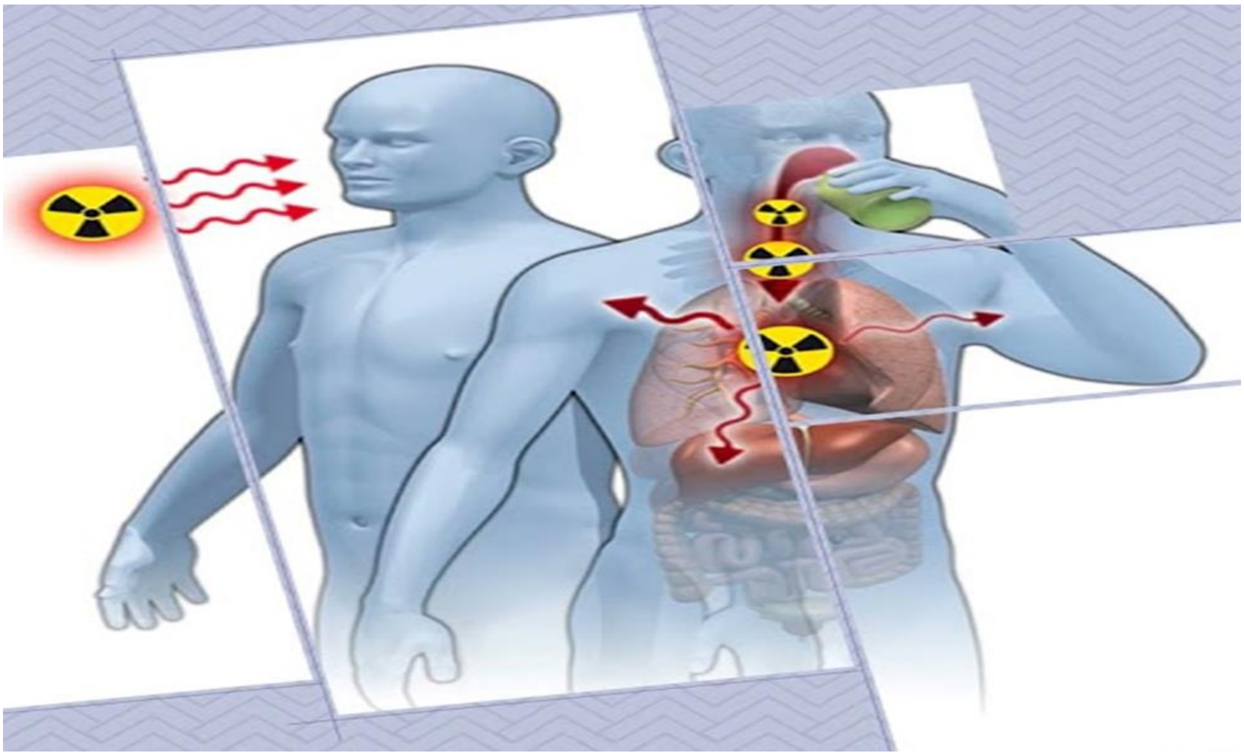
Law of Bergonie and Tribondeau
1st Lecture



Prepared and Presented by:

Lecturer Dr/ Arshed Shaker
Lecturer Dr/ Ayad Abdelsalam
Assist. Lecturer Dr/ Noor sabah

3rd year, 1st course

Teaching of Biological Radiation hazards

College of Technology & Health Sciences
Radiology Techniques Department

Law of Bergonie and Tribondeau

What is Radiobiology?

Radiobiology is the study of the effects of radiation on biological systems.

How does radiation damage cells?

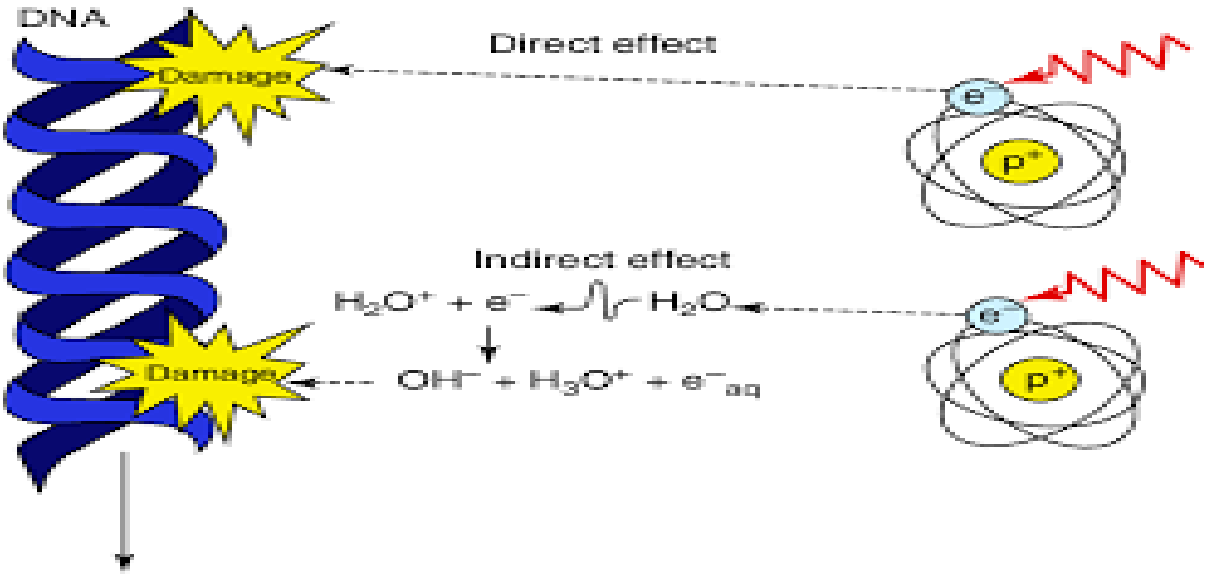
Radiation damages cells by causing breaks within the structure of DNA. There are two primary mechanisms by which this damage occurs.

