lec 8

Dr.Zainab Ali Hussein

Healing , Repair , Regeneration
Cell Injury – Reversible & Irreversible Injury

Introduction

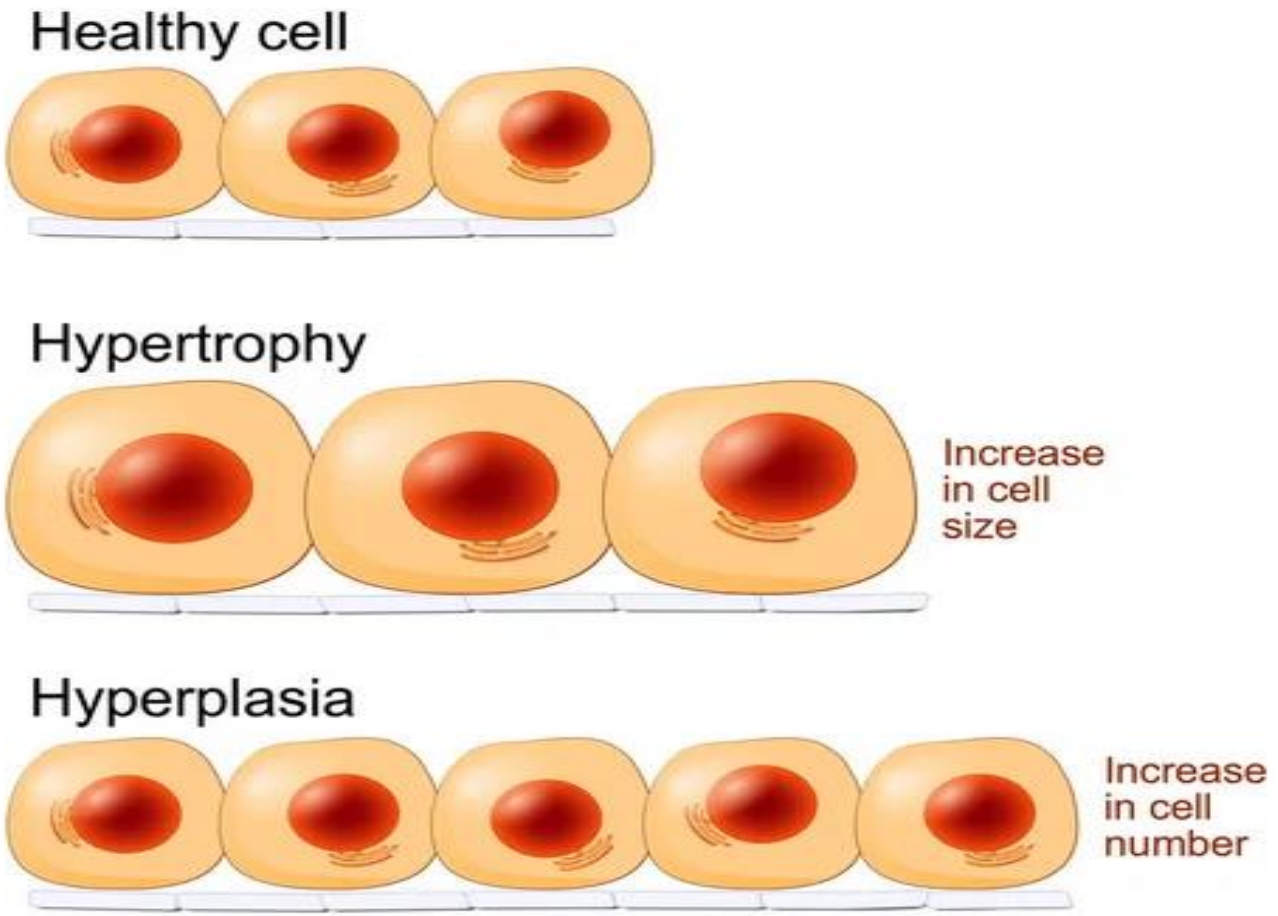
- Disease begins with cell injury and ends with healing or scarring.
- Understanding injury → explains organ failure, inflammation, necrosis, and repair.

Cell Injury

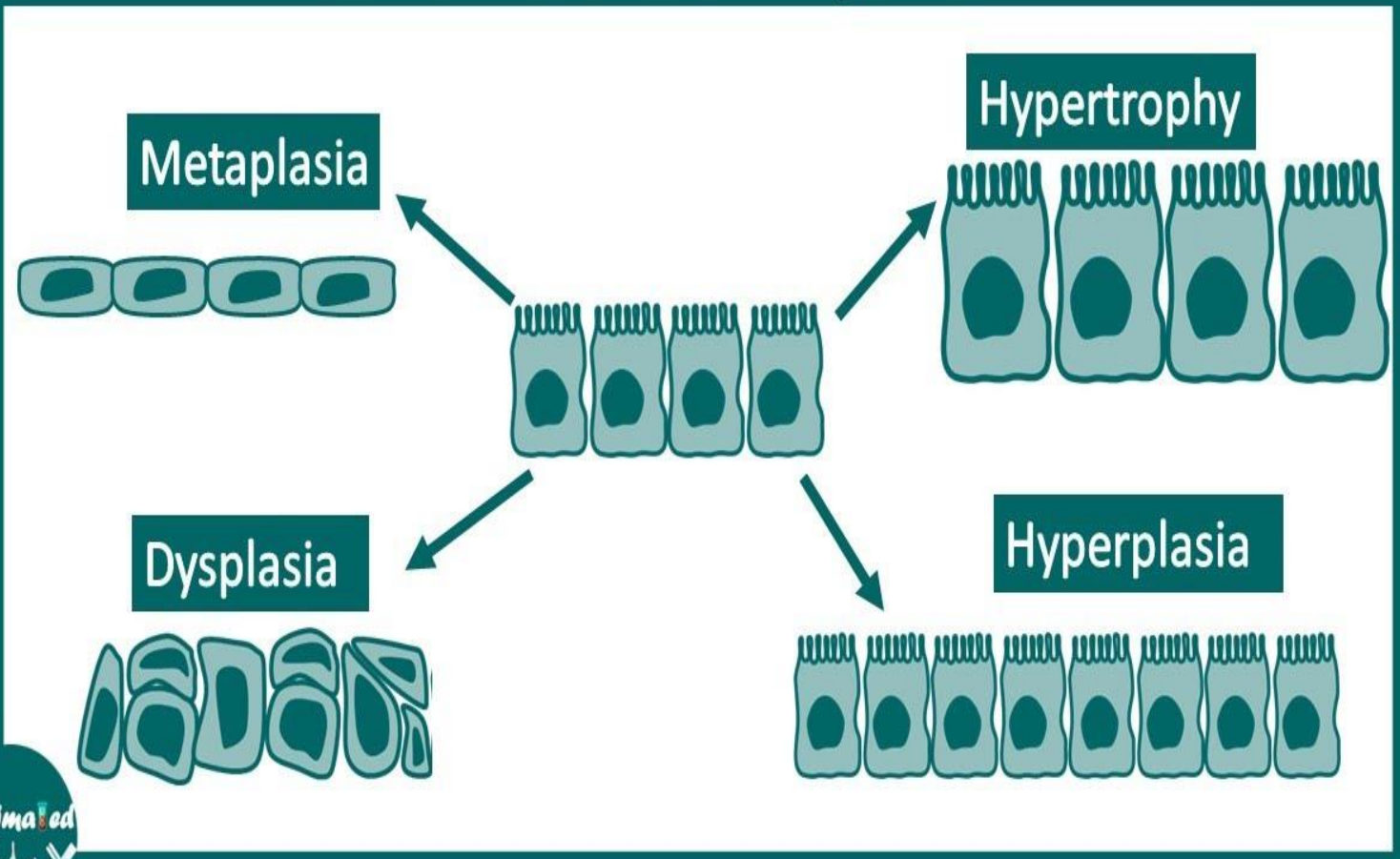
- A state where a cell can no longer maintain homeostasis.
- Begins after adaptive mechanisms are exhausted.
- Mild injury → reversible.
- Severe/prolonged injury → irreversible → cell death.
- Influenced by type of cell, duration of stress, and severity.

