Ionizing radiation hazard symbol

2007 ISO radioactivity danger logo.

RADIATION INJURY - The Effect of Ionizing Radiation

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Clinical applications of Radiation

- Diagnostic radiology
- Radiotherapy: Malignant neoplasms
- Radiation therapy for other diseases: Radioactive Iodine, radiation for keloids/hypertrophic scars

Scope

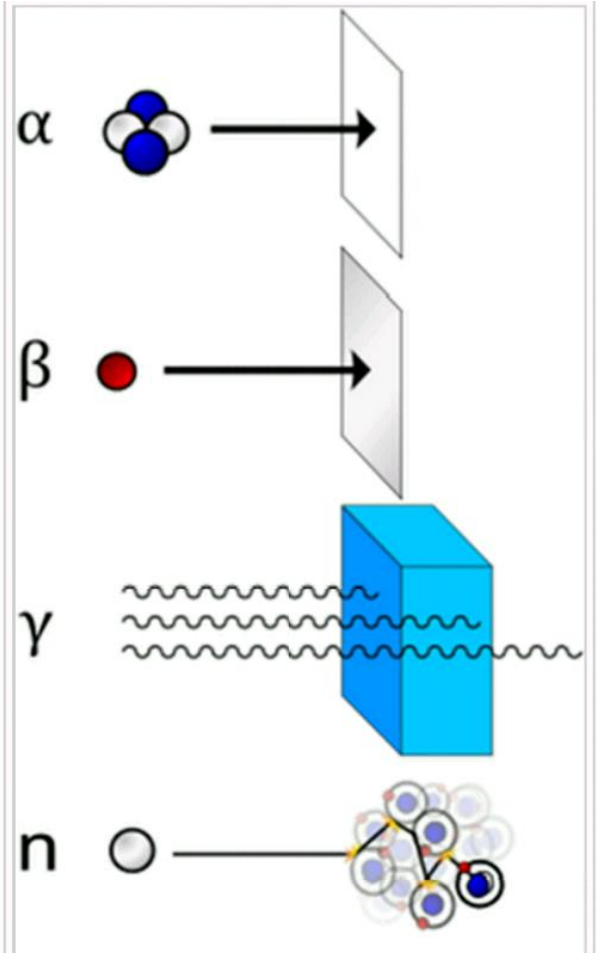
- The nature and effects of ‘ionizing radiation’ and ‘non ionizing radiation’ in cells, tissue and the individual

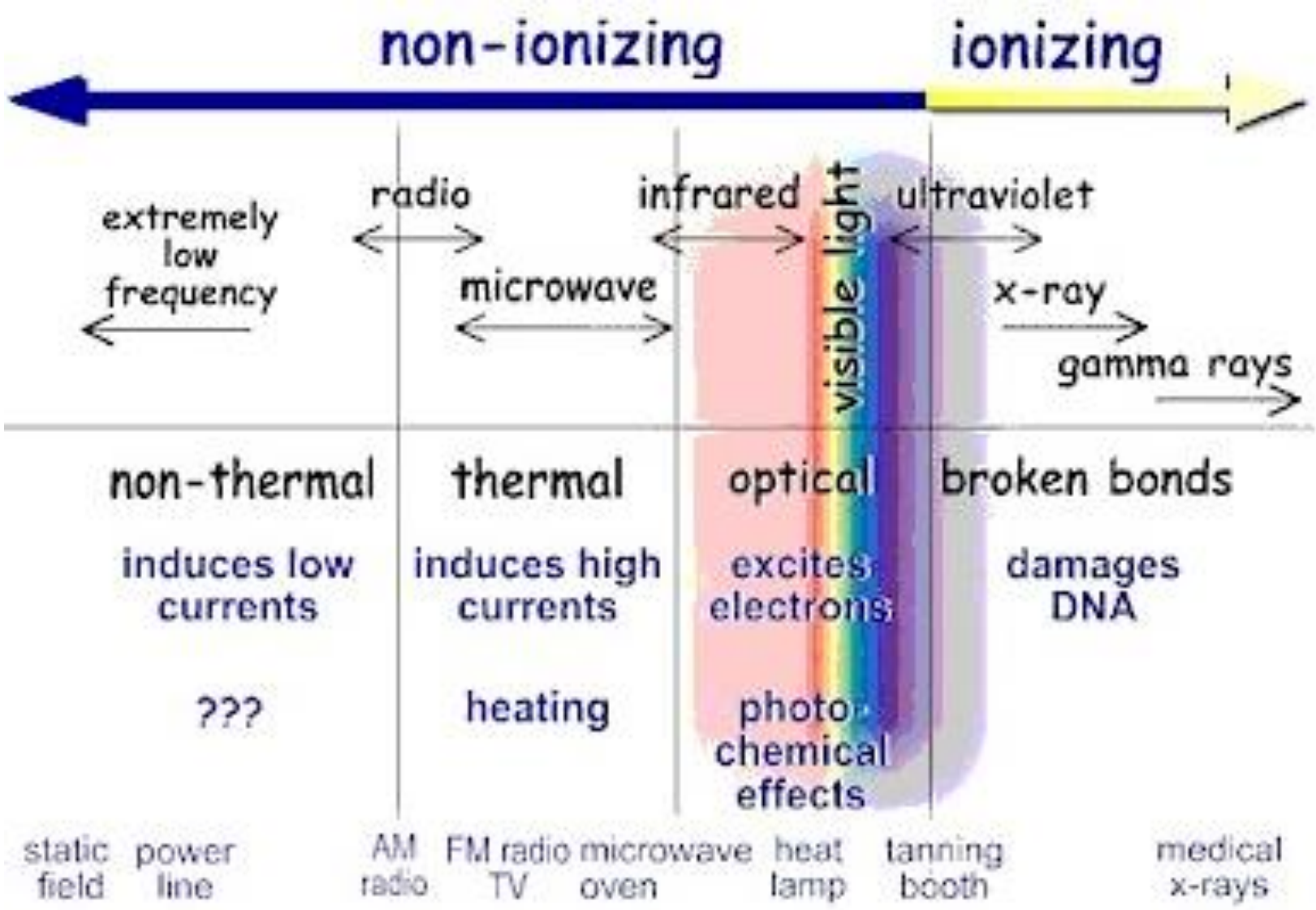
Objectives

- To understand the physical nature of radiation
- To understand the cellular changes induced by radiation
- To discuss tissue and organ changes due to ionizing radiation in humans
- To discuss the sequelae of total body irradiation

Radiation

- Energy bearing particles or waves travel through a vacuum
- Includes travel through matter containing media
- This media is not required for their propagation.



