Cellular Radiobiology I and II

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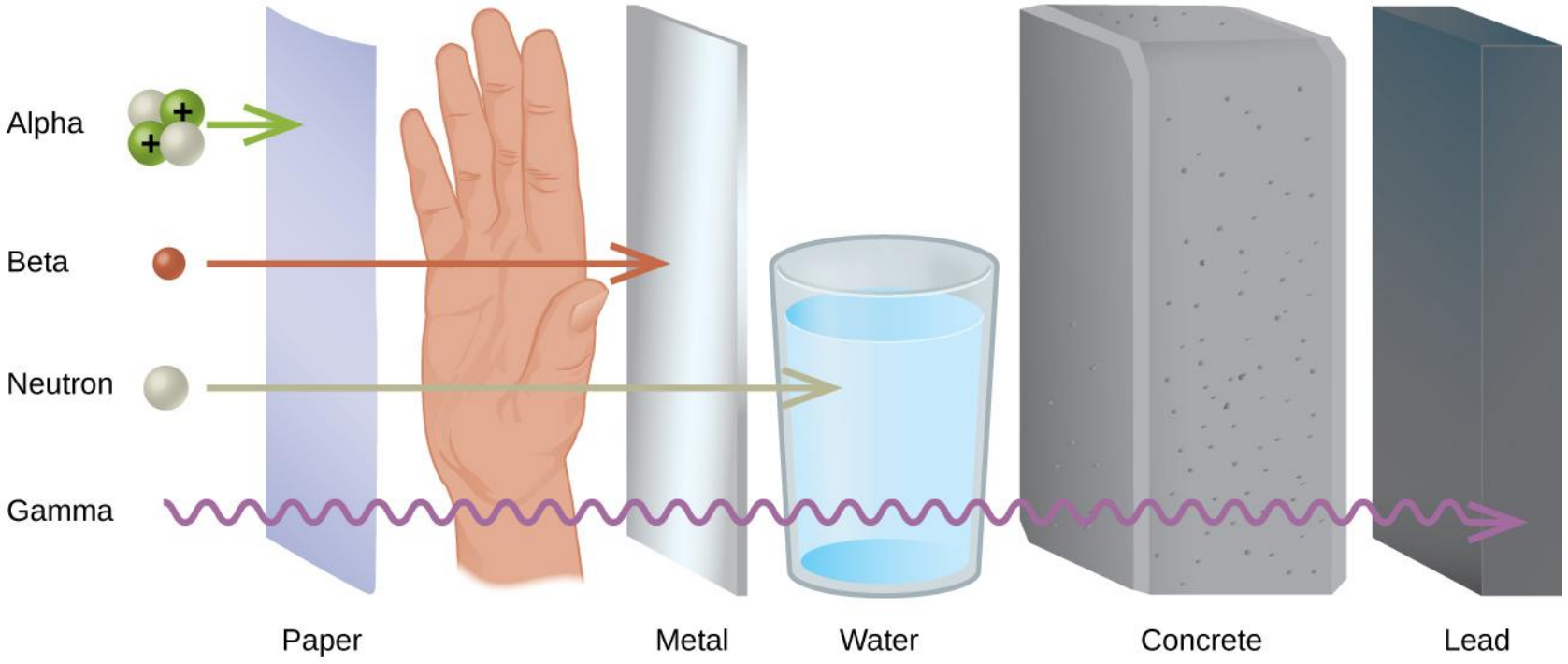
pnri.dost.gov.ph /PNRIDOST

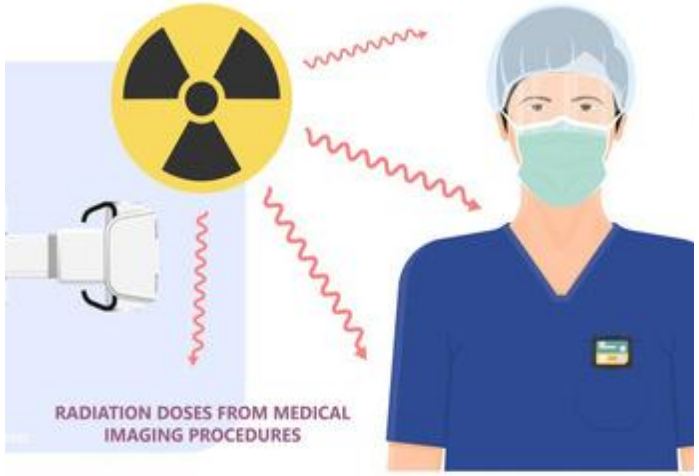
Ionizing radiation

A type of radiation of such energy that it can **detach electrons from atoms or molecules**, which **causes changes at the atomic level** when interacting with matter including living organisms. It usually involve the **production of ions** (electrically charged atoms or molecules) – hence the term "ionizing" radiation.

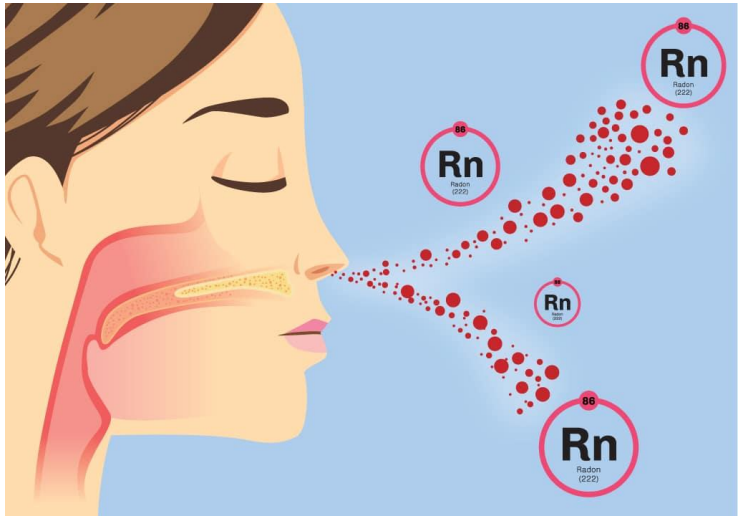


https://www.iaea.org/newscenter/news/what-is-radiation

Radiation hazards



Exposure from medical procedures



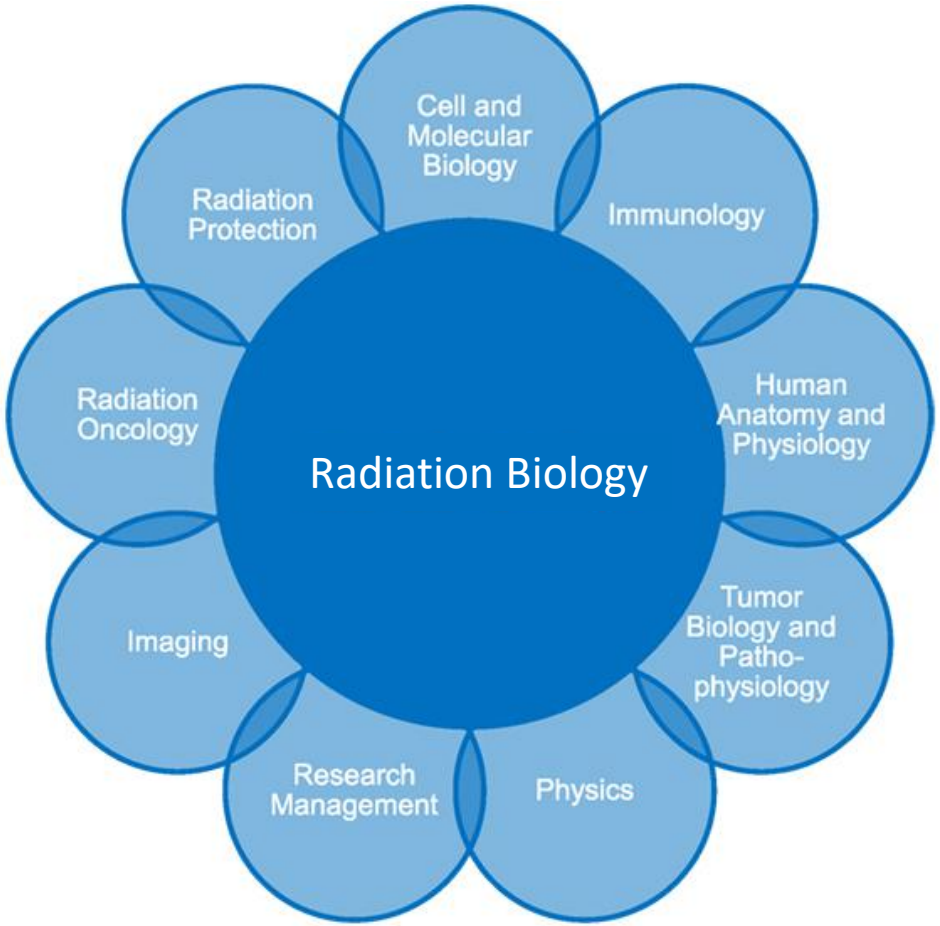
Radon breathers

Nuclear accidents

Tissues and organs are composed by cells of different kinds, and damage to these cells leads to development of radiation health effects.

Radiation Biology

- a branch of science that deals with the **action of ionizing radiation on biological tissues and living organisms**
- a combination of two disciplines: **radiation physics** and **biology**



Radiation biology is an **emerging** and **strongly interdisciplinary field** with significant contributions from a number of preclinical and clinical disciplines *(Combs et al., 2017)*.

https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2017.00226/full

Impacts of radiation at cellular level

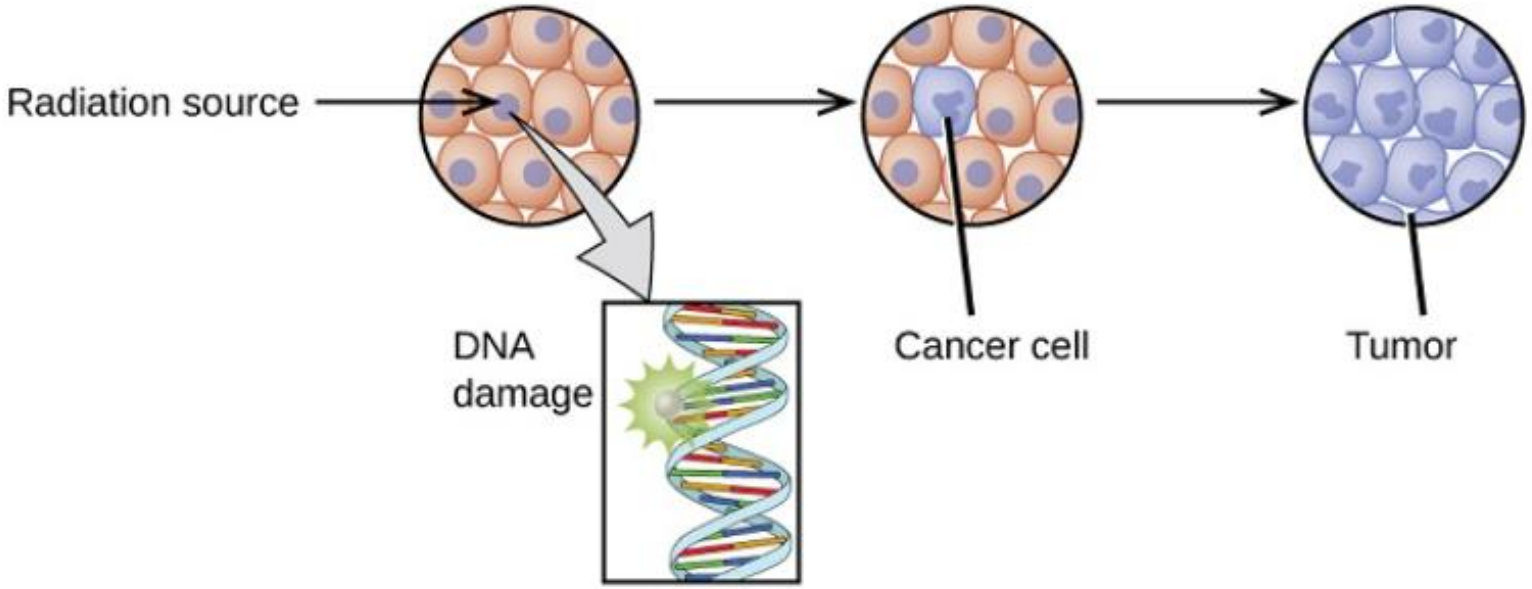
The cell **repairs itself** and it goes back to normal.

The cell damage is **not repaired** or is **incorrectly repaired**, so the cell is changed (mutated). This change may eventually lead to cancer.

