

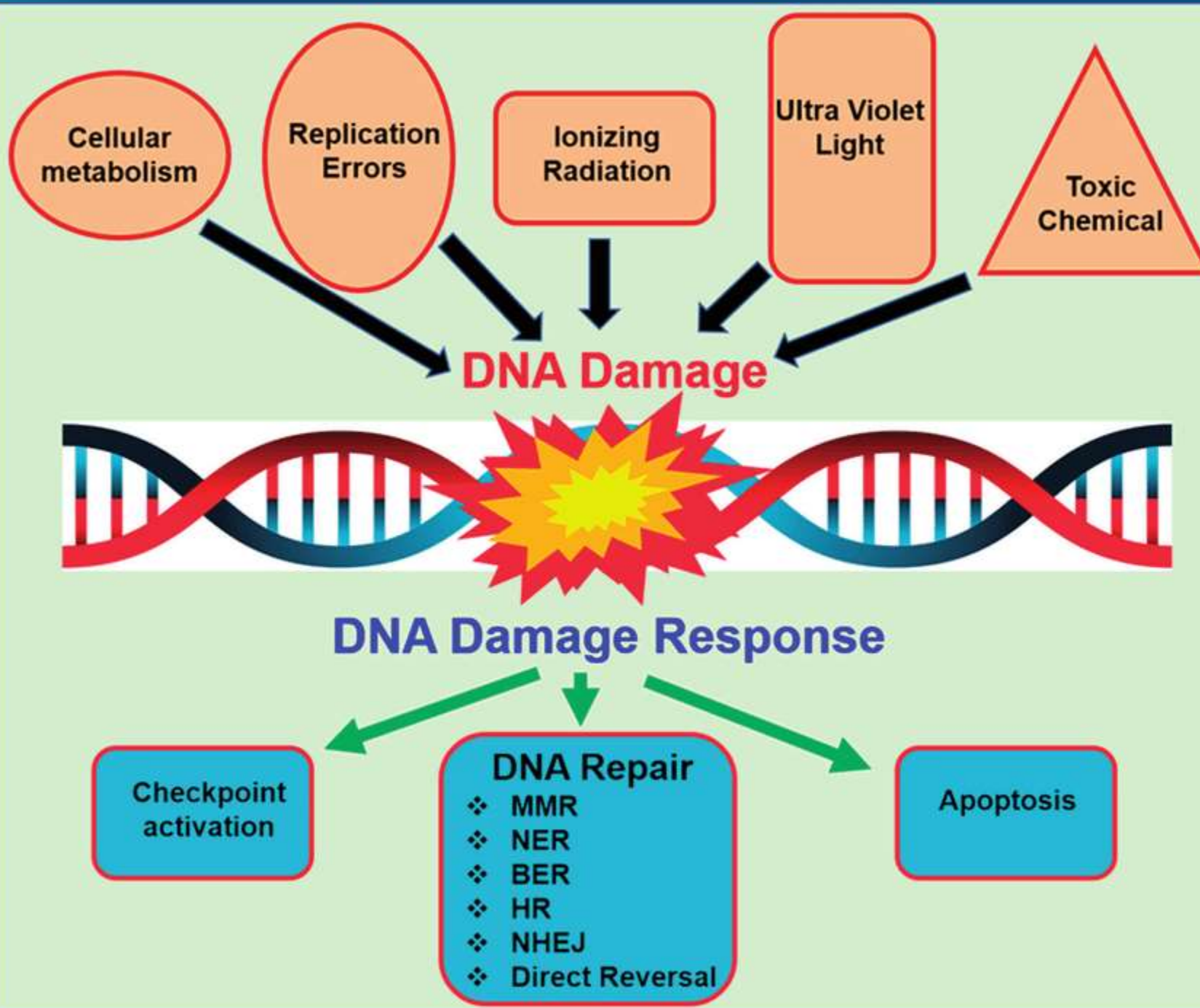
General and Molecular Genetics

DNA Damaging Agents

By: Shozab Seemab Khan (PhD Scholar)

DNA Damaging Agents

- ❖ DNA-damaging agents are **chemicals, physical factors, biological processes or environmental agents** that can cause alterations in the DNA structure, which need DNA repair and can also lead to mutations, cell death, or cancer.
- ❖ These agents can act on DNA directly or indirectly by generating reactive species that interact with DNA.