Adaptive Cellular Responses

- Hypertrophy: increased cell size (e.g., LV hypertrophy).
- Hyperplasia: increased cell number (e.g., endometrial hyperplasia).
- Atrophy: decreased cell size and function (e.g., muscular atrophy).
- Metaplasia and dysplasia: substitution of one adult cell type by another one .


Healthy cell
Hypertrophy
Increase in cell size
Hyperplasia
Increase in cell number

Cellular adaptation



Major Causes of Cell Injury

- Hypoxia/Ischemia: reduced O_2 → ATP depletion → major mechanism of injury.
- Physical agents: burns, freezing, radiation, trauma.
- Chemical agents: poisons, alcohol, drugs like paracetamol.
- Infectious agents: viral, bacterial, parasitic.
- Immunologic: autoimmune diseases, allergies.
- Genetic defects: enzyme deficiencies.
- Nutritional imbalance: protein deficiency, vitamins, obesity.

Hypoxia and Ischemia

- Hypoxia = low oxygen; ischemia = reduced blood flow.
- Leads to cell swelling, lactic acidosis, ribosome detachment.
- Common in MI, stroke, shock, severe anemia, CO poisoning.

Infectious and Immune-Mediated Injury

- Viruses: cause direct cell lysis or induce immune attack.
- Bacteria: exotoxins/endotoxins → overwhelming injury.
- Parasites: mechanical + immune reactions.
- Autoimmune: body attacks itself (e.g., lupus).

Genetic and Nutritional Factors

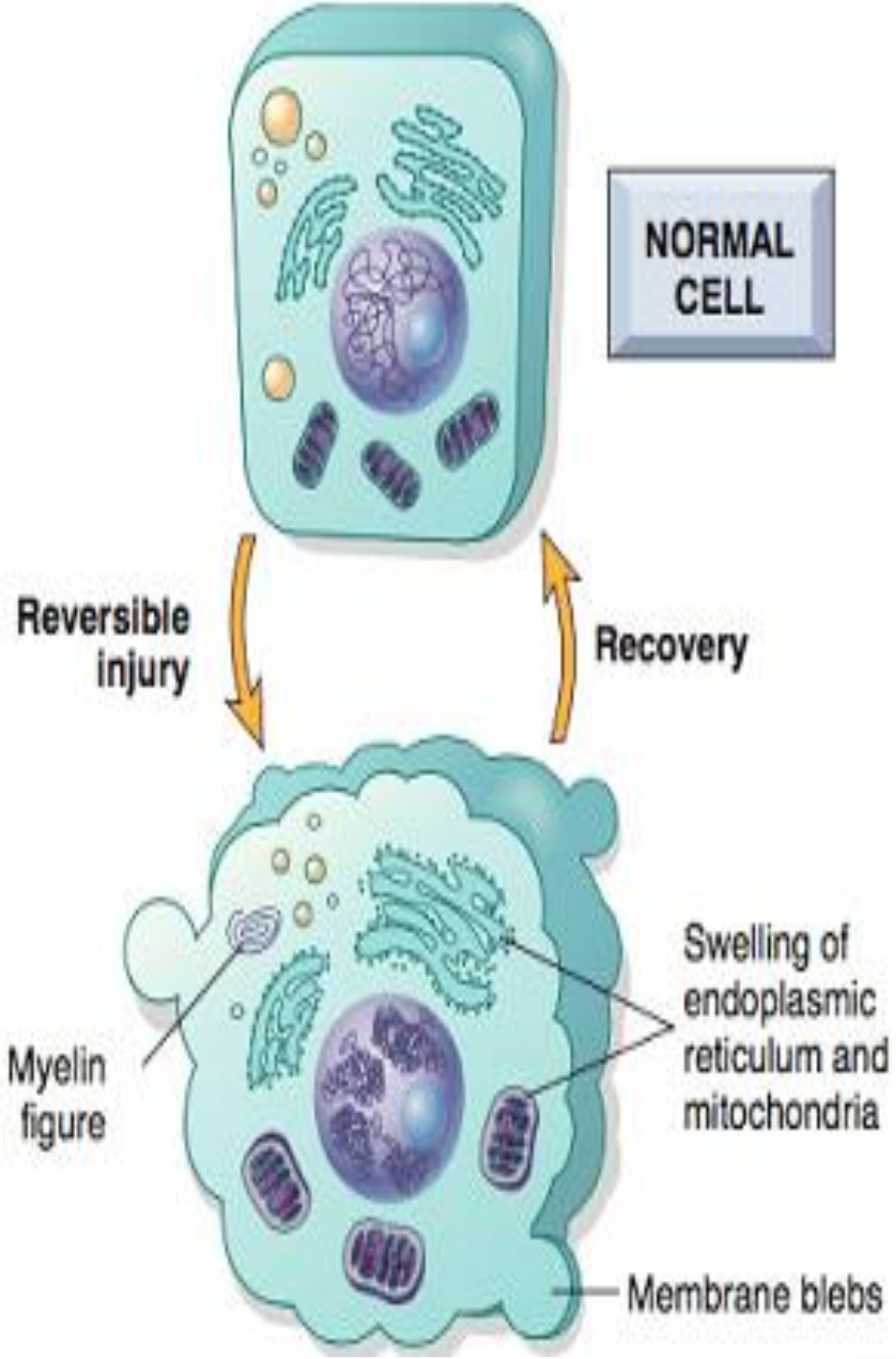
- Gene mutations
- Severe malnutrition → atrophy, decreased repair.
- Obesity → chronic inflammation + metabolic stress.