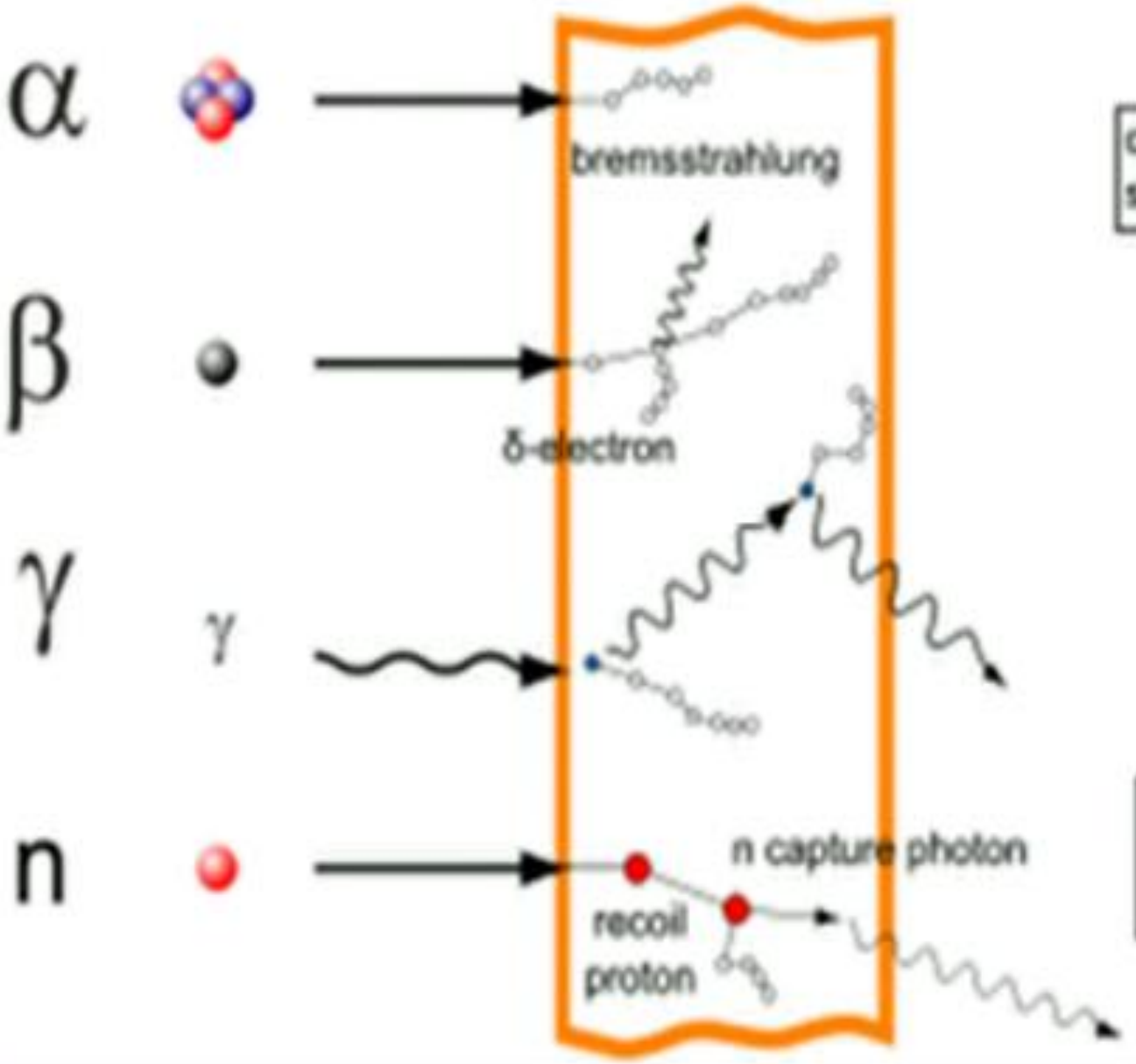

non-ionizing
ionizing
extremely low frequency
radio
microwave
infrared
visible light
ultraviolet
x-ray
gamma rays
non-thermal
thermal
optical
broken bonds
induces low currents
induces high currents
excites electrons
damages DNA
???
heating
photo-chemical effects
static field
power line
AM radio
FM radio TV
microwave oven
heat lamp
tanning booth
medical x-rays

Radiation- Ionizing or Non Ionizing

- Ionizing
- Non ionizing

Ionizing radiation

Interaction of ionizing radiation with matter



charged particles interact strongly and ionize directly

neutral particles interact less, ionize indirectly and penetrate farther

Quantity	Particle detector	CGS units	SI units	Other units
Disintegration rate		curie	becquerel	
Particle flux	geiger counter, proportional counter, scintillator			counts per minute, particles per cm^2 per sec
Energy Fluence	thermoluminescent dosimeter, Film badge dosimeter		$\frac{\text{joule}}{\text{metre}^2}$	
Beam energy	proportional counter	electronvolt	joule	
Linear energy transfer	derived quantity	$\frac{\text{MeV}}{\text{cm}}$		$\frac{\text{keV}}{\mu\text{m}}$
Kerma	ionization chamber, semiconductor detector, quartz fiber dosimeter, Kearny Fallout Meter	$\frac{\text{esu}}{\text{cm}^3}$	$\frac{\text{coulomb}}{\text{kilogram}}$	roentgen
Absorbed dose	calorimeter	rad	gray	rep
Equivalent dose	derived quantity	rem	sievert	
Effective dose	derived quantity	rem	sievert	BRET
Committed dose	derived quantity	rem	sievert	banana equivalent dose

Quantity	Particle detector	CGS units	SI units	Other units
Disintegration rate		curie	becquerel	
Particle flux	geiger counter, proportional counter, scintillator			counts per minute, particles per cm^2 per sec
	thermoluminescent		joule	
Absorbed dose	calorimeter	rad	gray	
Equivalent dose	derived quantity	rem	sievert	
Effective dose	derived quantity	rem	sievert	
Committed dose	derived quantity	rem	sievert	
Committed dose	derived quantity	rem	sievert	equivalent dose