There is too much damage to the cell, and the **cell dies**.

http://cdc.gov/radiation-health/about/health-effects-of-radiation.html

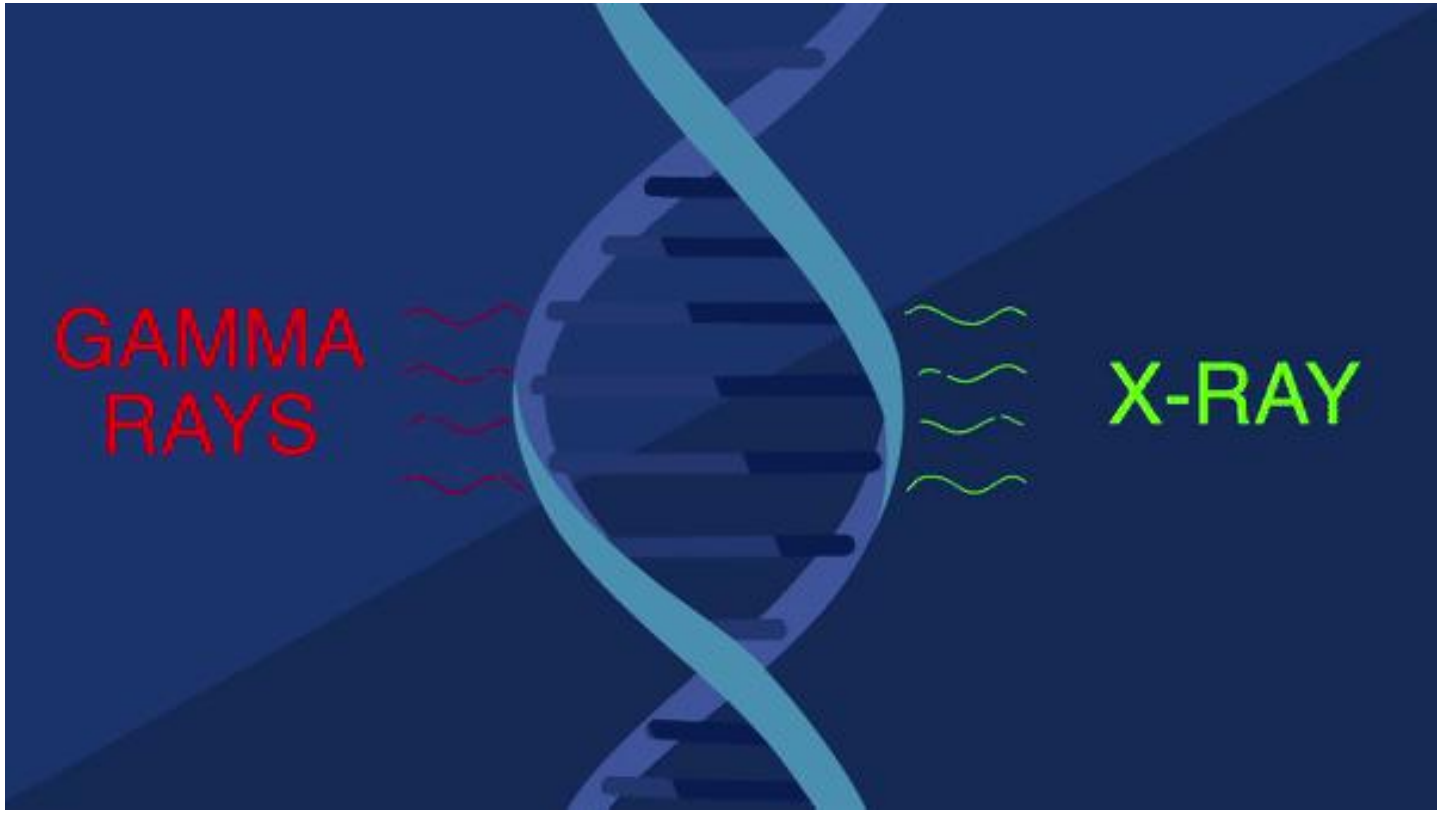
If damage is not properly repaired, the cells may divide in an uncontrolled manner and cause cancer



- **Primary target** for cell damage from ionizing radiation is deoxyribonucleic acid (DNA) in chromosome of cell's nuclei.
- The **most radiation-sensitive biomolecule** in living tissue is **DNA**.
- Damage to DNA that leads to most of observed macroscopic biological effects.

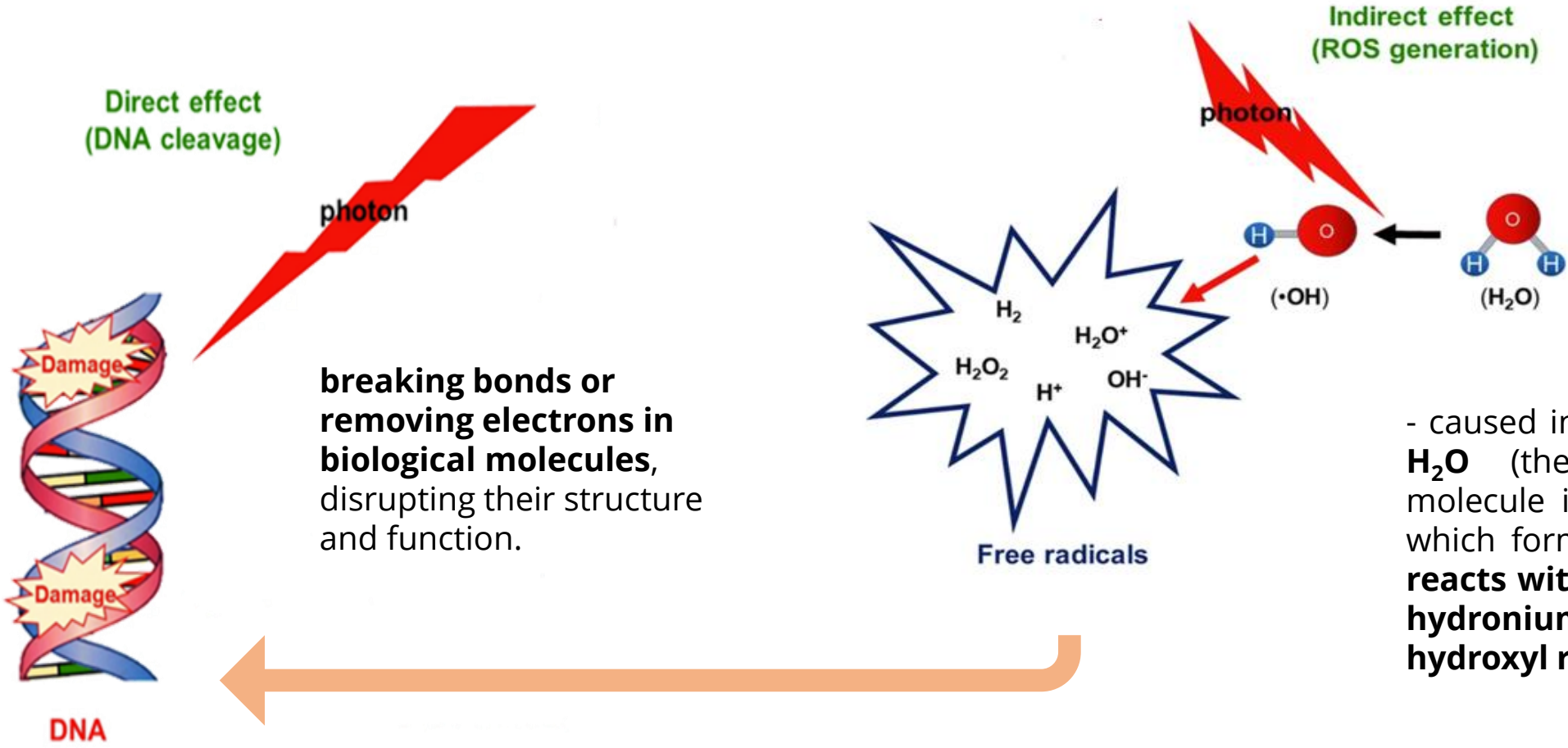
https://chem.libretexts.org/Courses/Harper_College/CHM_110%3A_Fundamentals_of_Chemistry/02%3A_Radiation-_Pros_and_Cons/2.04%3A_Biological_Effects_of_Radiation

How does ionizing radiation cause damage to DNA?



https://steemit.com/science/@biolegria/ionizing-radiation-and-the-efficiency-of-the-dna-repair-mechanism

Direct effect and Indirect effect

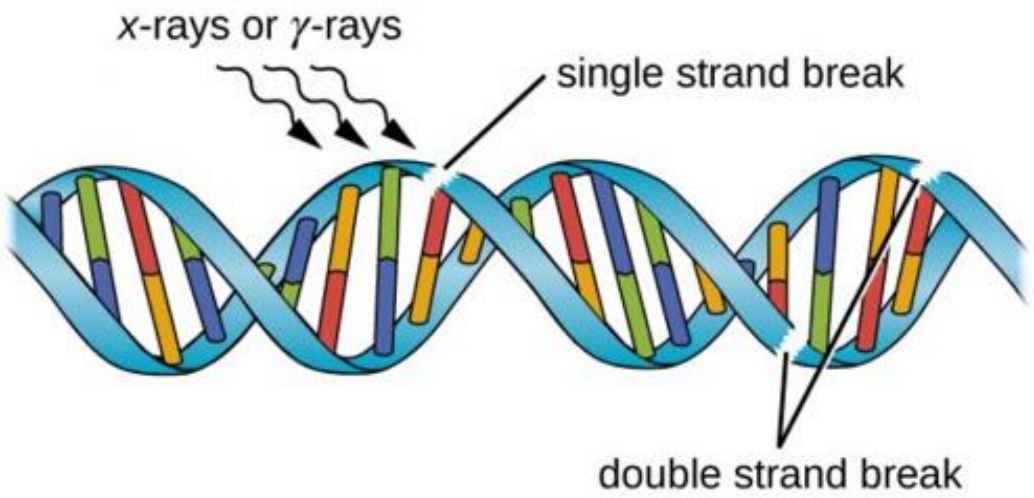


breaking bonds or removing electrons in biological molecules, disrupting their structure and function.

- caused indirectly by **ionizing H_2O** (the most abundant molecule in living organisms), which forms a **H_2O^+ ion that reacts with water, forming a hydronium ion and a hydroxyl radical**.

https://www.sciencedirect.com/science/article/pii/S0048969721014996

DNA lesions



Ionizing radiation such as that created by radioactive decay or in cosmic rays causes breaks in DNA strands.

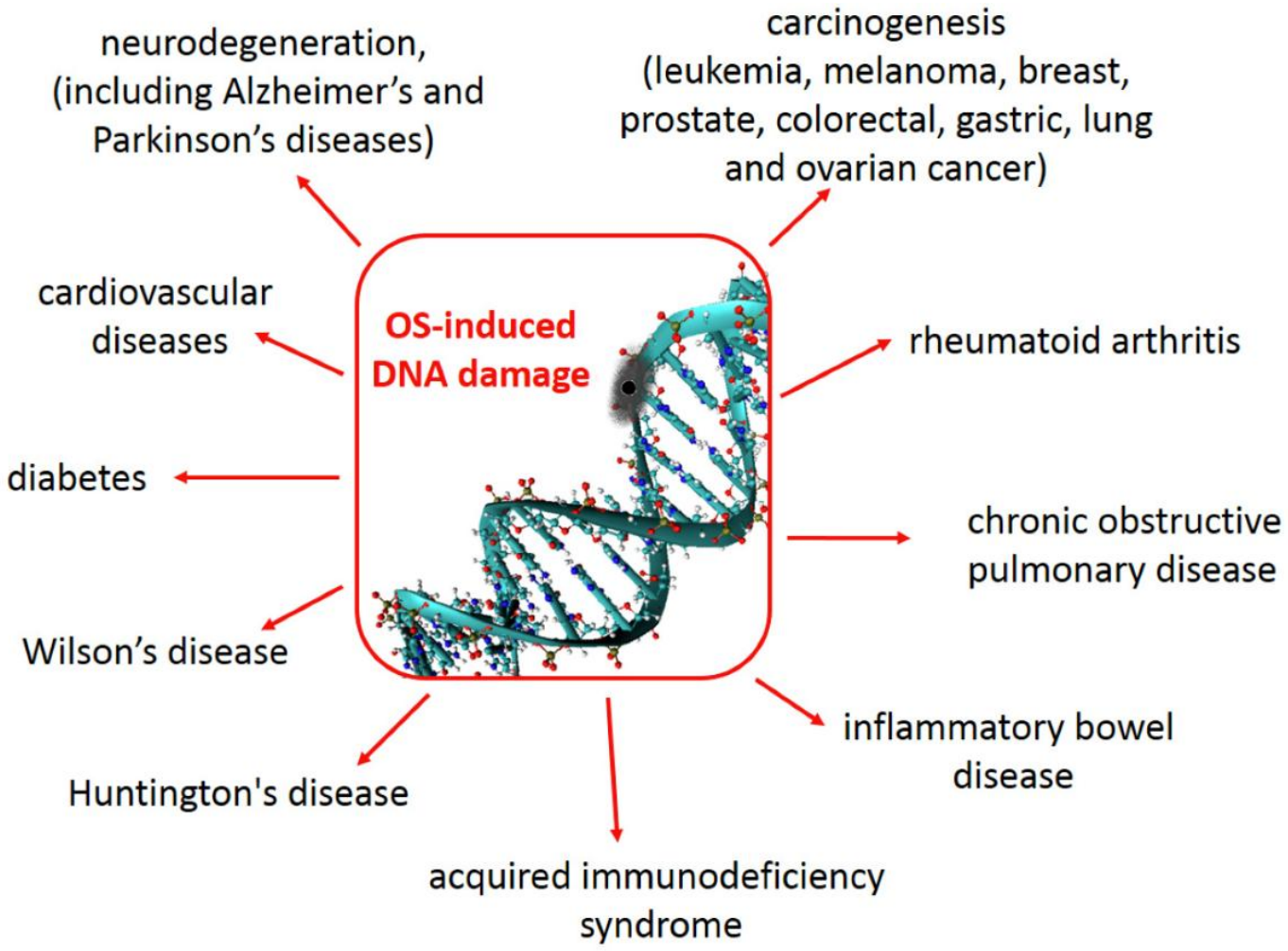
These premutagenic lesions alter the structure and possibly the base-pairing.