1. Chemical DNA-Damaging Agents

- ❖ These are substances that can interact directly with DNA or affect cellular processes to induce DNA damage.
- ❖ **i. Alkylating Agents**
- ❖ **Mechanism:** Add alkyl groups to DNA bases, leading to mispairing or DNA strand breaks.
- ❖ **Examples:**
 - ❖ Mustard gas (e.g., nitrogen mustards)
 - ❖ Cyclophosphamide
 - ❖ Methyl Methane Sulfonate (MMS)

1. Chemical DNA-Damaging Agents

❖ii. Cross-Linking Agents

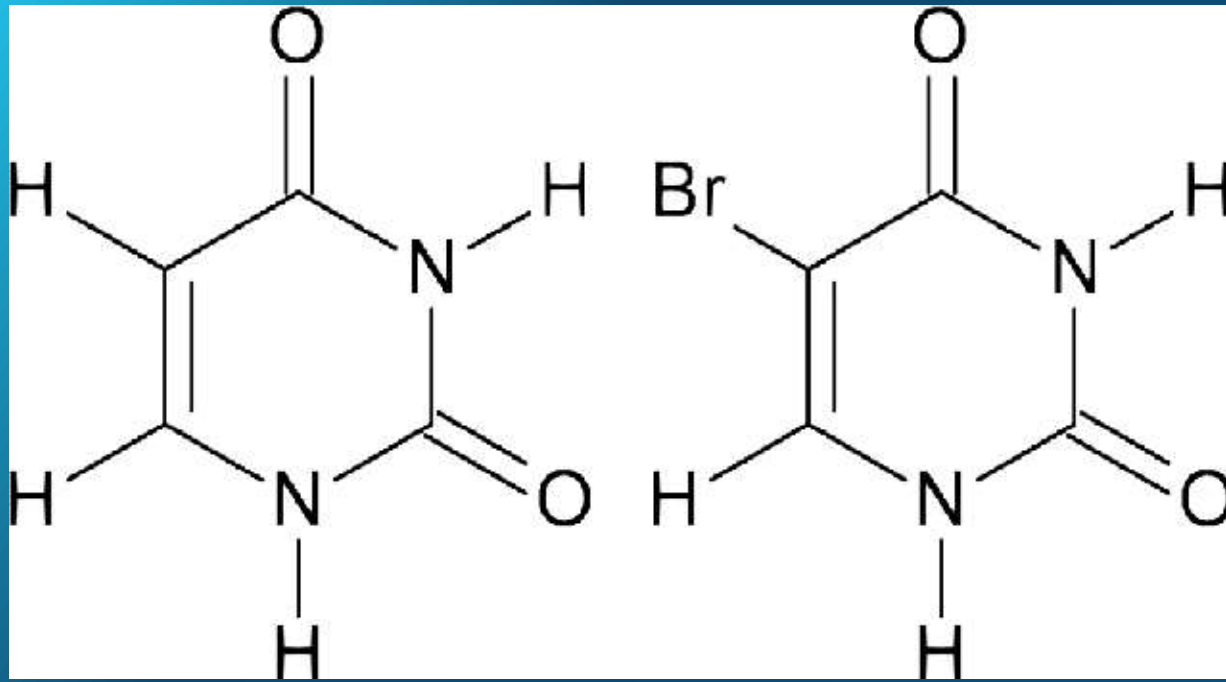
❖**Mechanism:** Create covalent bonds between DNA strands or between DNA and proteins, disrupting replication and transcription.

❖**Examples:** Cisplatin, Mitomycin C

❖iii. Base Analogues

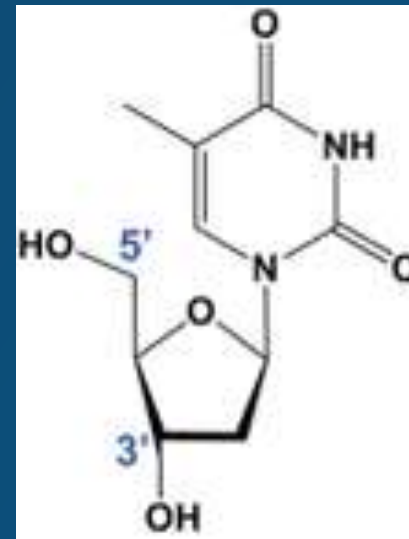
❖**Mechanism:** Mimic natural DNA bases but pair incorrectly, causing mutations.

❖**Examples:** 5-bromouracil, Azidothymidine (AZT)

