SAWA UNIVERSITY

HISTOPATHOLOGY
1

CELL INJURY AND CELL DEATH

Sawa University — جامعـــــة ســـــــاوة الاهلية

College of health and medical techniques — كليـــــة التقنيـــات الصحيـة والطبيـة

Department of Medical Laboratories — قسم تقنيات المختبرات الطبية

Third Stage — المرحلـــــــــــة الثالثة

محاضرة رقم 3 — الجانب النظري

Lecture No. 3 — Theoretical

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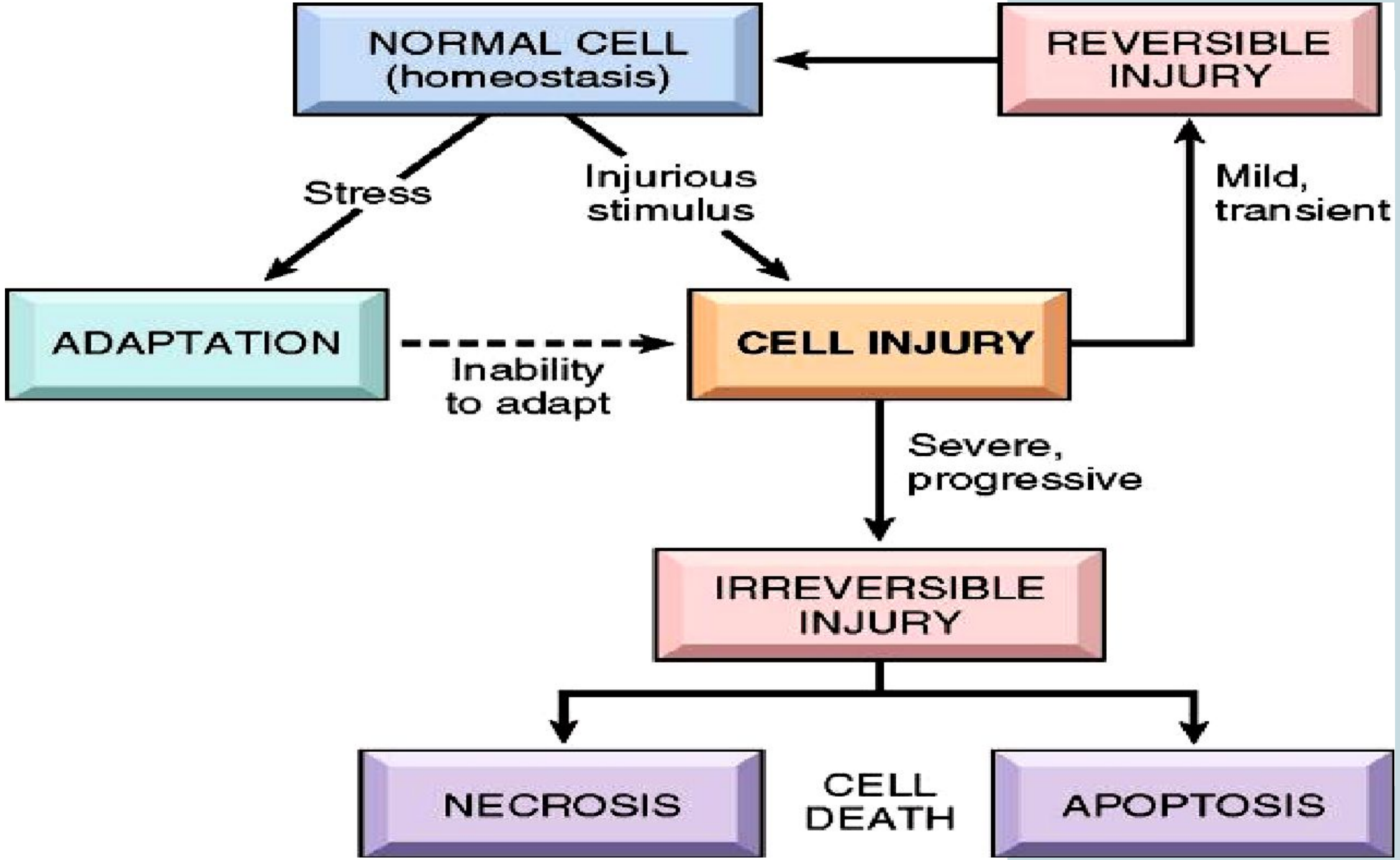
OBJECTIVE

- Define cell injury and explain its main causes.
- Knowing the types of cell Injuries and how to distinguish them microscopically.
- Differentiate between necrosis and apoptosis.