Mechanisms of Cell Injury

- Final common pathways regardless of cause:
- – ATP depletion
- – Mitochondrial damage
- – Calcium influx
- – ROS accumulation
- – Membrane damage
- – DNA damage

Reversible Cell Injury

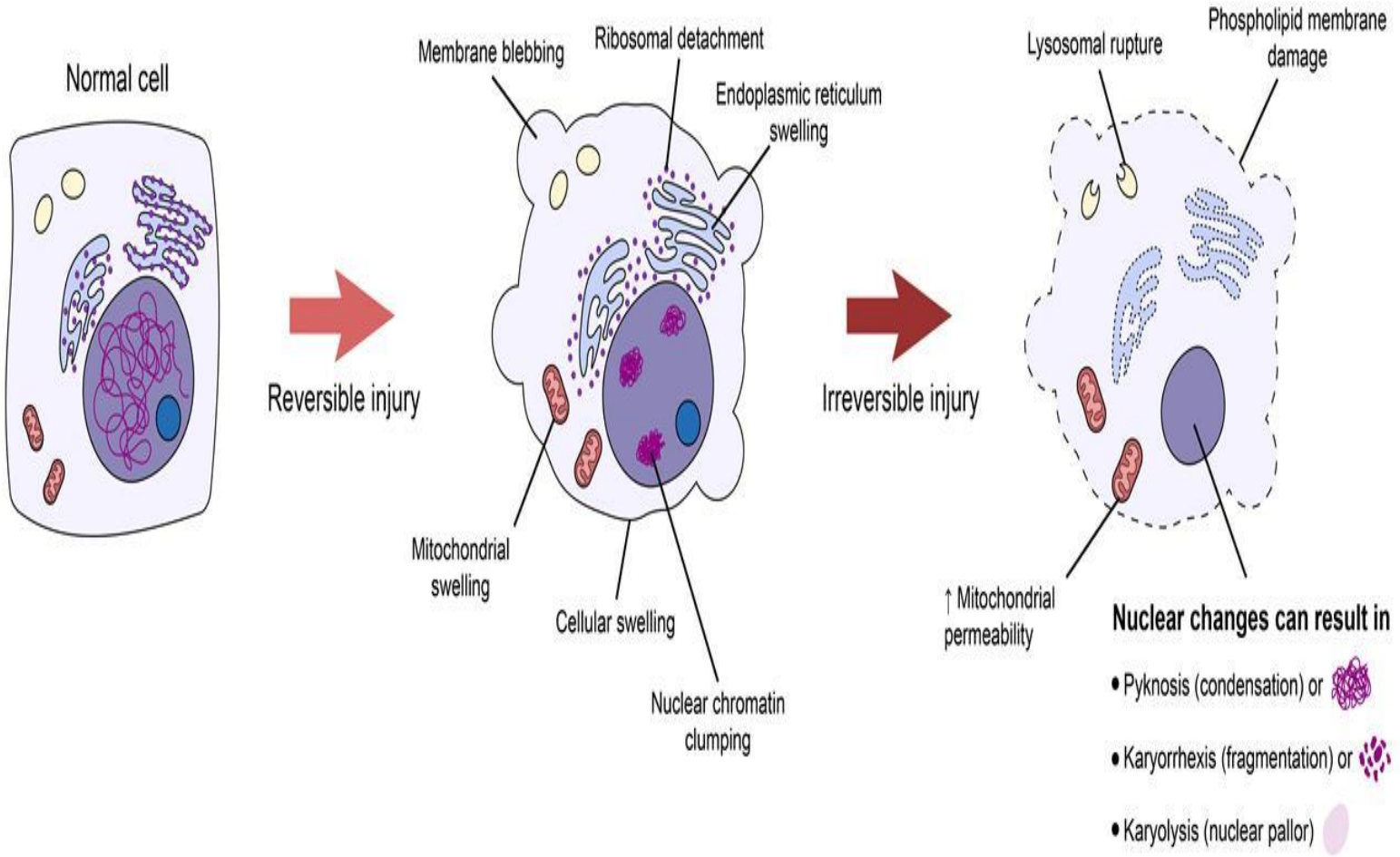
- • Membranes remain intact.
- • Features:
- – Cell swelling (hydropic change).
- – Membrane blebs.
- – ER swelling.
- – Fatty change (liver, myocardium).
- – Mild nuclear changes.
- • Fully reversible if stress removed quickly.


NORMAL CELL
Reversible injury
Recovery
Myelin figure
Swelling of endoplasmic reticulum and mitochondria
Membrane blebs

Irreversible Cell Injury

- • Point of no return.
- • Severe mitochondrial dysfunction and membrane damage.
- • Lysosomal rupture → cell digested.
- • Nuclear changes:
- – Pyknosis: shrinkage.
- – Karyorrhexis: fragmentation.
- – Karyolysis: dissolution.

Cell Injury

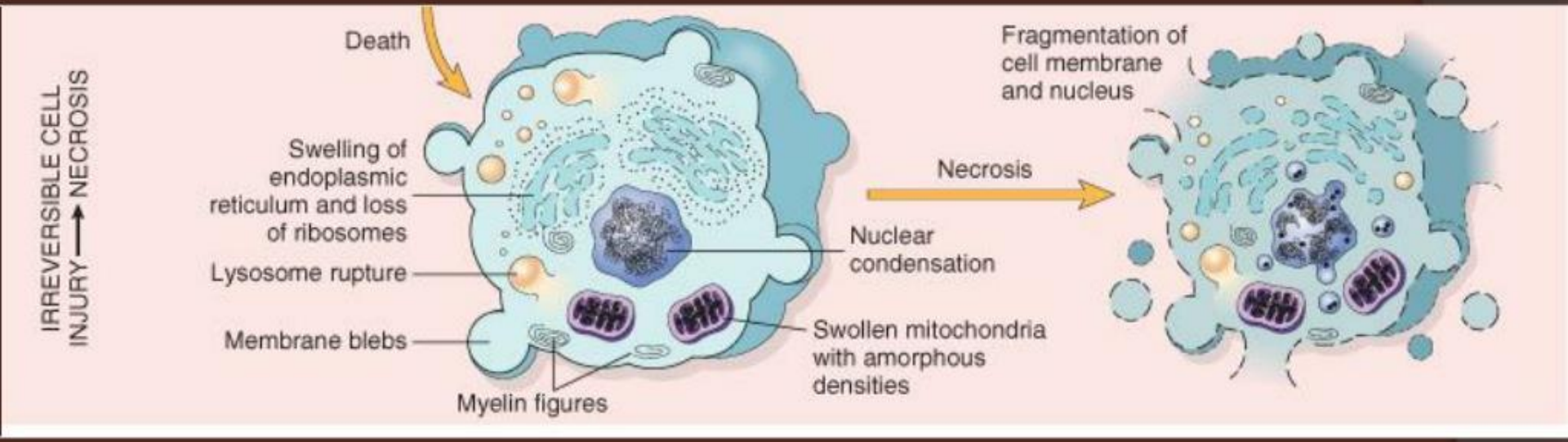


Moises Dominguez

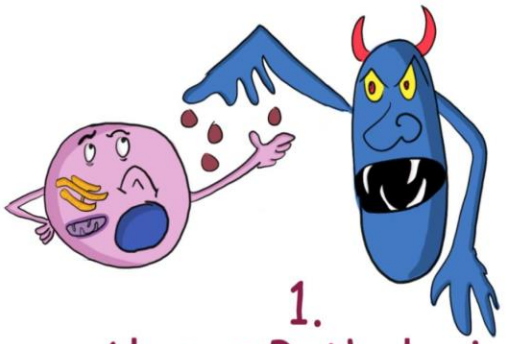
Necrosis

- Uncontrolled cell death.
- Always associated with inflammation.
- Cell contents leak out → immune activation.