Up to 50–100 such reactions per second might occur in a skin cell during exposure to sunlight but are usually corrected within seconds by photolyase reactivation or nucleotide excision repair.

Uncorrected lesions can inhibit polymerases, cause misreading during transcription or replication, or lead to arrest of replication.

https://wou.edu/chemistry/courses/online-chemistry-textbooks/ch450-and-ch451-biochemistry-defining-life-at-the-molecular-level/chapter-12-dna-damage-repair-and-mutations/

Oxidative stress and DNA damage



Galano, A., Tan, D-X., and Reiter, R.J. (2018) Molecules 23(3)530

Exposure modes and effects

Physical effects of radiation depend on the **amount of exposure**, not on whether a person is ever exposed to radiation.

High-dose exposure
Exposed to a large amount of radiation

Low-dose exposure
Exposed to a small amount of radiation

Short-term effects (ACUTE)

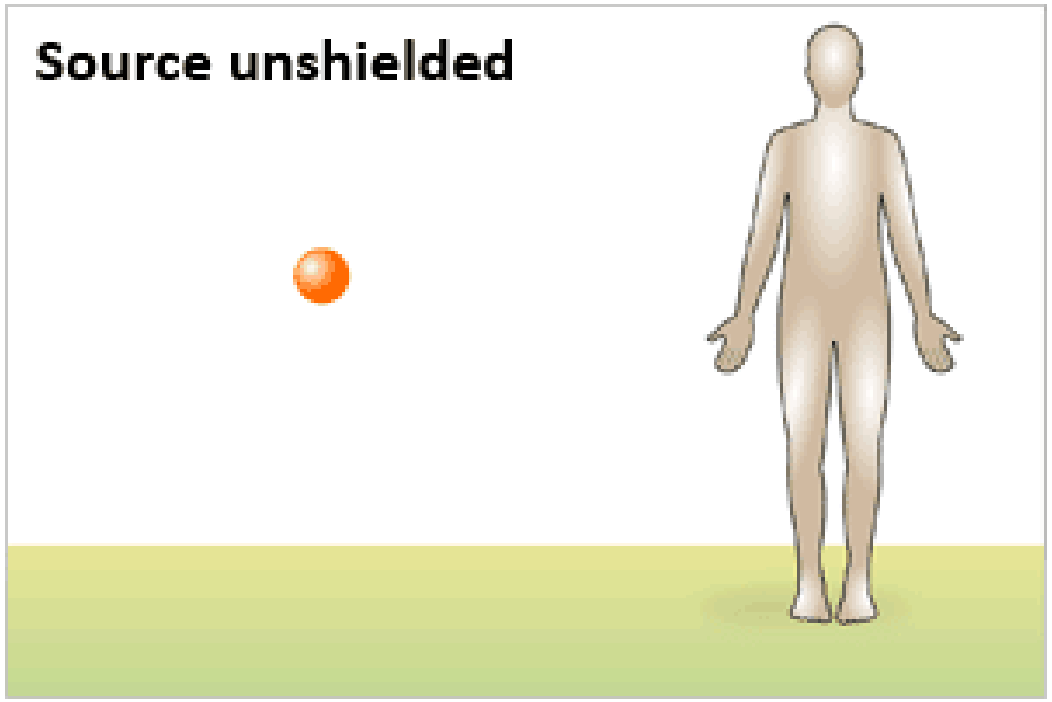
Acute Radiation Sickness (ARS)
(rapid cell death over short period of time)

Long-term effects (CHRONIC)

Delayed somatic effects
(cancer, mutations, birth defects)

https://www.env.go.jp/en/chemi/rhm/basic-info/1st/03-01-01.html

Radiation exposure

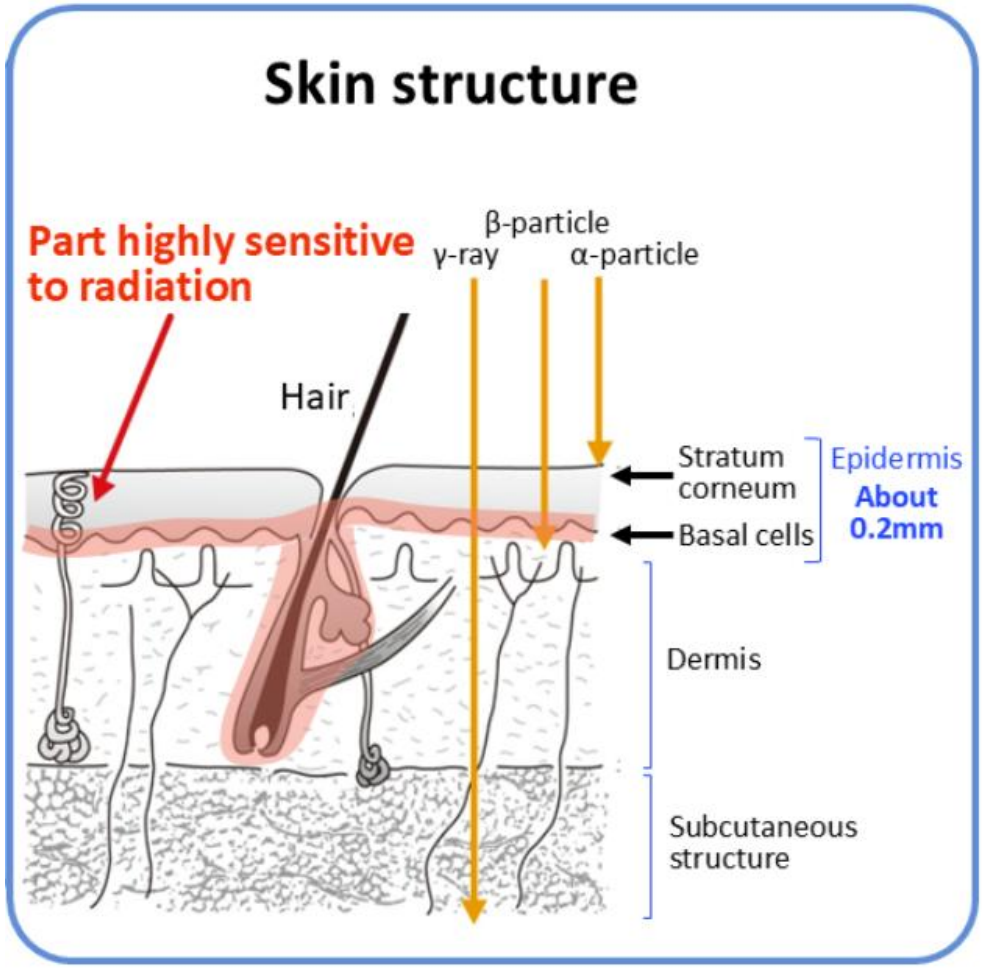


Radiation exposure occurs when all or part of the body absorbs **penetrating** ionizing radiation from an external radiation source.

Radiation exposure also occurs after internal contamination, i.e., when a radionuclide is ingested, inhaled or absorbed into the blood stream.

https://remm.hhs.gov/exposureimage.htm

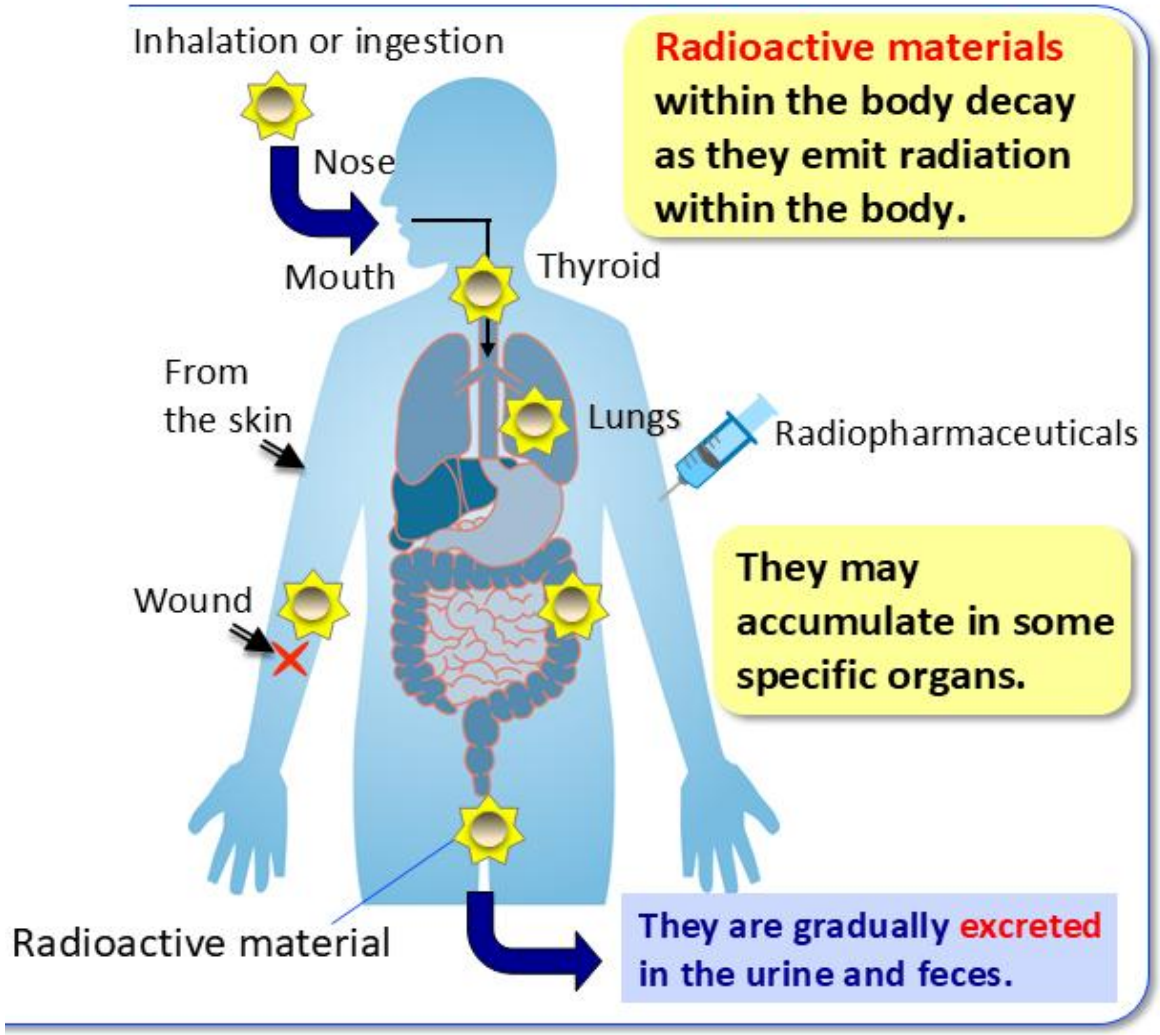
External exposure and skin



- **α (alpha)-particles** having **weak penetrating power**, stop at the epidermis and therefore do not produce any effects
- **β (beta)-particles adheres to the surface of the body for an extended period of time** and affect the skin's basal cells and hair-root cells that have high sensitivity to radiation

https://www.env.go.jp/en/chemi/rhm/basic-info/1st/02-01-03.html

Internal exposure



Radioactive materials incorporated into the body emit radiation within the body.

Accumulation in some specific organs may occur depending on the types of radioactive materials.

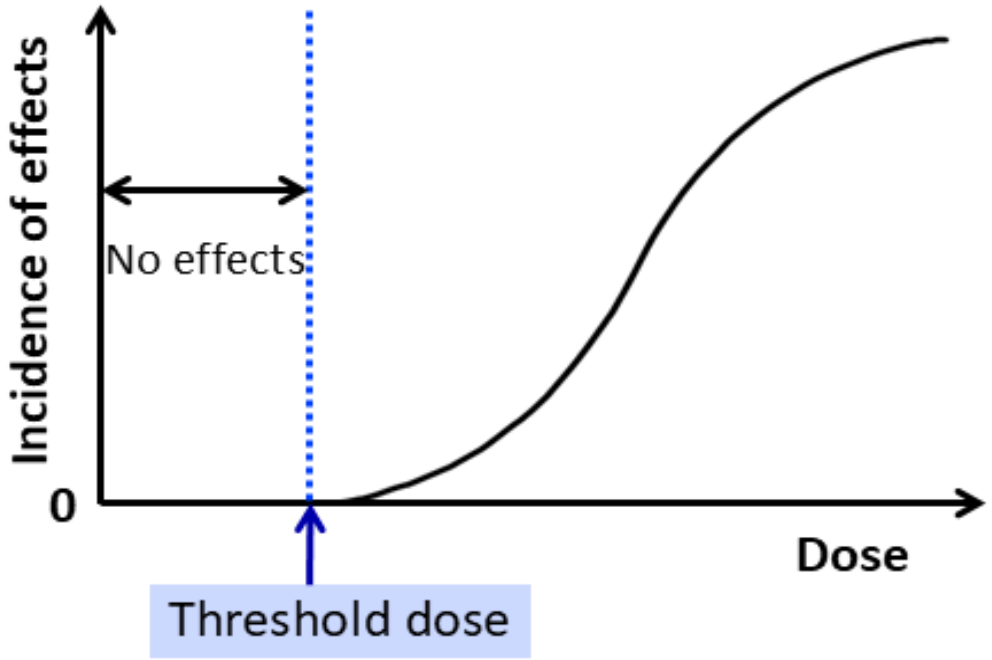
Strontium, having similar properties to calcium, tends to **accumulate in calcium-rich parts** such as **bones** once it enters the body; **cesium**, because of its properties **similar to potassium**, tends to be **distributed throughout the body.**

Iodine, being a constituent element of thyroid hormones, tends to **accumulate in the thyroid**, whether it is radioactive iodine or stable iodine.

https://www.env.go.jp/en/chemi/rhm/basic-info/1st/02-01-04.html

Deterministic effects

Deterministic effects are those which normally **have a threshold**: above this, the severity of the effect increases with the dose.



