

# RADIATION BIOLOGY

## Definition

**Radiation** is a process in which energetic particles or energetic waves travel through vacuum or media.

**Radiobiology** (also known as radiation biology) is the study of the action of ionizing radiation on living things.

## History

The history of discovery of different types of radiation can be summarized as follows:

- \* Sir Frederick William **Herschel**, 1738-1822, Germany, discovered the planet Uranus and its major moons (Titania and Oberon). He was the first person who discovers the existence of *infrared radiation*.



- \* Johann Wilhelm **Ritter**, 1776 – 1810, Germany, discovered *Ultraviolet*.



- \* Heinrich **Hertz**, German 1857 – 1894, detected *Radio waves* in 1887, therefore, some prefer to call Hertz the “Father of Radio” and the unit of radio frequency is called the “hertz”.

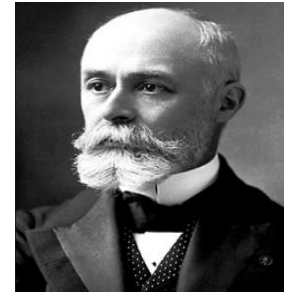


- \* Wilhelm Conrad **Rontgen**, 1845 – 1923. The German physicist who discovered the radiation known today as *X-rays* or Röntgen rays in 1895. In 1901 Röntgen was awarded the first Nobel Prize in Physics. He published the first X-ray photograph of his wife's hand, also he subjected his fingers to X-rays and observed the acute effects of radiation (his fingers burned).



## RADIATION BIOLOGY

- \* Antoine Henri **Becquerel** (France, 1852- 1908). In 1896, he discovered that uranium salts emitted rays that resembled X-rays in their ability to penetrate solid objects. Henri Becquerel, Pierre Curie, Marie Curie won the Nobel Prize in Physics 1903.



- \* Pierre **Curie** (1859-1906) & **Marie Curie** (1867-1934) together with Antoine Becquerel won the 1903 Nobel Prize in Physics for their investigations of *radioactivity*. Marie won a 1911 Nobel Prize in Chemistry for discovering Radium, Polonium. The health dangers of radioactive substances were not well known and Marie died of cancer.



- \* Ernest **Rutherford** (1871-1937) discovered two distinctive types of radiation emitted by thorium and uranium which he named *alpha and beta*. Also he named the radiation discovered by Paul **Villard**, a French chemist as *gamma*. He found out that this radiation had a much greater penetration power than alpha and beta.



- \* Victor **Hess** was an Austrian scientist who discovered *cosmic rays* during a series of hazardous balloon flights in 1912. He won the 1936 Nobel prize in physics for his work on the phenomena.

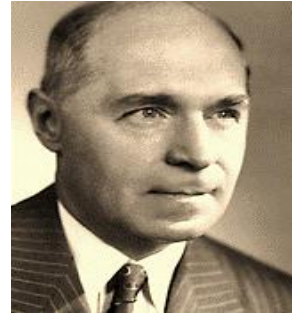


- \* James **Chadwick** (1932) discovered *neutron radiation* and *isotopes*.

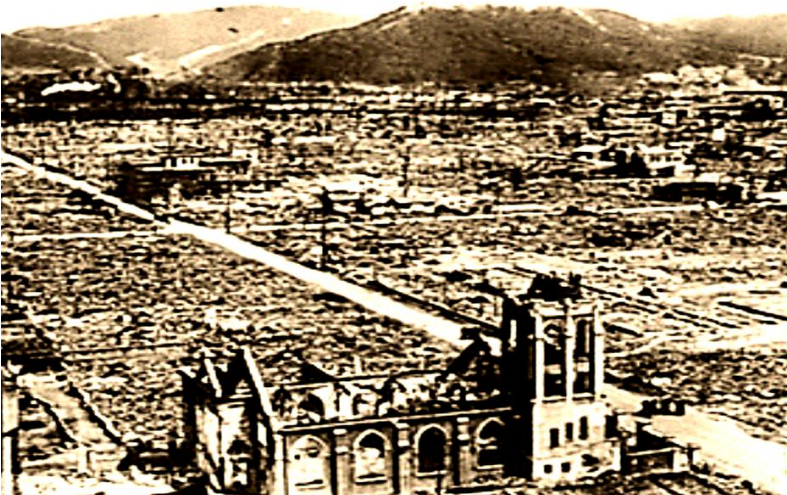
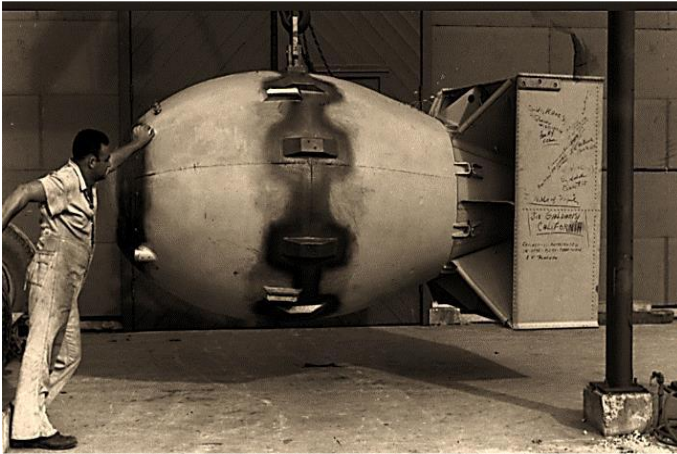


## RADIATION BIOLOGY

- \* Hermann Joseph **Muller** (1890-1967) recognized the *genetic effects of radiation* in 1927 including the cancer risk, and he obtained critical evidence of the abundant production of gene mutations and chromosome changes by X-rays. In 1946, he was awarded the Nobel Prize for his findings.



- \* **The atomic bombings of Hiroshima and Nagasaki, 1945** resulted in a large number of incidents of radiation poisoning, allowing for greater insight into its symptoms and dangers.



# RADIATION BIOLOGY

## Uses of radiation

### **A. In medicine**

1. Detection of broken bones & tumor masses by using X-rays.
2. Diagnosis of thyroid gland diseases by injection a radioactive substance (e.g. Iodine isotope).
3. Detection of several infectious diseases & hormonal disturbance by radioimmunoassay.
4. Decontamination of medical equipment & products by using ultra violet (UV) & gamma ( $\gamma$ ) rays.
5. Treatment of cancers (radiotherapy) by using gamma ( $\gamma$ ) ray.

### **B. In communication**

All modern communication systems use forms of electromagnetic radiation that vary in their intensity according to changes in:

1. **Sounds** (e.g. phone)
2. **Words** (e.g. fax)
3. **Pictures** (e.g. internet)

### **C. In science**

1. Determination the composition & age of materials by using radioactive atoms.
2. Determination the pathways taken by pollutants through the environment.

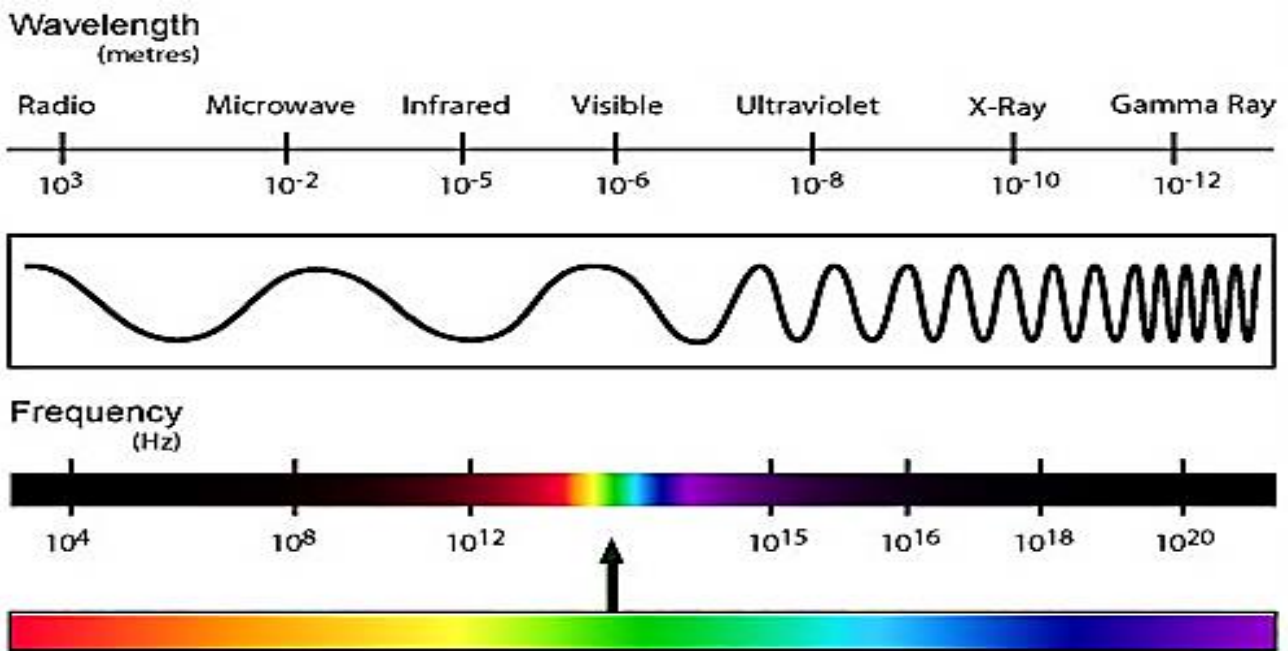
## Types of Radiation

Electromagnetic radiations can be classified in several types of radiation according to their **wave length** & **frequency** which are shown in the following spectrum. A smaller wavelength corresponds to a higher energy according to the equation:

$$E = h c / \lambda$$

(**E** = Energy; **h** = Planck's constant; **c** = speed of light;  **$\lambda$**  = wavelength).

# RADIATION BIOLOGY



Two types of radiation are commonly differentiated:

## A. Non-ionizing Radiation:

The non-ionizing radiation consists of electromagnetic waves that are not energetic enough to detach electrons from atoms or molecules, thus can't ionizing them. These include radio waves, microwaves, infrared, and visible light.

### 1. Visible light

Light is a very narrow range of electromagnetic radiation of a wavelength that is visible to the human eye (about 400–700 nm). The red light has the longest wavelength of visible light, while violet light has the shortest wavelength and the remainder (orange, yellow, green, blue) are lie between them as shown in the above spectrum. Bright sunlight provides an irradiance of just over 1 kilowatt per square meter at sea level, from which only 445 watt is visible light.

### 2. Infrared

Infrared (IR) light is electromagnetic radiation with a wavelength between 700 nm and 300 micrometers. From 1 kilowatt of bright sunlight energy, 527 watts is infrared radiation.

### 3. Microwave

Microwaves are electromagnetic waves with wavelengths ranging from as long as one meter to as short as one millimeter.

### 4. Radio waves

Radio waves have the longest wavelength among the non-ionizing radiation waves that reach to thousands meters. They are either *naturally* occurring radio waves that are resulted from lightning and astronomical objects, or can be generated *artificially* to be used for (fixed & mobile communication, broadcasting, radar, satellite communication, and computer networks).