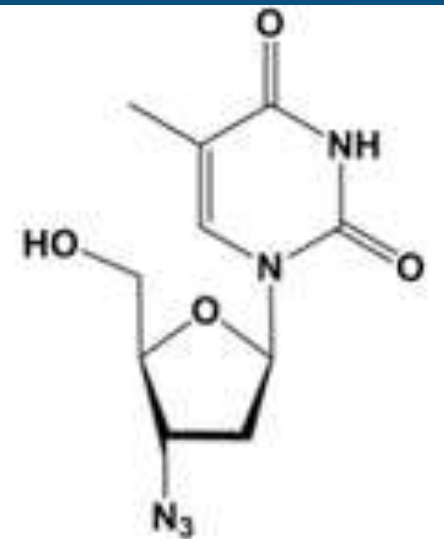


Uracil

5-bromouracil



Thymidine



Azidothymidine (AZT)
Zidovudine

1. Chemical DNA-Damaging Agents

❖iv. Intercalating Agents

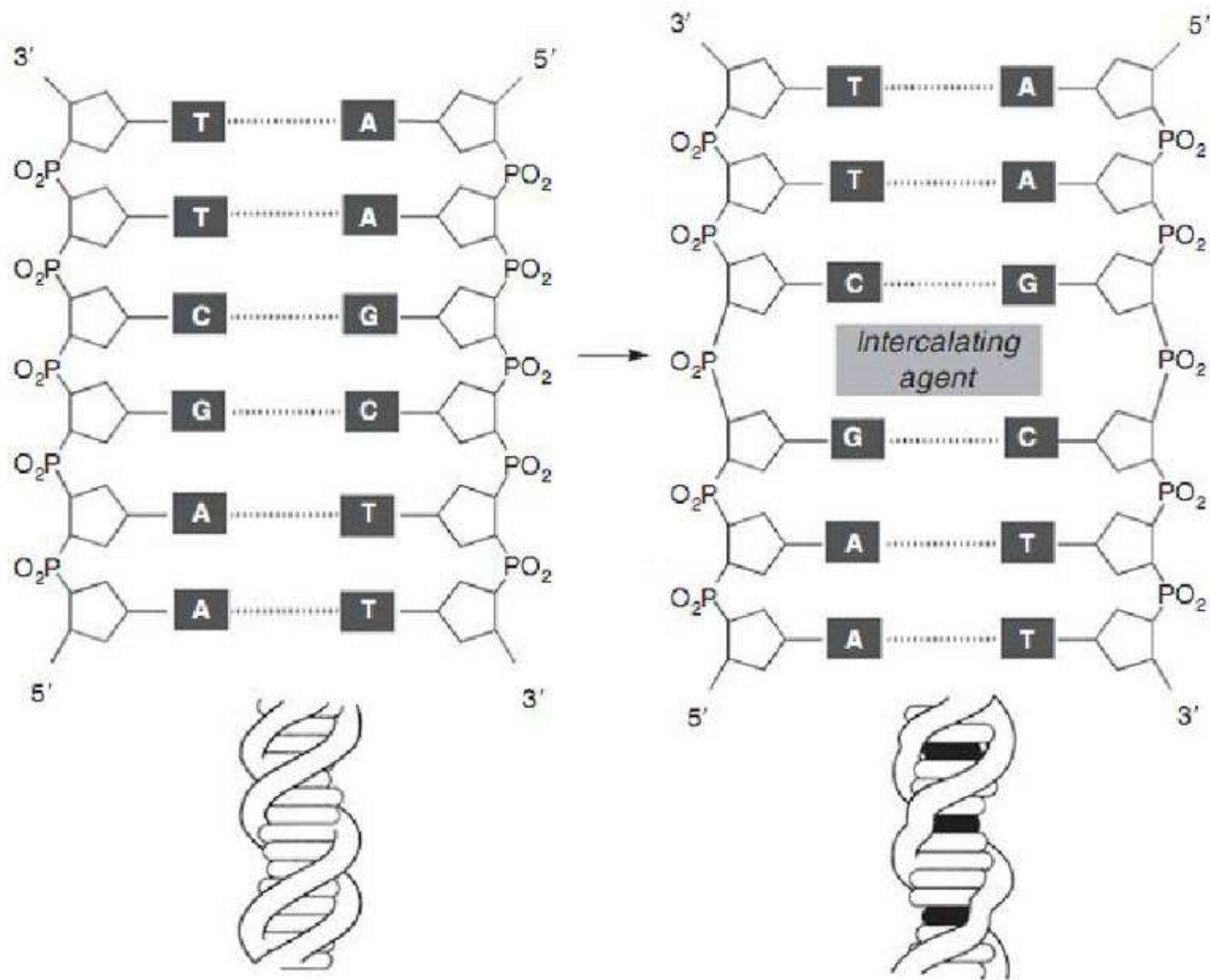
❖**Mechanism:** Insert themselves between DNA base pairs, causing structural distortion.