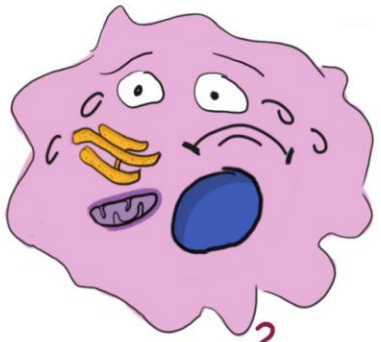
IRREVERSIBLE CELL INJURY- NECROSIS



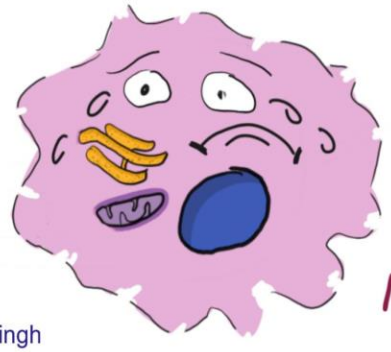
Necrosis



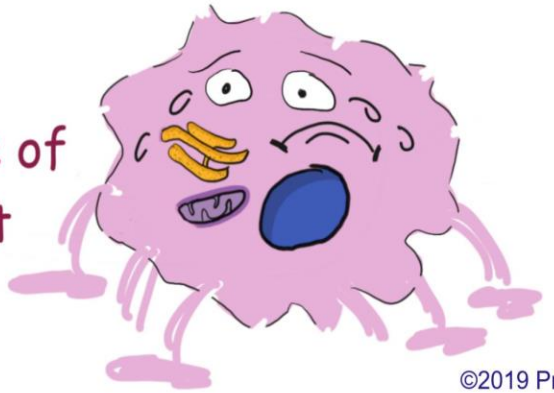
1. Always Pathological



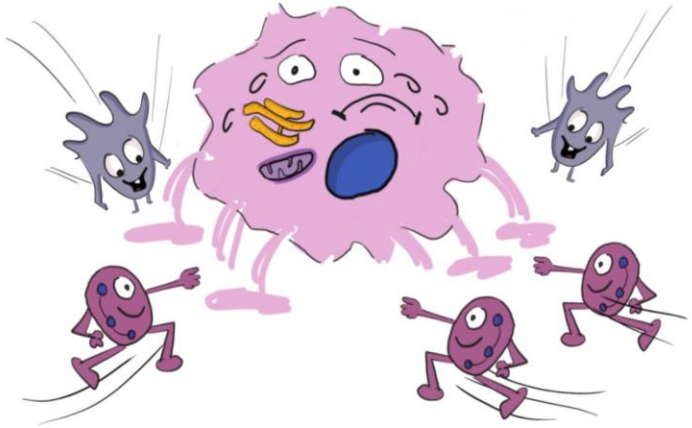
2. Cell Enlargement



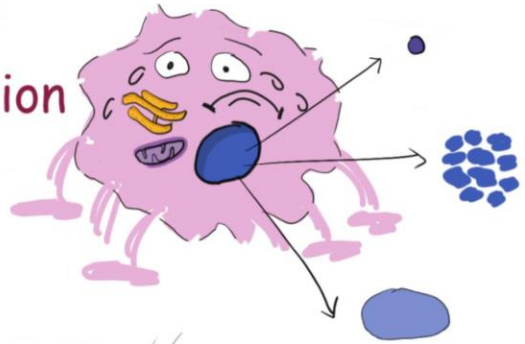
3. Loss of Membrane Integrity



4. Leakage of Content



5. Inflammation



6. Nuclear Degeneration

Types of Necrosis

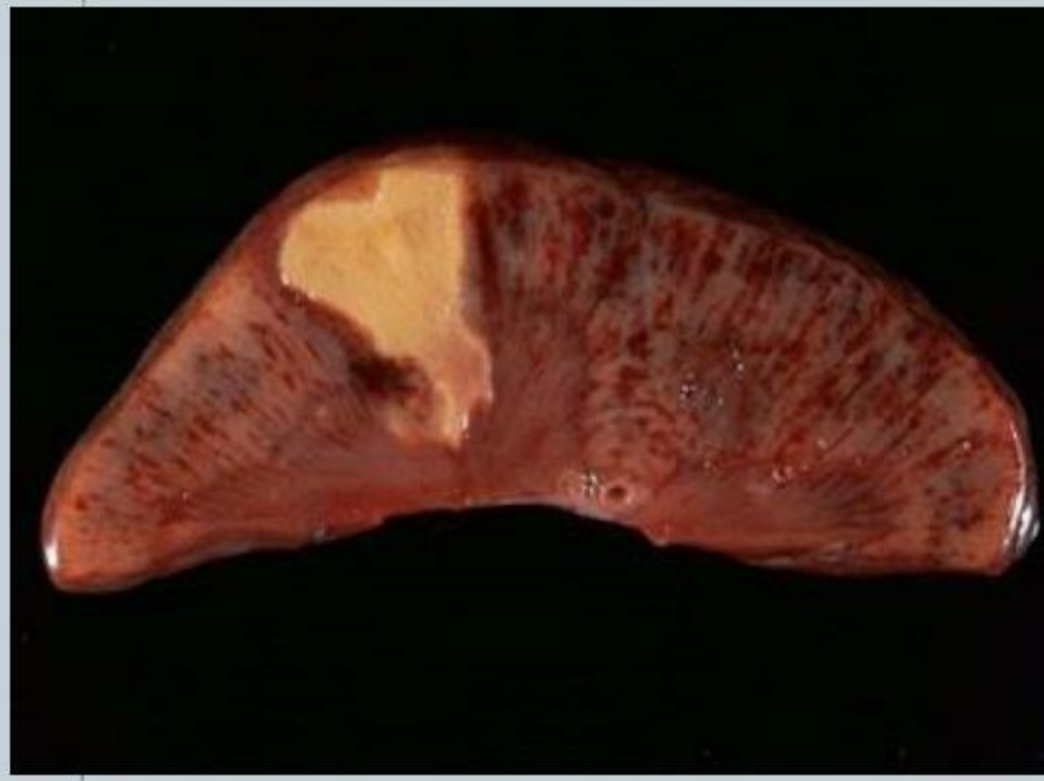
- Coagulative: ischemia, architecture preserved (heart, kidney).
- Liquefactive: brain infarcts, abscesses.
- Fat necrosis: pancreatitis, fat saponification.
- Caseous: TB, cheesy appearance.
- Fibrinoid: immune vasculitis.
- Gangrene: limb ischemia ± infection.