### 5. Ultraviolet radiations (UV)

Ultraviolet radiation has the shortest wavelength among the non-ionizing radiation waves that lie between 400 nm and 125 nm. From 1 kilowatt of bright sunlight energy, only 32 watt is UV radiation. UV radiation is considered as non-ionizing radiation because its energy is less than binding energy of the outer electron to an atom which is equal to 3.1 electron volt (eV), so it can't detach electron from its atom but it can cause excitation in biological system and resulting in serious damage.

## B. Ionizing radiation:

Ionizing electromagnetic radiations have energies larger than (10 eV) which is a typical binding energy of an outer electron to an atom or organic molecule. So exposure to ionizing radiation causes damage to living tissue, resulting in skin burns, radiation sickness and death at high doses and cancer, tumors and genetic damage at low doses. Ionizing radiations are all radiations on the short-wavelength end of the electromagnetic spectrum with a wavelength of 125 nm or less (lower wavelength means higher frequency and higher energy) which includes:

1. Alpha particles
2. Beta particles
3. X-ray
4. Gamma ray
5. Free neutrons & Cosmic ray.

# RADIATION BIOLOGY

## Radioactive Materials

### *Atomic number (Z):*

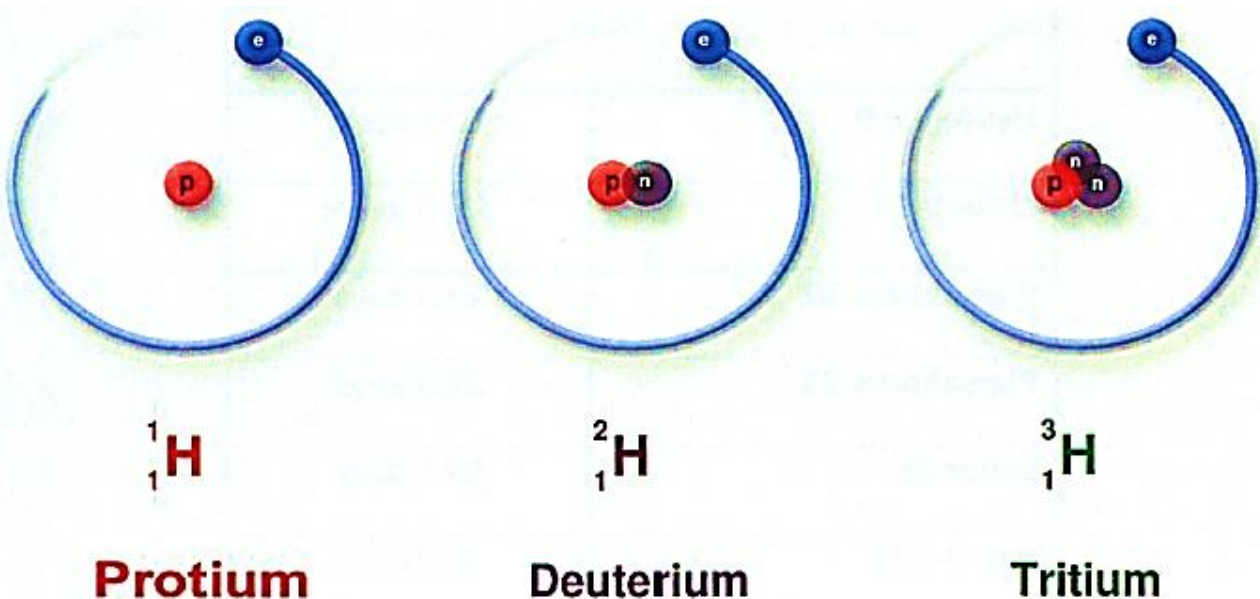
It is the number of protons within the atom's nucleus and is equal to the number of electrons in the neutral (non-ionized) atom.

### *Mass number (A):*

It is the number of nucleons (both protons and neutrons) in the nucleus of an atom.

### *Isotopes:*

They are variants of a particular chemical element which differ in neutron number, although all isotopes of a given element have the same number of protons in each atom. The term isotope is derived from Greek word *isos* (equal) and *topos* (place), meaning different isotopes of a single element occupy the same position on the periodic table. For example; carbon-12, carbon-13, and carbon-14 are three isotopes of the element carbon with mass numbers 12, 13, and 14 respectively. The atomic number of carbon is 6, which means that every carbon atom has 6 protons, so that the neutron numbers of these isotopes are 6, 7, and 8 respectively. Also hydrogen has three naturally-occurring isotopes, each isotope has one proton, its identity is given by the number of neutrons. They are protium ( $^1\text{H}$ ) with zero neutron, deuterium ( $^2\text{H}$ ) with one neutron, and tritium ( $^3\text{H}$ ) with two neutrons.



# RADIATION BIOLOGY

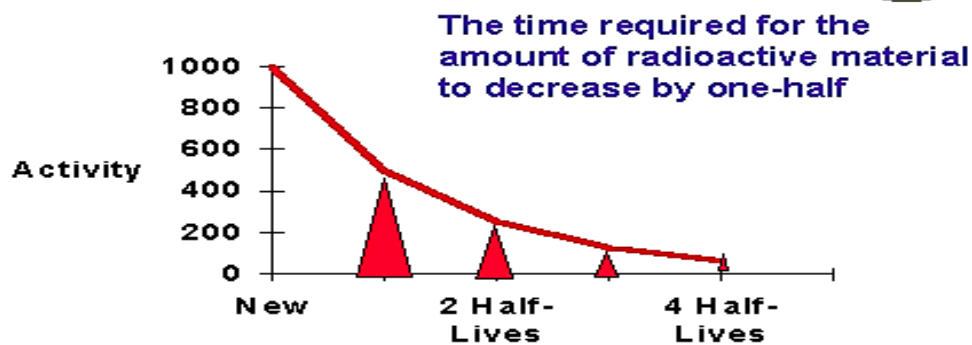
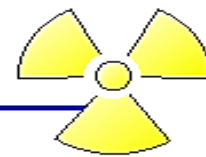
## **Radioactivity:**

It is a natural and spontaneous process by which the unstable atoms of an element emit or radiate excess energy in the form of particles or waves. These emissions are collectively called ionizing radiations.

## **Half-life**

It is the time required for a given amount of some radioactive material to be reduced to one-half of its original activity.

### Half-Life



Radioactive materials decay at exponential rates unique to each radioisotope, thus the half-life values for radioisotopes vary widely. For example, the following table shows half-lives for commonly used radioisotopes:

<b>Radioisotope</b>	<b>Half-Life</b>
Hydrogen-3	12.3 years
Carbon-14	5730 years
Phosphorus-32	14.3 days
Phosphorus-33	25.3 days
Sulfur-35	87.6 days
Iodine-125	60.1 days



# RADIATION BIOLOGY

## *Radioactive isotope (radionuclide):*

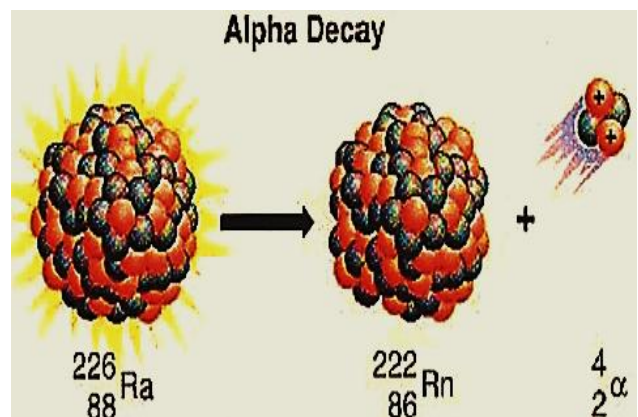
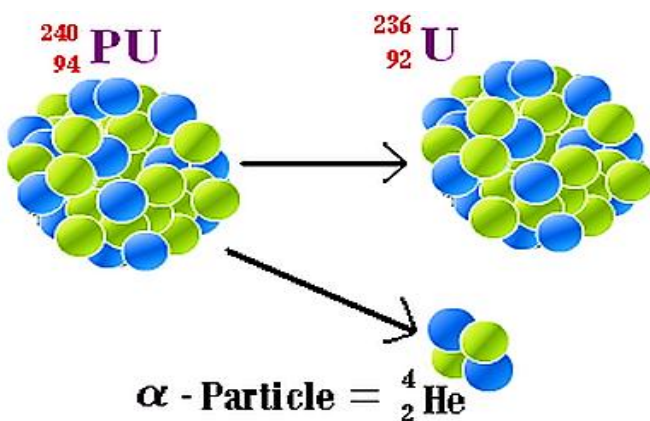
It is an atom that has excess nuclear energy, making it unstable unless emit this excess energy from the nucleus as new radiation or a new particle, or transfer this excess energy to one of its electrons, causing it to be ejected and then becomes more stable. Naturally occurring radionuclides fall into three categories:

1. **Primordial radionuclides** are mainly originated from the interior of stars which are not yet completely decayed because their half-lives are so long such as uranium and thorium.
2. **Secondary radionuclides** are derived from the decay of primordial radionuclides and have shorter half-lives such as radiogenic isotopes.
3. **Cosmogenic isotopes** are continually being formed in the atmosphere due to cosmic rays such as carbon-14.

## Types of Radioactive Decay

### 1. Alpha Particles

Alpha decay is a radioactive process in which a particle with two neutrons and two protons is ejected from the nucleus of a radioactive atom. The particle is identical to the nucleus of a helium atom. Because alpha particles contain two protons, they have a positive charge of two. Further, alpha particles are very heavy and very energetic compared to other common types of radiation. Examples of highly poisonous alpha-emitters are radium, radon, and polonium which are very heavy elements because the nuclei of these atoms are very “neutron rich” which makes emission of the alpha particle possible.

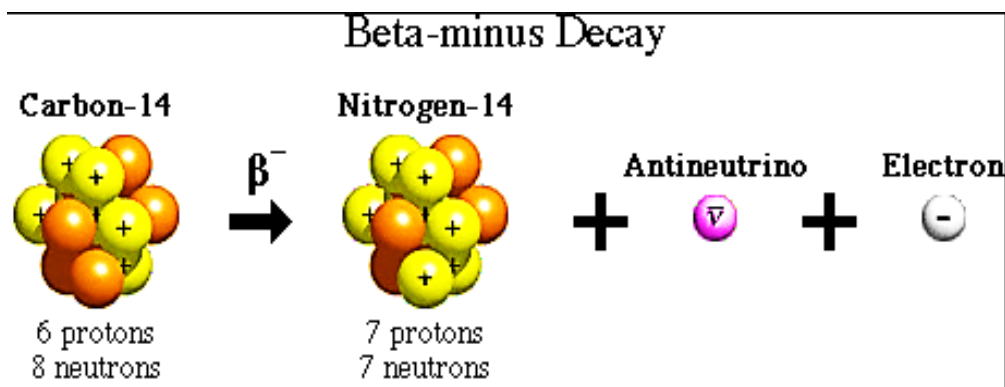


## 2. Beta Particles

Beta decay is a radioactive process in which an electron is emitted from the nucleus of a radioactive atom, along with an unusual particle called an **antineutrino** / **neutrino** which is an almost massless particle that carries away some of the energy from the decay process. Because this electron is from the nucleus of the atom, it is called a beta particle to distinguish it from the electrons which orbit the atom. Like alpha decay, beta decay occurs in isotopes which are “neutron rich”. There are two types of beta decay:

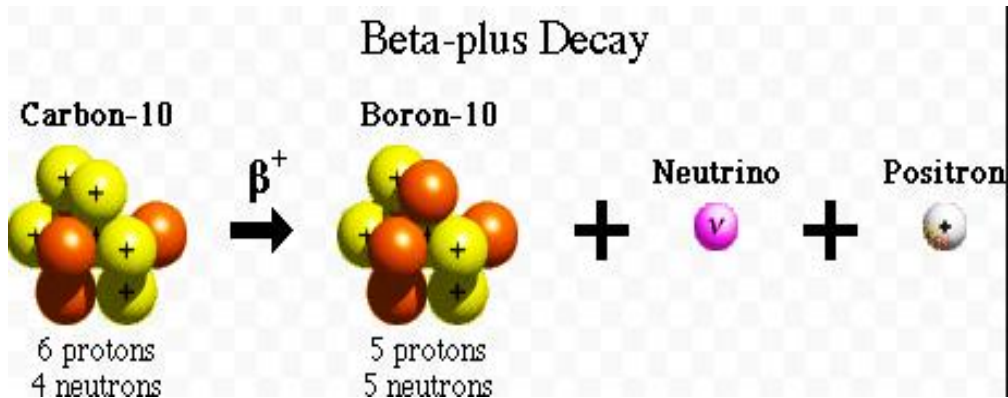
### A. *Beta-minus ( $\beta^-$ ) radiation*

During beta-minus decay, a **neutron** in an atom's nucleus turns into a proton, an electron and an antineutrino. The electron and antineutrino fly away from the nucleus, which now has one more proton than it started with. Since an atom gains a proton during beta-minus decay, it changes from one element to another. For example, after undergoing beta-minus decay, an atom of carbon (with 6 protons) becomes an atom of nitrogen (with 7 protons).



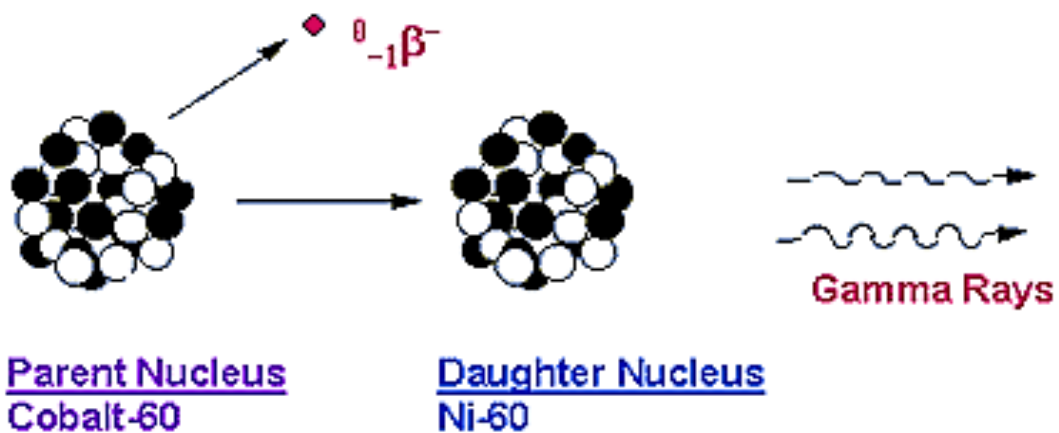
### B. *Beta-plus ( $\beta^+$ ) radiation*

During beta-plus decay, a **proton** in an atom's nucleus turns into a neutron, a positron and a neutrino. The positron and neutrino fly away from the nucleus, which now has one less proton than it started with. Since an atom loses a proton during beta-plus decay, it changes from one element to another. For example, after undergoing beta-plus decay, an atom of carbon (with 6 protons) becomes an atom of boron (with 5 protons). Although the numbers of protons and neutrons in an atom's nucleus change during beta decay, the total number of particles (protons + neutrons) remains the same.



### 3. Gamma ray

Gamma ( $\gamma$ ) radiation consists of photons which have neither mass nor electric charge. Gamma radiation can be emitted as a result of beta decay, and may also be emitted following certain nuclear reactions or the absorption of a thermal neutron by a nucleus. Important gamma emitters including technetium-99<sup>m</sup>, and cobalt-60 which are used in nuclear medicine and cesium-137 that is used for calibration of nuclear instruments.

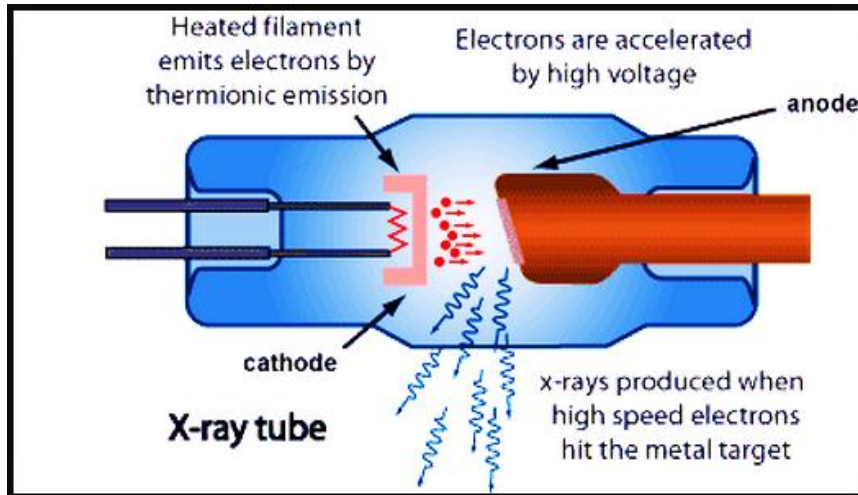


### 4. X-ray

X Rays are electromagnetic waves or photons not emitted from the nucleus, but normally emitted by energy changes in electrons. These energy changes are either in electron orbital shells that surround an atom or in the process of slowing down such as in an X-ray machine. Over a century ago in 1895, Roentgen discovered a device called a *Crooke's tube*, which was a glass envelope under high vacuum, with a wire element at one end forming the cathode, and a heavy copper target at the other end forming the anode. When a high voltage was applied to the electrodes, electrons

# RADIATION BIOLOGY

formed at the cathode would be pulled towards the anode and strike the copper with very high energy. Roentgen discovered that very penetrating radiations were produced from the anode, which he called **X-rays**. Medical x-ray machines in hospitals use the same principle as the Crooke's Tube to produce x-rays.

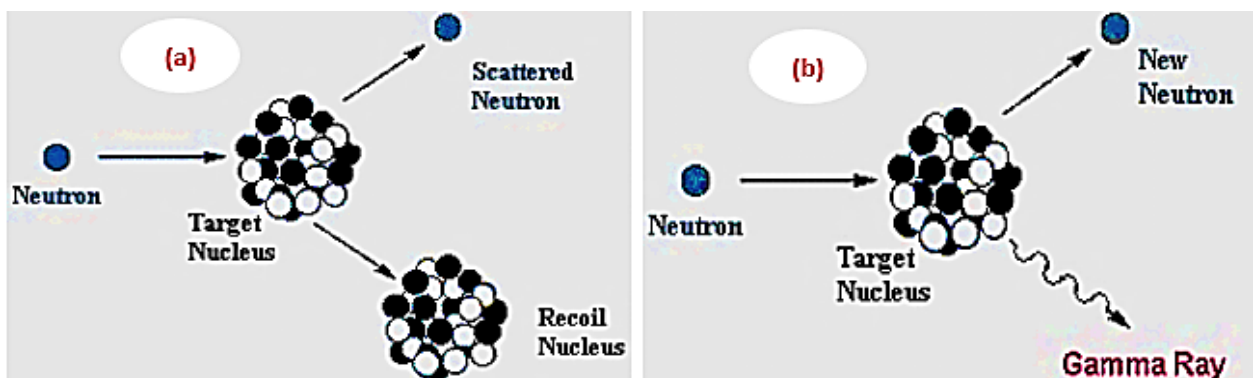


## 5. Neutron radiation

Neutrons are neutral particles with approximately the same mass as a proton and may be emitted during either spontaneous or induced nuclear fission, nuclear fusion processes, or from any other nuclear reactions. Neutrons are not directly ionizing radiation, but produce secondary events that occur as collisions with matter called scattering events & capture events:

### 1) Scattering events (neutrons with high speed & energy):

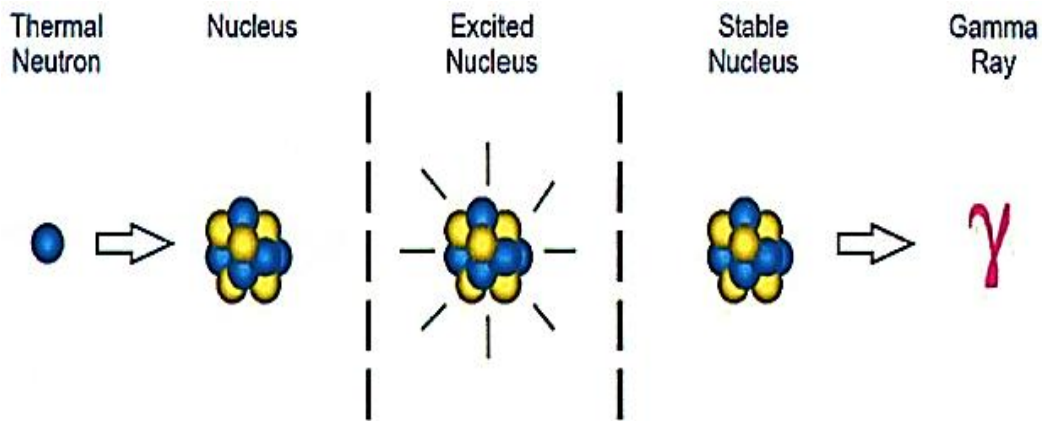
- a) **Elastic scattering event** occurs when a neutron collides with a nucleus and imparts a portion of its energy to the target nucleus and scattered away from it. This energized nucleus called a **recoil nucleus** will move throughout the material causing excitation and ionization events.
- b) **Inelastic scattering events** occurs when a neutron is absorbed by the target nucleus, then a gamma ray and a less energetic neutron emitted from the target.



# RADIATION BIOLOGY

## 2) Capture event (neutron with low speed & energy):

After a neutron has lost a significant portion of its kinetic energy through scattering events it is called **thermal neutron** that may be absorbed by a target nucleus in a capture event because neutron has no electric charge and can enter a nucleus more easily than positively charged protons which are repelled electrostatically. The result of this event is that the mass number of new atom increases by one and become unstable, and will undergo one of many possible nuclear decay (such as emitting gamma ray) to return to its stable status. Therefore, neutrons are the only type of ionizing radiation that can make other objects, or material, radioactive in a process called **neutron activation** to produce radioactive sources for use in medical, academic, and industrial applications.