INTRODUCTION

- Cells maintain homeostasis under normal physiological conditions.
- When exposed to stress, they can adapt, become injured, or die.
- Cell injury : is a variety of changes of stress that a cell suffers due to external or internal environmental changes
- Cell injury occurs when adaptive capacity is exceeded


NORMAL CELL
(homeostasis)
REVERSIBLE
INJURY
Stress
Injurious
stimulus
Mild,
transient
ADAPTATION
Inability
to adapt
CELL INJURY
Severe,
progressive
IRREVERSIBLE
INJURY
NECROSIS
CELL
DEATH
APOPTOSIS

Causes of Cell Injury:

- **1- Hypoxia (O2 Deprivation)** : It means the interference with aerobic respiration of cells and Hypoxia should be differentiate from **ischemia** (loss of blood supply) .

Causes of Hypoxia (O2 Deprivation).

- **a.** Ischemia (decrease O2 supply).
- **b.** Anemia (decrease O2 carrying capacity of blood).
- **c.** Co poisoning (displace O2 from Hb).
- **2-Physical agents:** including trauma, heat, cold, radiation, and electric shock

3- **Chemical agents and drugs:** including therapeutic drugs, poisons, environmental pollutants, and alcohol and narcotics.

4- **Infectious agents:** including viruses, bacteria, fungi, and parasites

5- Immunologic reactions: including autoimmune diseases and cell injury following responses to infection, hypersensitivity reaction to some drugs like penicillin.

6- **Genetic derangements:** such as chromosomal alterations and specific gene mutations.

7- **Nutritional imbalances:** including protein–calorie deficiency or lack of specific vitamins, as well as nutritional excesses(obesity).

8-Aging: Can result in diminished ability of cells to response to exogenous stimuli & injury& eventually cell death.

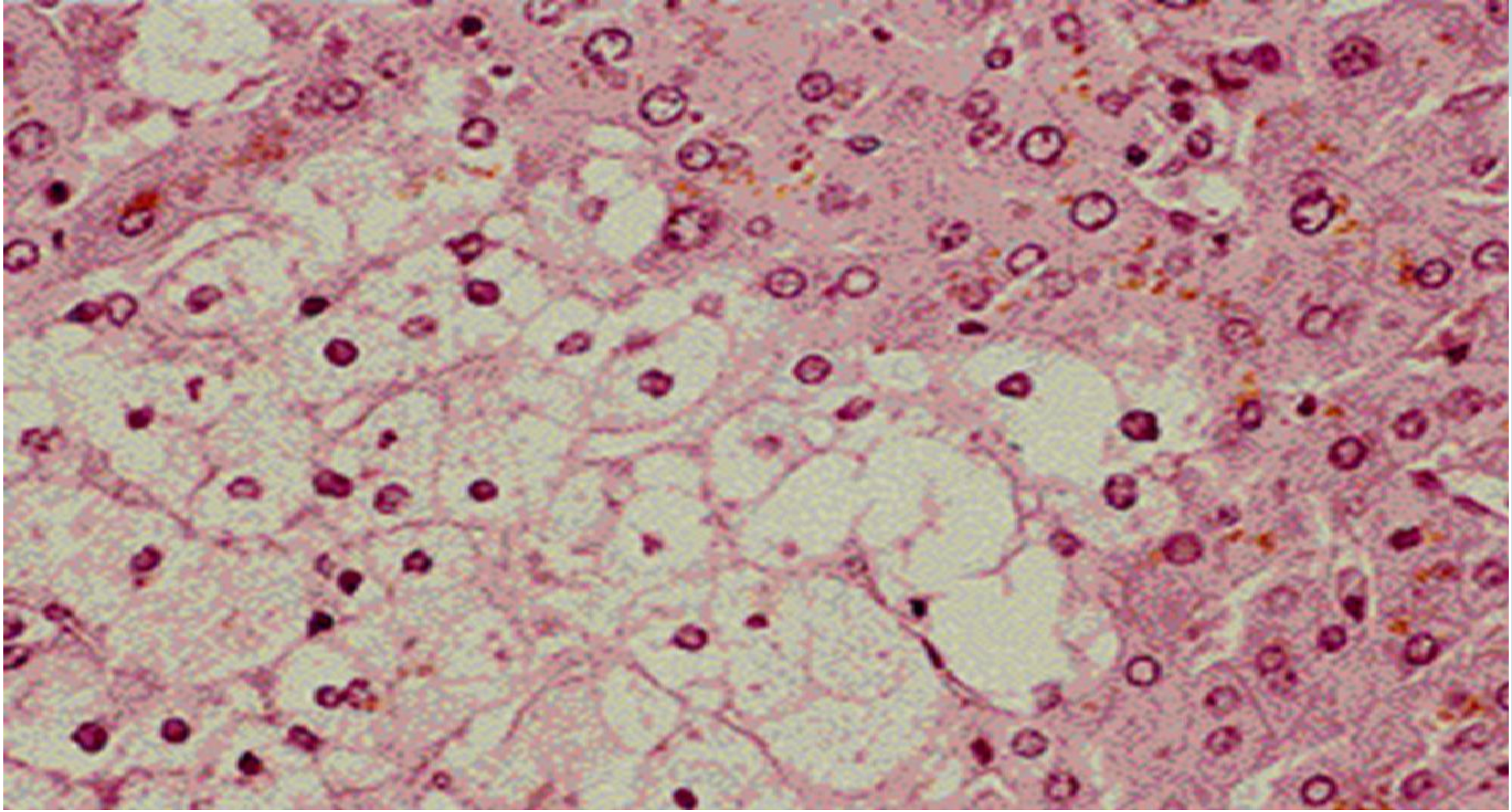
Types of cell injuries:

- **1. Reversible: If the change in the cellular environment is greater than the capacity of the cell to adapt and then return to its normal environment.**

Morphology of reversible injury:

1. Cellular swelling: is the earliest manifestation of almost all forms of injury to cells. When it affects many cells, it causes pallor, increased turgor, and increased weight of the affected organ.

On microscopic examination, small clear vacuoles may be seen within the cytoplasm; these represent distended and pinched-off segments of the endoplasmic reticulum(ER). This pattern of nonlethal injury is sometimes called hydropic change or vacuolar degeneration.The cytoplasm of injured cells appears red (eosinophilic) when stained with hematoxylin and eosin (H&E) due to the loss of RNA, which binds the blue hematoxylin dye. The eosinophilia becomes more pronounced with progression toward necrosis.

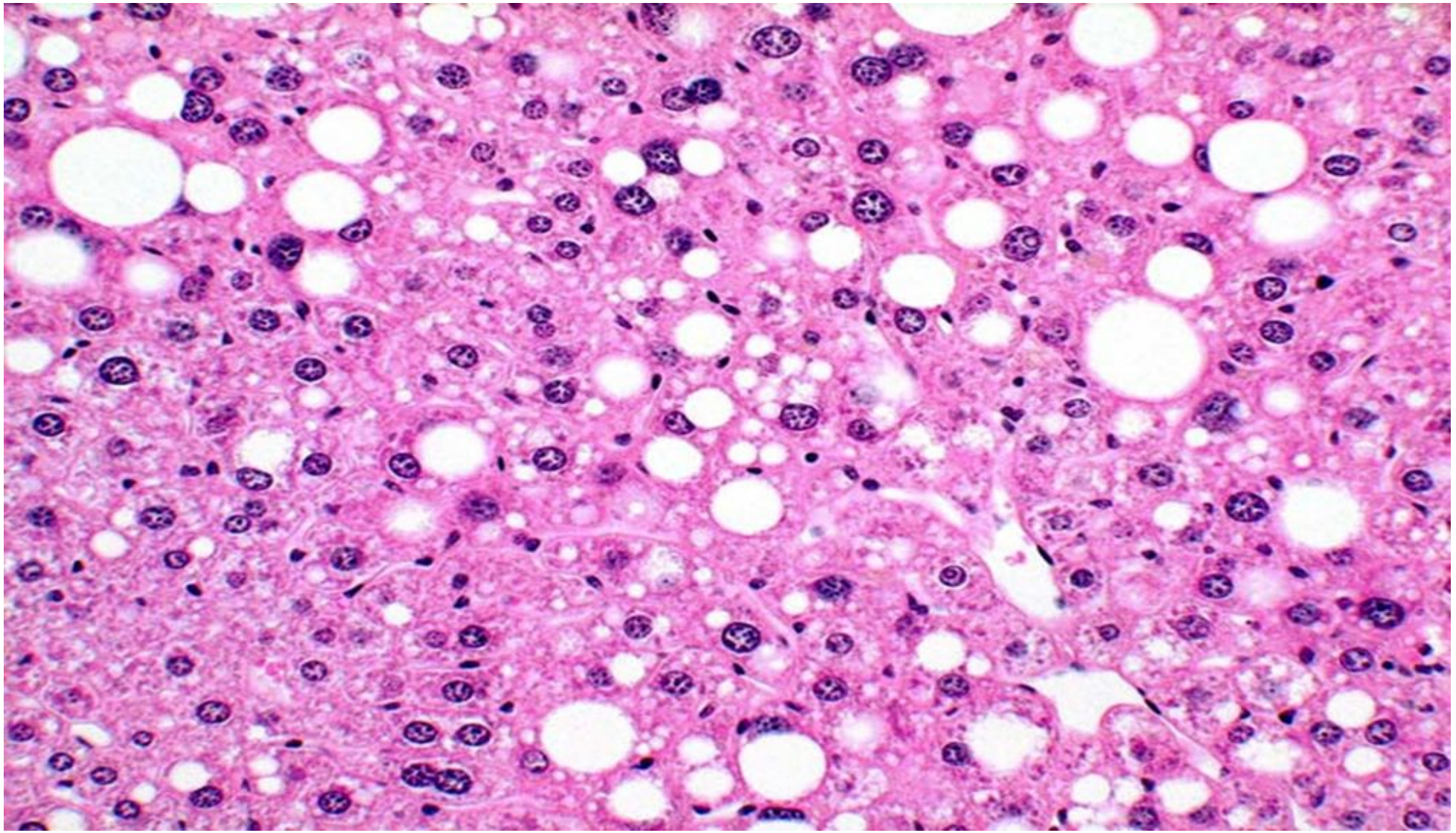


The affected hepatocytes are distended by accumulated water that imparts cytoplasmic pallor. (hydropic swelling)

2. Fatty change: occurs in organs that are actively involved in lipid metabolism (e.g., liver). It results when a toxic injury disrupts metabolic pathways and leads to rapid accumulation of triglyceride-filled lipid vacuoles.

Gross lesions is organ enlargement and lightening in colour. This is due to the high lipid content increasing the organ's volume

Microscopic Lesions the large, clear lipid droplets that fill the cytoplasm .



Fatty change in liver

2. Irreversible: if the injurious stimulus is persistent or severe, the cell suffers **irreversible injury** and ultimately undergoes **cell death.**

- **Cell death**: With continuing damage, the injury becomes irreversible, at which time the cell cannot recover and it dies.
- The removal of damaged, unneeded, and aged cells through *cell death* is a normal and essential process in embryogenesis, the development of organs, and the maintenance of homeostasis into adulthood.

Types of cell death:

1. Unprogrammed means, **Necrosis:** Severe mitochondrial damage with depletion of ATP and rupture

Lysosomal and plasma membranes are typically associated with necrosis. Necrosis occurs in many commonly encountered injuries, such as those following ischemia, exposure to toxins, various infections, and trauma.

2. Programmed cell death means, Apoptosis: a term derived from an ancient Greek word for the falling of leaves in the autumn. Apoptosis is a pathway of cell death in which cells activate enzymes that degrade the cells' own nuclear DNA and nuclear and cytoplasmic proteins.

Table 2.1 Features of Necrosis and Apoptosis

Feature	Necrosis	Apoptosis
Cell size	Enlarged (swelling)	Reduced (shrinkage)
Nucleus	Pyknosis, karyorrhexis, karyolysis	Fragmentation into nucleosome-size fragments
Plasma membrane	Disrupted	Intact; altered structure, especially orientation of lipids
Cellular contents	Enzymatic digestion; may leak out of cell	Intact; may be released in apoptotic bodies
Adjacent inflammation	Frequent	No
Physiologic or pathologic role	Usually pathologic (culmination of irreversible cell injury)	Often physiologic, means of eliminating unwanted cells; may be pathologic after some forms of cell injury, especially DNA damage

Morphology of irreversible injury

1. Necrotic cells show increased *eosinophilia* in H&E stains, attributable in part to the loss of cytoplasmic RNA and in part to the accumulation of denatured cytoplasmic proteins (which bind the red dye eosin).

2. The necrotic cell may have a glassy homogeneous appearance as a result of the loss of glycogen particles and the cytoplasm becomes vacuolated and appears moth-eaten by enzyme.