Types of Necrosis

- **Coagulation Necrosis –** Denaturation of proteins
- **Liquefaction Necrosis –** Rapid hydrolysis of tissue
- **Enzymatic Fat Necrosis –** Action of lipases
- **Caseous Necrosis –** Intermediate pattern involving coagulation and liquefaction
- **Gangrenous Necrosis –** Coagulation necrosis with modification
- **Fibrinoid Necrosis –** Coagulation necrosis modified by deposition of blood components

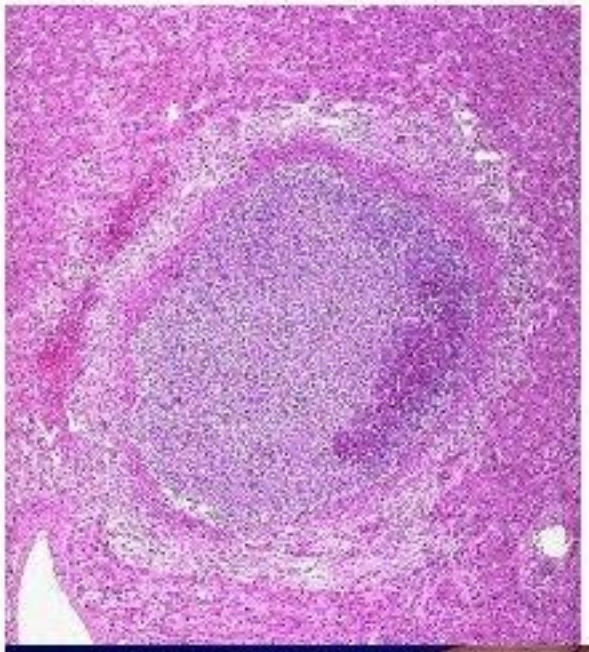
Coagulative Necrosis

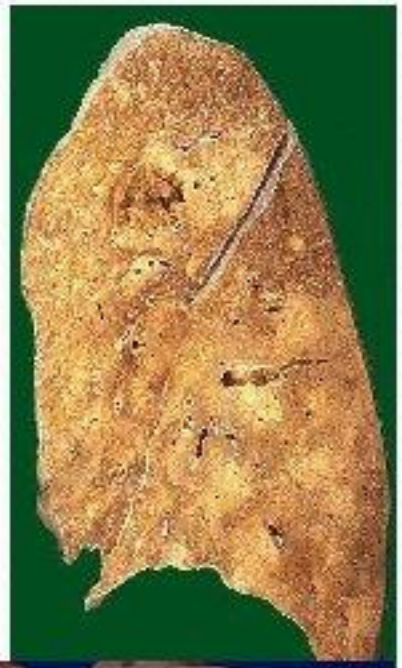
- Caused by ischemia
- Denaturation of structural proteins
- Enzymatic digestion of cells
- Architecture of tissue preserved
- Occurs in organs like heart, spleen, kidney
- Does not occur in brain