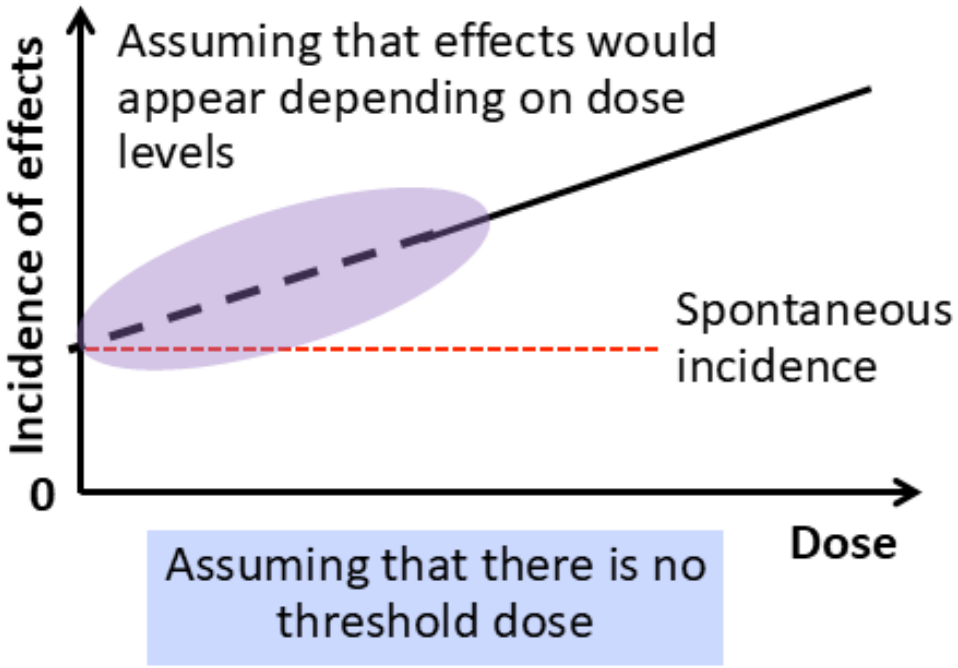
Threshold dose – a dose level, at which specific symptoms appear in 1% of the population exposed to the same dose of radiation

(2007 Recommendations of the International Commission on Radiological Protection (ICRP))

https://www.env.go.jp/en/chemi/rhm/basic-info/1st/02-01-04.html

Stochastic effects

Stochastic effects are those arising from **chance**: **the greater the dose, the more likely the effect**.

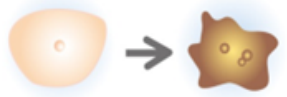


Effects of radiation exposure under certain doses are not clear because effects of other cancer –promoting factors such as smoking and drinking habits are too large.

The ICRP specifies the standards for radiological protection for such low-dose exposures, assuming that they may have some effects as well.

https://www.env.go.jp/en/chemi/rhm/basic-info/1st/02-01-04.html

Classification of radiation effects

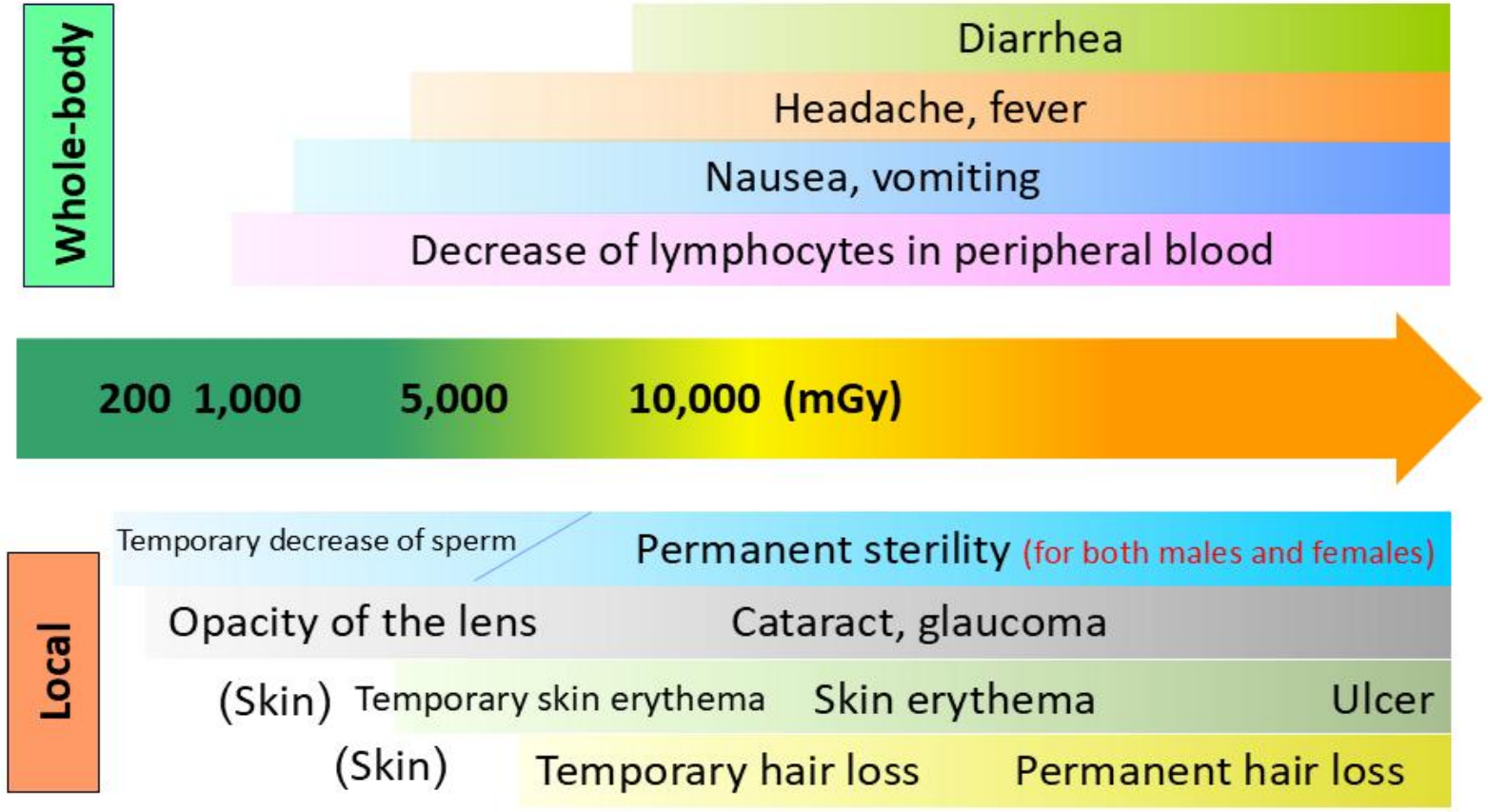
Categories of effects		Incubation period	e.g.	Mechanism of how radiation effects appear
Physical effects		Within several weeks = Acute effects (early effects)	Acute radiation syndromes*1 Acute skin disease	Deterministic effects (tissue reactions) caused by cell deaths or cell degeneration*2 
Physical effects		After the lapse of several months = Late effects	Abnormal fetal development (malformation)	
Physical effects		After the lapse of several months = Late effects	Opacity of the lens	
Physical effects		After the lapse of several months = Late effects	Cancer and leukemia	Stochastic effects due to mutation
Heritable effects		After the lapse of several months = Late effects	Hereditary disorders	

*1: Major symptoms are vomiting within several hours after exposure, diarrhea continuing for several days to several weeks, decrease of the number of blood cells, bleeding, hair loss, transient male sterility, etc.

*2: Deterministic effects do not appear unless having been exposed to radiation exceeding a certain dose level.

https://www.env.go.jp/en/chemi/rhm/basic-info/1st/02-01-04.html

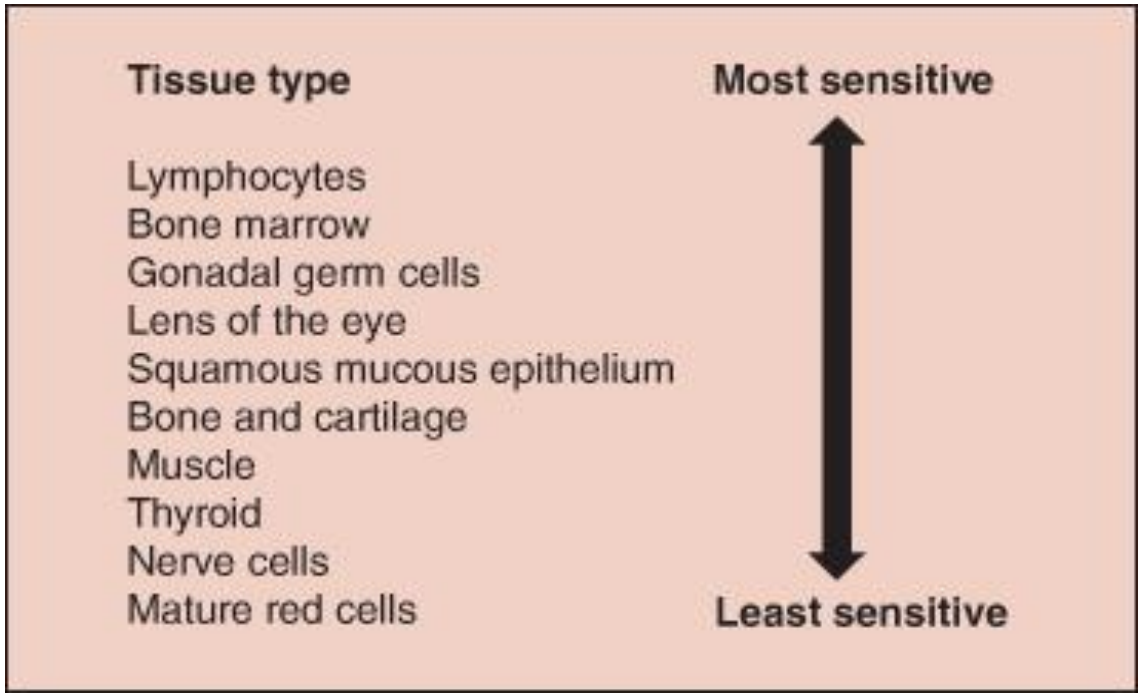
Whole body exposure and Local exposure



- Radiation exposure at levels exceeding 100 mGy at one time may cause effects on the human body due to cell deaths.
- Organs highly sensitive to radiation are more likely to be affected with a small amount of radiation.

Prepared based on the report of the Health Management Study Committee of the Nuclear Safety Commission (2000), etc.
https://www.env.go.jp/en/chemi/rhm/basic-info/1st/03-03-01.html