3. Nuclear changes appear in one of three patterns, all due to the breakdown of DNA:

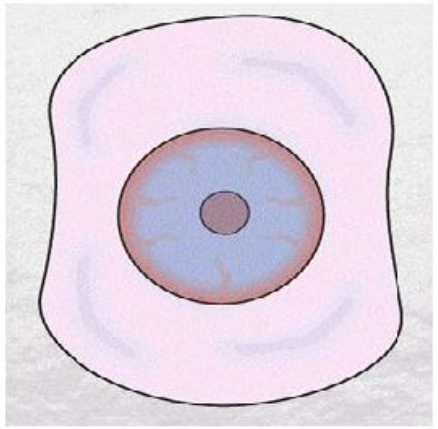
a. Karyolysis: The basophilia of the chromatin may fade due to loss of DNA because of enzymatic degradation by endonucleases.

b. Pyknosis: characterized by nuclear shrinkage and increased basophilia. Here the chromatin condenses into a dense, shrunken basophilic mass.

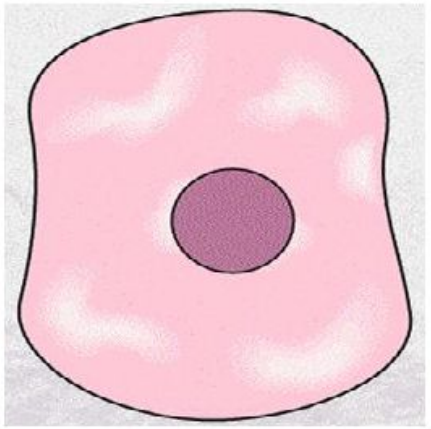
c. Karyorrhexis: the pyknotic nucleus undergoes fragmentation. With the passage of time (1 or 2 days),

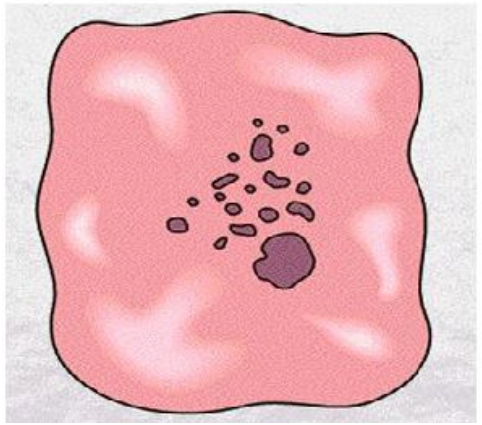
the nucleus in the necrotic cell totally disappears.