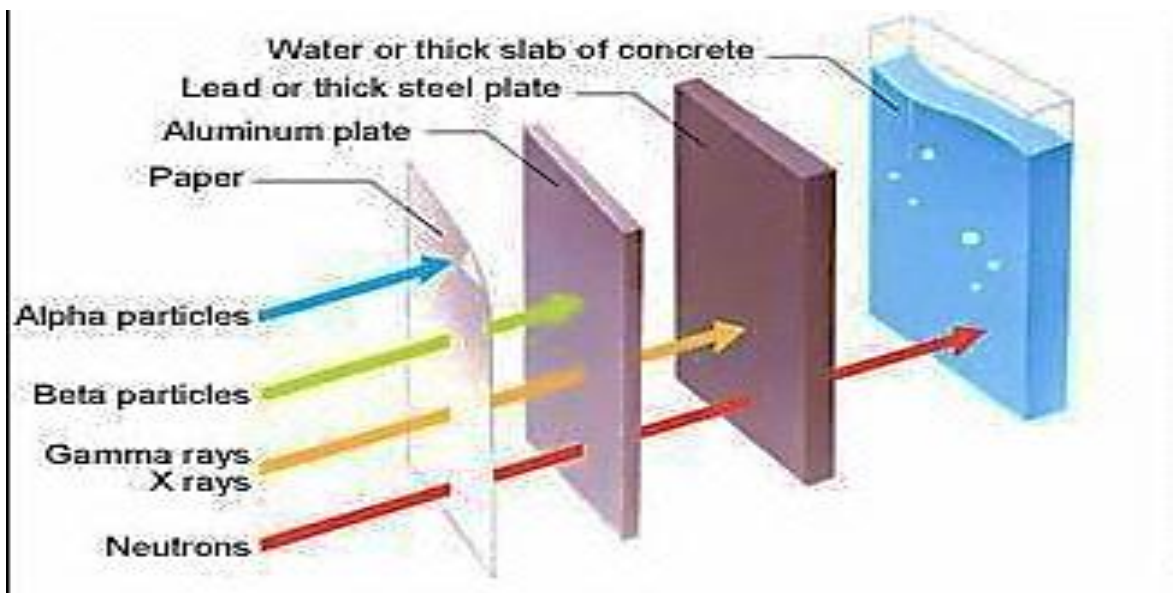


## Properties of Ionizing Radiations

The various types of ionizing radiations and their different properties can be summarized in the following table & Figure:

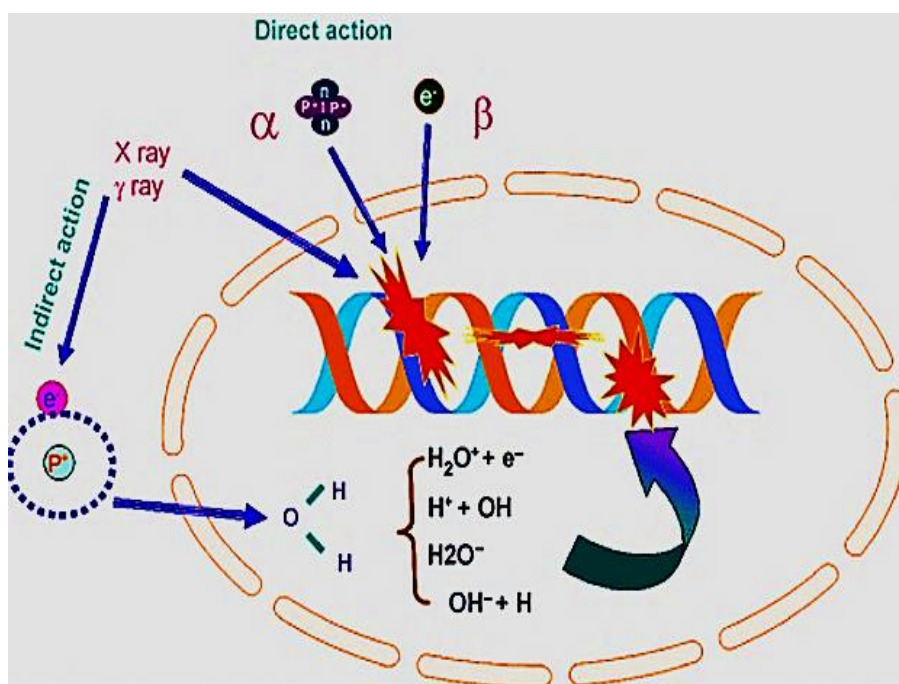
Radiation	Type of Radiation	Mass (AMU)	Charge	Shielding material
Alpha	Particle	4	+2	Paper, skin, clothes
Beta	Particle	1/1836	±1	Plastic, glass, light metals
Gamma & X-ray	Electromagnetic Wave	0	0	Dense metal, concrete, Earth
Neutrons	Particle	1	0	Water, concrete, polyethylene, oil

# RADIATION BIOLOGY



## Radiation Interactions with Matter

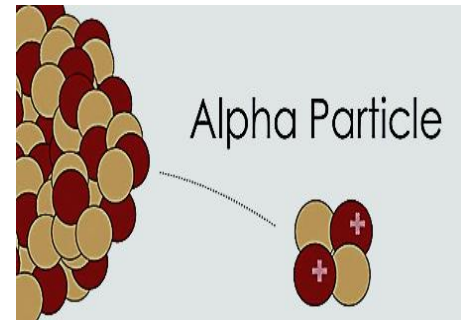
Ionizing radiation may be divided into directly and indirectly ionizing for the understanding of biological effects. Most of the *particulate radiation* ( $\alpha$ , and  $\beta$  particles) are directly ionizing and disrupt the atomic structure of absorbing matter. In contrast, *electromagnetic radiation* (X, and  $\gamma$  rays) are indirectly ionizing because they do not produce biological damage themselves but produce secondary electrons (charged particles) after energy absorption in the matter.



# RADIATION BIOLOGY

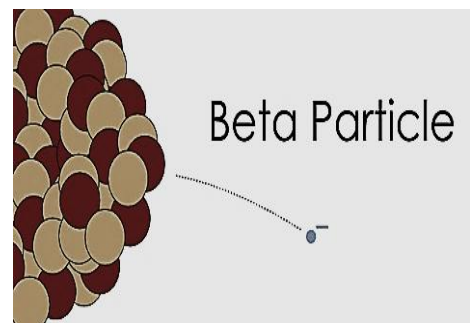
## Alpha ( $\alpha$ ) particles:

Because they are positively charged and heavy particles (2 protons + 2 neutrons) with higher mass and lower velocity, therefore alpha particles are highly ionizing and quickly losing their energy and weakly penetrate in body tissue and can be stopped and fully absorbed by low density material with a thickness of few millimeters such as paper, and clothes.



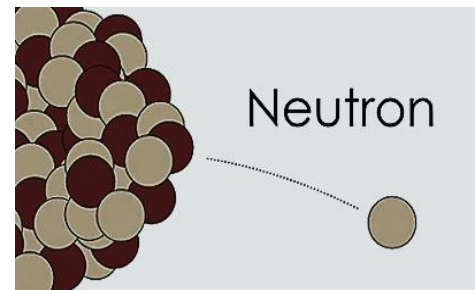
## Beta ( $\beta$ ) particles:

They have lower mass, less energetic, and higher velocity than alpha particles with a single negative charge, therefore, they can penetrate tissues to a greater depth but do not penetrate further than the skin of human body and can be stopped by plastic material with a thickness of few centimeters or metal material with a thickness of few millimeters.



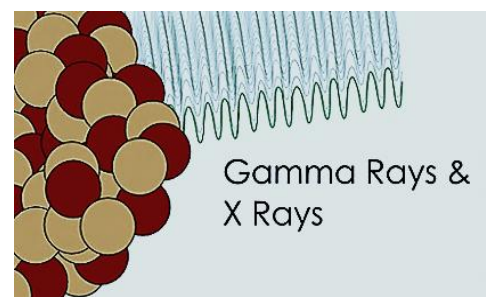
## Neutrons:

Because they are uncharged (neutral), so they are more penetrated than charged particles and produce ionizing of matter indirectly via secondary events. They can travel great distances in air (100s to even 1000s meters), and several meters in solid matters, so they can be stopped only with hydrogen rich shielding such as concrete or water.



## Electromagnetic radiation (X, and $\gamma$ rays):

Gamma ray originate from the nucleus, while X-ray originate from electron cloud of atom. Both of them are types of photons (massless & uncharged) that progress at the speed of light, so they can deeply penetrate through matter further than alpha and beta particles and need more dense material to be stopped such as dense metal, concrete, or earth. They are indirectly ionizing because they do not produce chemical and biological damage themselves but produce secondary electron after absorption their energy by matter.



## Sources of Radiation

### A. Natural Sources

There are many natural sources of radiation which have been present since the earth was formed, so we are all exposed to ionizing radiation from natural sources at all times. There are three major sources of naturally occurring radiation:

#### *1. Cosmic radiation:*

Charged particles from the sun and stars interact with the earth's atmosphere and magnetic field to produce a shower of cosmic radiation consists of **positively charged particles**, as well as **gamma radiation**. The exposure of an individual to cosmic rays is greater at higher elevations than at sea level because at higher elevations the amount of atmosphere shielding decreases and thus the dose of cosmic rays increases.

#### *2. Terrestrial radiation*

When the earth was formed four billion years ago, its ground, rocks, building materials and drinking water contained many radioactive materials such as **radium, uranium** and **thorium** which are ingested with food and water. Also **radon gas** is originated from the decay of natural uranium in soil, and when it is inhaled by human emits alpha radiation that cause lung cancer. The dose from terrestrial sources also varies in different parts of the world according to the concentrations of uranium and thorium in their soil.

#### *3. Internal Source*

We have various radioactive isotopes inside our bodies from birth such as **potassium-40, tritium ( $^3\text{H}$ ), carbon-14**, and **lead-210**. The variation in dose from one person to another is not as great as the variation in dose from cosmic and terrestrial sources.

### B. Man - made Sources

In the last century, artificial sources of radiation have been added to the naturally occurring sources, so people may be exposed to these sources either as **public** exposure or **occupational** exposure:

#### *1. Public exposure:*

The majority of people may exposed to radiation for one or several times during their life from the following sources:

*a) Medical X-ray* for diagnosis of several disease such as chest X-ray.