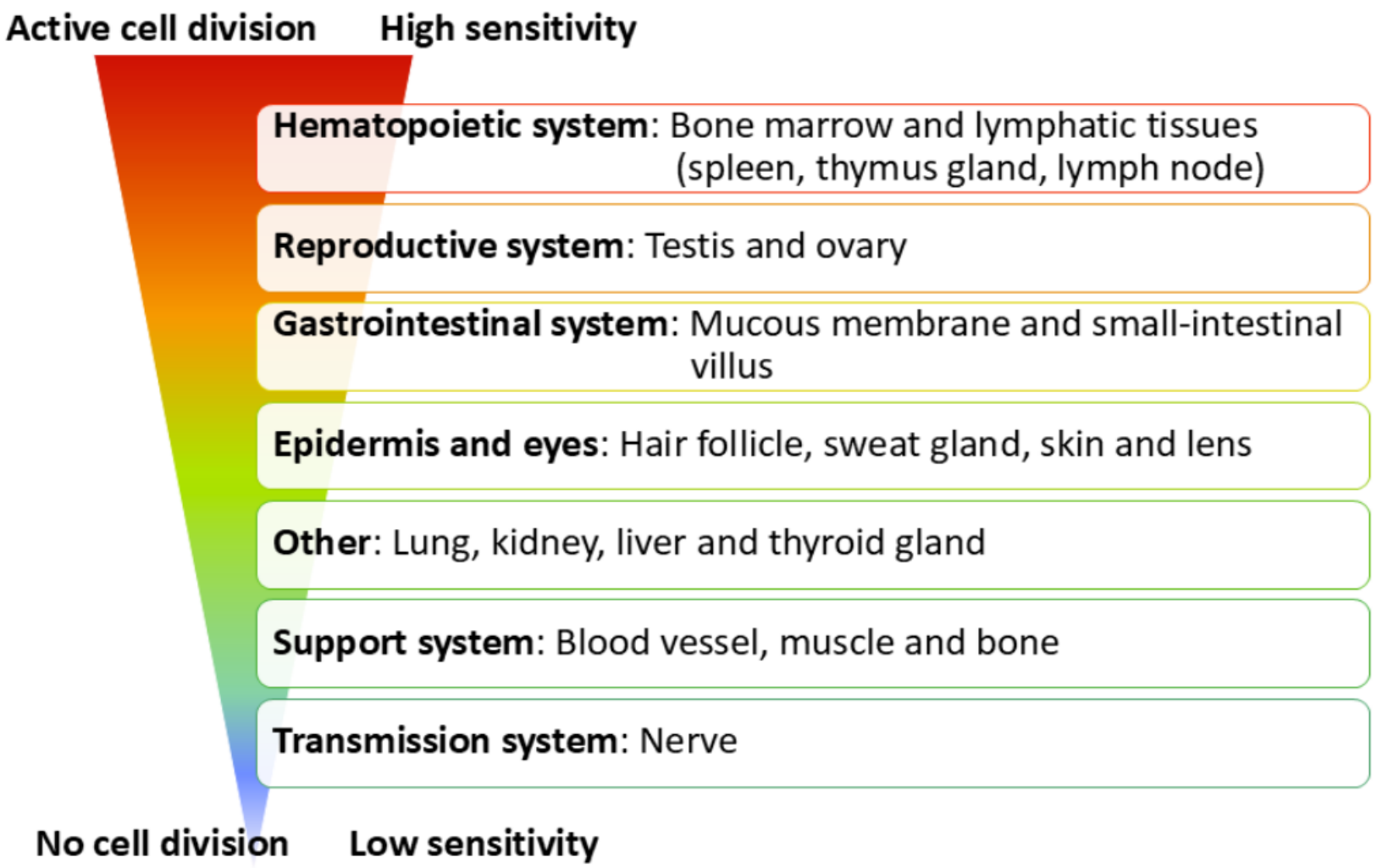
Cell and Tissue Radiosensitivity to Radiation



Not all living cells are equally sensitive to radiation.

Generally, tissues that have a **high rate of cell division or differentiation** are the **most radiosensitive.**

Cell and Tissue Radiosensitivity to Radiation



https://www.env.go.jp/en/chemi/rhm/basic-info/1st/03-02-06.html

Individual Sensitivity

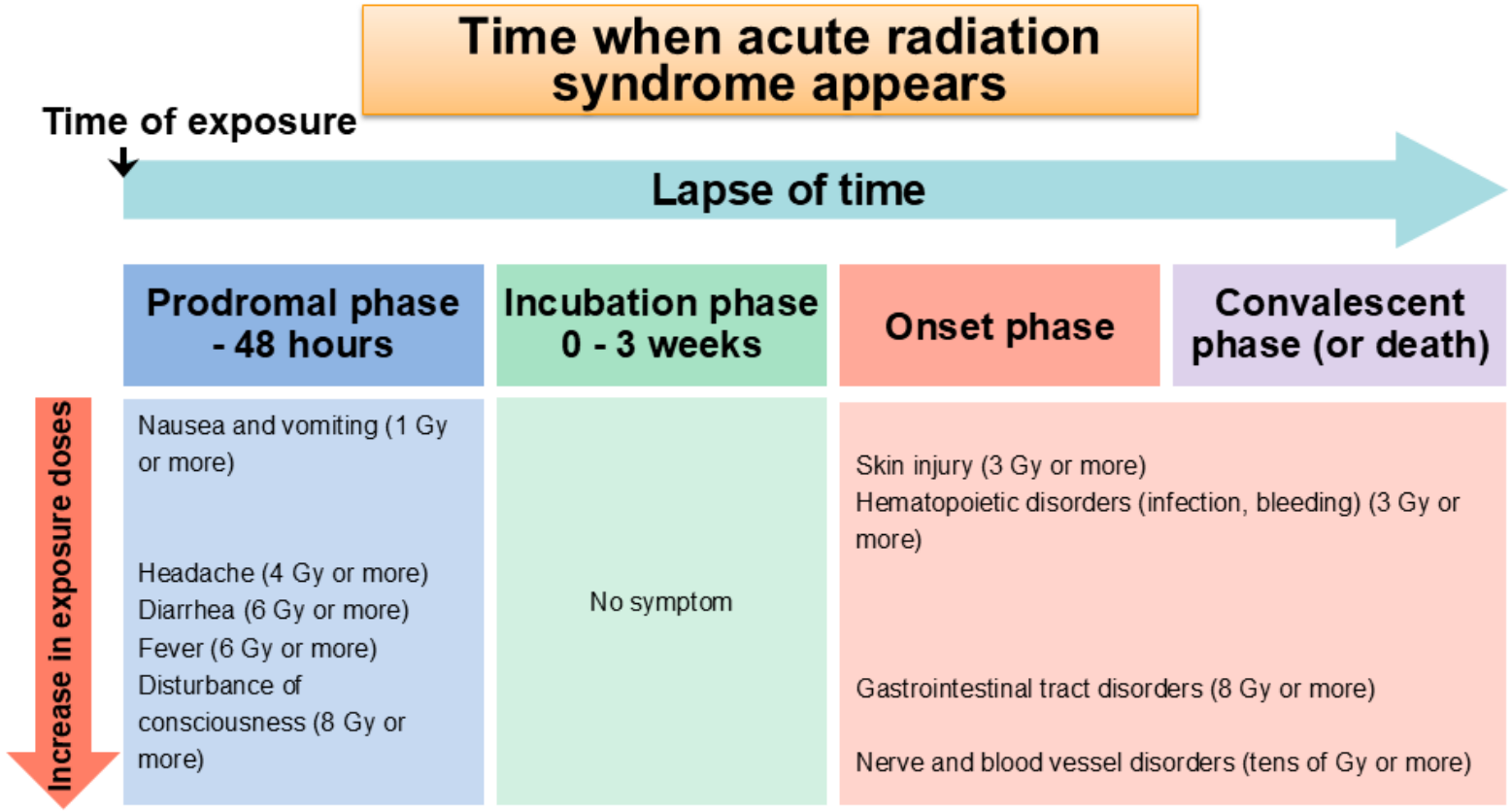
Some people are **more vulnerable** to the effects of radiation, including:

- Developing fetuses (the most vulnerable)
- Infants
- Children
- The elderly
- Pregnant women
- People with compromised immune systems

https://www.cdc.gov/radiation-health/about/health-effects-of-radiation.html

Acute Radiation Syndrome (ARS)

Acute Radiation Syndrome (ARS) is an **acute illness** caused by **radiation exposure** of the entire body by a high dose of penetrating radiation in a **very short period of time.**



Acute radiation syndromes observed in the case of a single whole-body exposure to radiation exceeding 1 Gy (1000 mGy).

https://www.env.go.jp/en/chemi/rhm/basic-info/1st/03-02-06.html

Acute Radiation Syndrome (ARS)

- **Hematopoietic**
  - Stem cell creation/division system breaks down, blood cell losses

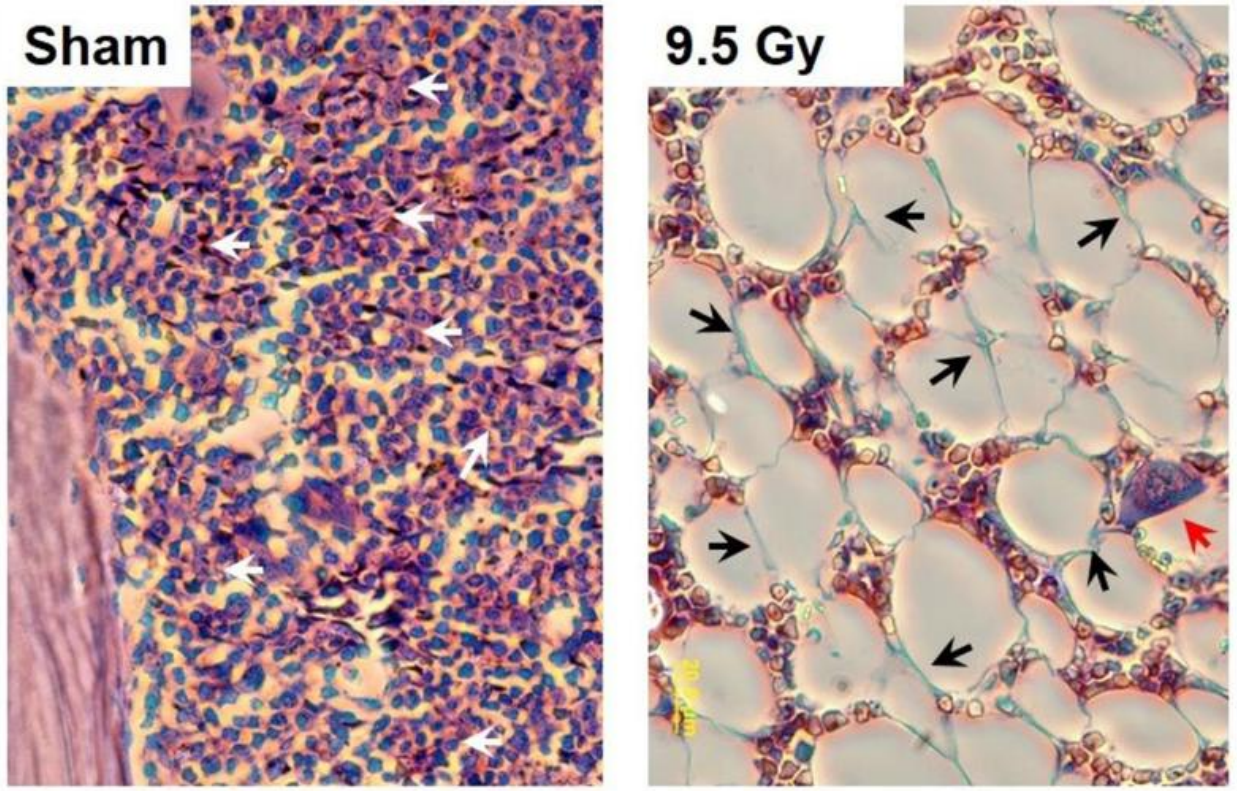
- **Gastrointestinal**
  - Stem cells in villi fail to reproduce, stopping nutritional uptake

- **Neurovascular (cerebrovascular)**
  - Straight up blasting of endothelial cells, edema (cell fluid leakage) from blood vessels, associated drop in intracranial pressure

Garau, M. M. et al., Reports of Practical Oncology and Radiotherapy, 16 no. 4 (2011): 123-130

Acute Radiation – Hematopoietic

Hematopoietic cells



Courtesy of MDPI AG (Basel, Switzerland). License CC BY.

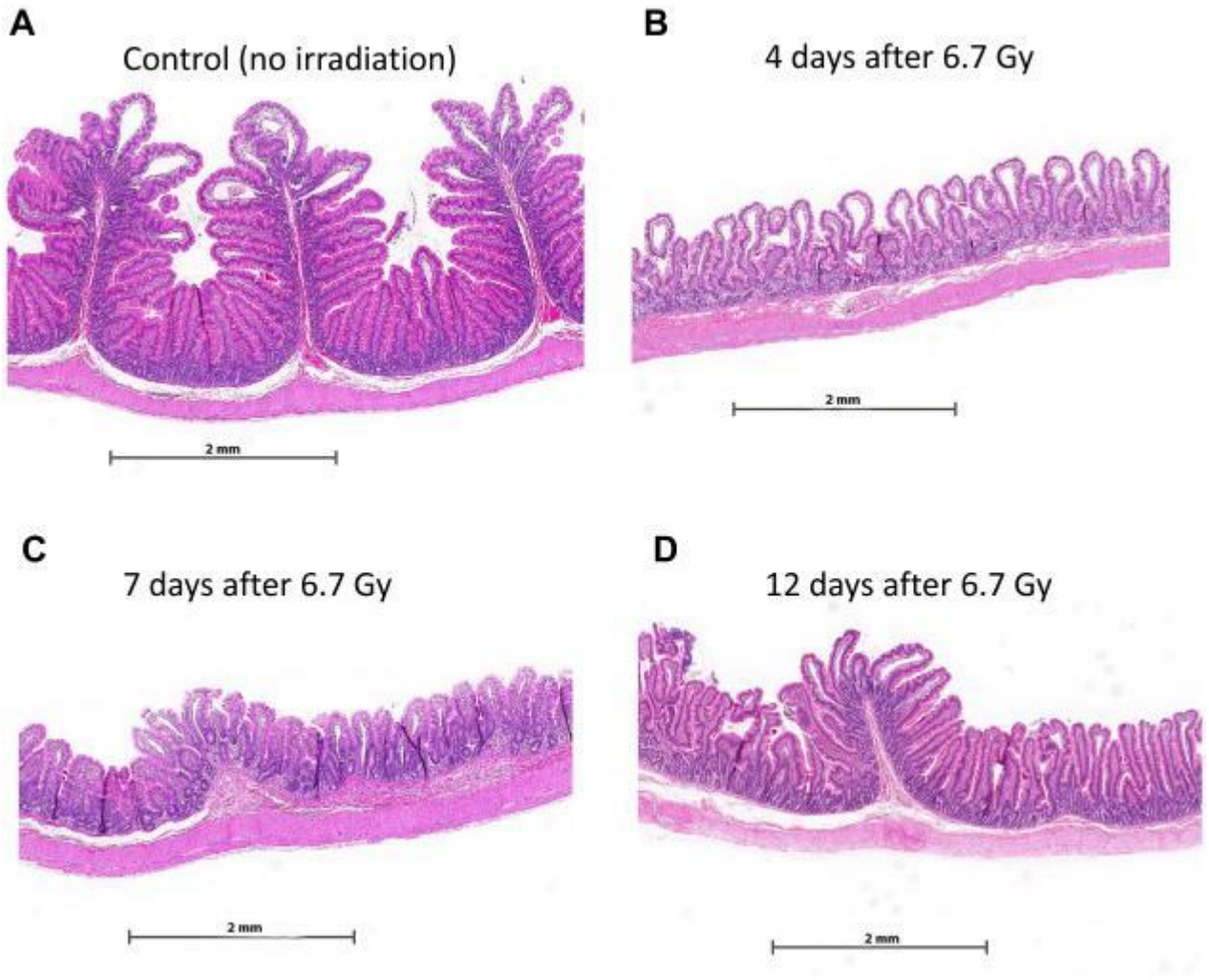
Mouse bone marrow tissue after 9.5Gy radiation exposure

Black arrow- Presence of the open reticular meshwork of the stromal cells

Red arrow- large macrophage containing phagocytized hematopoietic cells

N.I. Gorbunov, P. Sharma. Protracted Oxidative Alterations in the Mechanism of Hematopoietic Acute Radiation Syndrome. Antioxidants, 4(1):134 (2015).