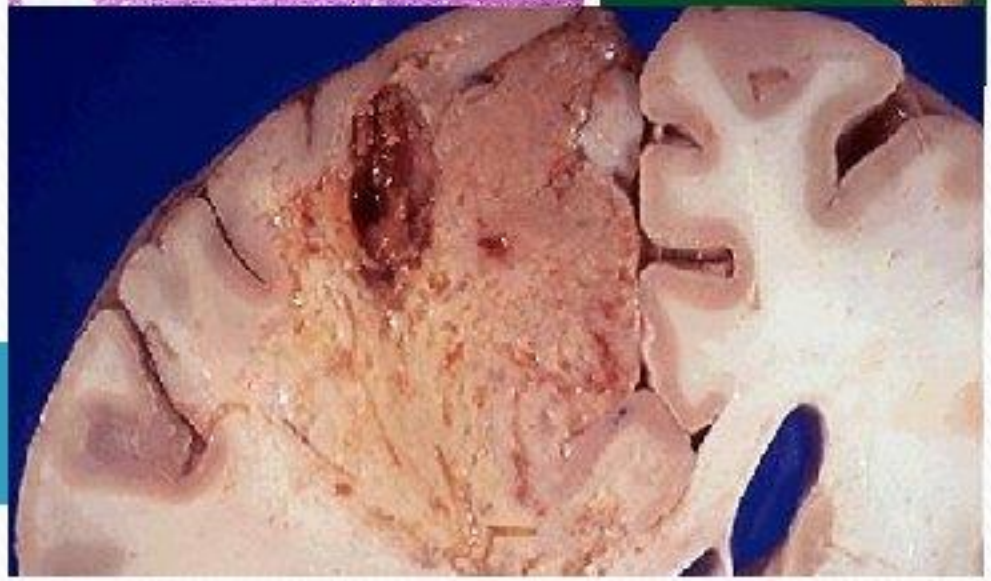


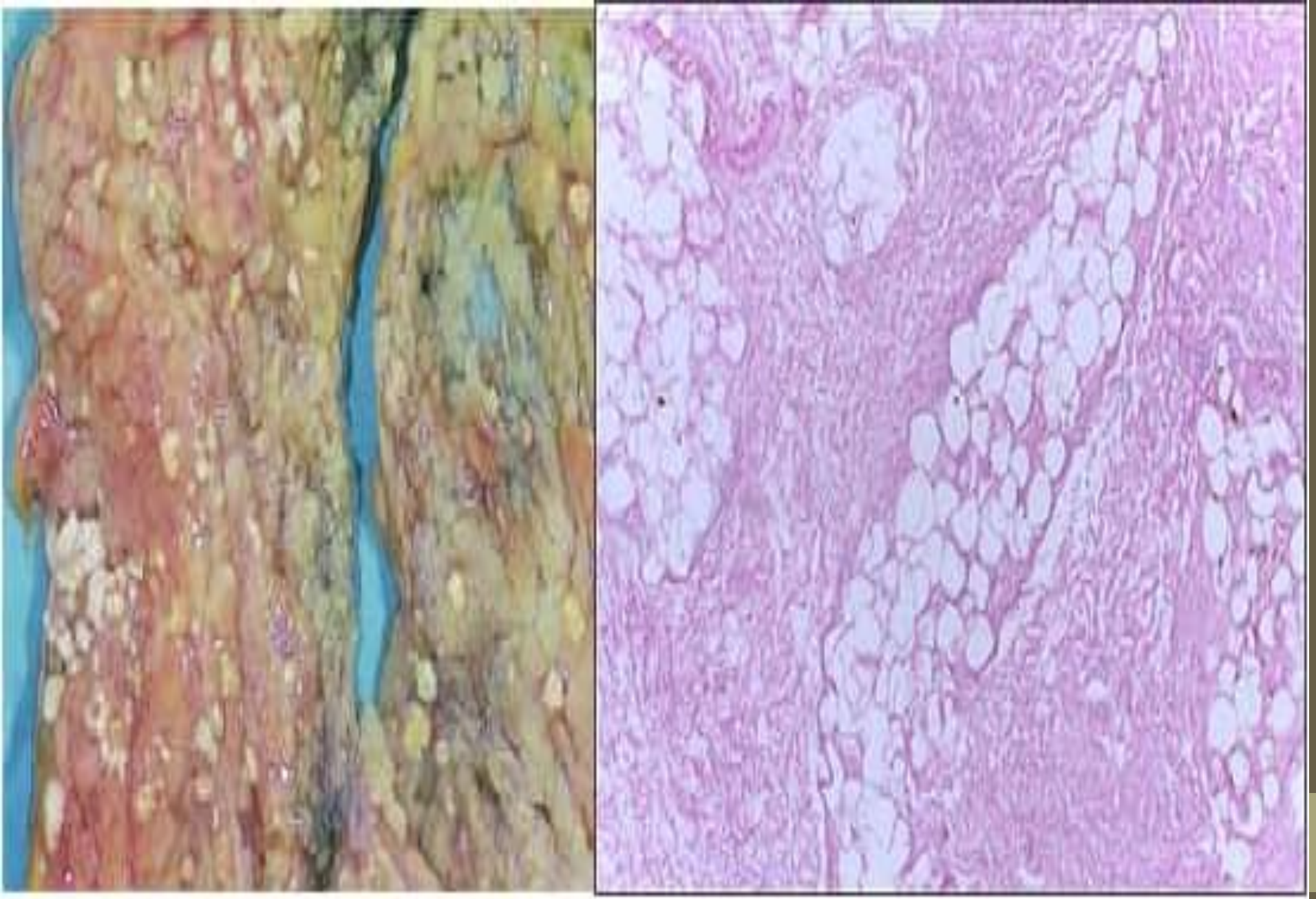
Liquefactive necrosis

- Focal infections (pus)
- CNS infarcts
- Center liquefies and digested tissue is removed by phagocytosis