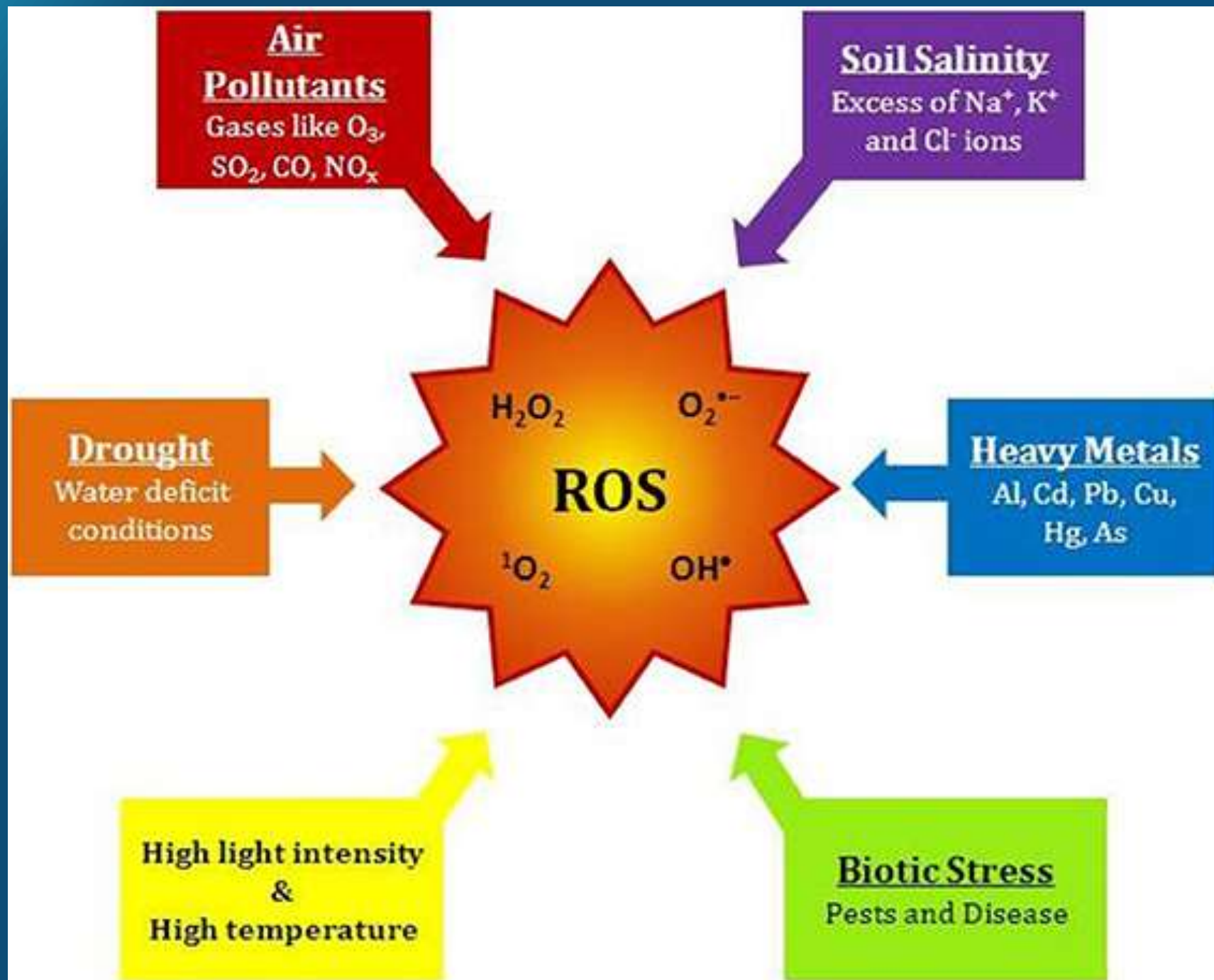
❖**Examples:** Ethidium bromide, Doxorubicin

❖v. Reactive Oxygen Species (ROS)

❖**Mechanism:** Oxidize DNA bases, causing strand breaks and lesions.