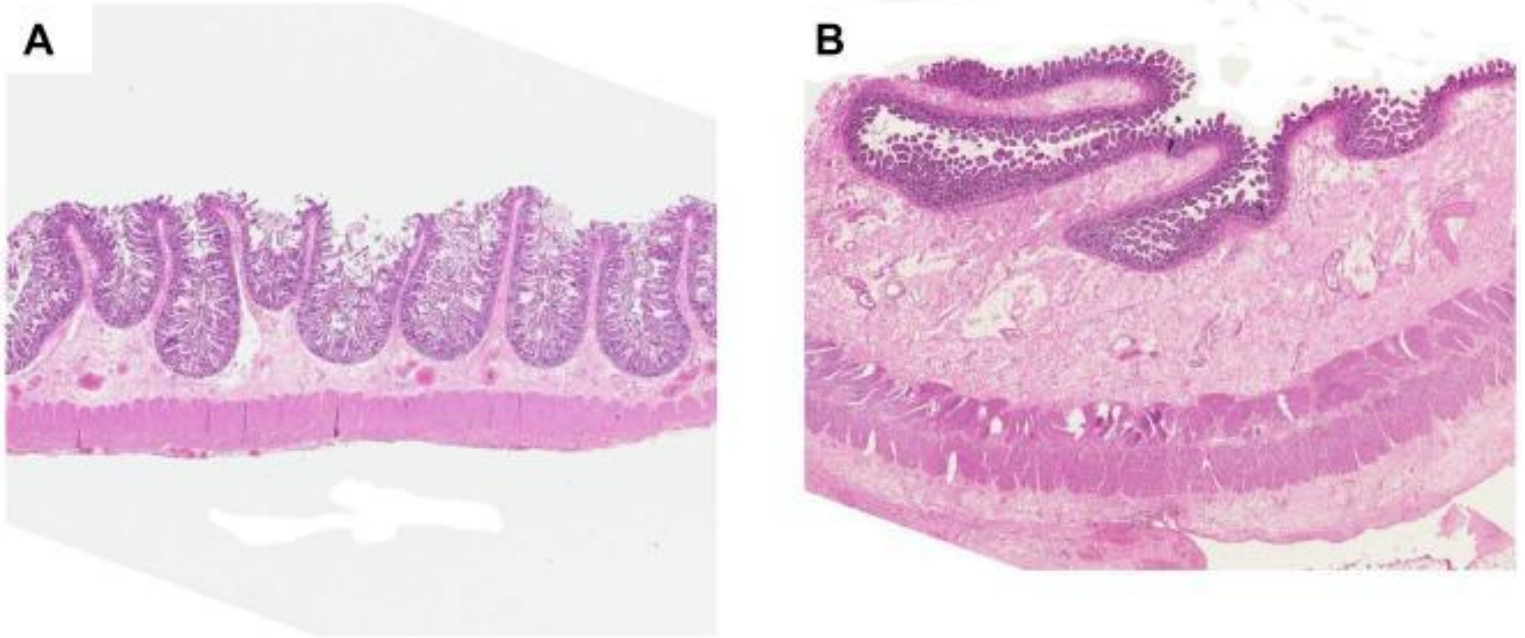
Acute Radiation – Gastrointestinal



Proximal jejunum from A.) unirradiated Rhesus macaque and B-D.) Rhesus macaque, 4, 7 and 12 days after exposure to single-dose irradiation (6.7 Gy).

Hauer-Jensen, M. et al., Radiation enteropathy – pathogenesis, treatment and prevention. Nat. Rev. Gastroenterol. Hepatol., 11:470 (2014).

Acute Radiation – Gastrointestinal

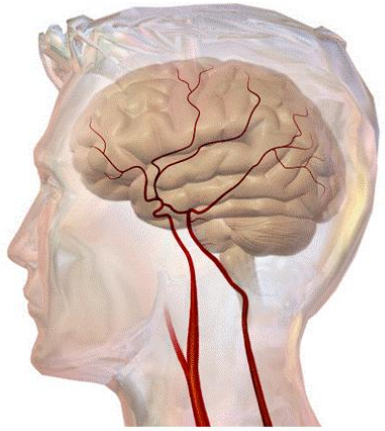


A.) Normal intestine (original magnification 0.5X) and B.) resected small intestine from a woman with severe delayed radiation enteropathy.

Note atrophic mucosa and severe fibrosis in submucosa and subserosa (original magnification 0.5X, same as panel A).

Hauer-Jensen, M. et al., Radiation enteropathy – pathogenesis, treatment and prevention. Nat. Rev. Gastroenterol. Hepatol., 11:470 (2014).

Acute Radiation – Cerebrovascular



Cerebrovascular syndrome occurs at doses higher than 20 Gy and is characterized by a **very short prodromal and latent phases.**

Symptoms:

- Headache
- abnormal cognition
- neurological deficits
- somnolent state
- loss of consciousness and eventual death

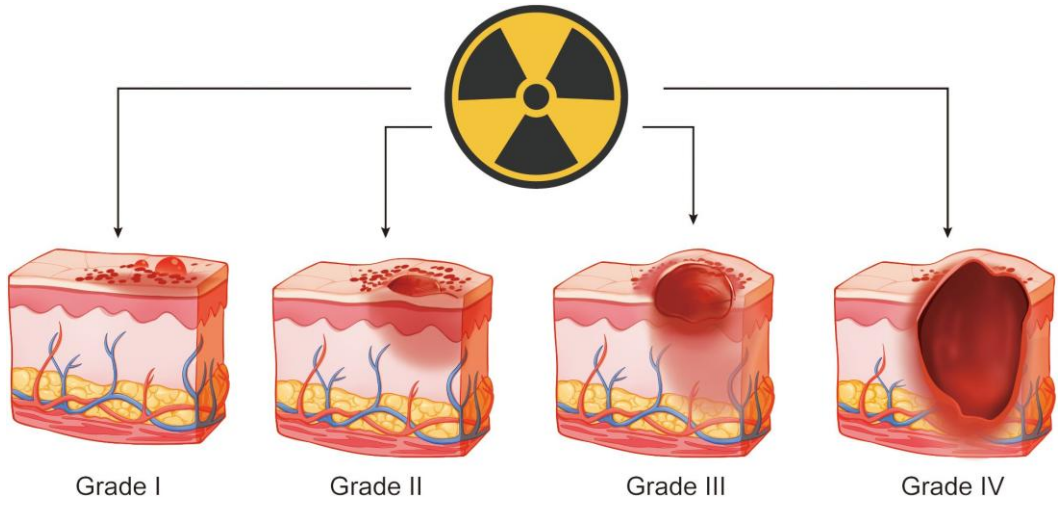
Proposed mechanism: The damaging effects of radiation on endothelial cells and vascular leak with edema and consequently an increase in intracranial pressure.

https://howradiologyworks.com/acute-radiation-syndromes/

Cutaneous Radiation Injury (CRI)

You may experience a Cutaneous Radiation Injury (CRI) when you are exposed to certain radioactive materials that give off the following:

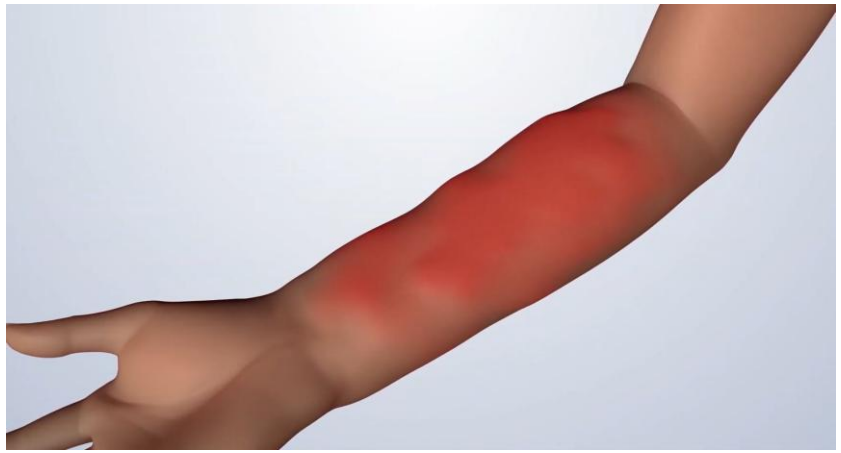
- Beta particles
- Penetrating gamma radiation
- Low-energy X-rays



If you experience Acute Radiation Syndrome (ARS) you may develop CRI. Not everyone who develops CRI will have ARS.

https://www.cdc.gov/radiation-emergencies/signs-symptoms/cutaneous-radiation-injury.html

Cutaneous Radiation Injury (CRI)



Symptoms of CRI can appear from a few hours to several days after exposure.

The early signs and symptoms of CRI include the following:

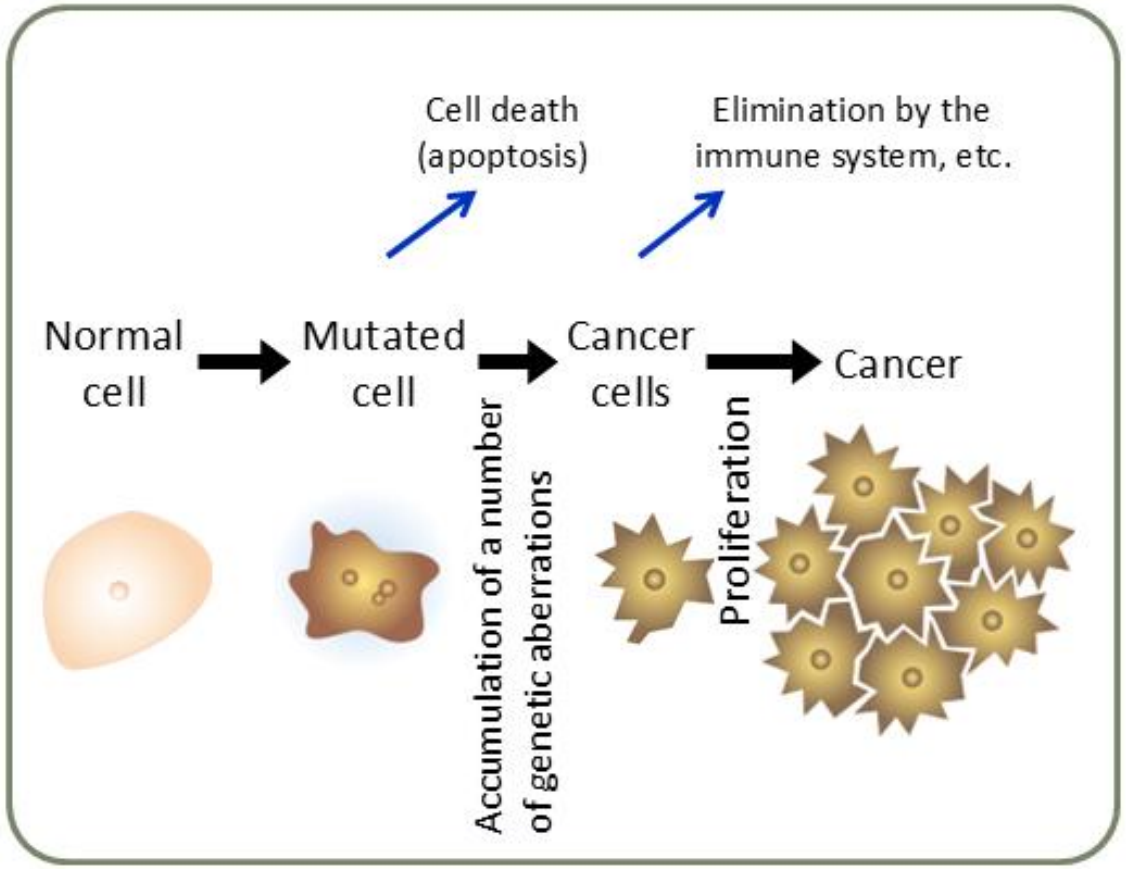
- Itchiness
- Tingling
- Skin redness (erythema)
- Swelling caused by a buildup of fluid (edema)