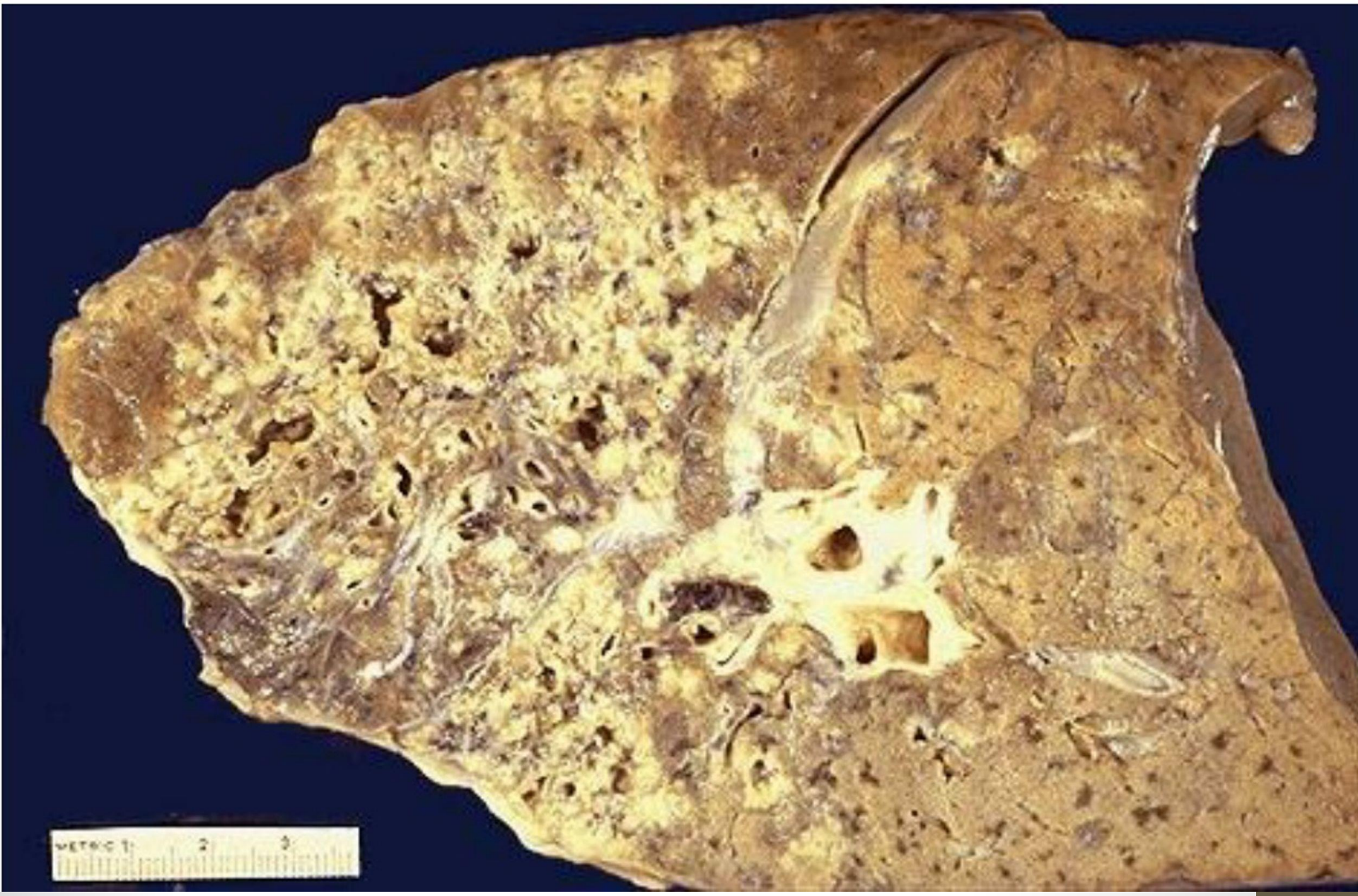




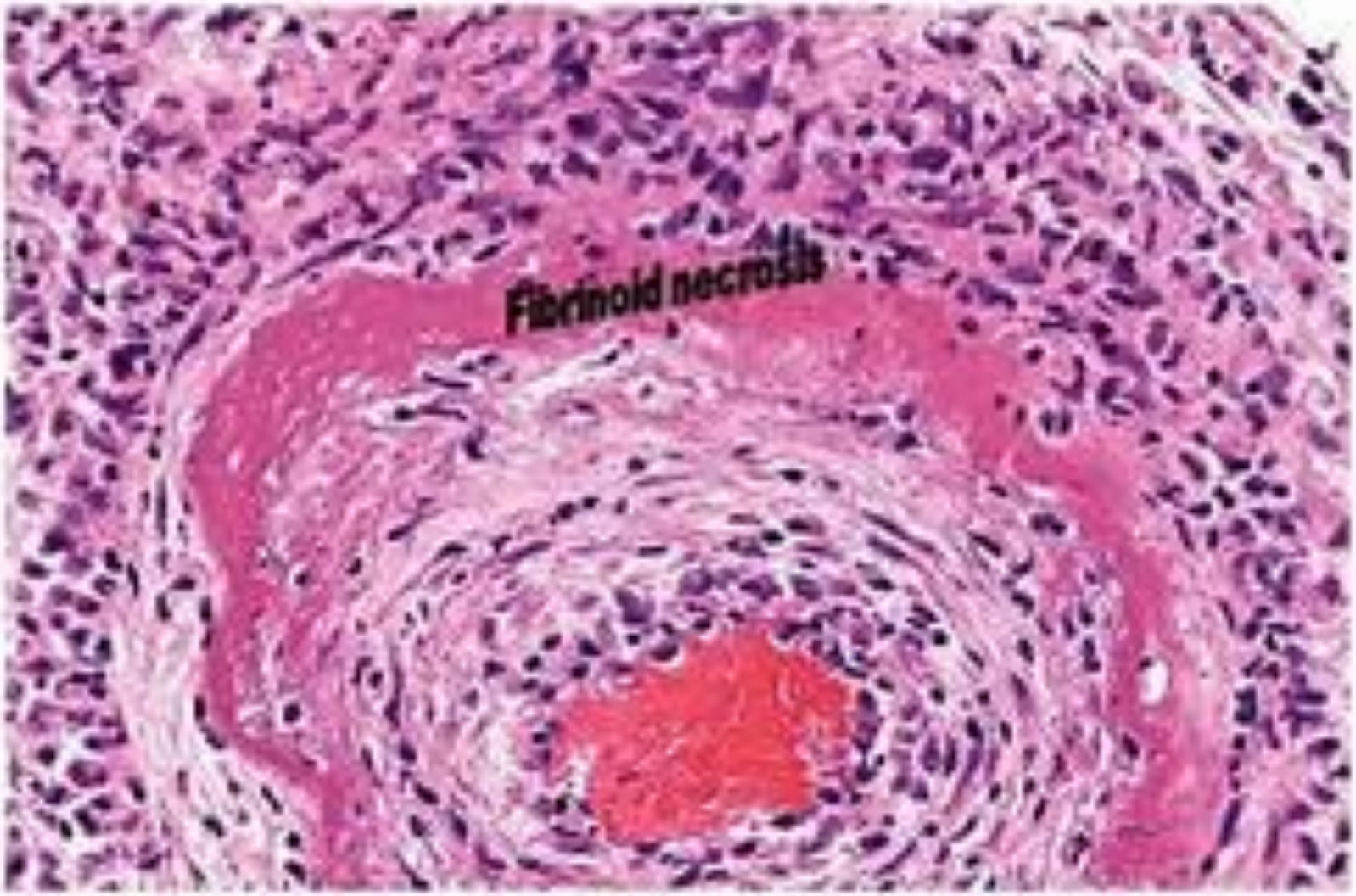


Fat necrosis of breast

CASEOUS NECROSIS, TB



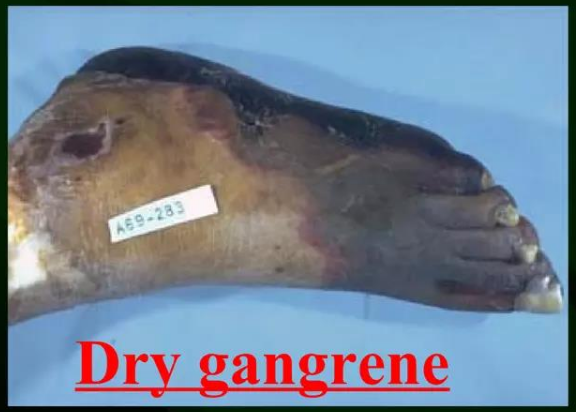
FIBRINOID NECROSIS



3) Gangrenous Necrosis (Surgical term):

- Generally the lower leg, that has lost its blood supply and has undergone coagulation necrosis. When bacterial infection is superimposed, Coagulative necrosis is modified by the liquefactive action of the bacteria and the attracted leukocytes (so-called **wet gangrene**).
- **Dry gangrene:** Is a form of infarction that results from ischemia and when there is secondary no infection because it gets dry. Characterized primarily by Coagulative necrosis without liquefaction. Dead tissue has mummified appearance (e.g. diabetic foot).

Wet gangrene



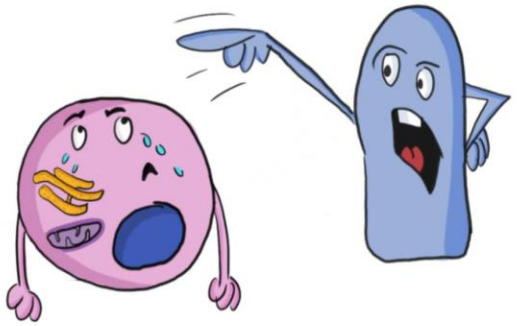
Dry gangrene

Apoptosis

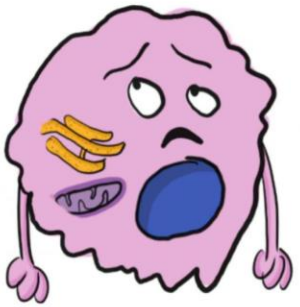
- Programmed cell death.
- No inflammation.
- Seen in DNA damage, viral infections, hormone withdrawal,aging.

Apoptosis

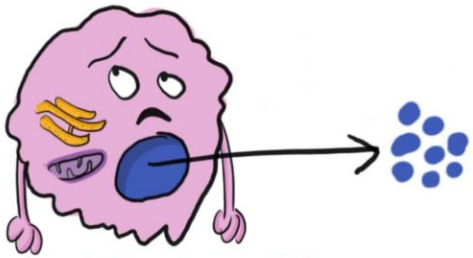
Creative-Med-Doses



1. Elimination of Unwanted cells
Programmed Cell Death

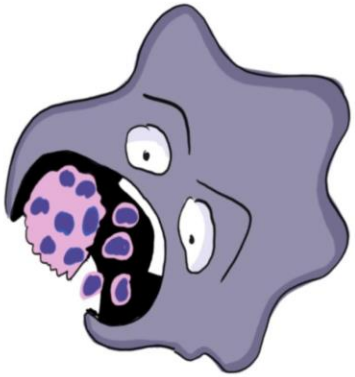


2. Cell Shrinks



3. Nuclear Fragmentation

4.
Apoptotic Bodies



5.
Phagocytosis of
Apoptotic Bodies
(No Inflammation)

Healing and Tissue Response

- After cell death, body attempts:
  - Regeneration (replace with same cells)
  - Repair (scar formation)
- Depends on cell type and ECM integrity.