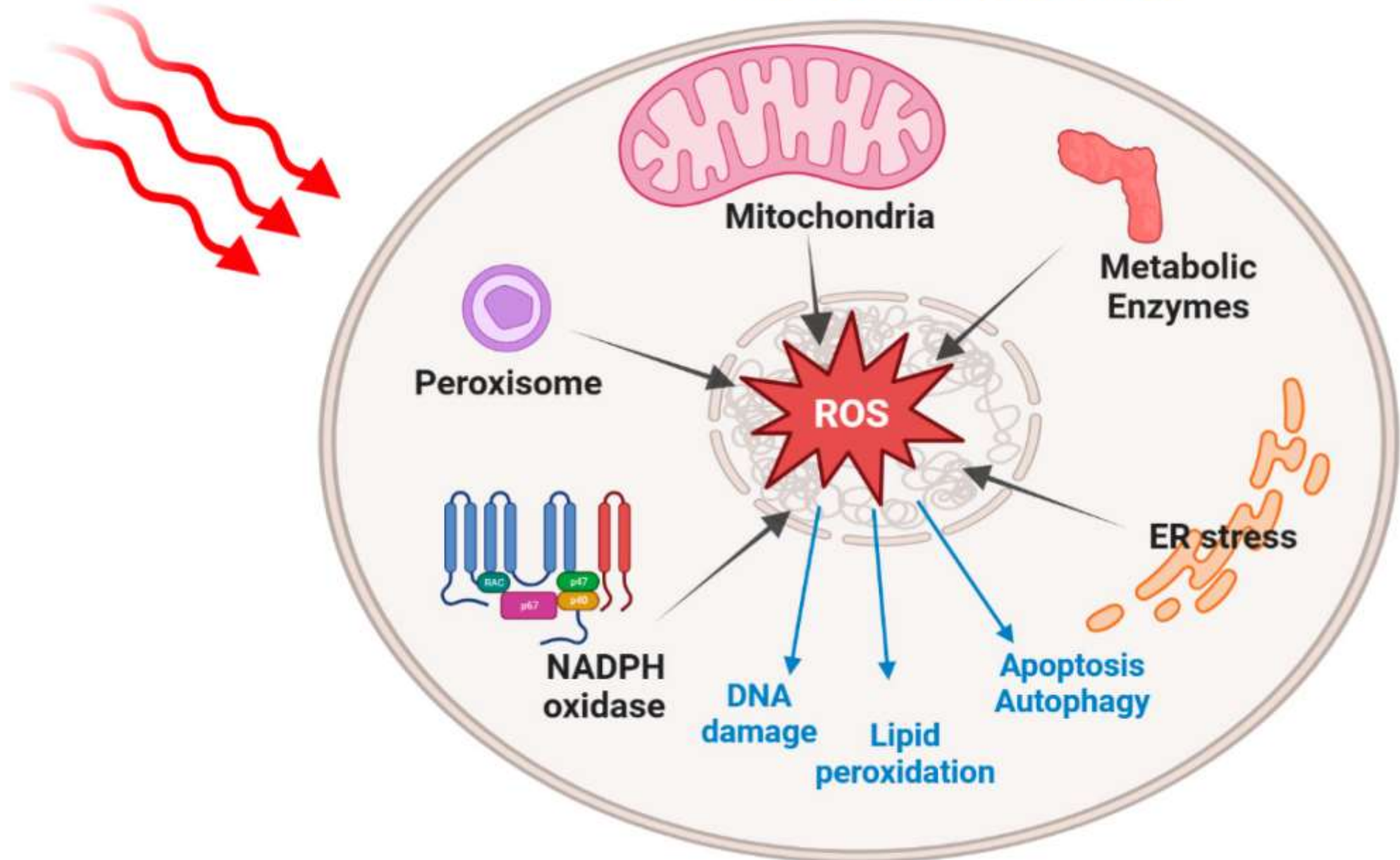
❖**Examples:** Hydrogen peroxide (H_2O_2), superoxide anion (O_2^-), hydroxyl radical ($\bullet\text{OH}$).





Extracellular source of ROS
-Radiation, Xenobiotics

Intracellular source of ROS



2. Physical DNA-Damaging Agents

- ❖ Physical factors, particularly forms of radiation, can induce direct DNA breaks or ionize molecules to generate reactive species.

- ❖ **i. Ionizing Radiation**

- ❖ **Mechanism:** Causes single-strand or double-strand breaks and base damage.

- ❖ **Examples:**

- ❖ X-rays

- ❖ Gamma rays

2. Physical DNA-Damaging Agents

❖ii. Ultraviolet (UV) Radiation

❖**Mechanism:** Induces pyrimidine dimers, mainly thymine-thymine dimers, which block DNA replication.

