

RADIATION PATHOLOGY

RADIATION: Any form of energy carried across space

IRRADIATION: Application of radiant energy to tissues

SOURCES:

- Natural (background radiation)
 - 1-**Cosmic rays** solar (sun)- galactic (stars): Ultraviolet (UV) rays, infrared rays, & atomic particles
NB: Ozone layer prevents harmful doses & substances from reaching us.
 - 2-**Radioactive substances in earth crust**, these emit radiant energy (**radioactive decay**) e.g.: uranium 234,235 & 238 (natural isotopes)
- Artificial
 - Industrial products –Nuclear explosions (weapons)- Nuclear power plants which may be a source of leakage or accidental release in atmosphere, of damaging radiation resulting in atmospheric pollution¹.

TYPES OF RADIATION

- NON IONIZING: Electromagnetic waves(EMW) of long wave length e.g. Radio waves, infrared waves & ultraviolet waves or rays
- IONIZING:
 - a- Atomic particles or particulate radiation (atomic energy/nuclear energy)
 - b- Electromagnetic waves(EMW) of short wave length e.g.: X rays & gamma rays *NB: UV rays may cause ionization and damage if there is prolonged exposure*

USES of RADIATION

- 1) In Industry: sterilization and pasteurization- energy generators(nuclear power plants produce heat and electricity from fission reactions)- microwave ovens and radio and TV
- 2) War: atomic weapons e.g. bombs
- 3) Science: geology and archeology (carbon dating)- oceanography
- 4) Medicine:

Diagnosis

- Radiodiagnosis:** X-rays- CT scans- MRI(magnetic resonance imaging) for lesions of bone /soft tissue. Use of dyes can show lesions in GIT (barium swallow) Blood vessel abnormalities (angiography) and urinary tract abnormalities (pyelography)
- Tissue diagnosis-Electron microscope
- Functional diagnosis

- PET (positron emission tomography): Where a radioactive tracer is injected, and the time taken for it to circulate is a measure of left ventricular contractility.
- Radioactive iodine is taken up by suspicious thyroid nodules for diagnosis of cold & hot (active) nodules (a measure of activity of thyroid cells in the nodule)

Treatment(Nuclear medicine / radiotherapy) especially cancer(palliative or curative) e.g. Cobalt 60

Others : e.g. sterilization of sutures, short wave treatment for joint disorders, diathermy(surgical procedure by heat application) and radioisotopes for thyroid disorders

Definitions:

Radioactivity: SPONTANEOUS change of unstable atomic nuclei(radioisotope) to another stable state, with the emission of radiant energy

Radioisotope or radionucleide: A radioactive form of an element (i.e. atoms of the same substance containing different number of neutrons) NB to stabilize an atom the number of neutrons must = number of protons in nucleus. A radioisotope is therefore an **unstable nucleus** with increased or decreased number of neutrons

Unstable atom/element/molecule emits ionizing radiation till a stable new atom is formed,

N.B. Isotope: different forms of the same element e.g. $^{12}\text{C}_{12}$ & $^{14}\text{C}_{14}$ --- $^{12}\text{C}_{12}$: **Isotope (stable)** since atomic number = atomic weight - $^{14}\text{C}_{14}$ **radioactive form of isotope (radioisotope)** where number of neutrons is more than protons

Ion: positively or negatively charged atom (an atom which has lost an outer electron has a +ve charge & an atom, which has gained an outer orbit electron, has a -ve charge). These charged atoms react with one another forming **free radicals** which are also highly reactive because they carry unpaired electrons in the outer shell.

MODE OF ACTION OF IONIZING RADIATION

1. Direct or Target theory:

Direct injury (inactivation/ alteration of) :

-DNA:

- Damage to mitotic spindle** causes suppression in mitotic activity
- DNA structural abnormalities:** Gene damage and chromosomal damage e.g. point mutation –translocation-amplification and chromosomal fragmentation (dysjunction with abnormal random fusion) (structure abnormality)
- DNA functional abnormality:** abnormal gene expression (functional abnormality)

-Enzyme injury

-Cell and nuclear membrane injury

2. **Indirect or Poison theory:** 1 or more hits affect water molecules in cell or tissue causes ionization of water resulting in free radical (H, OH)(chemical injury) and formation of hydrogen peroxide (H₂O₂) (chemical injury)