Tissue Regeneration

- Labile tissues: constant turnover (skin, GI, marrow).
- Stable tissues: can proliferate if stimulated (liver, kidney tubules).
- Permanent tissues: cannot regenerate (neurons, myocardium).

Growth Factors in Healing

- PDGF: fibroblasts, smooth muscle, vessels.
- VEGF: angiogenesis.
- FGF: wound repair.
- TGF-β: collagen synthesis, fibrosis.
- EGF: epithelial proliferation.
- HGF: liver regeneration.
- IL-6: primes hepatocytes.

Extracellular Matrix (ECM)

- Provides structural support.
- Components: collagen, elastin, fibronectin, proteoglycans.
- Basement membrane integrity is essential for regeneration.

Scar Formation

- Hemostasis: clotting, platelet activation.
- Inflammation: neutrophils → macrophages.
- Granulation tissue: fibroblasts, new vessels.
- Collagen deposition: Type III → Type I.
- Remodeling: increased strength, never 100%.

Primary vs Secondary Intention

- Primary: clean surgical wounds, minimal scar.
- Secondary: large wounds, ulcers, burns.
- More granulation tissue.
- More contraction.
- Larger scar.

DIFFERNCES BETWEEN HEALING BY PRIMARY AND SEONDARY INTENTION

FEATURES	HEALING BY PRIMARY INTENTION	HEALING BY SECONDARY INTENTION
CLEANLINESS	CLEAN	NOT CLEAN
INFECTION	NOT INFECTED	INFECTED
MARGINS	SURGICALLY CLEAN	IRREGULAR
SUTURES	USED	NOT USED
HEALING	SMALL GRANULATION TISSUE	LARGE GRANULATION TISSUE
OUT COME	LINEAR SCAR	IRREGULAR WOUND
COMPLICATION	NOT FREQUENT	FREQUENT

WOUND HEALING

FIRST INTENTION

clean, uninfected surgical incision

Injury

SECOND INTENTION

Large , irregular wound

Factors Affecting Healing

- Systemic:

  Diabetes, malnutrition, steroids, anemia, smoking.

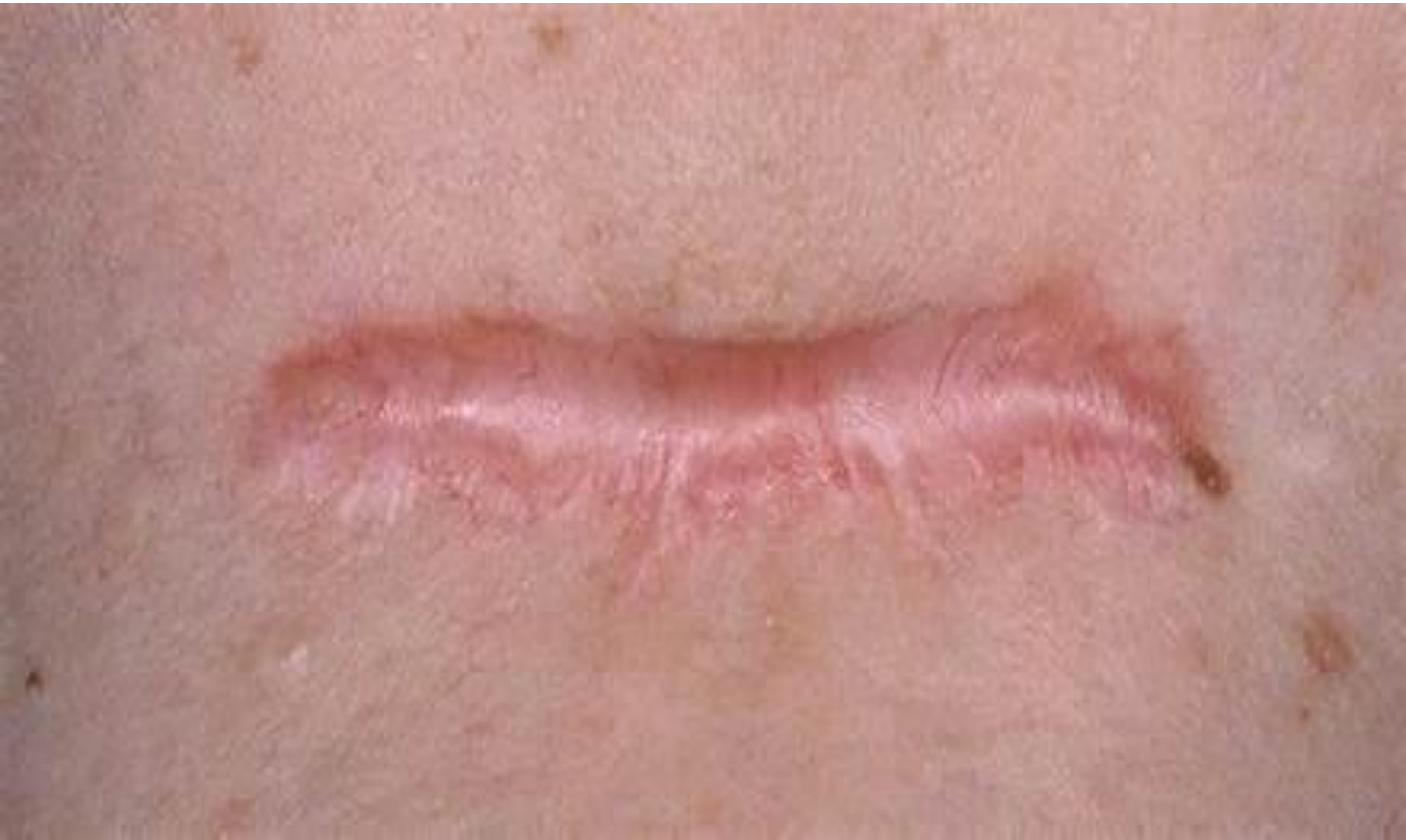
- Local:

  Infection, ischemia, mechanical stress, radiation, foreign bodies.

Complications of Healing

- Dehiscence.
- Chronic non-healing ulcers.
- Keloids (Type III collagen).
- Hypertrophic scars.
- Excess granulation tissue.
- Contractures.
- Organ fibrosis (cirrhosis, pulmonary fibrosis).

Keloid scar



the end