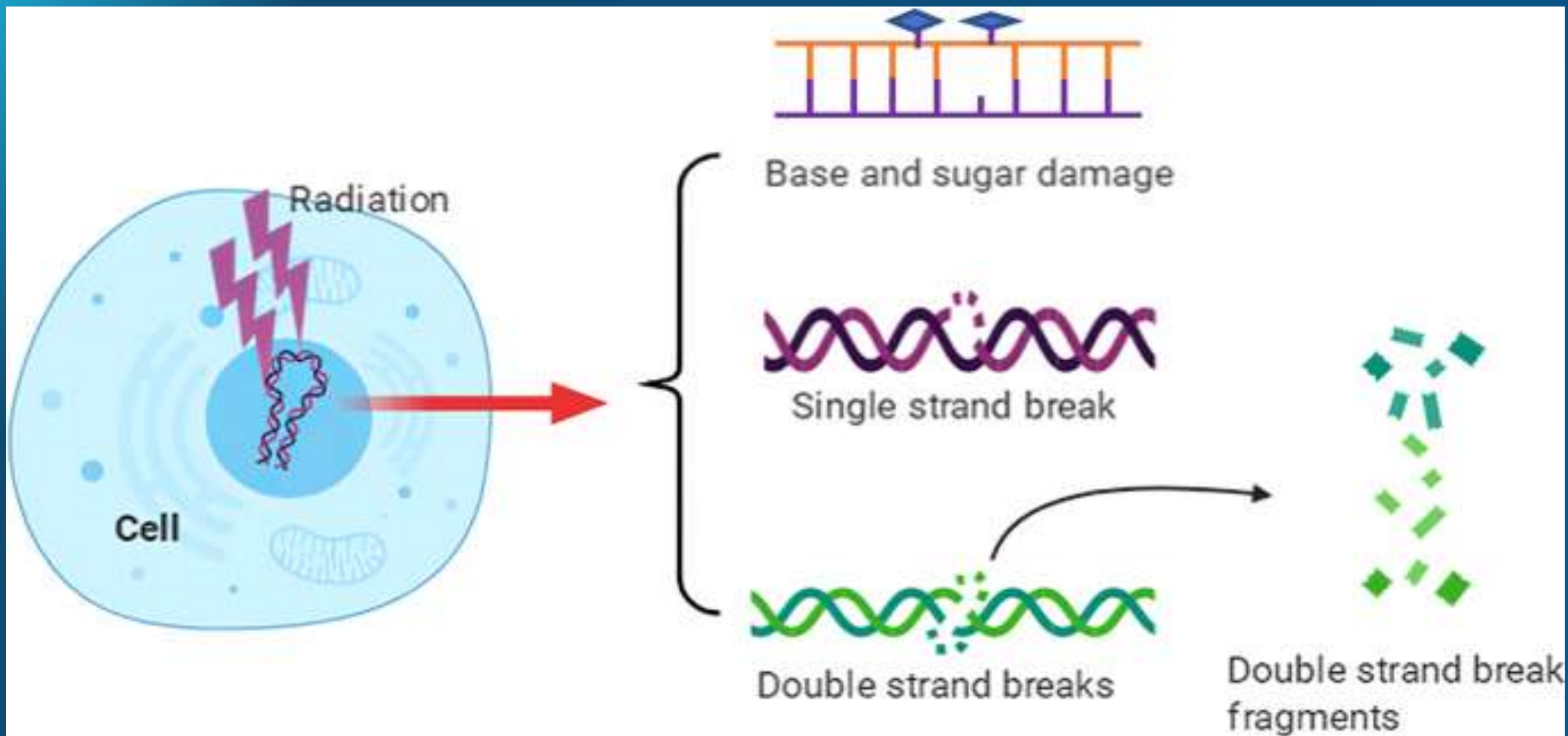
❖**Examples:**

❖UV-A, UV-B, and UV-C radiation.

❖iii. Heat

❖**Mechanism:** Causes deamination and DNA strand breakage.

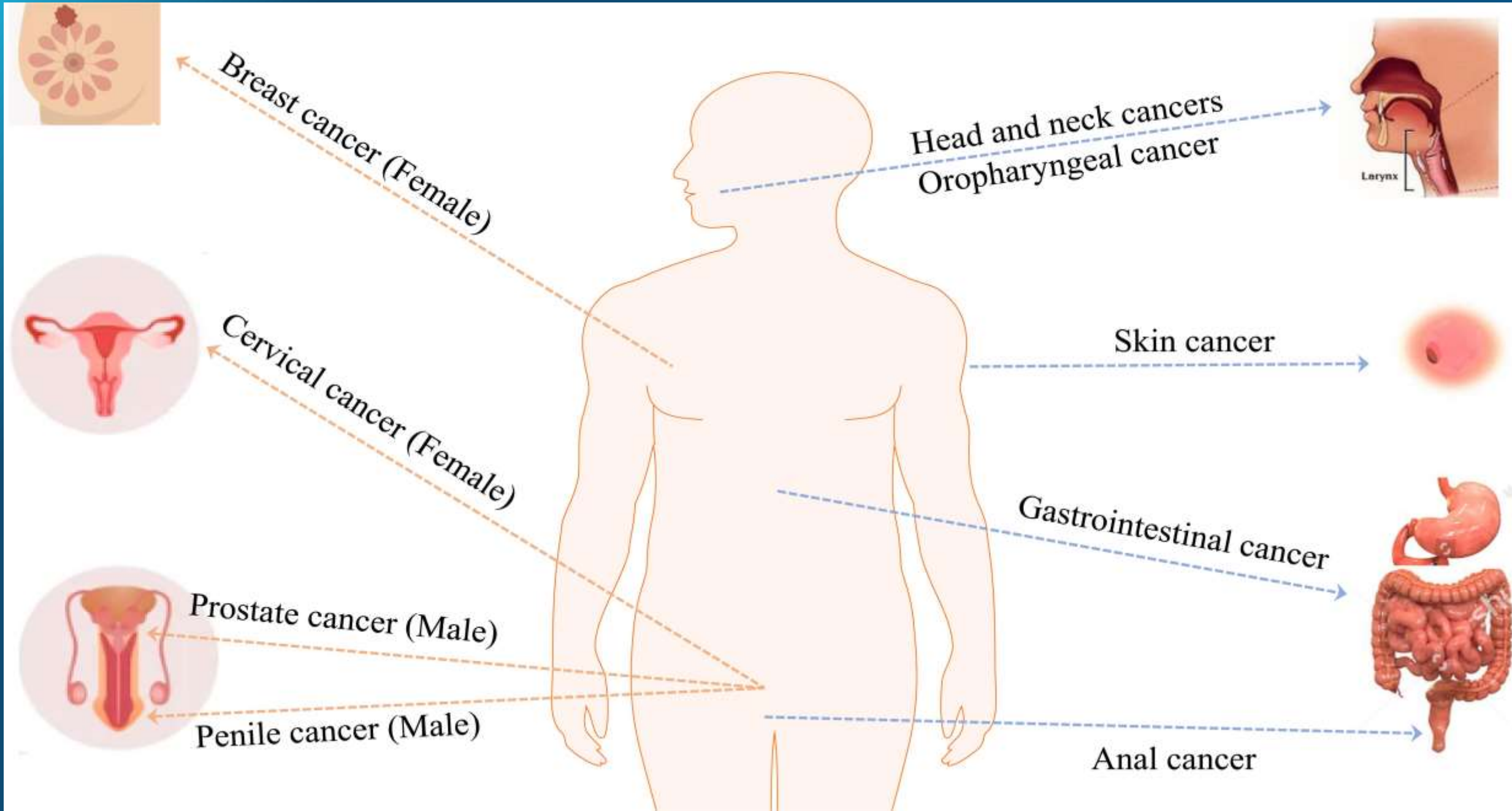
❖**Example:** Prolonged exposure to high temperatures.