Units of Dose

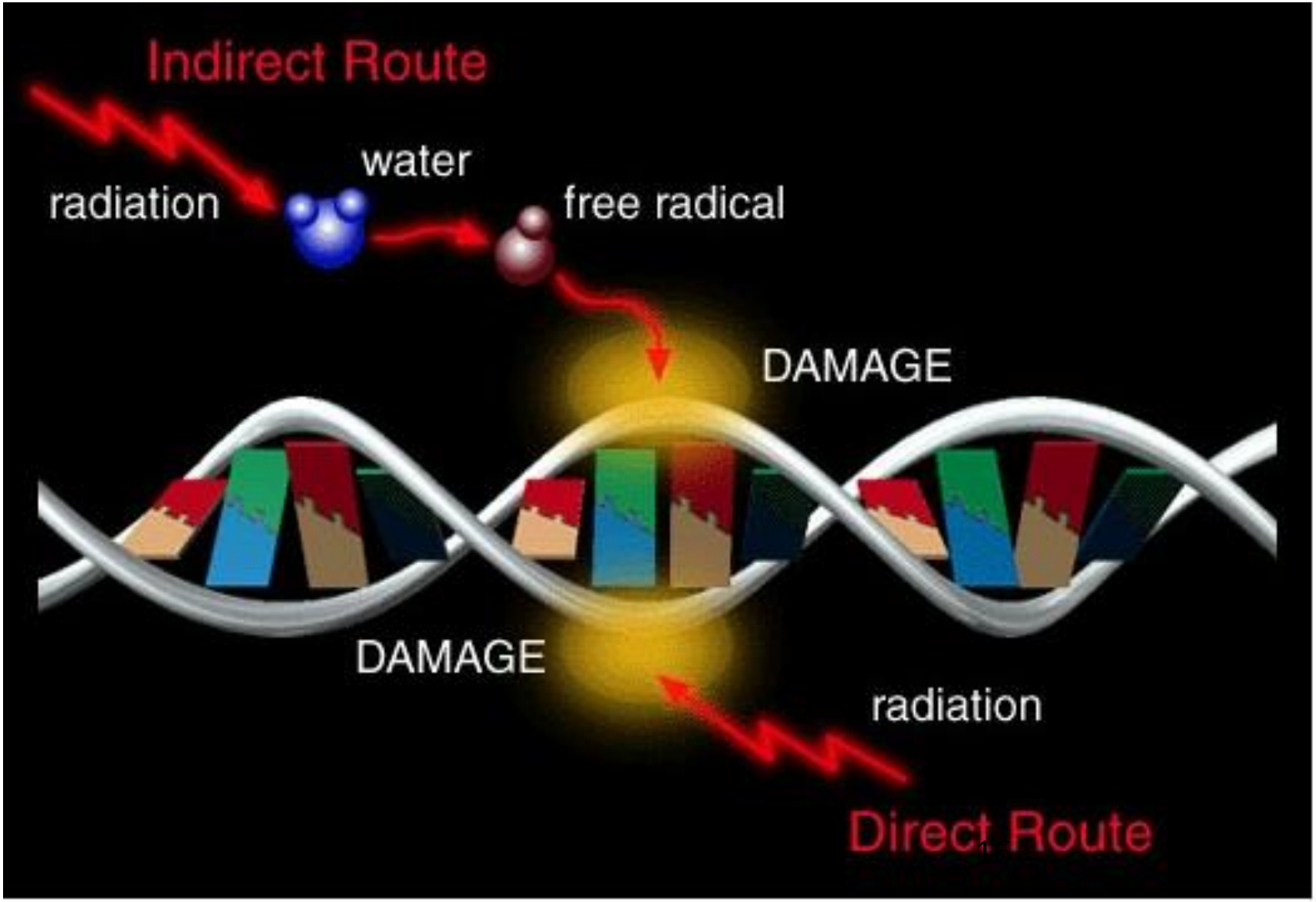
- **Gray (Gy)** – The Unit of ionizing energy absorbed (absorbed dose). I Gy = 1 J/Kg
- **Sievert (Sv)** – The Unit of absorbed dose taking account of Linear Energy Transfer (LET).
- For **α particles- 1Sv = Gy x20, β particles: 1Sv = Gy x1, γ**

LD-50 limit for CHO-K1 cell line irradiated by photons (blue curve) and by carbon ions (red curve).

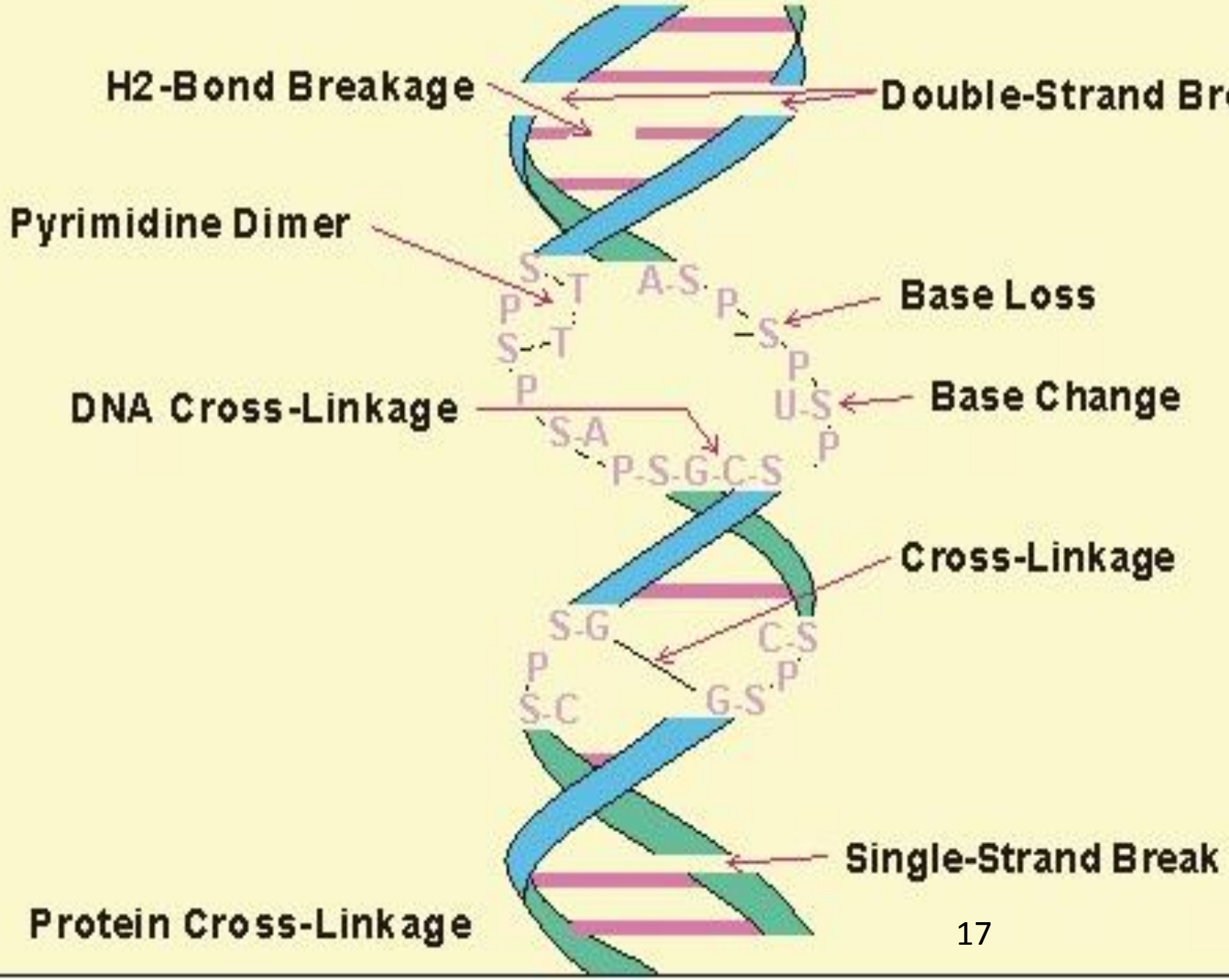
Effects of Ionizing Radiation

- **Target Theory –** injury results to ionization of specific cellular components.
- Targets include nucleic acids, enzymes and proteins that bear the SH group
- **Poison Theory –** injury results from ionization and production of free radicals. This results in membrane injury