Direct Radiation Damage

Radiation impacts sufficient energy to DNA bonds to directly cause breaks.

Indirect Radiation Damage

Indirect damage occurs when radiation interactions outside of the DNA to produce free radicals which in turn damage DNA.



- A free radical is an atom or molecule carrying an unpaired electron in an outer shell.
- Hydroxide (OH^-) is the most common free radical produced by radiation within the body. Hydroxide is produced in the body through interaction of water (H_2O).

DNA Strand Breaks

What is DNA?

DNA (deoxyribonucleic acid) is shaped like a double helix. Each side of the helix is known as a "strand."

DNA Composition

Backbone comprised of deoxyribose (a sugar) and a phosphate group bound together by covalent bonds.

Nucleobases (base pairs) encode genetic information. The four bases are Cytosine (C), Guanin (G), Adenine (A), and Thymine (T). Importantly, only C-G and A-T pairs are allowed.

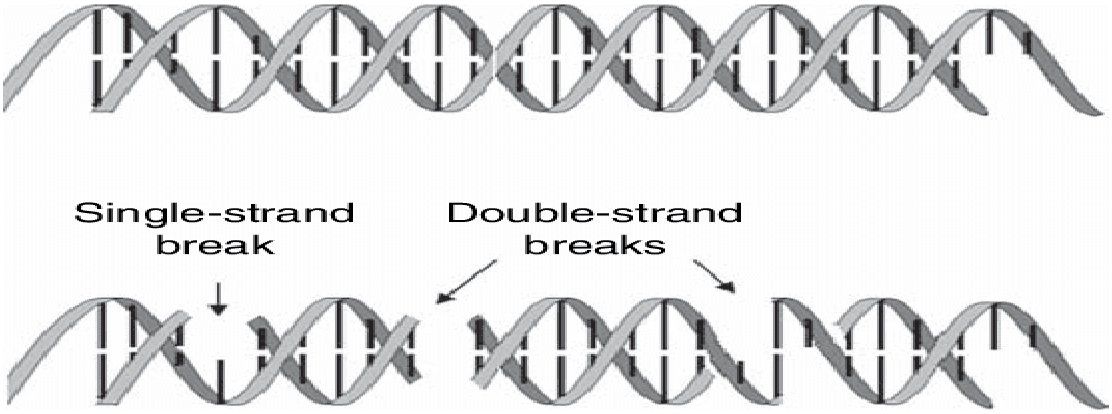
Single Strand Breaks

Single strand breaks occur when only one strand is damaged. This type of DNA damage in considered *sub-lethal* because they can generally be repaired.

When multiple single strand breaks occur close together on the same strand, the damage may be non-repairable (i.e. lethal).

Double Strand Breaks

Double strand breaks occur when both strands are broken within a few base pairs. This type of DNA damage in generally non-repairable and may result in cell death, sterilization (inability to reproduce), or mutation.



Factors Influencing Radiosensitivity

Law of Bergonie and Tribondeau

The law of Bergonie and Tribondeau states: The radiosensitivity of a cell is directly proportional to reproductive rate and is inversely proportional to its degree of differentiation.

1. The **law of Bergonie and Tribondeau** is that the radiosensitivity of a biological tissue is directly proportional to the mitotic activity and inversely proportional to the degree of differentiation of its cells. This law underpins the field of radiation-oncology, although such a general law may not apply precisely in all cases.

Usually neoplastic cells are more radiosensitive than the cells from which they originate; in fact, they reproduce much faster than healthy cells.

Cellular differentiation describes the extent to which a tumour resembles the normal tissue from which it derives. The more it differs from healthy tissue, the greater its radiosensitivity will be.

This means that radiosensitivity increases with:

- Increased rate of cell division
- Low degree of specialization (stem cells are very radiosensitive)
- Higher metabolic rate
- Increased oxygenation
- Increased length of time they are actively proliferating

2. Cell Cycle Stage

The cell cycle is the series of distinct phases leading to duplication of DNA and, ultimately, cell division. The cell cycle is of interest because the radiosensitivity of a cell is dependent upon its stage in the cell cycle.

