydrogen bonds. These four bases are arranged in a very specific manner to form a specific gene in every living species and provide the unique characteristics to these species.

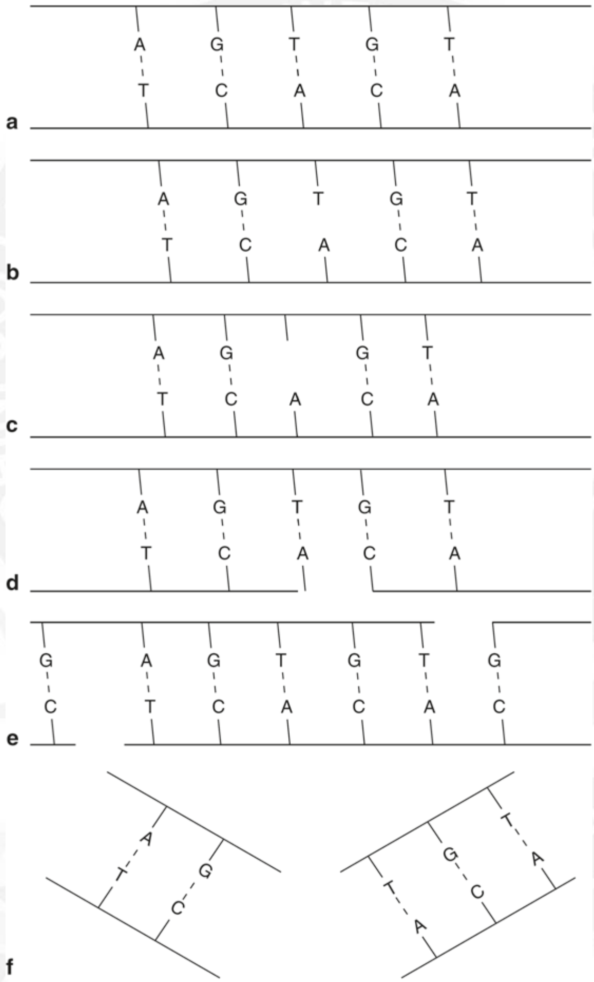
Radiation damage to the DNA molecule can be due to

(a) Loss of a base

(b) Cleavage of the hydrogen bond between bases

(c) Breakage of one strand of the DNA molecule (single strand)

(d) Breakage of both strands of the DNA molecule (double strand)



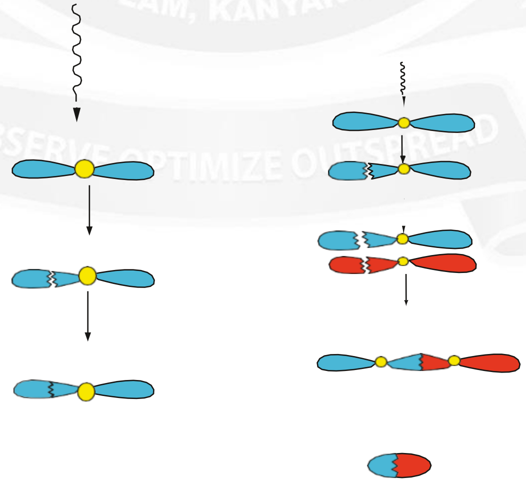
These radiation effects on DNA molecules are illustrated in Fig. These changes result in so-called mutations, which have adverse effects on the genetic codes. The number of mutations increases with increasing radiation exposure. At low-dose exposures, the breaks are single stranded and can be repaired by join- ing the broken components in the original order. At higher exposures, however, double strand breaks occur and the odds for repair decrease. Also, high-LET radiations cause more damage to the DNA molecule because of the double strand breaks. If the cell is not repaired, it may suffer a minor functional impairment or a major consequence (cell death). If DNA damage occurs in germ cells, future offspring may be affected.

Chromosome

Chromosomes are likely to be affected by mutations of the DNA molecules.These aberrations are categorized as chromatid aberrations and chromosome aberrations. In chromatid aberrations, irradiation occurs after DNA synthesis prior to mitosis and thus only one chromatid will be affected. On the other hand, in chromosome aberrations, irradiation occurs after mitosis prior to DNA synthesis and hence the broken chromatids will be duplicated producing daughter cells with damaged chromosomes.

In single-strand breaks, the chromosome tends to repair by joining the two fragments in a process called restitution, provided sufficient time is allowed. The cell becomes function- ally normal and replicates normally However, if the fragments are replicated during DNA synthesis prior to restitution, two strands with centromeres and two strands without centromeres will be produced. Random combination of these fragments will then produce acentric and dicentric chromatids Such chromosomes suffer severe consequences due to the mismatch of genetic information.