Effects: These react with DNA, enzymes & cell and nuclear membranes resulting in damage

UNITS OF RADIATION

Roentgen (R): measure for X-rays and gamma rays

RAD (r) : measure of how much radiation is absorbed by target area for any form of radiation(energy absorbed per unit mass) NB: This is now replaced by the **gray (Gy)** (1Gy=100r)

Because different types of ionizing radiation penetrate tissues to varying degrees & since different tissues vary in their sensitivity to radiation. The doses are corrected to dose equivalents e.g.:

- **RBE:** relative biological effect measures the amount of cell damage produced by a specific form of radiation. 1 R gama rays produces a certain amount of damage in bone marrow whereas the same dose causes less damage in connective tissue
- **REM:** roentgen equivalent in man i.e. amount of cell damage by a specific form of radiation compared to same dose of another form of radiation. 1 R x ray produces less damage than 1 R gamma rays. The **sieverts** unit (Sv) has now replace the rem 1Sv=100rem)

NB permissible dose of radiation for ages 18-25years is 5 rem / year

EFFECTS OF RADIATION

on non living tissue (elements) it produces radioisotope

on living tissue, it **DEPENDS ON:**

- 1) **Dose:** Mild doses produce no visible effects to mild effects . All cells die if dose 800-1000 rem
- 2) **Rate, duration of exposure, distance** from source and **Penetration** power
- 3) **Type of tissue**
 - Radiosensitive: actively mitotic cell e.g. labile cells
 - Radioresponsive: mitotic only on injury e.g. stable cells
 - Radioresistant: non mitotic e.g. permanent cells
- 4) **Oxygen effect.** The more vascularized, the more oxygenated and the higher the temperature, the more ionization of water and free radicals & H₂O₂ production is facilitated. NB :The angiogenesis accompanying malignant tumors raises the temperature of the tumor & its oxygen content

MANIFESTATIONS OF RADIATION DAMAGE

- Immediate effects (hours – days)
- Early effects (after 1 week)
- Late or delayed effects(months to years)

A) CELLS

- **Atrophy & Vacuolar Degeneration** of cells up to **necrosis** in addition to **an acute inflammatory reaction**
- **Later** followed by chronic inflammation and healing by fibrosis
- Very late, cells mutate

If the mutation is at the level of somatic cells a tumour occurs

Carcinogenesis (oncogenesis) but if it occurs at the level of the germ cell the result is **Genetic abnormalities (teratogenesis)** and the mutation is transmitted to offspring

B) TISSUE

-Blood vessels: **mild early**: dilatation, congestion and tissue shows edema (acute inflammatory changes) or **severe early damage** to vessel wall (fibrinoid necrosis), resulting in tissue hemorrhage, thrombophlebitis with resultant ischemia of tissue. More ischemia occurs later when **endarteritis obliterans occurs with chronicity**.

-Connective tissue: **early**: edema and acute inflammatory cells (PNLs & macrophages). **Later** chronic inflammation occurs and healing by fibrosis and scarring.

C) EFFECTS OF RADIATION ON INDIVIDUAL ORGANS

(during treatment)

1-**Skin**: Early: Acute radiodermatitis: (acute inflammation) erythema, swelling and epidermal desquamation or radiation ulcers due to surface necrosis

Later: Atrophy of skin appendages (alopecia and hypopigmentation)

Very late: Basal cell carcinoma or squamous cell carcinoma

2-**GIT**: Early: mucosal inflammation, ulceration & radiation colitis with diarrhea and pain

Late: fibrosis and atrophy leading to malabsorption

3-**Testis** and **ovary** (germ cells) early: destruction –late: fibrosis and sterility

4-**Lungs**: Acute respiratory distress syndrome (ARDS) – late: pulmonary fibrosis

5-**Haemopoietic & lymphopoietic: Bone marrow** depression: anemia, thrombocytopenia & leukopenia (pancytopenia) or total destruction of bone marrow (aplasia)

Lymph node atrophy or destruction with decrease lymphocytic count in peripheral blood; finally fibrosis

Later/delayed: **Leukemia-lymphoma**

6-**Bone**:

- Osteomyelitis- radiation necrosis

- Bone marrow hypoplasia or aplasia (destruction) with risk of leukemia later

- Osteosarcoma

7-**Others**: radiation nephritis, blood vessel: vasculitis and thrombosis (radiation vasculitis)

8-Long term effects: carcinogenesis or genetic defects (teratogenesis)

D) EFFECTS OF TOTAL BODY RADIATION

(1 dose exposure of all body as in radioactive fall out in accidents, wars & background radiation pollution)

SYSTEMIC

A. Early or acute radiation effects Sudden whole body exposure

(radiation syndrome)

- Radiation sickness or mild radiation syndrome : (**non –lethal**) 50-200 rem (0.5—2 Sv)
 Fatigue, anorexia and nausea (mild GIT syndrome)
 Transient drop in peripheral blood counts(mild)
- Haemopoietic syndrome: 200-600rem (2-6Sv) causing: BM depression: pancytopenia (**severe**)
- Gastrointestinal syndrome: 300-1000 rem(3-10Sv) producing: Severe diarrhea, vomiting(**Severe**) & GIT hemorrhage
- Cerebral syndrome: >1000 rem (10Sv) ending in convulsions and coma (**lethal**)

B Late effects (survivors of accidents with very low dose exposure or slow cumulative whole body exposure in industrial pollution & natural background radiation)

- Malignancy e.g. leukemia
- Genetic disorders (in offspring)
- Infertility & complications of fibrosis at various sites

LOCAL

Describe effects on various organs (see above)

RADIATION PROTECTION

- 1-Shield effect: lead aprons and concrete walls prevent penetration
- 2-Radiation surveillance and measurement: Dosimeters for personnel and Geiger counters & solid state detectors for checking the presence of radioactivity in environment
- 3-Bone marrow replacement can be life saving if done early in people who have been exposed to total body radiation (accidents, wars)
- 4-Chemical protection: cysteine and glutathione

NEOPLASMS AND RADIATION

Ionizing radiation may play a role in cancer treatment or cancer induction

- In **Cancer treatment(Radiotherapy)**: It depends on radiosensitivity of tumor cells. Radiosensitivity: Is the amount of damage produced in a tumor that is directly proportionate to & correlates with degree of mitotic activity of tissue or tumor. Actively mitotic cells are particularly vulnerable & with damage **of mitotic spindle**, mitotic activity & cell proliferation is inhibited within the tumor tissue this helps in confining the tumor &

preventing its spread. The other mode of action is **DNA & chromosomal damage**, which is incompatible with life of the tumor cell & the cell dies. Normal tissue survives the radiation dose since its rate of proliferation is lower than tumor

	Permanent cells (No mitotic ability)	Stable cells (Low mitotic ability)	Labile cells (High mitotic ability)
Degree of radiosensitivity	Radioresistant	Radioresponsive	Radiosensitive
Normal cells	Adult neurons Striated muscle	Muscle(smooth) CT Liver Endocrine organs Glial cells	Bone marrow Intestinal epithelium Hair follicles Gonads Skin
Tumors	Ganglioneuroma	Sarcomas Gliomas Hepatoma	Leukemia Lymphomas Germinoma (of gonads) Embryomas

1-**Curative by killing tumor cells** leading to spontaneous cure (Melanoma and Hypernephroma)

2-**Palliative** by -Decreasing tumor size through killing some cells Or inhibiting growth and therefore slowing tumor both primary & secondaries in addition to delaying spread

-Relief of pain by decreasing size of tumor and its pressure effects

-Control of hemorrhage by thrombosis and endarteritis obliterans

N.B. Monoclonal antibodies tagged with radioisotope can be used as a form of cancer therapy against cancer cells carrying the target antigens

- Cancer induction:** The dangers from this source have greatly increased in recent years. The ionizing activity of X-rays & atomic radiation produce many changes in nuclear DNA ranging from **single gene mutations** to **gross chromosomal abnormalities** with damage of chromosomes in the form of breaks & random fusion **producing mutant tumor cells (carcinogenesis)**.

Source of radiation	Possible tumors	Type of radiant energy
X-ray workers	Skin cancer-leukemia	Ionizing X-rays
Mining of radioactive substances	Lung cancer	Atomic energy(particulate & rays)
Atomic explosions	Skin cancer-leukemia-bone cancer	Atomic energy(particulate & rays)