Effects upon DNA



RADIATION DAMAGE TO DNA



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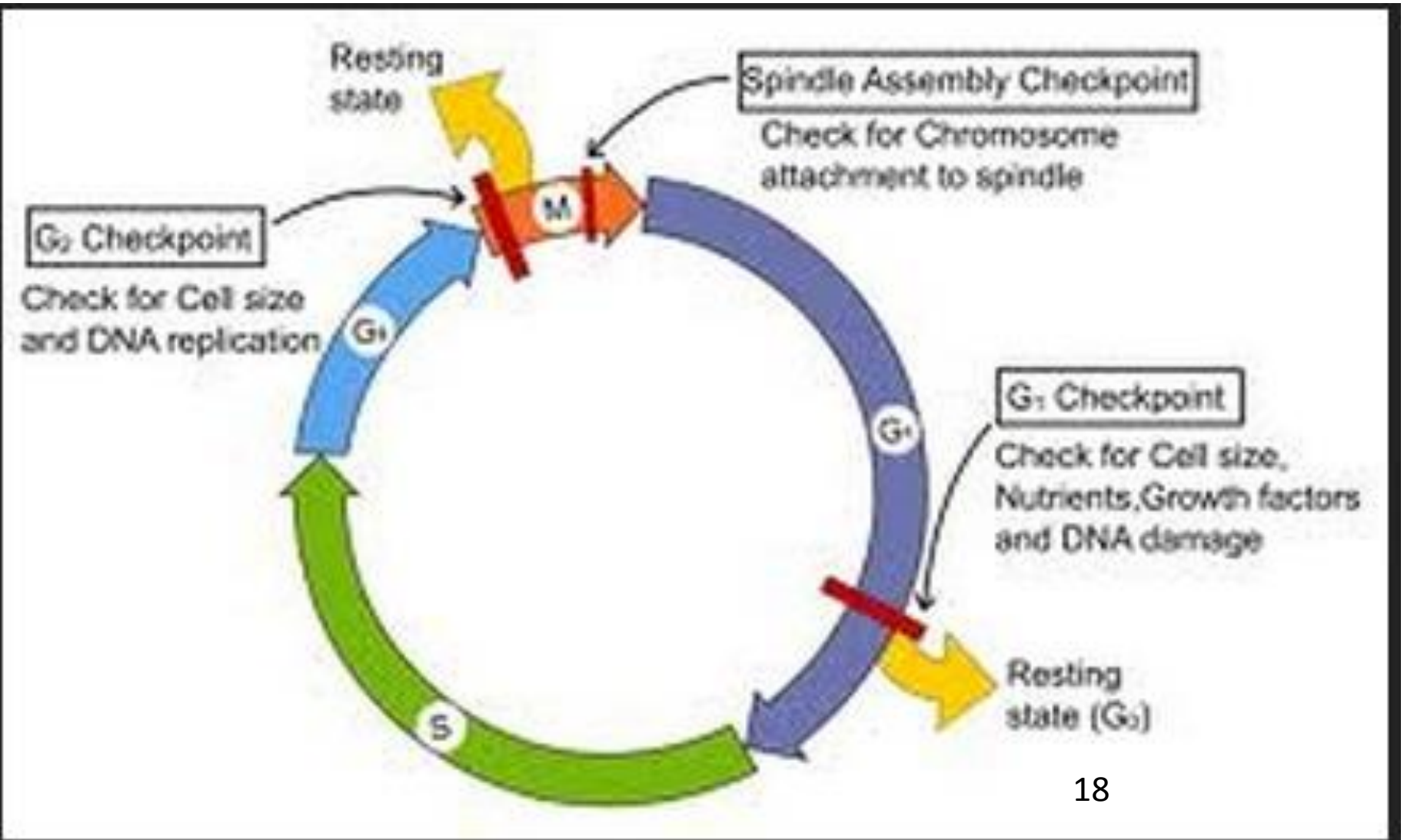