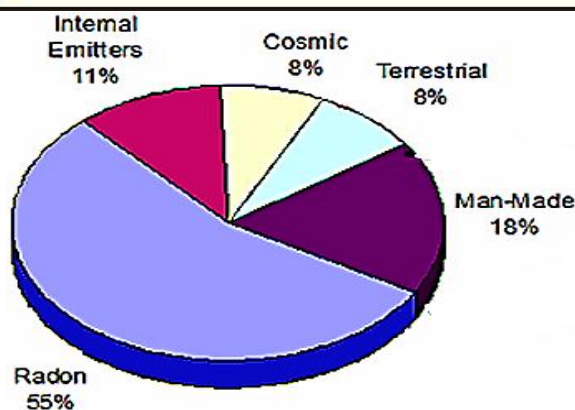
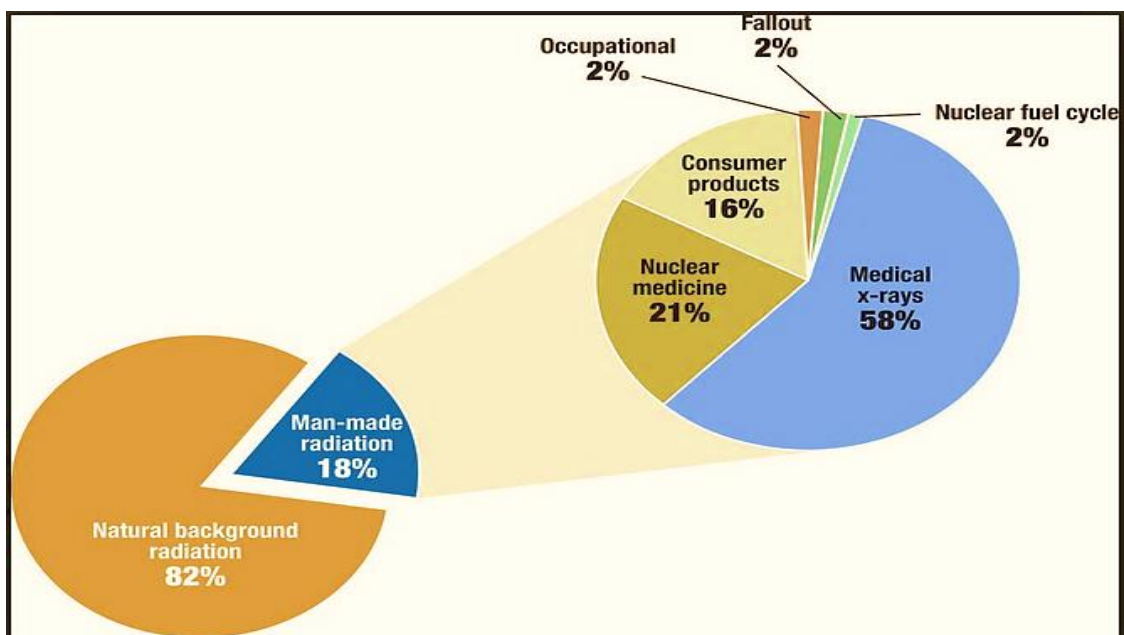
# RADIATION BIOLOGY

- b) Nuclear medicine** for therapy of cancer by using radioactive isotopes such as iodine -131, Technetium - 99, Cobalt-60, and Cesium-137.
- c) Consumer products** such as tobacco, building materials, fuels (gas, coal), ophthalmic glass, televisions, airport X-ray systems, smoke detectors, road construction materials, etc.
- d) Residual fallout** from nuclear weapons testing, shipment, and accidents.

## 2. Occupational exposure

Some workers are exposed to **artificial sources** of radiation commonly used in the manufacturing and service industries such as **nuclear fuel cycle** at a nuclear plant, X-ray machines and radiography.

As a whole, the average annual radiation dose to a member of the general population from natural sources (**Radon, Internal, Terrestrial, Cosmic**) is about 82%, while those come from man-made (**Medical X-ray, Nuclear Medicine, Consumer Products**) is about 18%.



## Types of Radiation Units

### 1. Measurement of Decay Rate

The amount of radioactive material in a given object contains unstable atoms which are continuously decaying, so the more unstable atoms, the greater the decay rate. This rate of decay is measured by two units:

- a) **Curie (Ci)** is a unit used to measure a radioactivity and related to the decay rate (disintegration rate), so One curie = 2,200,000,000,000 **disintegrations per minute ( $2.2 \times 10^{12}$  dpm)**. This means that every minute,  $2.2 \times 10^{12}$  atoms decay and give off radiation.
- b) **Becquerel (Bq)** is a unit also used to measure a radioactivity and one Becquerel is that quantity of a radioactive material that will have **60 dpm**. As a result, there are  $3.7 \times 10^{10}$  Bq in one curie.

### 2. Measurement of Exposure Dose

**Roentgen** (abbreviated 'R') (Pronounced: "renken") is a unit for measuring *exposure* only to gamma and x-rays. The roentgen is essentially a measure of how many ion pairs are formed in a given volume of air when it is exposed to radiation.

### 3. Measurement of Absorbed Dose

There are two units used to measure the absorbed dose of radiation:

- a) **Rad** (Radiation absorbed dose) is a unit used as a measure of energy absorbed by any material from any type of radiation, but it does not describe the biological effects of the different radiations.
- b) **Gray** (Gy) is a standard international (SI) unit also used to measure absorbed dose, and each 1 Gray = 100 rads.

### 4. Measurement of Equivalent Dose

Because not all radiation types has the same biological effect even for the same amount of absorbed dose, therefore, the *equivalent dose* is the quantity of radiation dose that is relative to the harm or risk caused by a given dose of radiation when compared to any other doses of radiation of any type. To determine equivalent dose, the absorbed dose is multiplied by a quality factor (Q) that is unique to the type of incident radiation.

***Equivalent dose = absorbed dose x quality factor***

The equivalent dose can be measured by a unit known as **Roentgen equivalent man (rem)**. For instance, *exposure* to (1Roentgen) of gamma radiation causes

# RADIATION BIOLOGY

an absorbed dose in a person of about (1 rad), which results in equivalent dose of (1 rem). However, an absorbed dose of (1 rad) from fast neutrons would result in equivalent dose of (10 rem). Since the rem is a fairly large unit, radiation exposure is usually recorded in millirem (1 rem = 1000 mrem). According to standard international (SI) units, **Sievert (Sv)** is a unit also used to measure equivalent dose, and each 1 Sievert = 100 rem.

## Types of Radiation Doses

**Dose** is the amount of radiation you receive and usually measured by (**mrem**), while **Dose Rate (intensity)** indicates how fast you receive the dose of radiation and usually measured by (**mrem/hr**). As discussed above the biological effectiveness of each type of radiation varies greatly depending largely on the type of radiation, type of tissue, and the period of time exposure. Therefore, there are several types of radiation dose that can be summarized as follows:

1. **Equivalent dose** is used to compare the biological effectiveness of different types of radiation on the same tissue. It is equal to the product of the absorbed dose in the tissue multiplied by the quality factor of radiation type, which is expressed by rem or Sievert (Sv).
2. **Effective dose** is used to estimate the risk of radiation in humans. It is sum of the products of equivalent doses to each organ/tissue and the tissue factor. The unit of effective dose is the Sievert (Sv).
3. **Collective dose** is defined as the dose received per person in Sv multiplied by the number of persons exposed per year that is generally used for protection purposes and in population response calculations.
4. **Chronic dose** means a person received a radiation dose over a long period of time.
5. **Acute dose** means a person received a radiation dose over a short period of time.

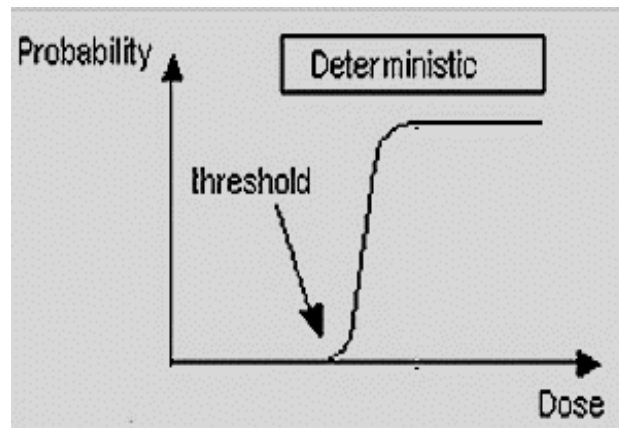
# RADIATION BIOLOGY

## Biological Effects of Radiation

Whether the source of radiation is natural or man-made, whether it is a small dose of radiation or a large dose, there will be some biological effects within the body. These different effects can be split into two categories; *Deterministic* and *Stochastic* effects:

### 1. Deterministic effect

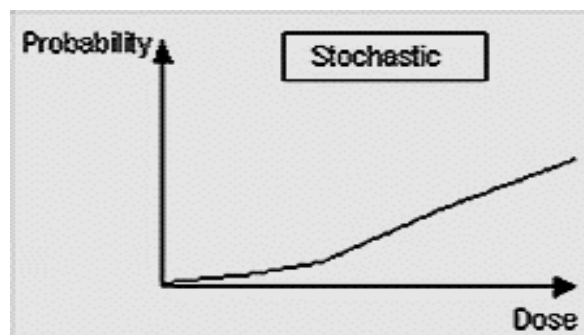
The *probability* of having this effects is not proportional to the absorbed dose because this effect has a *threshold*, below which the effect will not occur. However, the *Severity* of deterministic effect depends on absorbed dose which is related directly to the dose received such as cataract, hair loss, infertility, etc.



Organs	Effects	Threshold (mSv)	
		Acute dose (single)	Chronic dose (multiple /year)
Testis	Permanent infertility	> 3500	>2000
Ovary	Permanent infertility	>2500	>200
Eye	Cataract	>5000	>150

### 2. Stochastic effect

The *probability* of having this effect is directly proportional to the dose absorbed. There is no *threshold*, so any dose may or may not produce this effect, but the *severity* of stochastic effect is independent on the absorbed dose. Stochastic effect of radiation can cause cancers or genetic modifications.



# RADIATION BIOLOGY

## Mechanisms of Damage

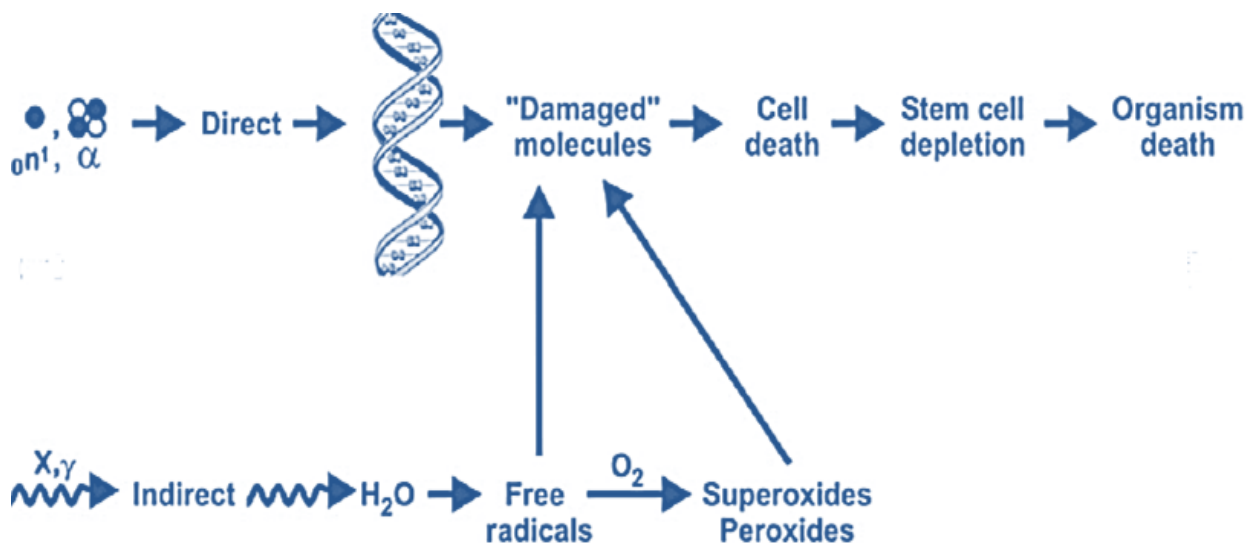
Ionizing radiation causes atoms and molecules to become ionized or excited. These excitations and ionizations can damage molecules that regulate vital cell processes (e.g. DNA, RNA, proteins) through two mechanisms:

### 1. Direct mechanism:

Radiation directly hit the atoms of the macromolecules; DNA, RNA, proteins, lipids, and carbohydrates which are critical to the survival of the cell, and then the cell may be destroyed.

