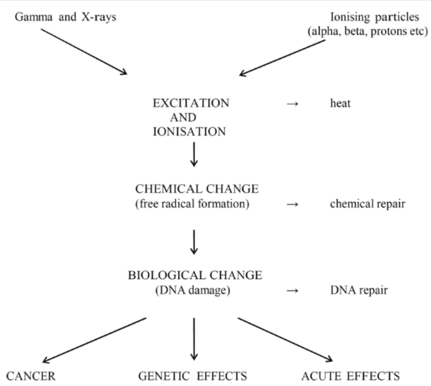
Development of Radiation Injury



Development of Radiation Injury

When they interact with living tissue, x-rays, gamma rays and other ionising particles eject fast electrons from atoms within the cell. These electrons in turn lose their energy by interactions with other large molecules causing ionisation and excitation.

Energy deposition in irradiated cells thus occurs in the form of ionised and excited atoms or molecules distributed at random throughout the cells. Although much of the actual energy absorbed by irradiated cells goes into producing excited molecules, it appears that most of this energy does not produce chemical reaction and is dissipated in the form of heat.

It is the ionisation that causes most of the immediate chemical changes in the vicinity of the event.

Ionisation results from the ejection of an orbital electron from a molecule, producing a positively charged or 'ionised' molecule. Such molecules are highly unstable and will rapidly undergo chemical change. This damage results in the production of 'free radicals', which are atoms or molecules containing unpaired electrons.

Free radicals are extremely reactive and may lead to permanent damage of the affected molecule, or the energy may be transferred to another molecule.

Because 80 percent of the cell is water, most energy deposited within the cell by radiation results in the production of aqueous free radicals, for example, OH *and H.*

Development of Radiation Injury (cont)

Chemical damage may be repaired before it is irreversible by recombination of the radicals, and the energy dissipated as fluorescence, phosphorescence, or vibrational energy. If unrepaired, chemical change will lead to biological damage.

The radiosensitive site of the cell has been identified as the deoxyribonucleic acid (DNA) molecule within the nucleus.

Interaction of Radiation with Tissue

The process by which x-ray or γ-ray photons are absorbed depends on their energy and the chemical composition of the absorbing material.

At high energies, the **Compton process** dominates. In this process the photon interacts with a loosely bound electron of an atom of the absorbing material. Part of the photon energy is given to the electron as kinetic energy. The photon, deflected from its original path, proceeds with reduced energy and may undergo further interactions. The net result is the production of **fast electrons**, many of which can ionise other atoms of the absorber, break vital chemical bonds, and initiate biological damage.

In the **photoelectric effect**, the photon gives up all its energy to the bound electron; some of which is used to overcome the binding energy of the electron and release it from its orbit, while the remainder is given to the electron as kinetic energy.

In radiotherapy, for example, with a cobalt-60 unit or a linear accelerator, the Compton process, which is independent of Z, is overwhelmingly important. As a consequence, the absorbed dose is approximately the same in soft tissue, muscle and bone.

In radiobiology, it doesn't matter which process dominates because most of the energy of the absorbed photons is converted into the kinetic energy of fast electrons. This energy is dissipated as the electrons move through the medium where they ionise and excite atoms with which they interact.

Linear Energy Transfer

Linear Energy Transfer (LET) accounts for all the energy liberated along the path of an ionising particle

Usually expressed as **keV per micrometer, keV/μm** (ie. Energy per Length).

LET determins if a type of ionising radiation is **sparsely** (x or γ rays), **moderately** (neutrons) or **densely** (α-particles) ionising

In general, particles of high-LET radiations (densely ionising) are more likely to produce change in a given volume of living matter, because their interactions are produced more closely together.

Direct action of Radiation

When radiation (x or γ rays, charged or uncharged particles) is absorbed in biological material, it may interact directly with the sensitive targets in the cells initiating the chain of events that lead to a biological change.

This is the dominant process for medium LET radiation (for example, neutrons) and is essentially the sole method of absorption for high LET radiation (for example, α-particles).

Indirect action of Radiation

Radiation may interact with other atoms or molecules in the cell (particularly water) to produce **free radicals**. If the radicals are formed within a critical distance of the target, they are able to diffuse far enough to reach and damage it

This is dominant for sparsely ionising radiation, for example, x-rays or γ rays

Radiolysis of water occurs when water is irradiated, it dissociates into other molecular products

When an atom of water (H2O) is irradiated, it is ionised and dissociates into two ions - an ion pair:

Ionisation: H2O + radiation → HOH+ + e-

Indirect action of Radiation (cont)

After this initial ionisation, a number of reactions can happen:
1. the ion pair may rejoin into a stable water molecule (and no damage occurs);
2. if the ions do not rejoin, it is possible for the negative ion (electron) to attach to another water molecule, producing a third type of ion:

Additional Ionisation: H2O + e- → HOH-

The HOH+ and HOH- are relatively unstable and can dissociate into still smaller molecules:

Dissociation: HOH+ → H+ + OH
HOH- → OH- + H

The **final result** of the radiolysis of water is the formation of an ion pair (H+ and OH-) and two free radicals (H *and OH*).

The ions can recombine (H+ and OH-), and hence no biological damage would occur. However, the free radicals are another story. They are highly reactive, unstable and exist with a lifetime of less than 1 ms. During this time, they are capable of diffusion through the cell and interaction at a distant site. Free radicals contain excess energy that can be transferred to other molecules to disrupt bonds and produce point lesions at some distance from the initial ionising event. **It is estimated that about two thirds of x- ray damage to mammalian cells is due to the OH*.**