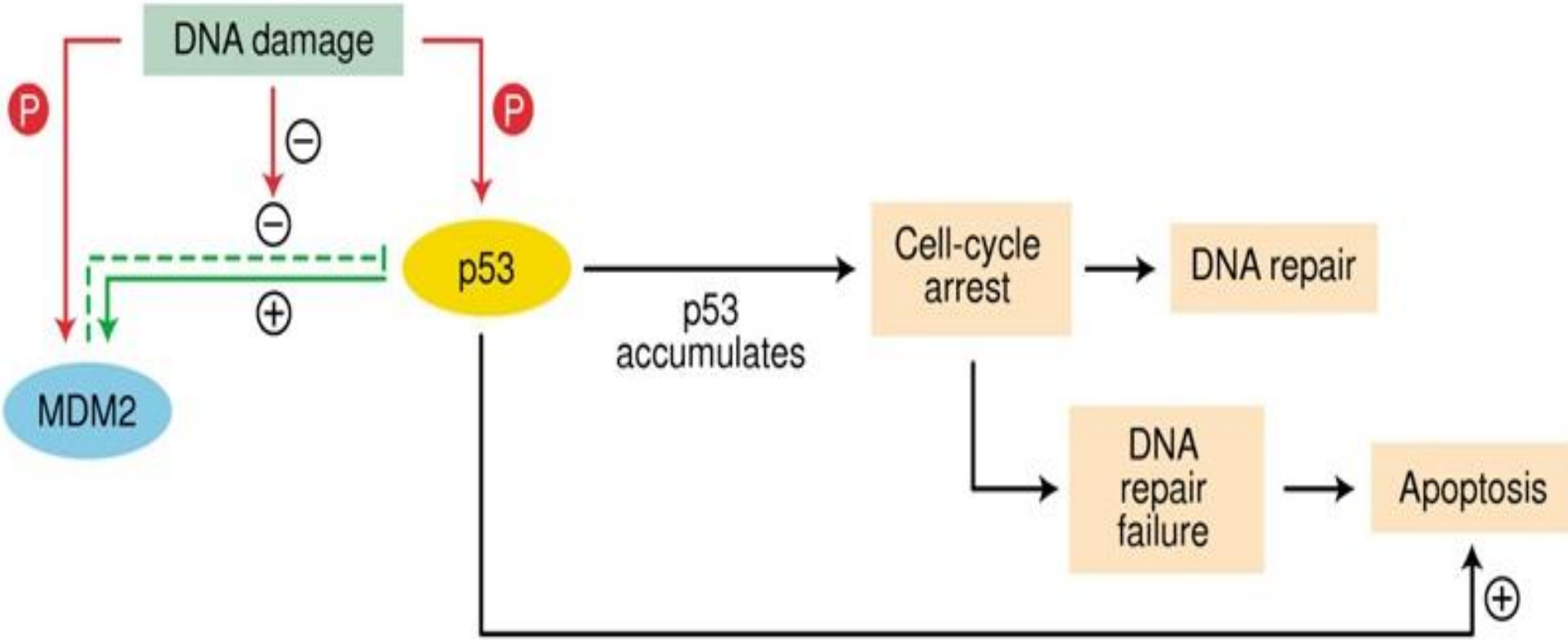
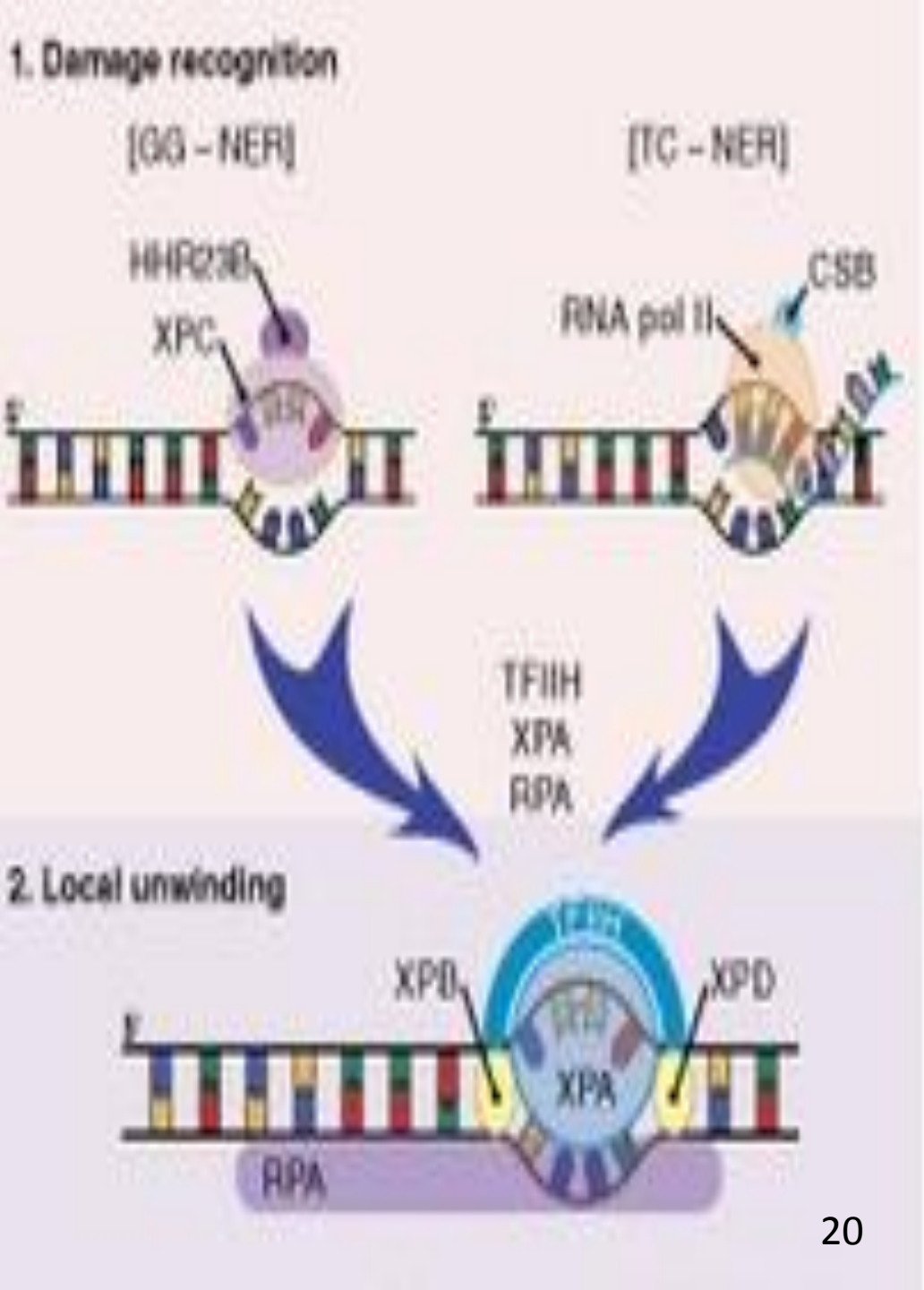
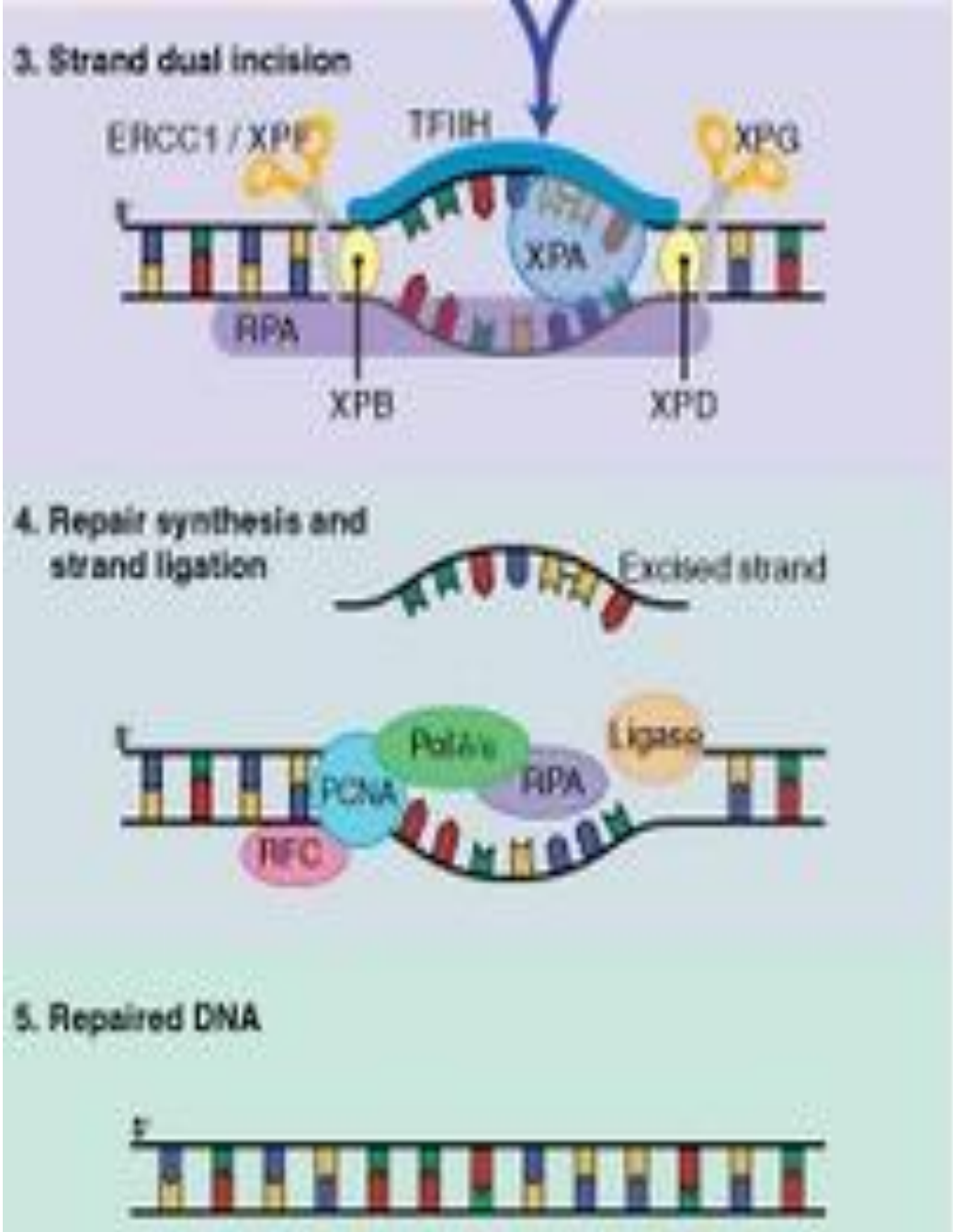
Cell Cycle Checkpoints