Normal

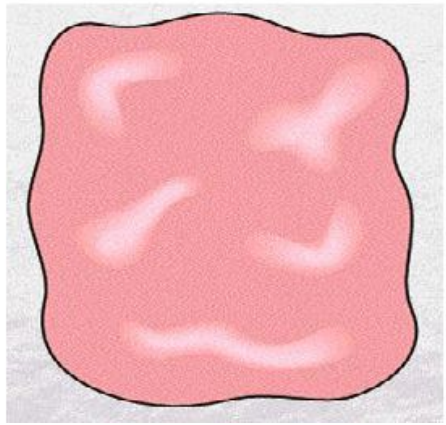


Pyknosis





Karyorrhexis

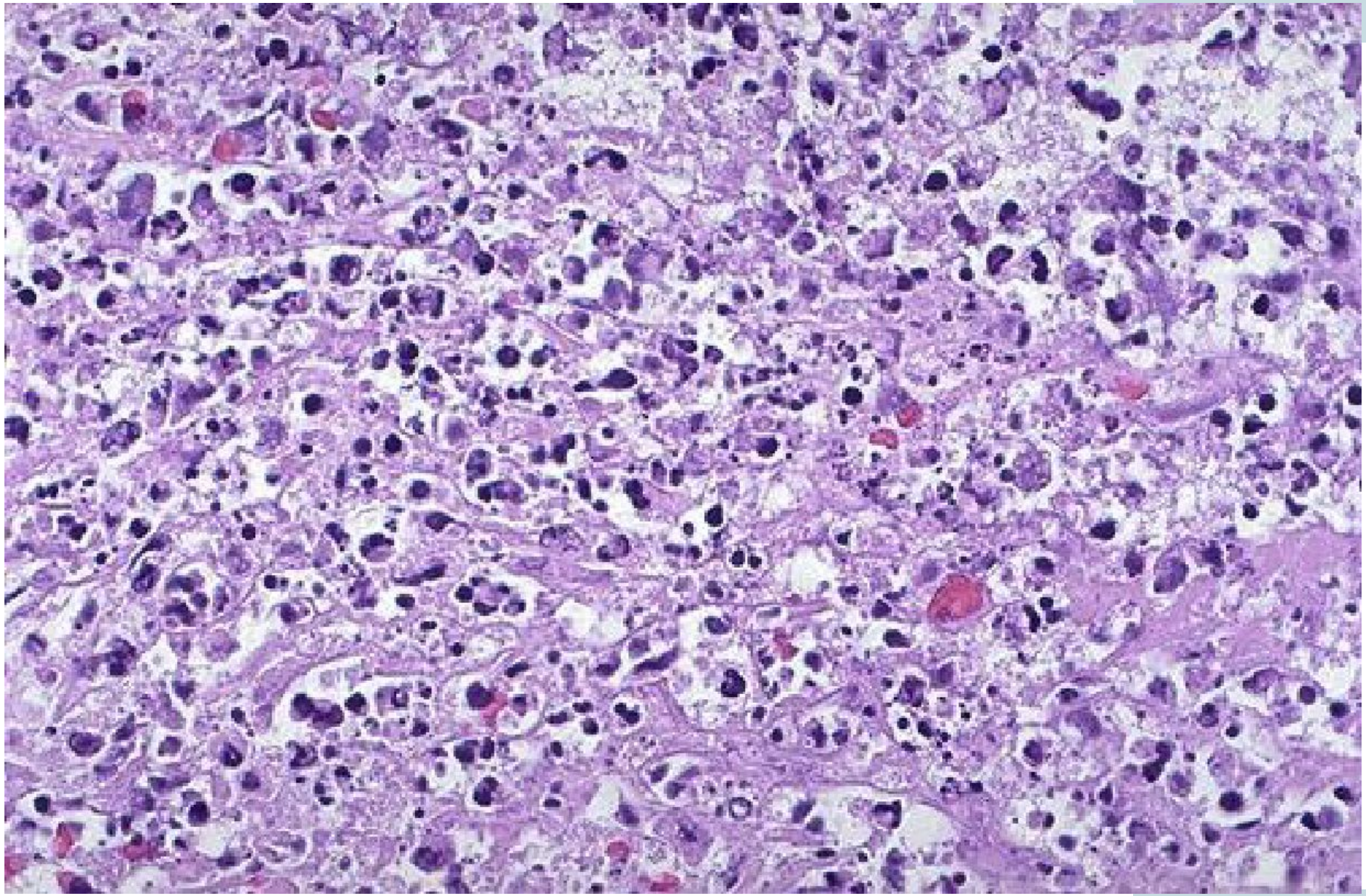


Karyolysis

Types of Necrosis:

 Depend on whether the enzymatic digestion is predominant or denaturation of proteins, these types include:

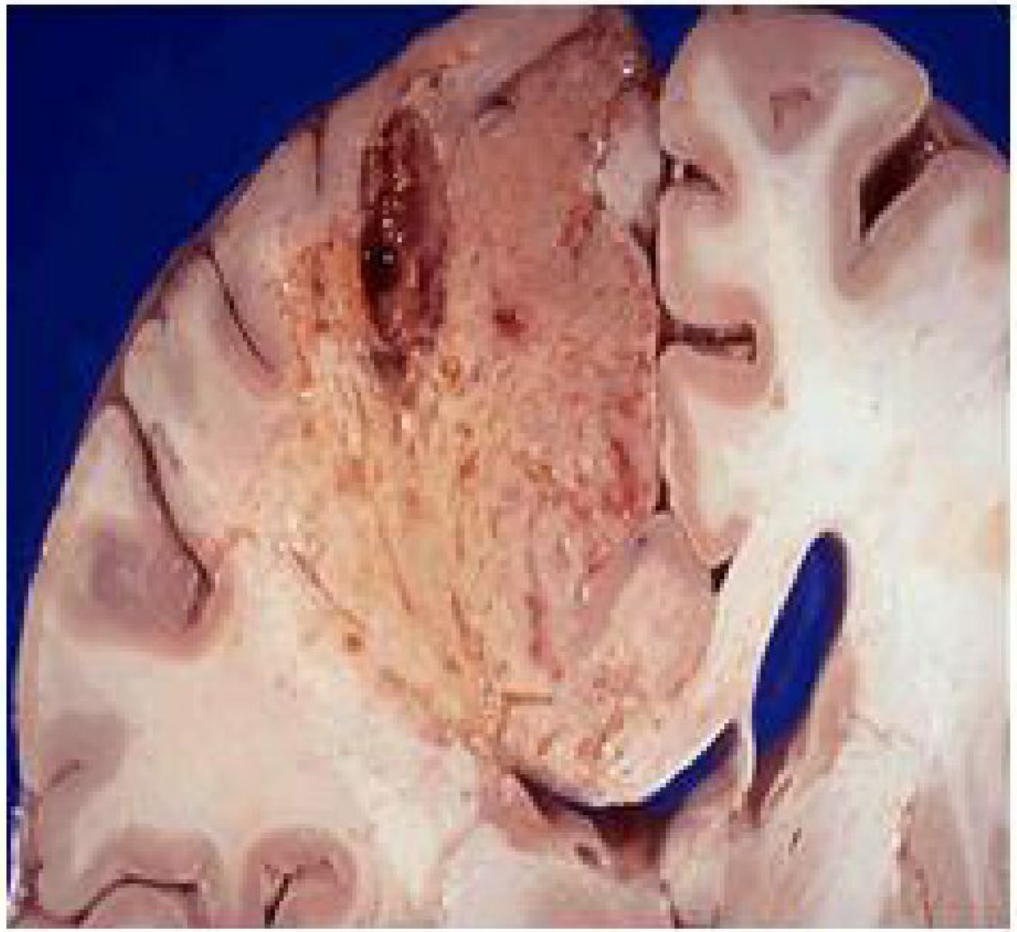
1. Coagulative necrosis: When there is marked cellular injury, there is cell death. This microscopic appearance of myocardium is a mess because so many cells have died that the tissue is not recognizable. Many nuclei have become pyknotic (shrunken and dark) and have then undergone karorrhexis (fragmentation) and karyolysis (dissolution). The cytoplasm and cell borders are not recognizable. Nuclei disappears, but cell appears normal . E.g. myocardial infarct