3. Biological DNA-Damaging Agents

- ❖ These are factors produced by living organisms or biological processes.
- ❖ **i. Viral Infection**
- ❖ **Mechanism:** Some viruses integrate their genomes into host DNA or induce replication stress.
- ❖ **Examples:**
 - ❖ Human papillomavirus (HPV)
 - ❖ Epstein-Barr virus (EBV)

Effects of Human papillomavirus (HPV)



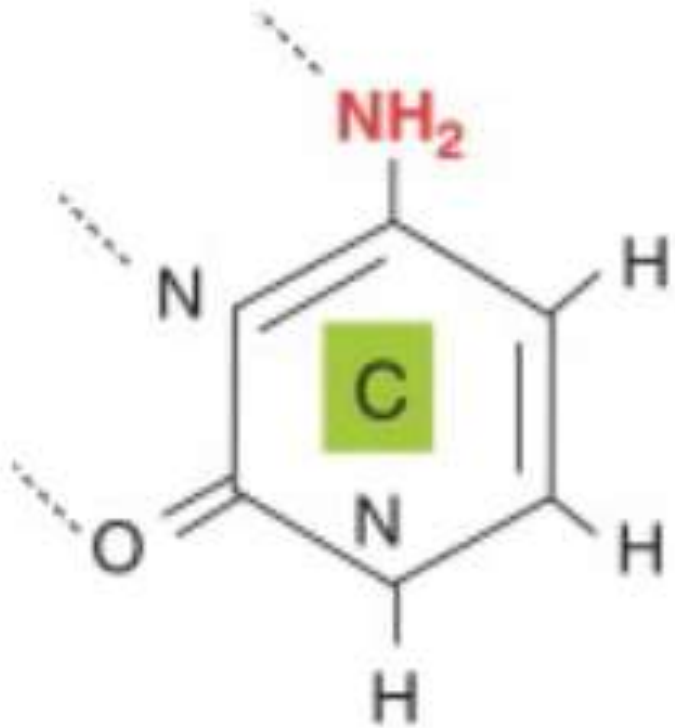
3. Biological DNA-Damaging Agents

❖ii. Endogenous Cellular Processes

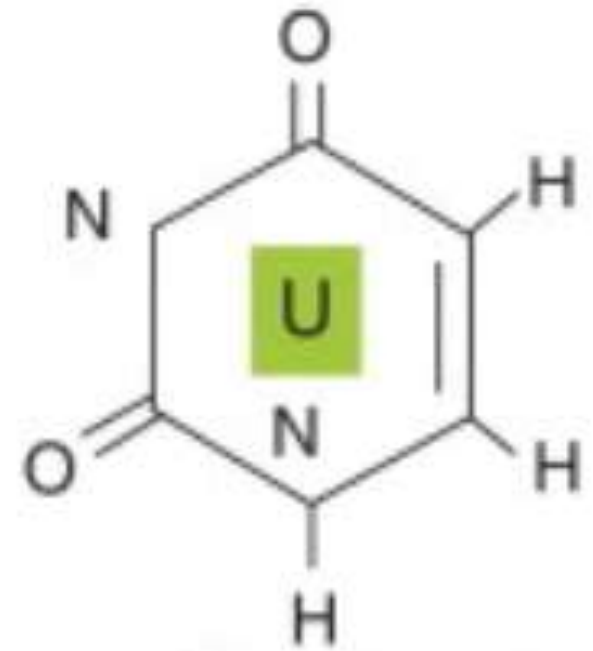
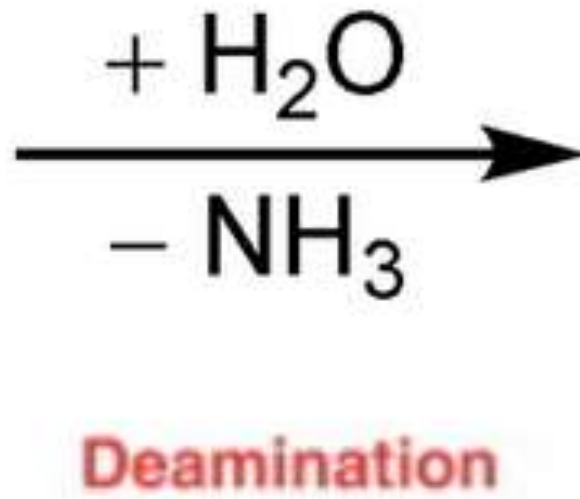
- ❖**Mechanism:** Errors during replication or repair generate DNA lesions.
- ❖**Examples:** Replication stress and Spontaneous base deamination (e.g., cytosine to uracil)