G1: First growth phase

The cell is performing normal functions and growing.

S: Synthesis phase

During the S phase, the cell replicates its DNA. S phase is the least radiosensitive phase of the cell cycle because the cell contains two copies of its DNA.

G2: Second growth phase

The cell is again performing normal functions and continues to grow.

M: Mitosis phase

The cell divides into two cells in a process called mitosis. Mitosis is the most radiosensitive phase both because mitosis is sensitive to disruption and because the cell is well oxygenated during this phase.

Temporal Aspects of Radiation Damage

Although radiation absorption is essentially instantaneous ($\sim 10^{-15}$ s), radiation damage accumulation from single strand breaks depends both on the temporal rate of damage and on the rate at which the cell repairs sublethal damage.

If DNA damage cannot be repaired, cell death may take between weeks and month depending on the type of cell. This is the reason for the delay in late effects described in the linear quadratic model.

<u>Applications of Bergonié and Tribondeau Law</u>

1. Radiotherapy Optimization

- Guides treatment planning by targeting rapidly dividing cancer cells
- Minimizes damage to slower-growing healthy tissues
- Informs fractionation of radiotherapy doses
    - Allows normal tissues to recover between treatments

- Effectively damages cancer cells

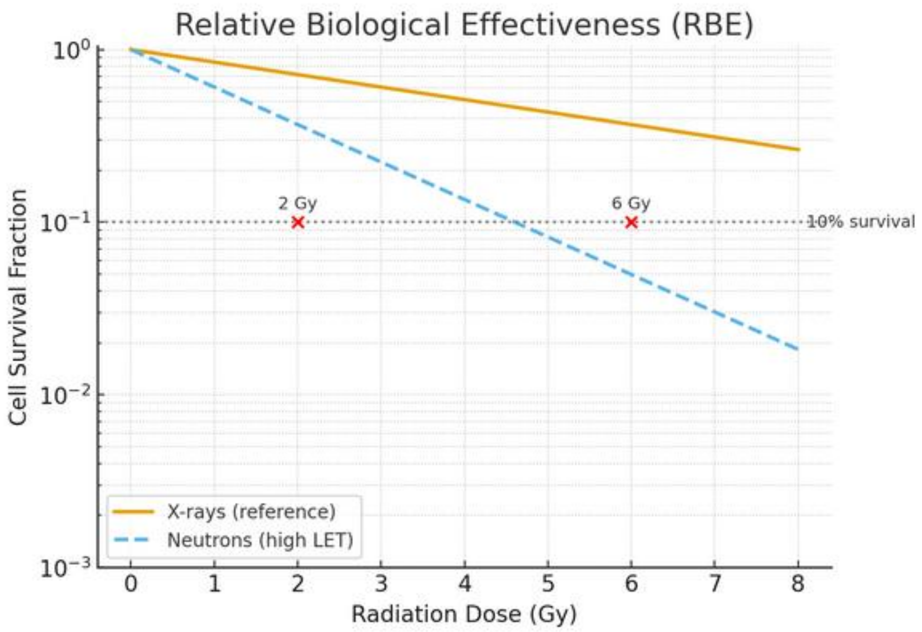
- Contributes to development of tissue weighting factors
  - Used to calculate effective dose
  - Assesses radiation risks to different organs

2. **Radiation Protection Strategies**

- Informs design of radiation shielding
- Helps determine safe exposure limits for body parts in various settings
  - Occupational exposure (nuclear power plant workers)
  - Medical settings (radiologists, technicians)
- Optimizes imaging protocols in diagnostic radiology
  - Balances image quality with radiation dose
  - Minimizes risks to radiosensitive organs (thyroid, breast)
- Aids space radiation protection strategies
  - Protects astronauts from cosmic radiation
  - Focuses on radiosensitive tissues (bone marrow, central nervous system)
- Guides development of radioprotective agents
  - Mitigates radiation-induced damage in clinical scenarios
  - Assists in emergency response planning (nuclear accidents)

Relative Biological Effectiveness (RBE)

Is a measure of the effectiveness of different types of ionizing radiation in producing a specific biological effect.



The figure showing **Relative Biological Effectiveness (RBE)**

- ❖ **Low-LET radiation (X-rays, γ-rays, β-rays):** lower RBE (≈1).
- ❖ **High-LET radiation (α-particles, neutrons, heavy ions):** higher RBE (can be 5–20 or more).
- ❖ RBE is **not a constant value**; it changes depending on biological conditions and dose.

- **X-rays (reference radiation):** require a higher dose (e.g., 6 Gy) to reduce survival to 10%.
- **Neutrons (test radiation):** require a lower dose (e.g., 2 Gy) to reduce survival to the same 10%.

RBE = 6/2=3

Example: What is the RBE for alpha radiation in killing 50% of epithelial cells?