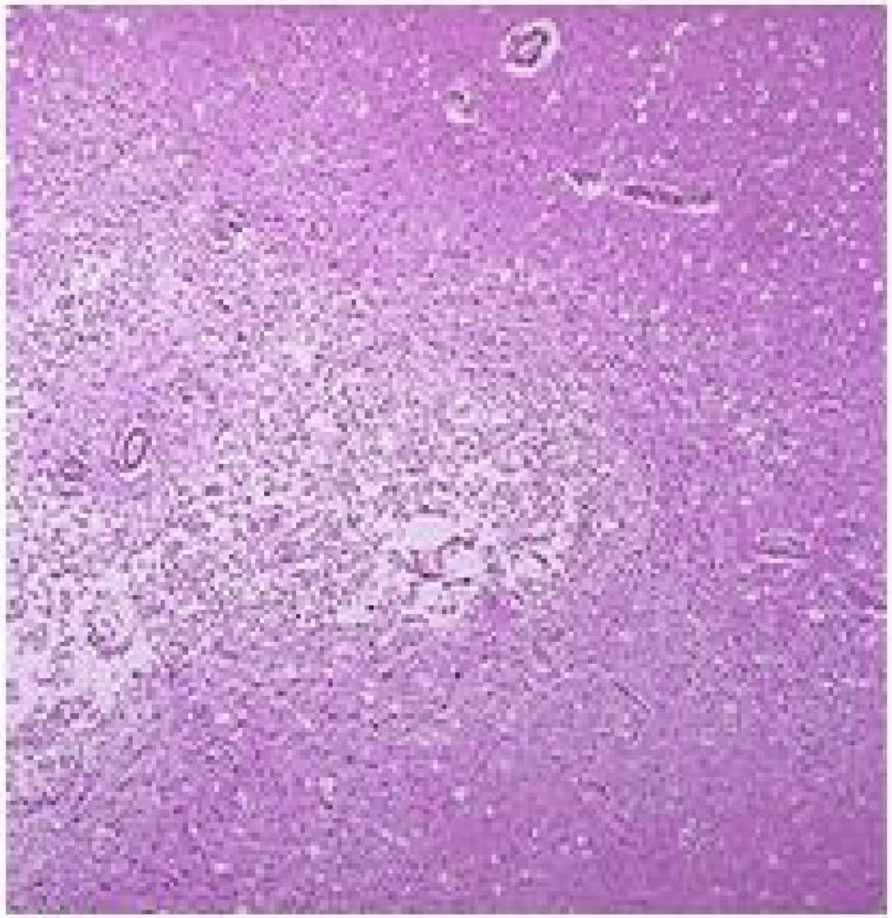


Myocardial infarct

2. Liquifactive Necrosis:

- **Suppurative infections** characterized by the formation of **pus** (liquefied tissue debris and neutrophils) in some focal **bacterial** or, occasionally, **fungal** infections (due to the action of inflammatory cells).
- unclear reasons, **hypoxic** death of cells within the **CNS** often evokes liquefactive necrosis.
- Liquefaction completely digests the dead cells. The end result is transformation of the tissue into a liquid viscous mass.
- **Enzymatic digestion** is predominant in this type of necrosis.
- In the liquefactive necrosis, there is **loss of both tissue architecture & cellular details**