Over time, other symptoms may develop depending on the site of the injury and the level of radiation exposure.

https://www.cdc.gov/radiation-emergencies/signs-symptoms/cutaneous-radiation-injury.html

Carcinogenesis

Carcinogenesis refers to the phenomena **transforming a normal cell into a cancer cell**, with the development of a cancer the culmination of a series of events stemming from the uncontrolled proliferation of malignant cells under the cumulative effect of multiple genetic changes.



https://www.env.go.jp/en/chemi/rhm/basic-info/1st/03-07-01.html

Carcinogens

- a substance, organism or agent capable of causing cancer

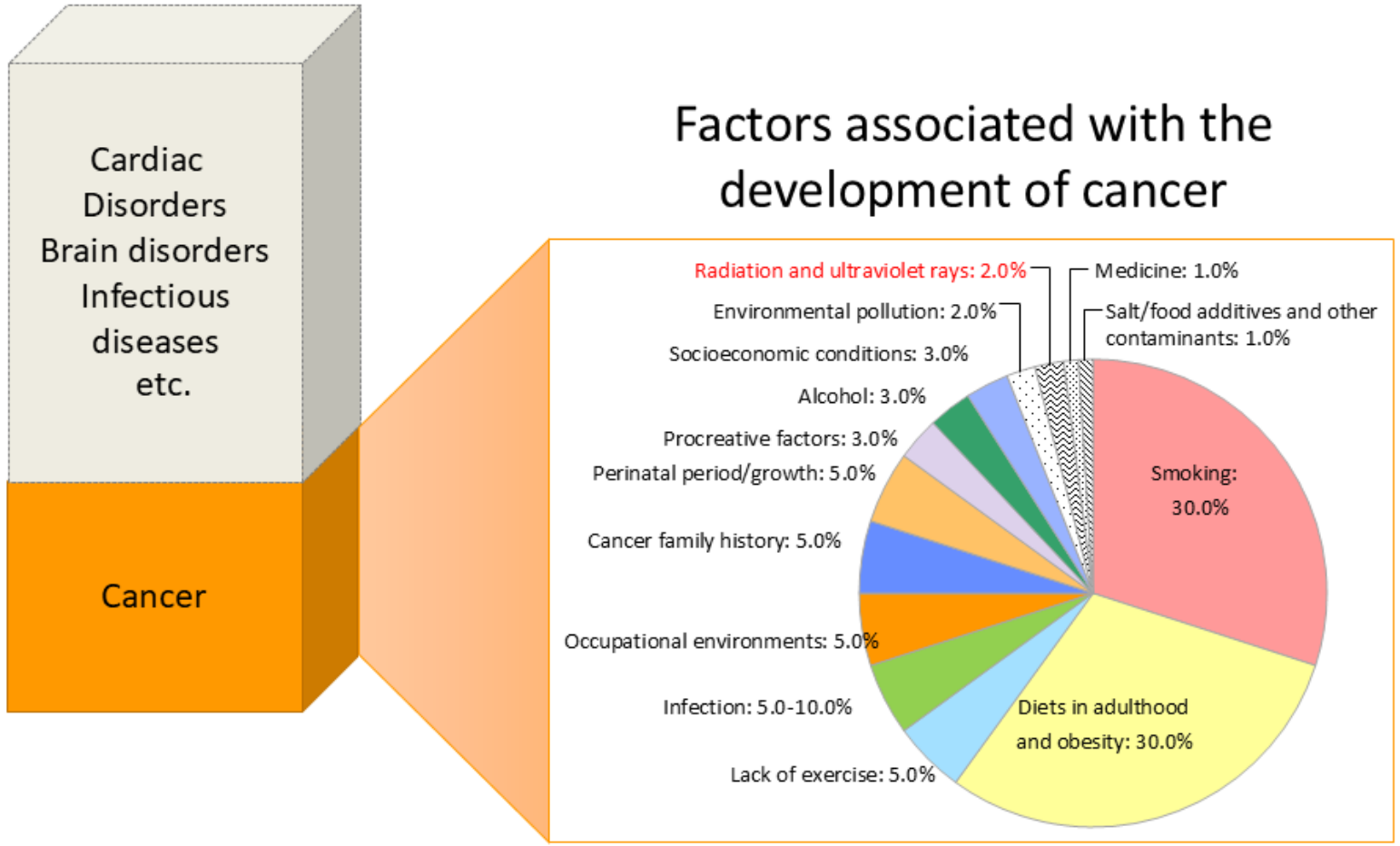
Physical Carcinogens
- Ultraviolet and ionizing radiation

Chemical Carcinogens
- Polycyclic hydrocarbons
- Asbestos
- Components of tobacco smoke
- Alcohol
- Aflatoxin (a grain contaminant)
- Arsenic (a drinking water contaminant)

Biological Carcinogens
- Viral infections such as hepatitis B and human papillomavirus (HPV)
- Bacterial infections, such as *Helicobacter pylori*
- Parasitic infections, such as *Schistosoma haematobium*

National Human Genome Institute, Glossary, Division of Genome Sciences (https://www.genome.gov/genetics-glossary/Carcinogen
Koya AI, Ibrahim SA. Carcinogenesis. 2024 Oct 2. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 38917272.

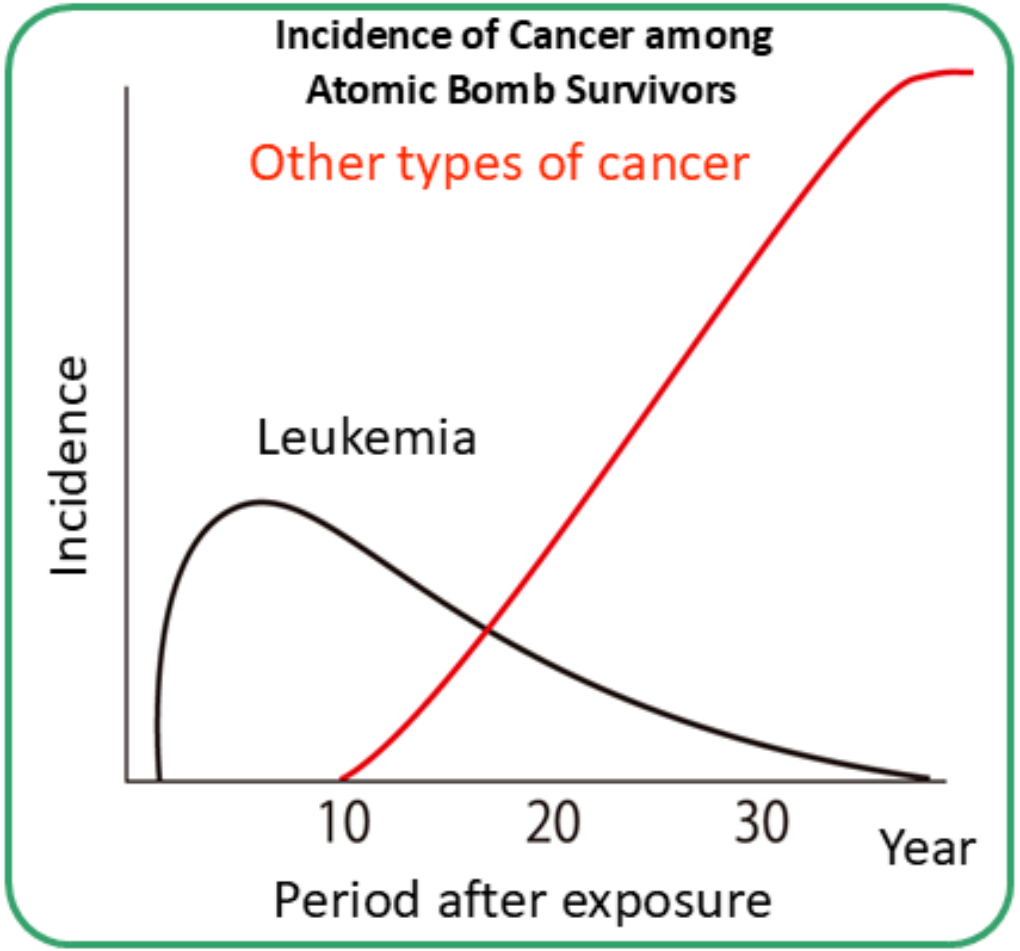
Factors Associated with Carcinogenesis



Source: Prepared based on Cancer Causes Control 1996.7.S55-S58

https://www.env.go.jp/en/chemi/rhm/basic-info/1st/03-04-04.html

Incidence of Cancer among Atomic Bomb Survivors



Among atomic bomb survivors, leukemia increased in around two years, but the incidence decreased thereafter. On the other hand, cases of solid cancer started to increase after an incubation period of around 10 years.

https://www.env.go.jp/en/chemi/rhm/basic-info/1st/03-07-01.html

Dose limits

In radiation protection, **dose limits** are set to **limit stochastic effects** to an acceptable level, and to **prevent deterministic effects** completely.

Table of dose limits for occupationally exposed workers and for the public.

Type of limit	Occupational	Public
Stochastic limits **Effective dose:**	20 mSv per year, averaged over defined periods of 5 years	1 mSv in a year
Deterministic limits **Annual equivalent dose in:**		
Lens of the eye	150 mSv	15 mSv
Skin	500 mSv	50 mSv
Hands and feet	500 mSv	-

Source of data: ICRP, 2007. The 2007 Recommendations of the International Commission on Radiological Protection. ICRP Publication 103. Ann. ICRP 37 (2-4).

Acute Gamma Radiation Syndrome

Turner, J. E. *Atoms, Radiation, and Radiation Protection*. Wiley-VCH, 2007. p. 421

Dose (Gy)	Symptoms	Remarks
0–0.25	None	No clinically significant effects.
0.25–1	Mostly none. A few persons may exhibit mild prodromal symptoms, such as nausea and anorexia.	Bone marrow damaged; decrease in red and white blood-cell counts and platelet count. Lymph nodes and spleen injured; lymphocyte count decreases.
1–3	Mild to severe nausea, malaise, anorexia, infection.	Hematologic damage more severe. Recovery probable, though not assured.
3–6	Severe effects as above, plus hemorrhaging, infection, diarrhea, epilation, temporary sterility.	Fatalities will occur in the range 3.5 Gy without treatment.
More than 6	Above symptoms plus impairment of central nervous system; incapacitation at doses above ~10 Gy.	Death expected.

Typical LD50 for acute radiation poisoning

Research studies

International Journal of Nanomedicine

Dovepress

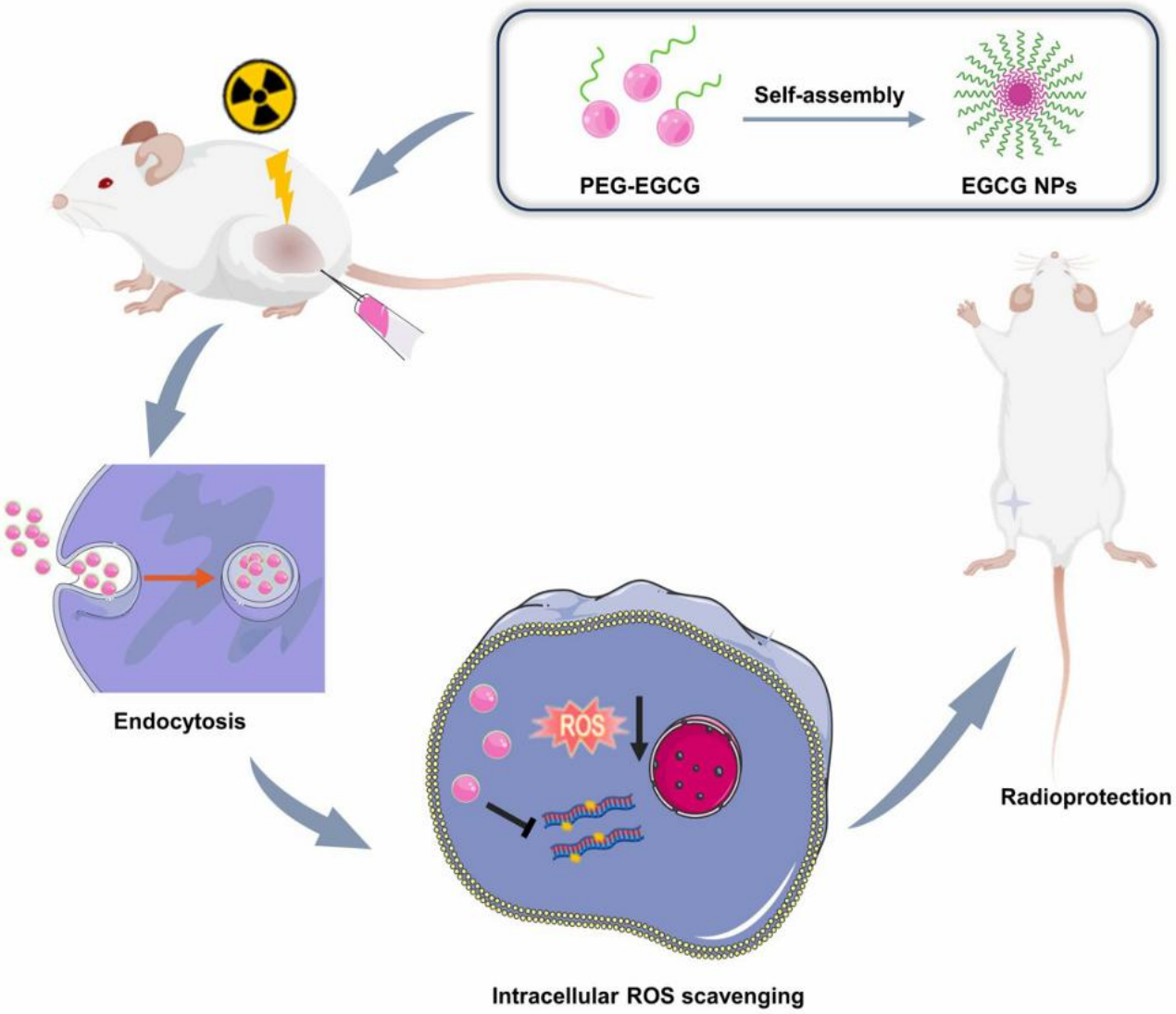
Open Access Full Text Article

ORIGINAL RESEARCH

Self-Assembled EGCG Nanoparticles with Enhanced Intracellular ROS Scavenging for Skin Radioprotection