Experimentation shows that it takes only 2 grays of alpha radiation to kill half of the cells, but when .the same cells are exposed to 250-kVp x-rays, it takes 6 grays to kill half of them

RBE = 6 / 2 = 3

For killing 50% of the cells, the RBE of alpha radiation is 3 (Alpha radiation is 3 times more - effective at "cell-killing" than x-rays are)

Linear Energy Transfer (LET)

Linear Energy Transfer (LET) is the **amount of energy deposited by ionizing radiation per unit length of tissue traversed**.
It is usually expressed in **keV/µm (kiloelectron volts per micrometer)**.

LET= de/dx

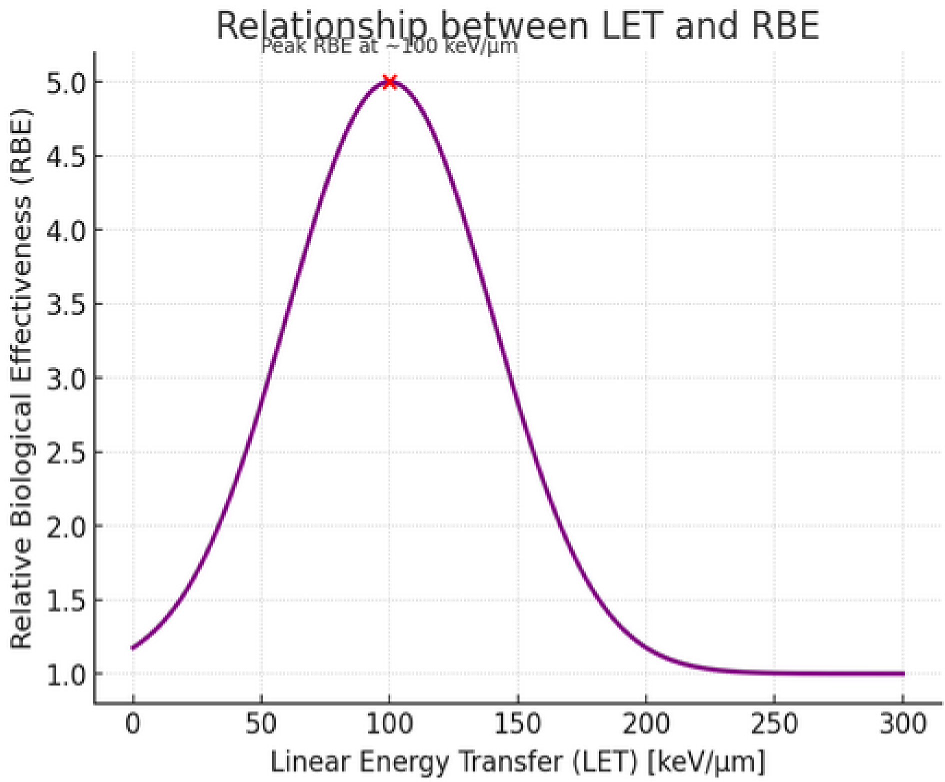
- **dE** = energy lost by the radiation
- **dx** = distance traveled in the absorbing medium

Types

- **Low-LET radiation**
  - Examples: X-rays, γ-rays, β-particles (electrons).
  - Characteristics: sparsely ionizing, produce isolated DNA damage, RBE ≈ 1.
- **High-LET radiation**
  - Examples: α-particles, neutrons, heavy ions.
  - Characteristics: densely ionizing, produce clustered DNA damage, harder to repair, higher RBE.

Relationship with RBE

- RBE generally **increases with LET** up to about **100 keV/µm**, which is the most efficient at causing double-strand breaks in DNA.
- Beyond that, RBE decreases (the "overkill effect") because extra energy is wasted after the cell is already lethally damaged.



- RBE **increases with LET** up to about **100 keV/µm** (most efficient for DNA double-strand breaks).
- After that, RBE **decreases** due to the **overkill effect** — extra energy is wasted once the cell is already lethally damaged.

MCQs on (Lecture 1)

1. What is **Radiobiology**?
   a) Study of light on human cells
   b) Study of heat effects on tissues
   c) Study of the effects of radiation on biological systems
   d) Study of cell metabolism
   e) Study of chemical mutagens
2. Radiation primarily damages cells by affecting:
   a) Cell wall proteins
   b) Cytoplasmic fluid
   c) DNA structure
   d) Mitochondria
   e) Ribosomes

3. Which of the following describes **direct radiation damage**?
   a) Free radicals attack DNA
   b) Radiation hits water molecules only
   c) Enzymes destroy genetic material
   d) Radiation directly causes DNA bond breaks
   e) None of the above
4. **Indirect radiation damage** is mainly caused by:
   a) DNA base mutations
   b) Protein misfolding
   c) Damage to mitochondria
   d) Free radicals produced by radiation interactions
   e) Cell membrane rupture
5. A **free radical** is defined as:
   a) A stable atom with paired electrons
   b) An atom/molecule with an unpaired electron
   c) A positively charged ion
   d) A neutral water molecule
   e) A radioactive isotope
6. The **most common free radical** produced by radiation in the body is:
   a) Hydrogen ion (H+)
   b) Superoxide (O2-)
   c) Hydroxide (OH-)
   d) Peroxide (H2O2)
   e) Carbon radical
7. Hydroxide radicals are mainly produced through the radiation interaction with:
   a) Lipids
   b) Proteins
   c) Water (H2O)
   d) DNA directly
   e) Oxygen gas
8. DNA is composed of a backbone made of:
   a) Proteins and fats
   b) Deoxyribose sugar and phosphate group
   c) Ribose and nucleotides
   d) Lipids and nitrogen bases
   e) Amino acids
9. Which are the four DNA bases?
   a) Uracil, Adenine, Guanine, Thymine
   b) Cytosine, Guanine, Adenine, Thymine
   c) Adenine, Cytosine, Uracil, Guanine
   d) Guanine, Adenine, Ribose, Uracil
   e) Thymine, Cytosine, Ribose, Guanine