### 2. Indirect mechanism:

Radiation interacts with water, also of water leading to the formation of *free radicals* such as hydrogen ( $H^*$ ) and hydroxyl ( $OH^*$ ) free radicals in a process called *radiolysis*. These fragments could combine to form toxic substances, such as superoxide & peroxides which can contribute to the destruction of the cell.

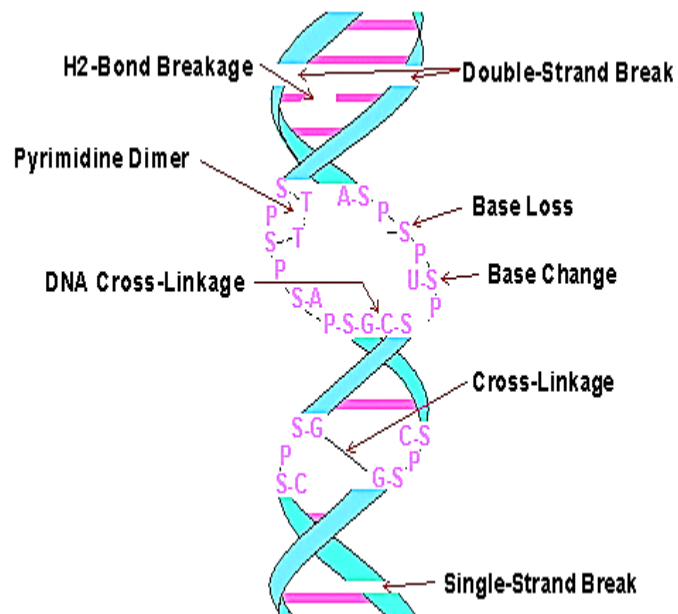


## Cellular damage of radiation

Injury to living tissue results from the transfer of energy to atoms and molecules in the cellular structure, especially DNA that lead to break chemical bonds or produce new chemical bonds and cross-linkage between macromolecules which is known as *genomic instability*. There are different types of damage to DNA produced by radiation (including ultra violet) as shown in the following figure:

# RADIATION BIOLOGY

1. Single-strand break
2. Double-strand break
3. Hydrogen bond breakage
4. DNA cross-linkage
5. Pyrimidine Dimer
6. Base change
7. Base loss



When the cell exposed to radiation, its DNA may be damaged due to physical and biochemical effects of radiation within a short time (fractions of seconds or few seconds), but within few minutes cells with damaged DNA undergo one of the following processes:

## 1. Cell death

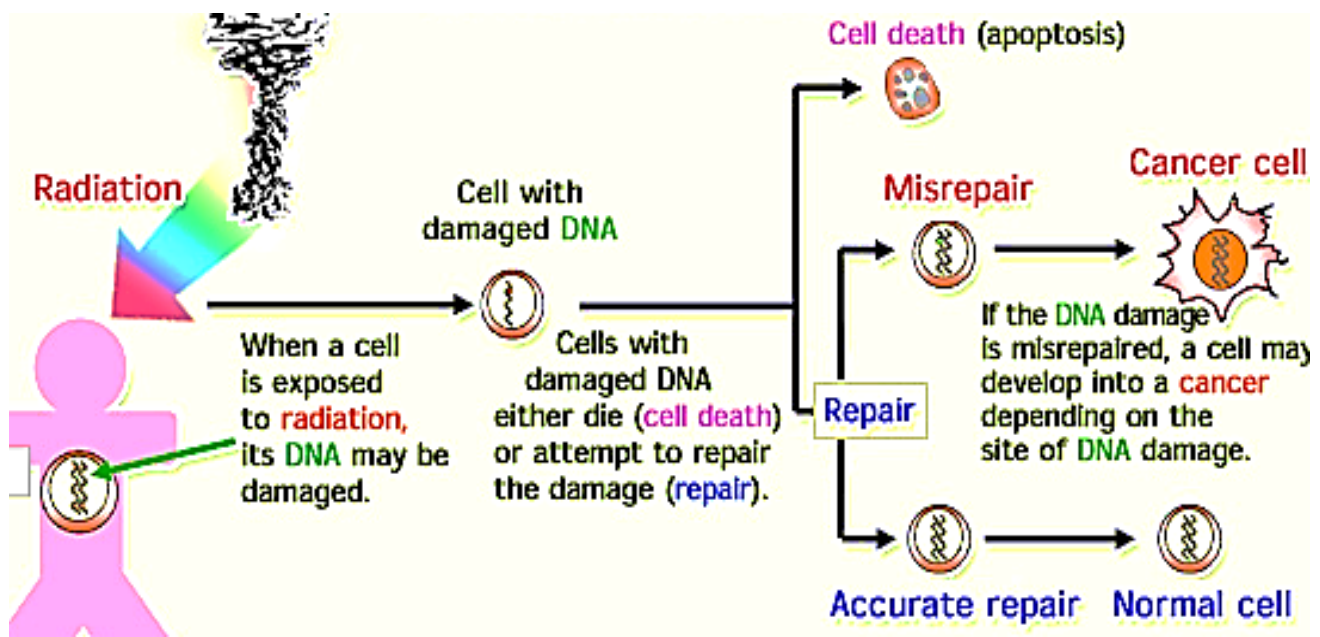
Any cell with damaged DNA should be suicide by activation a mechanism known as programmed cell death (**apoptosis**). At high doses, large numbers of cells were killed and clinical symptoms appear in hours-days-weeks or months because cells cannot be replaced quickly enough, and tissues fail to function.

## 2. Cell repair

Cell with damaged DNA attempt to repair this damage within minutes. If the damage is correctly repaired, the cell returns normal, but if the repair is incorrect (*Misrepair*), the cell survive with genomic instability which is over time cause big problems that can be grouped into two categories:

- a) Somatic damages which primarily arise from genomic instability in somatic cells of the irradiated person that are either appear early after exposure to radiation such as hair loss, infertility), or appear late after exposure to radiation such as cataract, and cancer.
- b) Genetic damages which arise from genomic instability in germ cells of the irradiated parents and seen in their offspring as genetic malformations.

# RADIATION BIOLOGY



## Determinants of Radiation Effects

The occurrence of health effects from exposure to ionizing radiation is a complicated function of numerous factors including:

### 1. Type of radiation

The type of radiations determine how far they can penetrate into tissue and how much energy they are able to transmit directly or indirectly to tissue.

### 2. The radiation dose

The higher the dose of radiation received the higher health effects.

### 3. The dose rate of radiation

A given dose will produce less effect if divided than if it were given in a single exposure.

### 4. Species Sensitivity

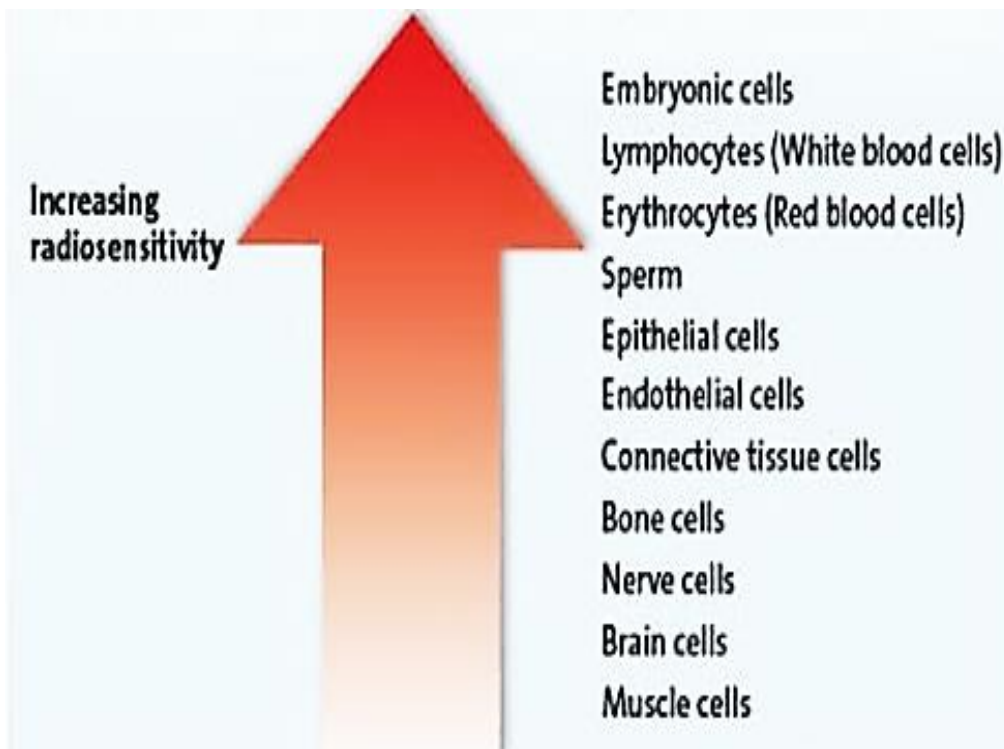
There is a wide variation in the radio-sensitivity of various species. The lethal dose for each species is expressed as the (*LD50/30*) which is the dose required for killing 50% of the individuals in a large population in a thirty day period. Lethal doses for plants and microorganisms are usually hundreds of times larger than those for mammals as shown in the following table:

# RADIATION BIOLOGY

Organism	LD <sub>50</sub> (rad)	Organism	LD <sub>50</sub> (rad)
Dogs, pigs	300	Cattle, rats, horses	630
Goats	350	Rabbits	800
MAN	400	Chickens	1000
Mice, monkeys	450	Insects	5000
Sheep	540	Turtles	15000
Fish	550	Bacteria/viruses	100000

## 5. Cell Sensitivity

Within the same individual, a wide variation in susceptibility to radiation damage exists among different types of cells and tissues. This radio-sensitivity has been expressed by (*Law of Bergoniè & Tribondeau*), in which the radiation sensitivity of a tissue is *directly* proportional to the *rate of proliferation* of its cells, and *inversely* proportional to the degree of *cell differentiation*. Therefore, the developing embryo is most sensitive to radiation during the early stages of differentiation (in the first trimester than in later trimesters). One exception to this law is mature lymphocytes, which are highly radiosensitive. It is possible to rank various kinds of cells in ascending order of radio-sensitivity:



## 6. Part of the body exposed

Extremities such as the hands or feet are able to receive a greater amount of radiation with less resulting damage than blood forming tissues found in the bone marrow.



## 7. The age of individual

As a person ages, cell division slows and the body is less sensitive to the effects of ionizing radiation. Once cell division has slowed, the effects of radiation are somewhat less damaging than when cells were rapidly dividing.

## 8. Area exposed

The larger the area exposed, the greater the overall damage to the organism. Therefore, in radiation therapy doses should be delivered to very limited areas (to tumor sites) rather than whole-body irradiation of the same dose.