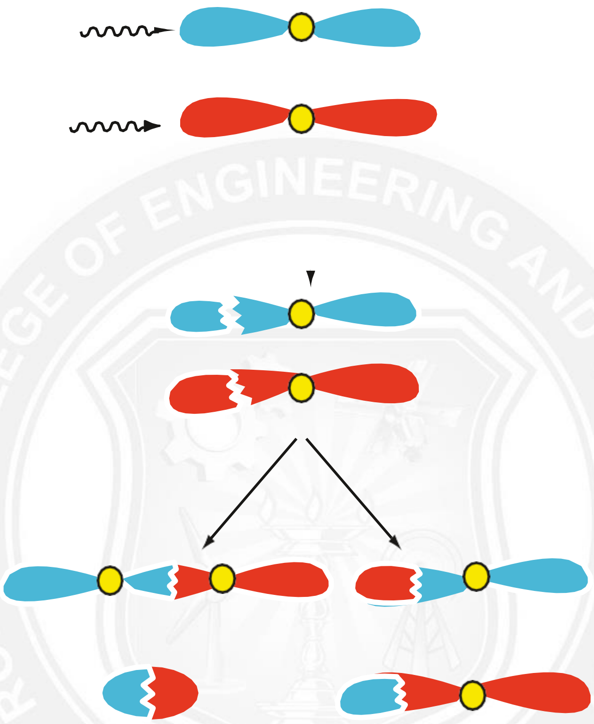
If radiation produces single-strand breaks in two separate chromosomes, then there are four ways of recombining the broken ends The dicentric and acentric combinations are similar to those formed after replication of single strands in the same chromosome shown in Fig. 15.7b. How- ever, these cells suffer severe consequences because of the mismatch of genetic information from two separate damaged chromosomes. The translocation is a process in which two fragments—one with a centromere from one chromosome and one without a centromere from another chromosome—combine to form a new chromosome In another, radiation can cause two breaks in one arm of a chromosome, resulting in three fragments, only two of which combine with the loss of the third. Such a process is called deletion Translocation and deletion, although not as harmful to the cell, cause late effects such as carcinogenesis and hereditary effects due to mismatch or loss of genetic



An alternative to deletion is the combination of all three fragments into a chromosome with changes along the broken line. This process is called inversion, which has all the original genetic material except a change in the sequence of genes and hence is not as detrimental to the cell.

Repair of chromosomes after irradiation depends on the sites of break in the DNA molecule or the chromosome, the total radiation dose, the dose rate, and the LET of the radiation. Chromosome aberrations by double-strand breaks occur more frequently at high-dose rates than at low-dose rates because of less time to repair and fewer chances of combining two fragments in correct sequence of genes. High- LET radiations cause more double-strand breaks in chromosomes than low-LET radiations, and thus repair becomes difficult in the former. For example, α-particles, protons, and neutrons will cause more chromosome aberrations than γ-rays.

Direct and Indirect Actions of Radiation

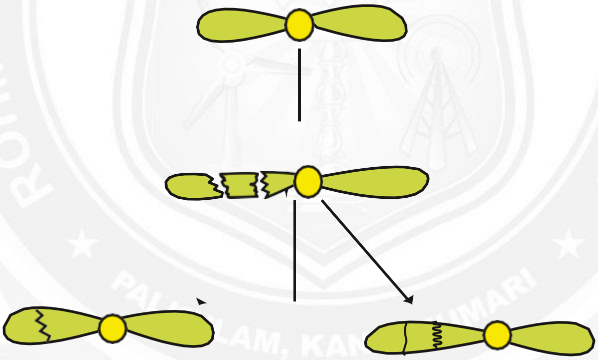


The DNA molecule of a cell is the most sensitive target to radiation. Radiation damage to the cell can be caused by the direct or indirect action of radiation on the DNA molecules. In the direct action, the radiation hits the DNA molecule directly, disrupting the molecular structure Such structural change leads to cell damage or even cell death. Damaged cells that survive may later induce carcinogenesis or other abnormalities. This process becomes **Dicentric Fragment**

In the indirect action, the radiation hits the water molecules, the major con- stituent of the cell, and other organic molecules in the cell, whereby

$$H_2O + \text{energy} \rightarrow H_2O^+ + e^-$$
$$H_2O + e^- \rightarrow HOH^-$$
$$H_2O^+ \rightarrow H^+ + OH\bullet \text{ (free radical)}$$
$$HOH^- \rightarrow OH^- + H\bullet \text{ (free radical)}$$
$$H^+ + OH^- \rightarrow H_2O$$
$$H\bullet + OH\bullet \rightarrow H_2O$$
$$OH\bullet + OH\bullet \rightarrow H_2O_2$$
$$H\bullet + O_2 \rightarrow HO_2\bullet \text{ (perhydroxyl radical)}$$

free radicals such as perhydroxyl (HO_2) and alkoxy (RO_2) are produced.



RADIATION DOSE AND ITS EFFECTS

3.4 Types of Biological effects

Biological Effects by radiation are of two types

1.Deterministic Effect (or) non-stochastic effect

2. Stochastic Effect

Deterministic Effect (or) Non-Stochastic Effect

Deterministic effects are also called non-stochastic effect. Deterministic effects are usually associated with high doses and are characterized by a threshold.

It has a threshold of doses below which the effect does not occur and above this threshold the damage increases with dose. The threshold may be varied from person to person

Deterministic effect includes

(i) Acute Radiation Sickness

(ii) Chronic Radiation Sickness

Acute radiation sickness