10. Base pairing in DNA follows the rule:
   a) A-G, C-T
   b) A-C, T-G
   c) A-T, C-G
   d) A-U, C-G
   e) G-G, A-A
11. A **single strand break (SSB)** in DNA is generally considered:
   a) Lethal
   b) Permanent
   c) Sub-lethal and repairable
   d) Unrelated to mutations
   e) Always mutagenic
12. Multiple single strand breaks close together can result in:
   a) Enhanced repair
   b) No effect
   c) Stronger bonding
   d) Non-repairable lethal damage
   e) Protein synthesis failure
13. **Double strand breaks (DSBs)** are usually:
   a) Easily repaired
   b) Non-harmful
   c) Sub-lethal
   d) Non-repairable and may cause cell death
   e) Protective for DNA
14. Double strand breaks can result in all of the following EXCEPT:
   a) Cell death
   b) Mutation
   c) Sterilization
   d) Enhanced cell growth
   e) Inability to reproduce
15. According to the **Law of Bergonie and Tribondeau**, radiosensitivity is proportional to:
   a) Cell differentiation
   b) Cell reproductive/mitotic rate
   c) Cytoplasmic volume
   d) Enzyme activity
   e) Cell size
16. Radiosensitivity is **inversely proportional** to:
   a) Rate of mitosis
   b) Degree of differentiation
   c) Oxygenation
   d) Cell proliferation
   e) Metabolic rate

17. Which type of cells are generally more radiosensitive?
   a) Neurons
   b) Muscle cells
   c) Cardiac cells
   d) Neoplastic (tumor) cells
   e) Cartilage cells
18. Why are tumor cells more radiosensitive than normal cells?
   a) They contain more DNA
   b) They reproduce faster
   c) They are highly differentiated
   d) They contain less oxygen
   e) They have stronger proteins
19. Radiosensitivity increases with:
   a) Lower oxygenation
   b) Higher specialization
   c) Reduced metabolic rate
   d) Increased oxygenation
   e) Increased differentiation
20. Which type of stem cells are most radiosensitive?
   a) Mature neurons
   b) Undifferentiated stem cells
   c) Mature red blood cells
   d) Skeletal muscle fibers
   e) Cartilage
21. The **cell cycle** consists of phases:
   a) M, T, P, C
   b) Z, Y, X
   c) G1, S, G2, M
   d) S1, S2, S3
   e) Pre, Post, Divide
22. In which phase does DNA replication occur?
   a) G1
   b) S phase
   c) G2
   d) M
   e) G0
23. The **least radiosensitive** phase of the cell cycle is:
   a) G1
   b) M
   c) G2
   d) S phase
   e) None of the above

24. The **most radiosensitive** phase of the cell cycle is:
   a) S
   b) G1
   c) Mitosis (M)
   d) G2
   e) G0
25. Radiation absorption occurs in approximately:
   a) 1 second
   b) 10–9 s
   c) 10–15 s
   d) 1 minute
   e) Several hours
26. If DNA damage is unrepaired, cell death can occur over:
   a) Few seconds
   b) Few minutes
   c) Few hours
   d) Weeks to months
   e) Immediately
27. The delay in late radiation effects is explained by:
   a) Cell differentiation law
   b) Linear quadratic model
   c) Cell repair mechanism
   d) DNA replication errors
   e) Bergonie's principle
28. Radiotherapy optimizes treatment by targeting:
   a) Mature neurons
   b) Rapidly dividing cancer cells
   c) Cartilage cells
   d) Muscle fibers
   e) Fully differentiated cells
29. One goal of radiotherapy fractionation is to:
   a) Destroy all healthy cells
   b) Increase oxygen toxicity
   c) Allow normal tissues to recover
   d) Prevent tumor shrinkage
   e) Avoid cancer cell damage
30. Radiation protection strategies include:
   a) Increasing exposure time
   b) Avoiding shielding
   c) Designing shielding and exposure limits
   d) Ignoring radiosensitivity
   e) Using no protective agents