DNA Repair


DNA damage
P
P
p53
MDM2
p53
accumulates
Cell-cycle
arrest
DNA repair
DNA
repair
failure
Apoptosis


1. Damage recognition
[GG - NER]
[TC - NER]
HHR23B
XPC
CSB
RNA pol II
TFIIH
XPA
RPA
2. Local unwinding
XPD
XPD
XPA
RPA


3. Strand dual incision
ERCC1 / XPF
TFIIH
XPG
XPA
RPA
XPB
XPD
4. Repair synthesis and strand ligation
Excised strand
Pol δ/ε
Ligase
PCNA
RPA
RFC
5. Repaired DNA
5'

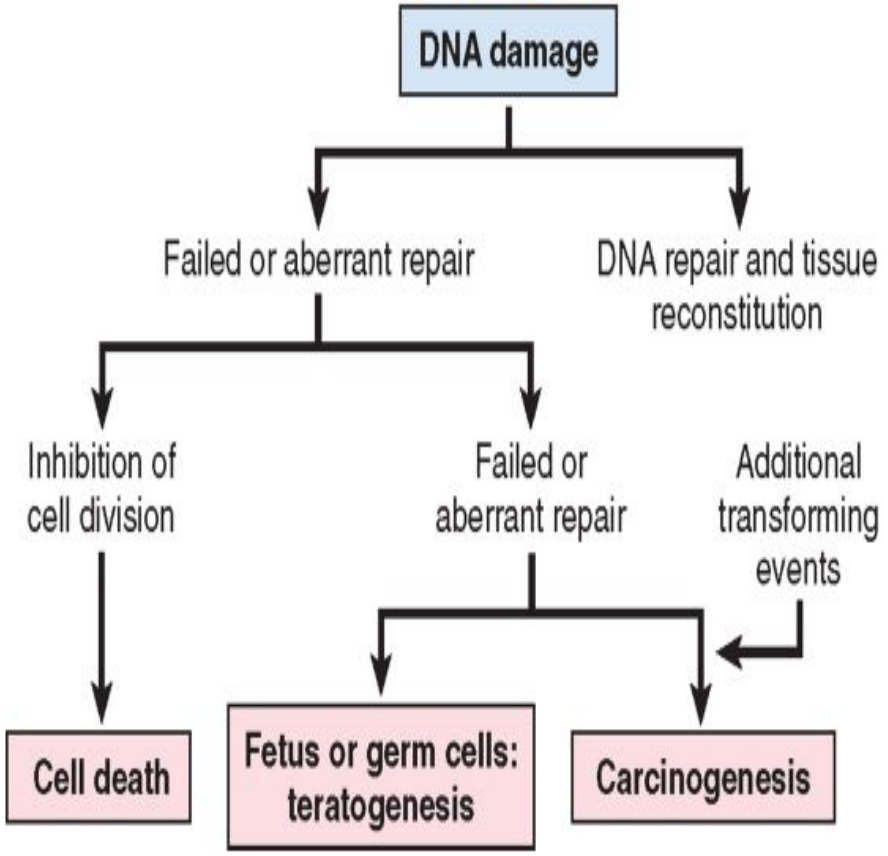
Effect on Cells: Chromosomal Changes

1. Deletions
2. Translocations
3. Fragmentation
4. Adhesion breaks between chromosomes
5. Polyploidy and aneuploidy

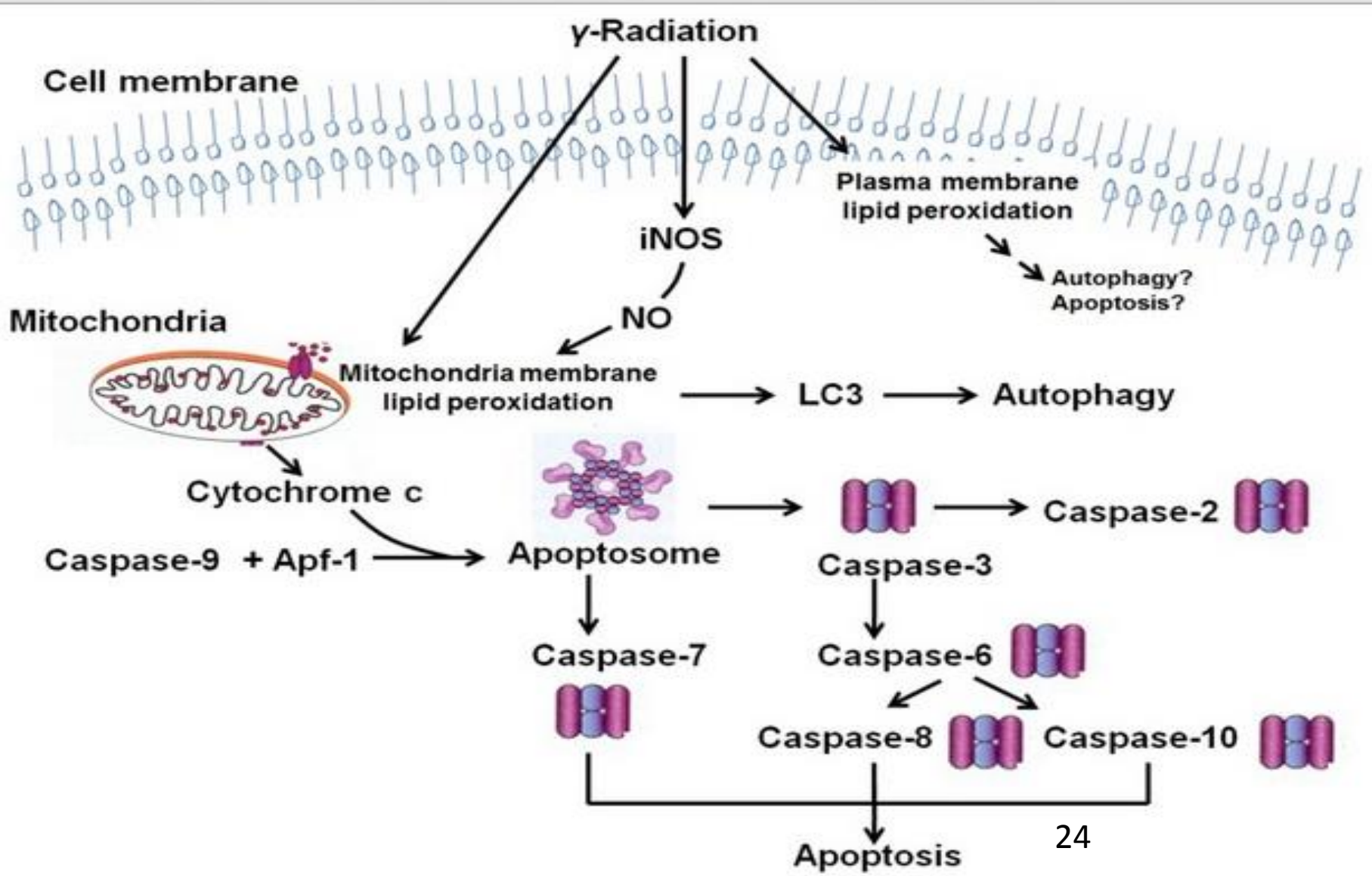
- The number of these mutations is related to the dose of radiation

Consequences

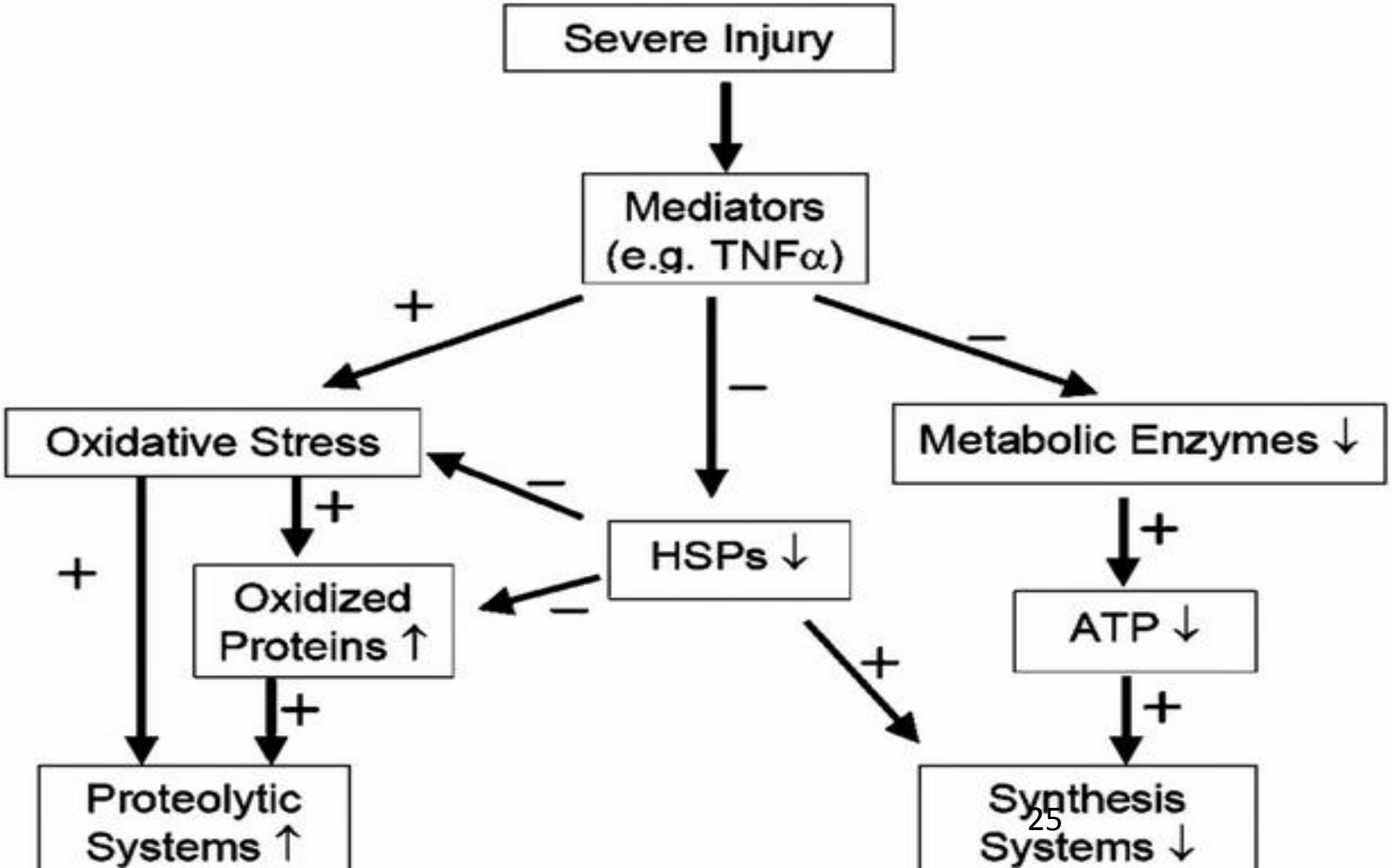
- Inhibition of cell division
- Germ-line mutations
- Carcinogenesis