## Health Effects of Radiation

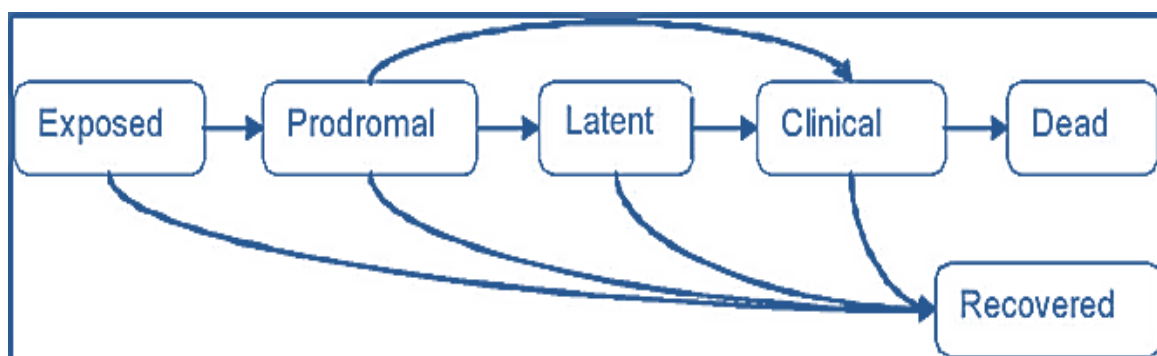
Health effects of ionizing radiation upon humans are often broadly classified into **prompt (short-term) effects** that appear immediately after exposure, and **delayed (long-term) effects** that appear months or years after exposure.

### Short-Term Effects

According to the part of body exposed and type of radiation, it can be classified into acute radiation syndrome (ARS), and cutaneous radiation syndrome (CRS).

#### A. Acute radiation Syndromes (ARS):

It is also known as *radiation sickness* or *radiation poisoning* that occurs after *whole or partial body exposure* to deeply penetrated radiation (gamma, neutron) in a very short period of time (usually minutes). The total health effects which present within 24 hours of exposure may last for several months and vary from mild and transient illness to death depending on the amount of radiation. Acute Radiation syndromes progresses in four phases:



# RADIATION BIOLOGY

## 1) *Prodromal phase*

The symptoms present in this initial phase appear in the first 2 days after brief exposure to radiation and include nausea, vomiting, diarrhea, abdominal pain, fever, and eye burning.

## 2) *Latent Phase*

During this phase, the subjective symptoms of illness may subside, and the individual may show signs of improvement, this improvement may be temporary. The length of this phase generally decreasing as dose increases. It may not be present at all for very large doses.

Dose (rad)	100-200	200-400	400-600	600-1000	> 1000
Latent Period (day)	> 30	18-28	8-18	< 7	3-5

## 3) *Manifestation Phase*

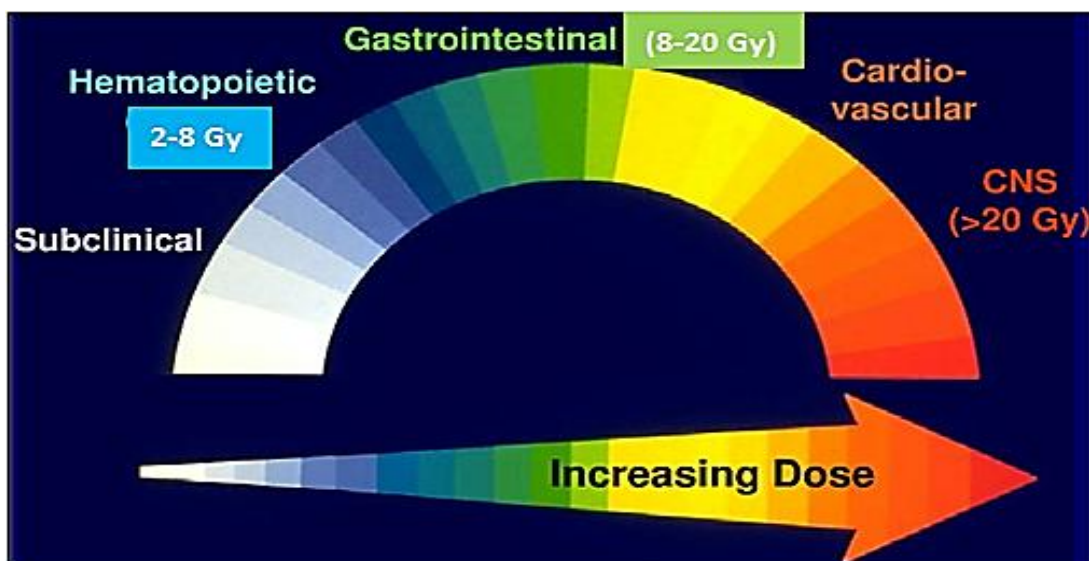
The manifestations of this phase are dependent on the dose received, so low doses result in hematopoietic syndrome, moderate doses result in gastrointestinal syndrome, while large doses result in neurovascular syndrome and rapid death.

## 4) *Recovery or Death Phase*

It is the final phase of acute radiation syndrome that include *either recovery* from radiation effect if the dose is below 800 rad up to 1,000 rad and the patient received adequate medical care, *or death* if the dose is above 1,000 rad.

Dose (rad)	100-200	200-400	400-600	600-1000	> 1000
Lethality%	0	0 - 50	20 - 70	50 - 100	100

According to the manifestation phase, acute radiation syndrome (ARS) can be divided into three syndromes:



## **a) Hematopoietic Syndrome:**

It occurs at doses in the range of 200 - 800 rad (2-8 Gy), that affect the bone marrow cells resulting in **pancytopenia** (severe depletion of all types of blood cells due to killing of precursor cells in the bone marrow) which is manifested by **Leukopenia** (less WBCs) that leads to infections; **Thrombocytopenia** (less blood platelets) leads to bleeding; and **Anemia** (less RBCs). This syndrome is often survivable, but death may occur within 60 days following exposure that can be prevented by bone marrow transplantation (BMT) & antibiotics therapy.

## **b) Gastrointestinal Syndrome:**

It occurs after doses greater than 800 up to 2000 rad (8-20 Gy) that cause severe damage to the mucosal lining of the gastrointestinal tract and usually results in death at about 1 week after irradiation due to infection, diarrhea and vomiting that could lead to electrolyte imbalance & dehydration. Intensive nursing with antibiotics, fluid, and electrolyte replacement can prevent early death from this syndrome, but these patients may die later due to damage to other organs.

## **c) Neurovascular Syndrome:**

It occurs following large doses of radiation >2000 rad (> 20Gy) that damaged cells of the central nervous system are damaged, so the affected individual undergoes a rapid illness, characterized by disorientation, body tremors, brain clot, shock and the latent period is very short or absent, and the patient would die within 1 or 2 days.

## **B. Cutaneous Radiation Syndrome (CRS)**

It occurs after **partial body exposure** to high energy **beta radiation**, which usually does not penetrate deeply enough in tissue to cause the 3 other sub syndromes of ARS (hematopoietic, gastrointestinal, neurovascular) but can cause major skin effect that is also known as radiation burn. Sometimes this occurs when radioactive materials contaminate a patient's skin or clothes. Phases of CRS are the same as for the ARS (Prodromal, Latent, Manifest Illness, and Recovery) with chronic or late effects, but without death. Within a few hours after irradiation, the **basal cell** layer of the skin is damaged causing a transient **erythema** (reddening of skin) associated with **itching** and **temporary hair loss**. However, very large doses over 1,000 rad can cause **alopecia** (Permanent hair loss), damaged sebaceous & sweat glands, **skin pigmentation**, ulceration or necrosis of the exposed tissue, and **desquamation** (shedding of the skin).

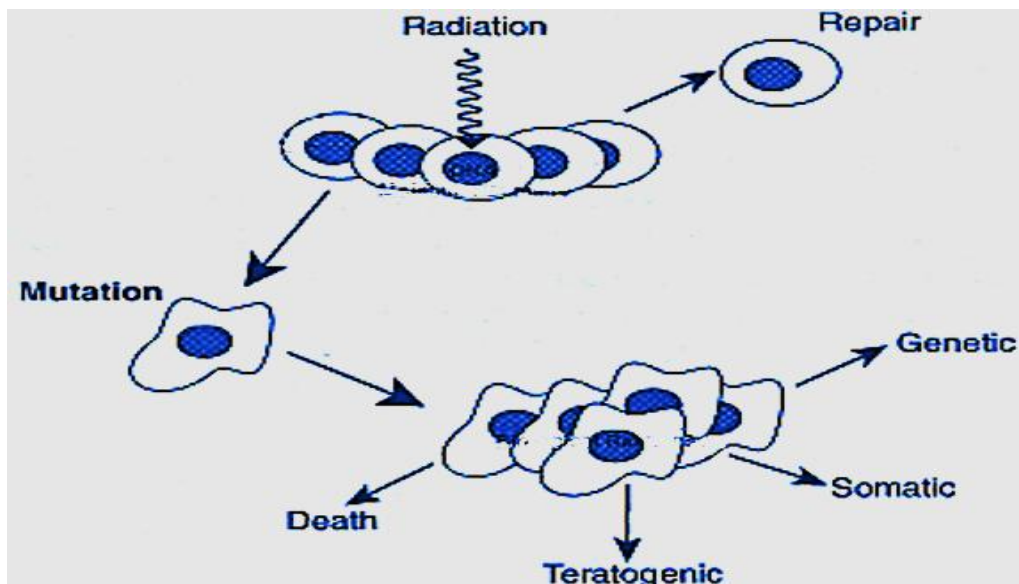
# RADIATION BIOLOGY



## Long-Term Effects of Radiation

Long-term (also known as delayed or chronic) effects of radiation are those which appear years after the original exposure and result either from previous acute (high-dose) exposures, or chronic low level exposure over a period of years. There are three categories of effects resulting from exposure to low doses of radiation:

1. **Genetic effect** that is suffered by the offspring of the individual exposed.
2. **Somatic effect** that is suffered by the individual exposed.
3. **Embryological (teratogenic) effect** that is suffered by a developing embryo/fetus exposed during pregnancy period.



## A. Genetic Effects

Ionizing radiation can permanently damage DNA in germ cells and lead to gene mutations which are passed to the offspring of the individual exposed. Genetic effects from low dose exposures have not been observed in human studies and difficult to be measured because:

- The fertilized egg produced from mutated germ cells may result in a nonviable organism which is aborted during the earliest stages of fertilization.
- The majority of mutations are recessive and do not appear unless both the mother and the father were affected with the same kind of genetic damage.

The genetic effects caused by radiation can be grouped as:

### 1. Dominant gene disorders:

Most cells from humans contain two sets of chromosomes with matched pairs of genes, one gene from each parent. The matched gene partners can differ, with one gene being dominant over its recessive partner gene. *Achondroplastic dwarfism* is an example of a dominant gene disorder that could be caused by ionizing radiation.



### 2. X-Linked Single-Gene Disorders:

Single-gene disorders associated with the X-chromosome are called X-linked effects. If a bad gene is present on the X-chromosome, it will invariably produce an effect in males because males only have one X-chromosome. *Muscular dystrophy* is an example of an X-linked effect that could be caused by ionizing radiation. However, if a female has one bad gene on an X-chromosome, but the other X-chromosome has a good gene partner, then the bad gene can behave as recessive and not show its effect unless both partner genes are defected.



### 3. Chromosome disorders:

Radiation exposure of the parents could lead to an abnormal number of chromosomes (*aneuploidy*) in their offspring, which could severely affect the unborn or newborn child. In most cases, *aneuploidy* will result in spontaneous loss of pregnancy. In the remaining cases, a severely affected child would be expected. *Down's syndrome* is an example of a consequence of aneuploidy caused by an extra copy of chromosome 21 (*trisomy 21*). People with aneuploidy have a significant reduction in their life expectancy, have abnormal body features, and are infertile.