31. In diagnostic radiology, optimization balances:
   a) Time vs. cost
   b) Image quality vs. radiation dose
   c) Patient comfort vs. staff training
   d) Speed vs. storage capacity
   e) Dose vs. technician experience
32. Radiosensitive organs include all EXCEPT:
   a) Thyroid
   b) Breast
   c) Skeletal muscle
   d) Bone marrow
   e) Central nervous system
33. In space missions, radiation protection mainly targets:
   a) Skin
   b) Bone marrow and CNS
   c) Hair follicles
   d) Nails
   e) Cartilage
34. Radioprotective agents are developed to:
   a) Increase DNA damage
   b) Mitigate radiation-induced damage
   c) Block oxygen supply
   d) Speed up mutations
   e) Destroy stem cells
35. Emergency planning for nuclear accidents requires:
   a) Ignoring radiosensitivity
   b) Allowing uncontrolled exposure
   c) Using radiation protection strategies
   d) Increasing patient doses
   e) Avoiding shielding
36. Radiosensitivity of a tissue depends mainly on:
   a) Color of tissue
   b) Tissue temperature
   c) Mitotic activity and differentiation
   d) Shape of cells
   e) Enzyme activity
37. The backbone of DNA is bound together by:
   a) Hydrogen bonds
   b) Covalent bonds
   c) Ionic bonds
   d) Van der Waals forces
   e) Metallic bonds

38. What describes **cell sterilization** due to radiation?
    a) Complete cell death
    b) Inability to reproduce
    c) Increased cell growth
    d) Reversible mutation
    e) Enhanced repair
39. Which factor does NOT increase radiosensitivity?
    a) High oxygenation
    b) Active proliferation
    c) High metabolic rate
    d) High differentiation
    e) Increased mitotic rate
40. Which phase allows the cell to grow and perform normal functions after DNA replication?
    a) S
    b) M
    c) G2
    d) G1
    e) G0
41. Got it ✅ I'll prepare **20 multiple-choice questions (MCQs)** from the text you provided. Each question will have 5 options (a–e) with the **correct answer in bold**.
42. Relative Biological Effectiveness (RBE) is a measure of:
    a) The amount of radiation absorbed per unit mass
    b) The energy of a photon
    c) The distance traveled by radiation in tissue
    d) **The effectiveness of different types of ionizing radiation in producing a biological effect**
    e) The speed of ionizing radiation
43. Linear Energy Transfer (LET) represents:
    a) The number of photons emitted per second
    b) **The amount of energy deposited per unit length of tissue**
    c) The mass of particles in a radiation beam
    d) The dose equivalent received by tissue
    e) The rate of radioactive decay
44. The unit of LET is:
    a) Gy (Gray)
    b) Sv (Sievert)
    c) J/kg
    d) **keV/µm**
    e) MeV
45. In the formula LET = dE/dx, **dE** stands for:
    a) Distance traveled
    b) Density of tissue
    c) Dose absorbed
    d) **Energy lost by the radiation**
    e) Electric charge

46. In the formula LET = dE/dx, **dx** stands for:
   a) **Distance traveled in the absorbing medium**
   b) Dose equivalent
   c) Energy deposition
   d) Radiation type
   e) Photon wavelength
47. Which of the following is an example of **low-LET radiation**?
   a) α-particles
   b) Neutrons
   c) **X-rays**
   d) Heavy ions
   e) Protons at low energy
48. Which of the following is an example of **high-LET radiation**?
   a) **α-particles**
   b) X-rays
   c) γ-rays
   d) β-particles
   e) UV rays
49. A characteristic of low-LET radiation is:
   a) Dense ionization
   b) **Sparsely ionizing, producing isolated DNA damage**
   c) High RBE (≥10)
   d) Strong overkill effect
   e) Non-ionizing
50. A characteristic of high-LET radiation is:
   a) Sparsely ionizing
   b) Easily repaired DNA damage
   c) Low biological impact
   d) **Clustered DNA damage, harder to repair**
   e) Low RBE
51.

---

52. Typical RBE value for low-LET radiation (e.g., X-rays, γ-rays):
   a) 5–10
   b) 2–4
   c) 0.5
   d) **≈1**
   e) 20
53.

---

54. High-LET radiation is generally associated with:
   a) Low ionization density
   b) **High RBE values**
   c) Low biological effectiveness
   d) Sparse DNA lesions
   e) Easily repairable damage
55.