Effect Upon Cell Membranes



Effects Upon Proteins



Radiosensitive cells

Comparing how much radiation affects different types of cells

Increasing radiosensitivity

- Embryonic cells
- Lymphocytes (White blood cell
- Erythrocytes (Red blood cells)
- Sperm
- Epithelial cells
- Endothelial cells
- Connective tissue cells
- Bone cells
- Nerve cells
- Brain cells
- Muscle cells

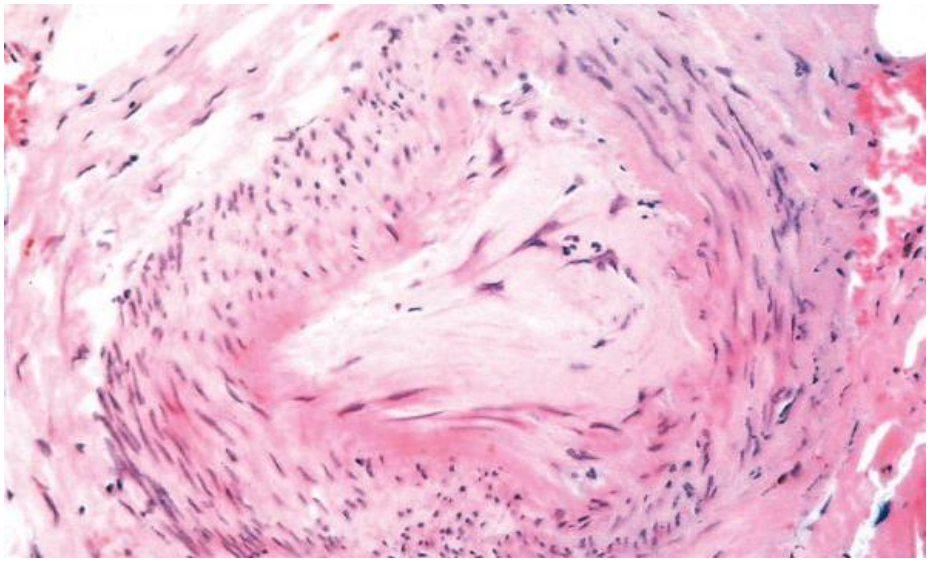
* Law of Bergonie and Tribondeau

Effect of Radiation on Tissues

- Acute
  - Occur hours to days following radiation exposure
  - Due to depletion of stem cells in an organ or tissue
  - Apparent when cell number reduction > cell regeneration
  - Further radiation exposure leads to tissue death, irreversible tissue damage
  - Bone marrow, skin, GIT

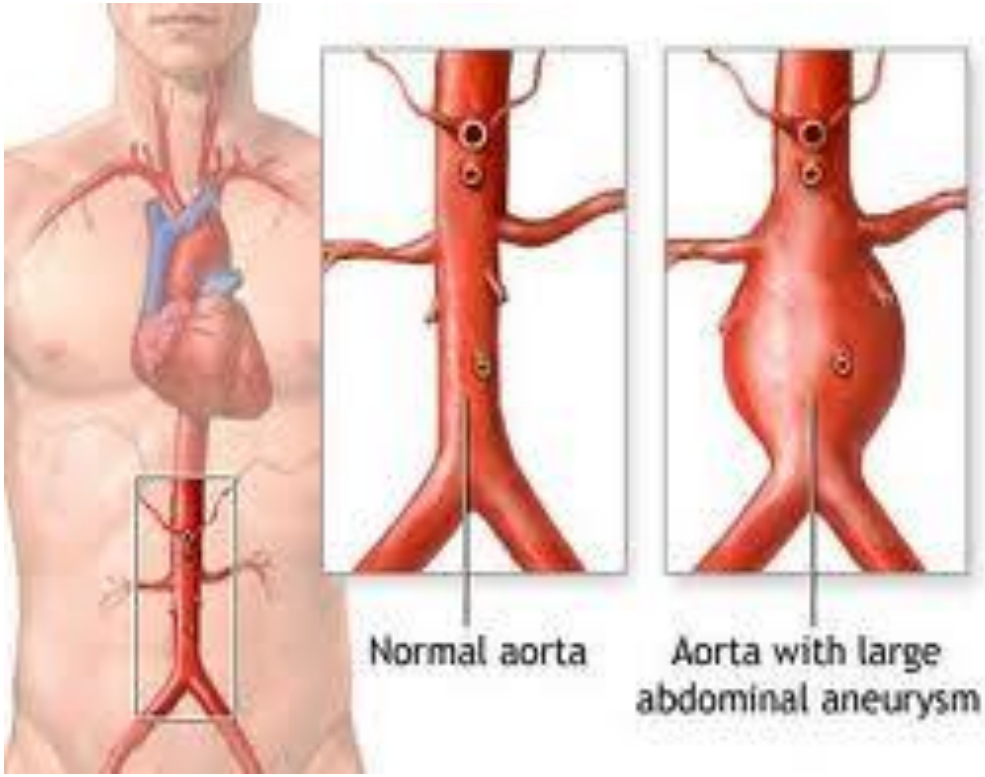
Effect of Radiation on small blood vessels

- Late
  - Occur months to years following radiation exposure
  - Related to endothelial damage → intimal thickening, occlusion → ischaemic



Effects, large blood bessels

- Due to injury involving vasa vasora
- Transmural necrosis
- Aneurisms



Heart

- Pericardium – Fibrosis
- Myocardium -Radiation induced cardiomyopathy – minimal inflammatory infiltrate
- Worse when cardiotoxic drugs are used
- Endocardium – valvular thickening, fibrosis, calcification
- Coronary – intimal foam cell accumulation

Nervous System

- Brain, spinal cord, peripheral nerve
- Neurons – resistant
- Injury to glial and oligodendrocytes
- Glial and vascular injury – vasogenic oedema due to Blood Brain Barrier Dysruption
- Endothelial vasculopathy
- Spinal cord – transient myelitis (2-4 months)
- Delayed myelitis (20-30 months)

Peripheral Nerves

- Fairly resistant
- Peripheral neuropathy
- Perineural inflammation and ganglionitis

Bone Marrow

- Highly sensitive
- Stem cell injury leading to pancytopenia
- Myelodysplasia may predominate

Other tissues

- Ovaries/Testes, highly susceptible – germ cell necrosis, supporting cells are retained
- Eye – optic neuropathy, lens opacity, retinal injury
- Lymphoid cells – disorders in homing and recirculation
- Endocrine – hyperplasia - hypoplasia

conclusion

- Ionizing induced injury affects the DNA/Proteins/lipid membranes
- Microvascular injury is associated with late injury
- Repair with fibrosis is an intermediate manifestation
- Long term - neoplasia

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