❖iii. Bacterial Toxins

- ❖**Mechanism:** Induce DNA damage directly or via inflammation.
- ❖**Examples:** Colibactin (produced by *Escherichia coli*)



Cytosine



Uracil

4. Environmental Agents

- ❖ Agents present in the environment that damage DNA include pollutants, chemicals, and lifestyle factors.
- ❖ **i. Carcinogens**
 - ❖ **Mechanism:** Form DNA adducts, induce strand breaks, or promote mutations.
 - ❖ **Examples:** Polycyclic aromatic hydrocarbons (PAHs), Benzene
- ❖ **ii. Heavy Metals**
 - ❖ **Mechanism:** Disrupt DNA repair mechanisms and generate reactive species.
 - ❖ **Examples:** Arsenic, Cadmium

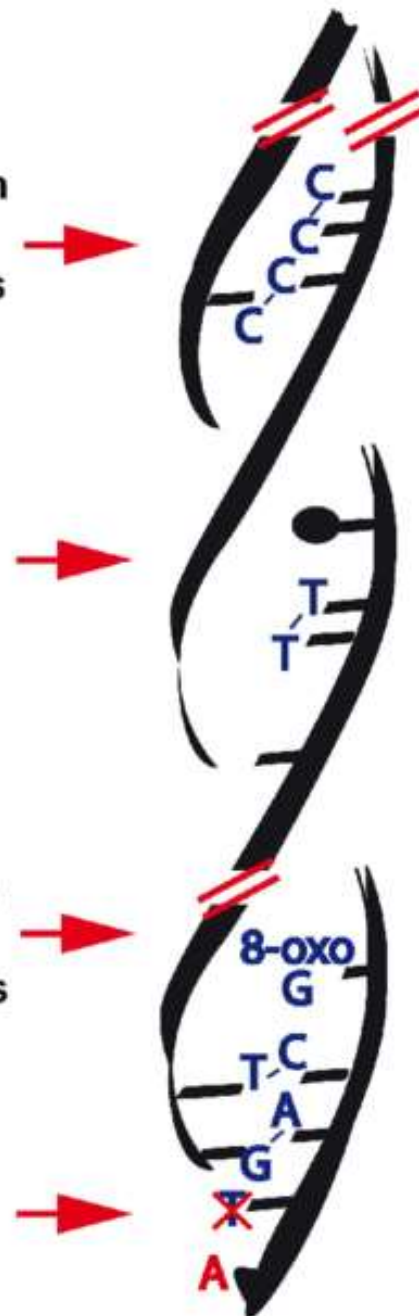
DNA DAMAGING AGENTS

Ionizing radiation
X-rays
Anti-tumor drugs

UV-light
chemicals

Oxygen radicals
Hydrolysis
Alkylating agents

Replication
errors



DNA LESIONS

Double strand breaks
Single strand breaks
Intrastrand crosslinks
Interstrand crosslinks

Bulky adducts
Pyrimidine dimers

Abasic sites
Single strand breaks
8-oxoguanine lesions

Bases mismatch
Insertions
Deletions

DNA REPAIR PATHWAYS

Non Homologous
End Joining (NHEJ)

Homologous
Recombination (HR)

Nucleotide
Excision
Repair (NER)

Base Excision
Repair (BER)

Mismatch
Repair (MMR)

Consequences of DNA Damage

❖ Cellular Effects:

- ❖ Activation of DNA repair pathways (e.g., MMR, NER, BER, HR, NHEJ)
- ❖ Cell cycle arrest
- ❖ Apoptosis or senescence if damage is irreparable.

❖ Long-term Effects:

- ❖ Mutations leading to cancer
- ❖ Genetic disorders
- ❖ Aging related disorders

*Thank
You!*