---

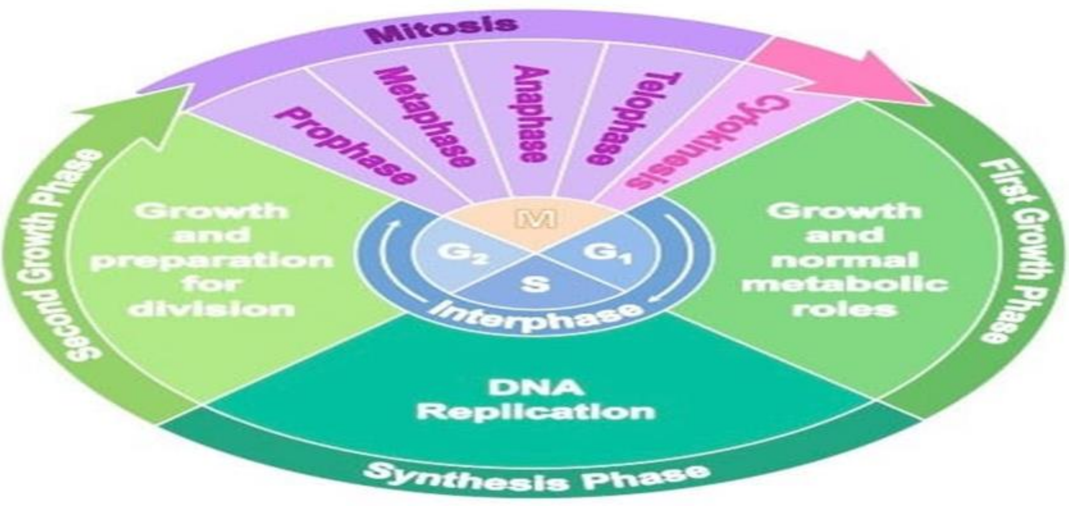
56. RBE generally increases with LET up to about:
   a) 50 keV/µm
   b) 75 keV/µm
   c) **100 keV/µm**
   d) 150 keV/µm
   e) 200 keV/µm
57. ---
58. At LET ≈ 100 keV/µm, radiation is most efficient at:
   a) Producing single-strand breaks
   b) Generating free radicals
   c) **Causing double-strand DNA breaks**
   d) Causing no biological damage
   e) Producing UV fluorescence
59. ---
60. What happens to RBE beyond 100 keV/µm?
   a) It keeps increasing indefinitely
   b) It becomes constant
   c) **It decreases due to the overkill effect**
   d) It becomes zero
   e) It oscillates
61. ---
62. The "overkill effect" means:
   a) **Extra energy is wasted after the cell is already lethally damaged**
   b) No biological damage occurs
   c) The tissue completely recovers
   d) RBE remains at maximum levels
   e) Radiation stops interacting with tissue
63. ---
64. Which of the following is **not** high-LET radiation?
   a) α-particles
   b) Neutrons
   c) Heavy ions
   d) **γ-rays**
   e) Low-energy protons
65. ---
66. Which statement is true about low-LET radiation?
   a) **Produces isolated DNA damage**
   b) Produces dense ionization tracks
   c) Has RBE > 10
   d) Strong overkill effect
   e) Causes mostly clustered double-strand breaks
67. ---
68. Which type of radiation has **the highest potential for clustered DNA damage**?
   a) X-rays
   b) γ-rays
   c) β-particles

d) **α-particles**
e) Microwave radiation

69. ---
70. At what LET value is RBE **maximized**?
a) 25 keV/µm
b) 50 keV/µm
c) **~100 keV/µm**
d) 150 keV/µm
e) 200 keV/µm

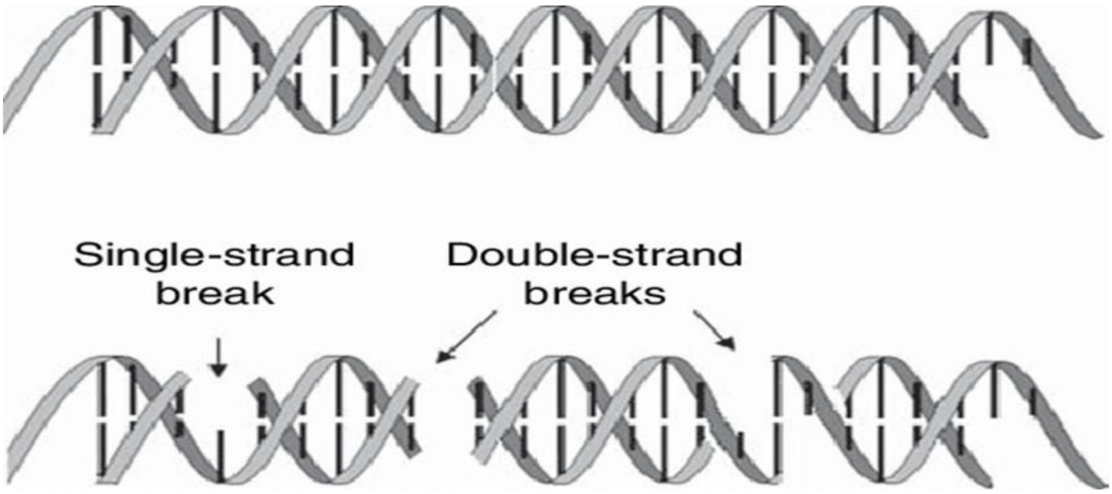
71. ---
72. Which of the following best describes the relationship between LET and RBE?
a) RBE decreases with increasing LET
b) RBE is unrelated to LET
c) RBE increases indefinitely with LET
d) **RBE increases with LET up to ~100 keV/µm, then decreases (overkill effect)**
e) RBE is constant for all LET values

73. ---
74. ✅ That's **20 MCQs** with answers bolded.
75. Would you like me to also put these into a **PowerPoint quiz format (with question + clickable correct answer)** for teaching, or just keep them as a written set?
76.