### 4. Multifactorial disorders:

Multifactorial disorders are likely associated with the effects of multiple genes in combination with lifestyles and environmental factors. Multifactorial disorders include congenital malformations such as:

- a) *Spina bifida* (split spine) is a congenital disorder caused by the incomplete closing of the embryonic neural tube. Some vertebrae overlying the spinal cord are not fully formed and remain unfused and open. If the opening is large enough, this allows a portion of the spinal cord to protrude through the opening in the bones.



- b)** Cleft palate is a congenital fissure in the roof of the mouth, resulting from incomplete fusion of the palate during embryonic development.



## **B. Somatic Effects**

Late somatic effects occur in somatic cells years after brief or chronic exposure to radiation such as carcinogenic and cataractogenic effects:

### **1. Carcinogenic Effect:**

Radiation can cause up to 10% of invasive cancers in most parts of the body, in all animals, and at any age. Cancer formation is stochastic effect usually take 10–15 years for solid tumors, and can take 2–10 years for leukemia. There are several evidences that confirmed the carcinogenic effect of radiation in human as summarized below:

- a) Painters** showed bone cancer resulting from accumulation of radium in their bones due to ingestion radium paint.

# RADIATION BIOLOGY

- b) Radiologists & Dentists** developed skin cancer resulting from frequent exposure to x-ray.
- c) Miners** have lung cancer as a result of the inhalation of large quantities of airborne radioactive materials mainly radon.
- d) Survivors of atomic bombing** of Hiroshima and Nagasaki showed a significant increase in the incidence of leukemia as well as thyroid and breast cancers.
- e) Children whose mothers were irradiated during pregnancy** showed an increased risk of leukemia.
- f) Patients exposed to high doses of x-ray for treatment** showed a significant increase in the cancer incidence of thyroid, brain, skin, breast and leukemia.

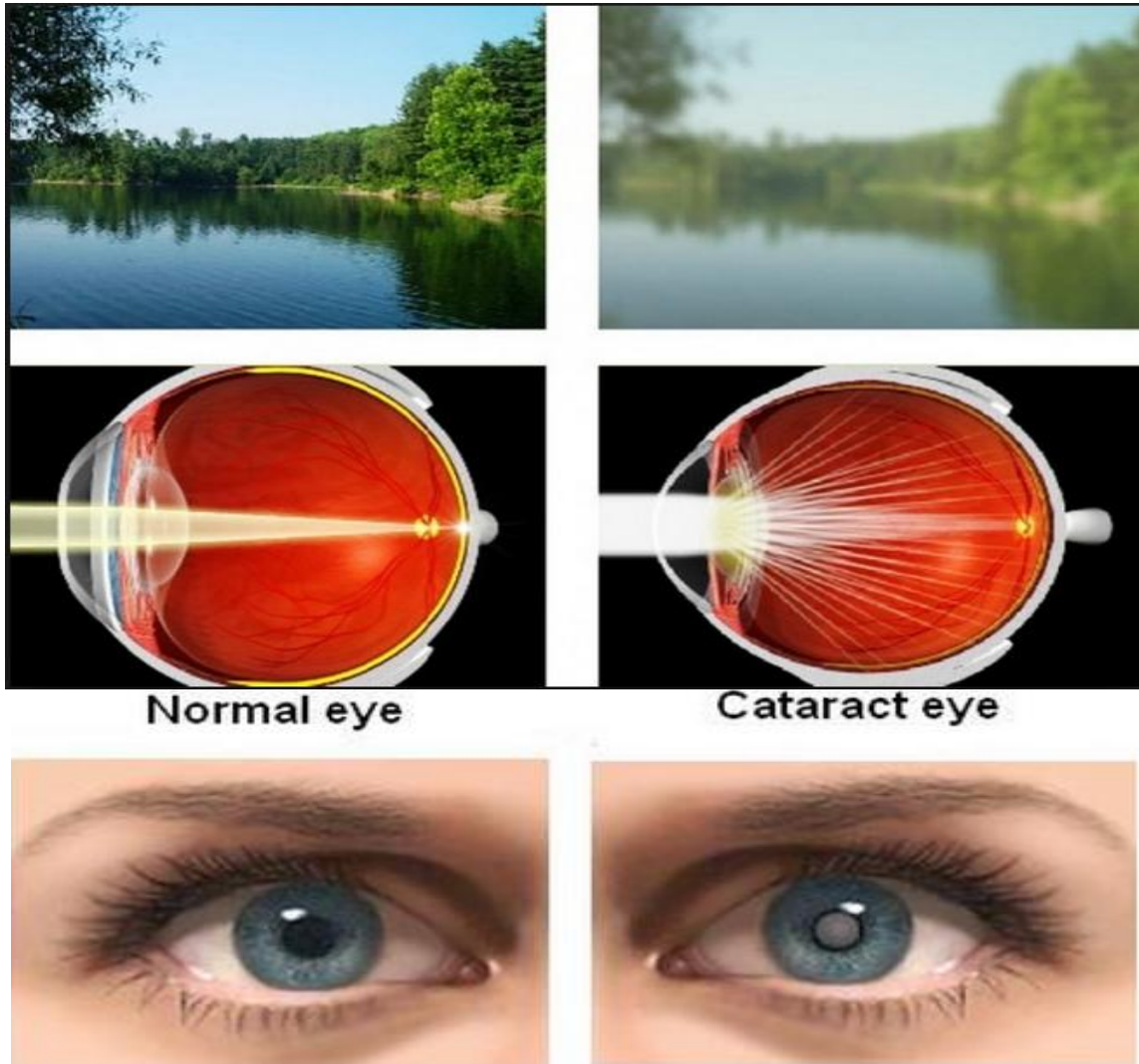


## 2. Cataractogenic Effect:

A cataract is a cloudy (opaque) area that forms in the normally clear lens of the eye which is the leading cause of blindness. A clouded lens in cataract eye allows less light to pass into the eye leading to blurred vision (images are not clear). Radiation in sufficiently high doses can induce the formation of cataracts which is a deterministic effect, meaning that it does not occur below a minimum threshold dose, and the severity of the cataract is related to the dose. The threshold dose is thought to be 200 rad (2 Gy). At doses of greater than 700 rad (7Gy), all people irradiated will develop cataract. The average latent period for cataract formation is approximately 15 years and appears to be inversely related to the dose received.



# RADIATION BIOLOGY



## **C. Embryological (Teratogenic) effects**

The **teratogen** (Greek word *tera*, meaning “monster.”) is any agent that alters fetal morphology or functions if the fetus is exposed during the critical stage of development, that may be physical (radiation), chemical (drugs), or biological (rubella viruses which cause German measles). Teratogenic effect is actually a special case of the somatic effect because the somatic cells of the embryo/fetus are exposed to radiation, not the reproductive cells of the parents. According to the law of Bergonie & Tribondeau, we know that the developing embryo is very radiosensitive and its response to irradiation depends upon; *total dose*, *rate of dose*, *type of radiation*, and *stage of development*.

# RADIATION BIOLOGY

A fetus undergoes three stages of development which are differing in their responses to irradiation:

## 1. Pre-implantation Stage:

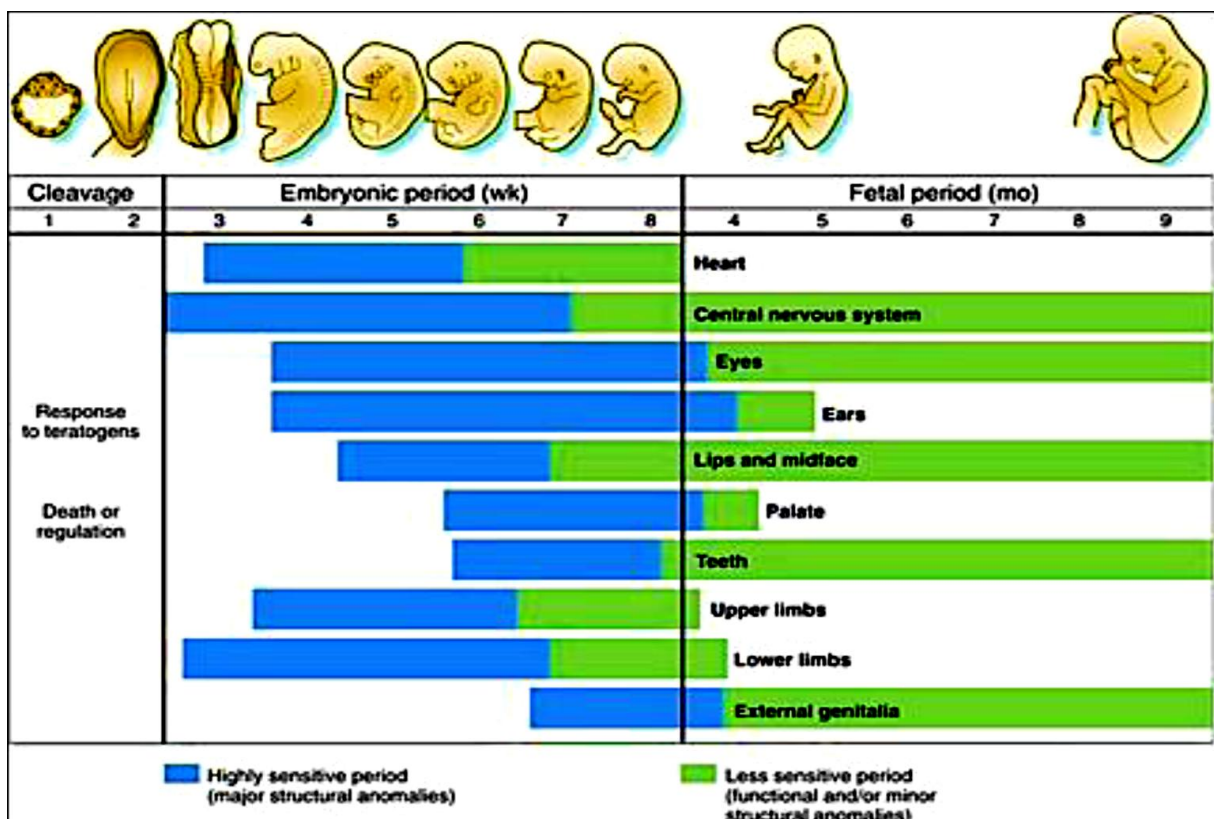
This stage originates with joining of the sperm & egg, and continues through day 9 when the zygote becomes deposited in the intrauterine wall. During this stage, the fertilized ovum is highly dividing and undifferentiated cells. Radiation damage during this stage can cause **death** either before birth (*intrauterine death*), or few days after birth (*neonatal death*).

## 2. Embryonic Stage:

This stage originates from the second to eighth week after conception. The cells differentiated to form specific organ systems. Radiation damage during this stage can cause **morphological abnormalities** which appear directly after birth such as *growth retardation* & *developmental abnormalities*.

## 3. Fetal Stage:

This stage starts following the end of major organogenesis and continue until term. The incidence of prenatal death and morphological abnormalities during this stage is negligible. The main radiation-induced effects during this stage are the **physiological abnormalities** which involve nervous system and sense organs and are not manifest until later in life such as *reduced intelligence (IQ)*, *behavioral changes*, and *cancer*.



# RADIATION BIOLOGY