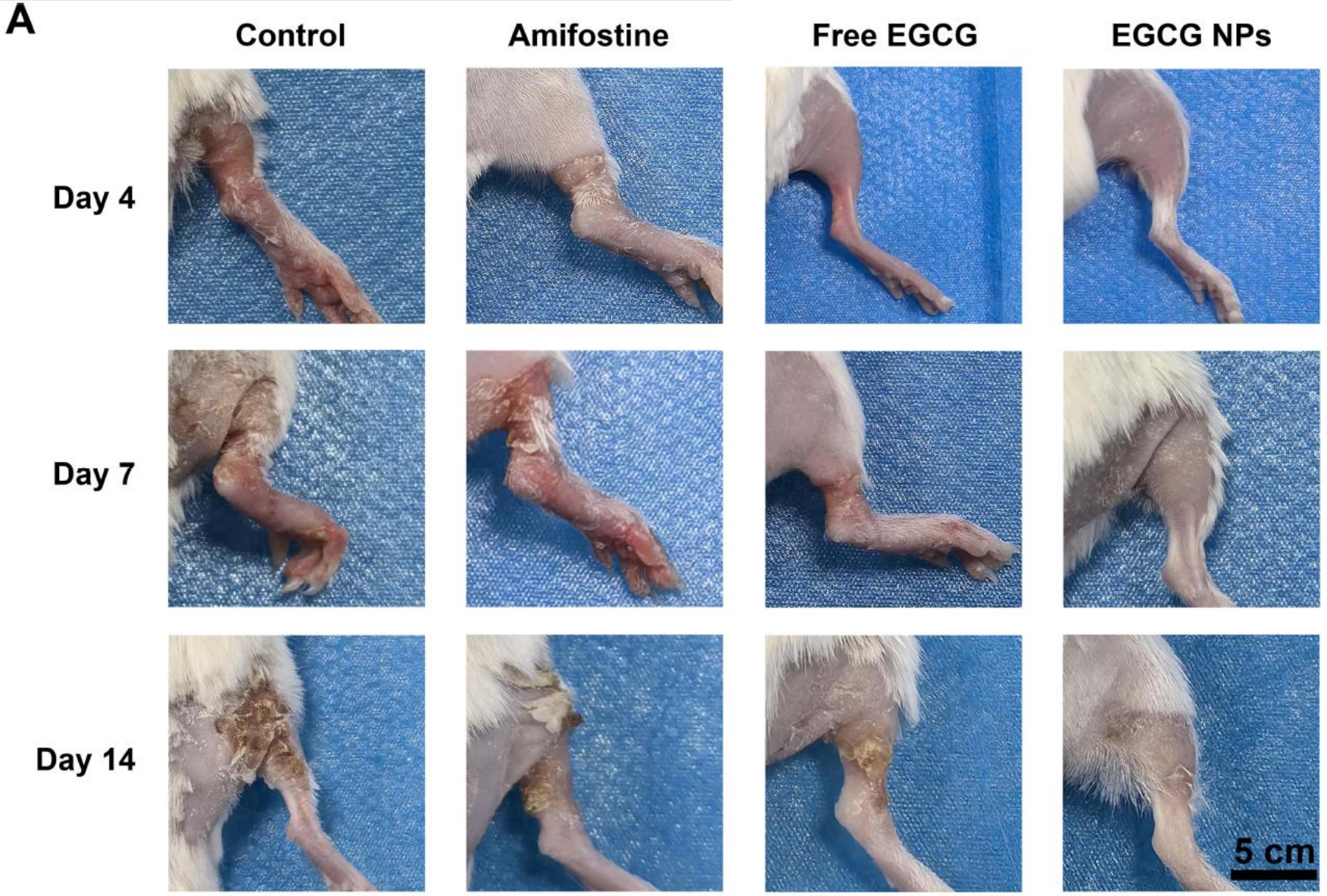
Xiaowen Han[1], Ruiling Xu[1], Yang Xia[2], Ying Liu[3], Shan Chen[3], Mingsong Shi[1], Zhiyan Zou[1], Yuanyuan Liang[1], Tingting Chen[1], Yufeng Tang[4], Wei Tang[3], Xiaoan Li[1,5], Liangxue Zhou[2,6,7]

Research studies



EGCG (Epigallocatechin gallate) NPs exhibited markedly improved radioprotective efficacy, effectively reducing skin edema and ulceration, alleviating pathological conditions such as interstitial edema, dermal fluid accumulation and inflammatory infiltration, decreasing the duration of skin injury, and promoting wound healing.

Research studies

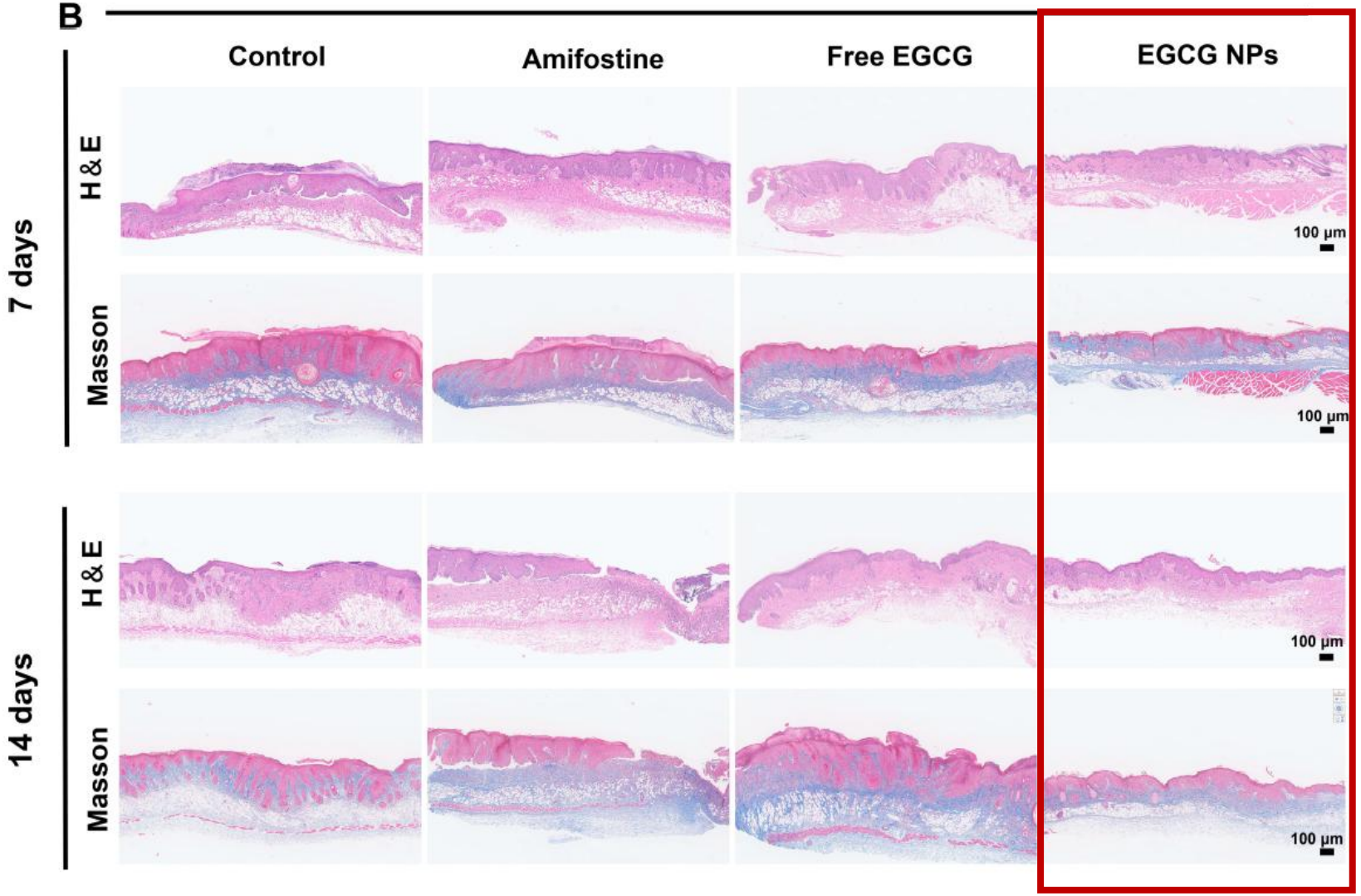


All groups exhibited obvious erythema, with the control group also presenting edema.

Control and amifostine - ulceration and desquamation
Free EGCG - dry desquamation and minor ulceration
EGCG NPs - slight desquamation without any ulceration

Control – moist desquamation and unhealed ulcers
Amifostine and Free EGCG – moderate edema and desquamation
EGCG NPs - substantial reduction in redness and swelling, with only minimal pigmentation

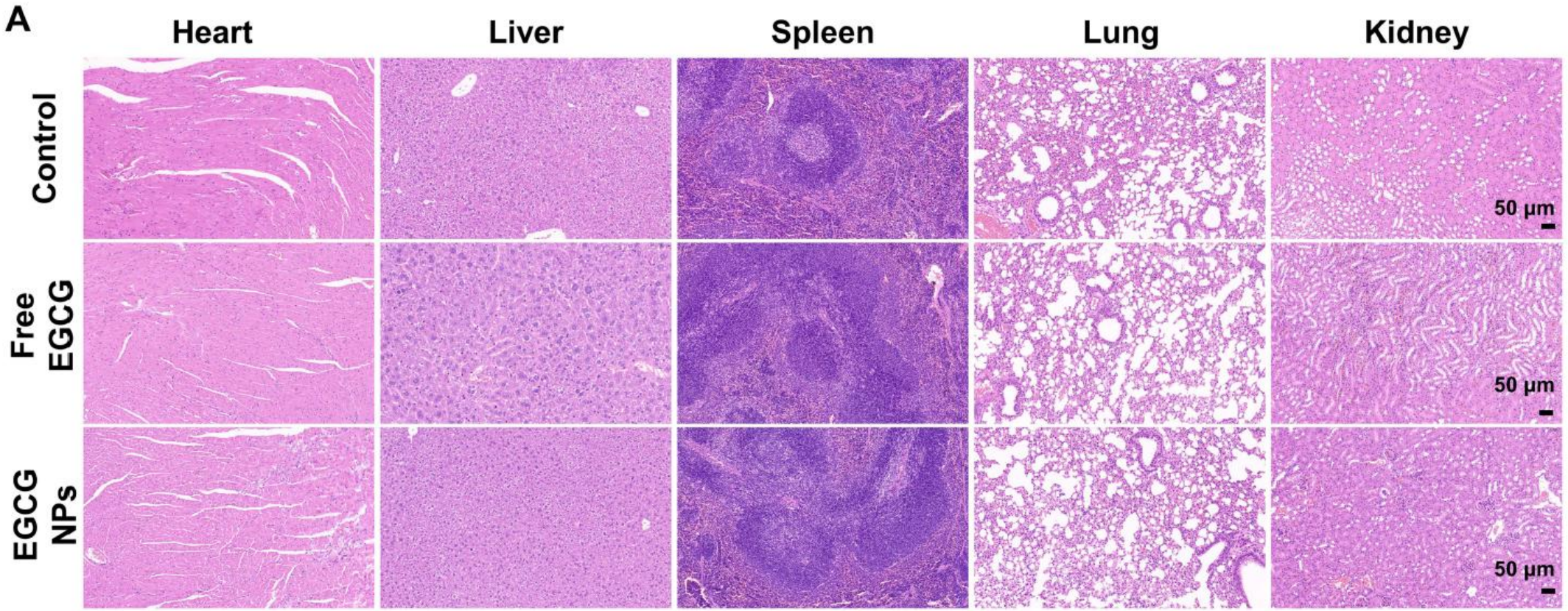
Research studies



EGCG NPs group exhibited completely intact epidermis and the lowest degree of epithelial keratosis.

EGCG NPs showed intact epidermis and comparable in thickness to uninjured tissue, with newly formed collagen showing a random orientation and accompanying hair follicle regeneration.

Research studies



EGCG NPs has no apparent toxic effects on the organ tissues of mice after administration.

THANK YOU!

For questions or concerns:

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