1. Which phase of the cell cycle involves **DNA replication**?
a) G1 phase
b) G2 phase
c) S phase
d) M phase
e) Cytokinesis

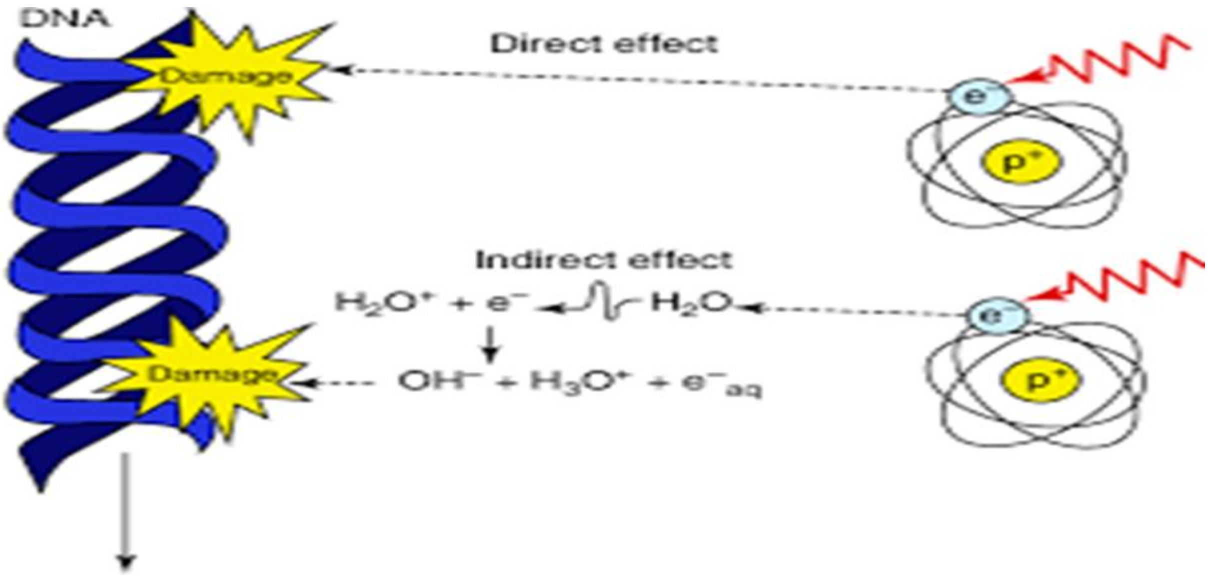
2. The **first growth phase (G1)** is mainly responsible for:
   a) DNA synthesis
   b) Chromosome condensation
   c) Cell division
   d) Growth and normal metabolic roles
   e) Cytokinesis
3. The **second growth phase (G2)** prepares the cell for:
   a) DNA synthesis
   b) Cell division (mitosis)
   c) Normal metabolic activities
   d) RNA degradation
   e) Apoptosis
4. During the **M phase**, the cell undergoes:
   a) DNA replication
   b) Protein synthesis
   c) Mitosis (Prophase → Metaphase → Anaphase → Telophase)
   d) Growth and repair
   e) Organelle duplication
5. Which phase is the **most radiosensitive** according to radiobiology?
   a) S phase
   b) G1 phase
   c) G2 phase
   d) M phase
   e) Interphase



1. A **single-strand break (SSB)** in DNA involves:
   a) Damage to both DNA strands
   b) Damage to nucleobases only
   c) Loss of the phosphate backbone

d) Damage to only one strand of the double helix
e) Complete DNA degradation

2. Single-strand breaks are generally considered:
a) Always lethal
b) Always mutagenic
c) Sub-lethal and repairable
d) Non-repairable
e) Protective for cells
3. A **double-strand break (DSB)** occurs when:
a) Only one strand is broken
b) Both strands are broken within a few base pairs
c) The sugar-phosphate backbone remains intact
d) Only nucleobases are altered
e) Chromosomes elongate abnormally
4. Double-strand breaks are usually:
a) Harmless
b) Easily repaired
c) Lethal and non-repairable
d) Strengthening DNA
e) Enhancing replication
5. Which outcome is most associated with **double-strand breaks**?
a) Enhanced cell metabolism
b) Faster DNA replication
c) Increased protein synthesis
d) Cell death, sterilization, or mutation
e) Improved DNA repair



1. Which organ is primarily responsible for filtering blood in the human body?
a) Heart
b) Lungs
c) Stomach
d) Kidneys
e) Liver

2. What is the SI unit of electric current?
a) Volt
b) Ampere
c) Ohm
d) Watt
e) Joule

3. Which planet is known as the "Red Planet"?
a) Venus
b) Mars
c) Jupiter
d) Saturn
e) Mercury

4. Who proposed the theory of relativity?
a) Isaac Newton
b) Nikola Tesla
c) Galileo Galilei
d) Albert Einstein
e) Stephen Hawking

5. In computer science, what does "CPU" stand for?
a) Central Programming Unit
b) Central Process Utility
c) Central Processing Unit
d) Computer Power Unit
e) Control Processing Utility