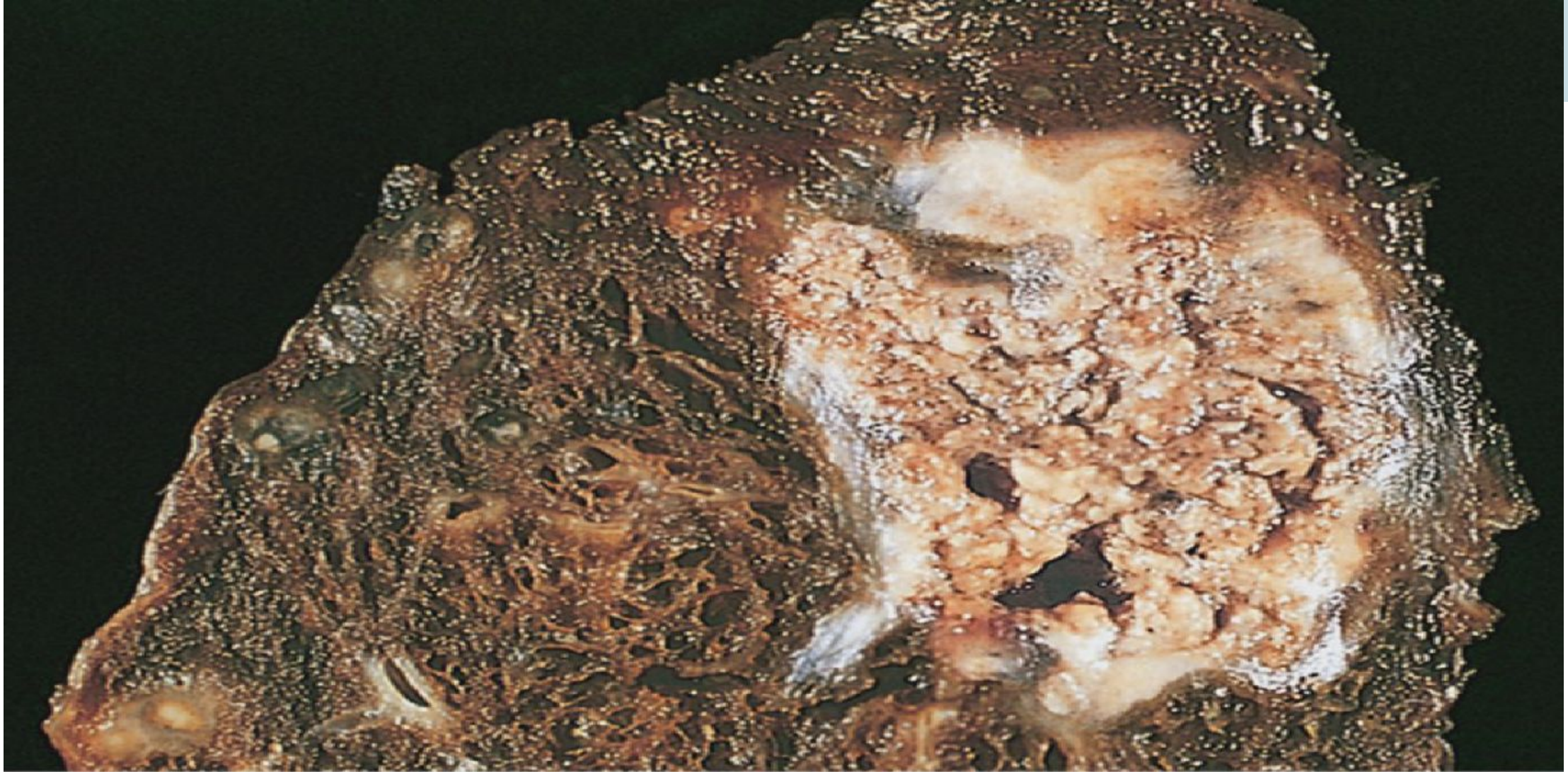


Liquefactive necrosis :-

3. Caseous necrosis: **“cheesy” necrosis** -normal cell structure gone but granular material remains , E.g. pulmonary TB specific form of coagulation necrosis typically caused by mycobacteria (e.g. tuberculosis).

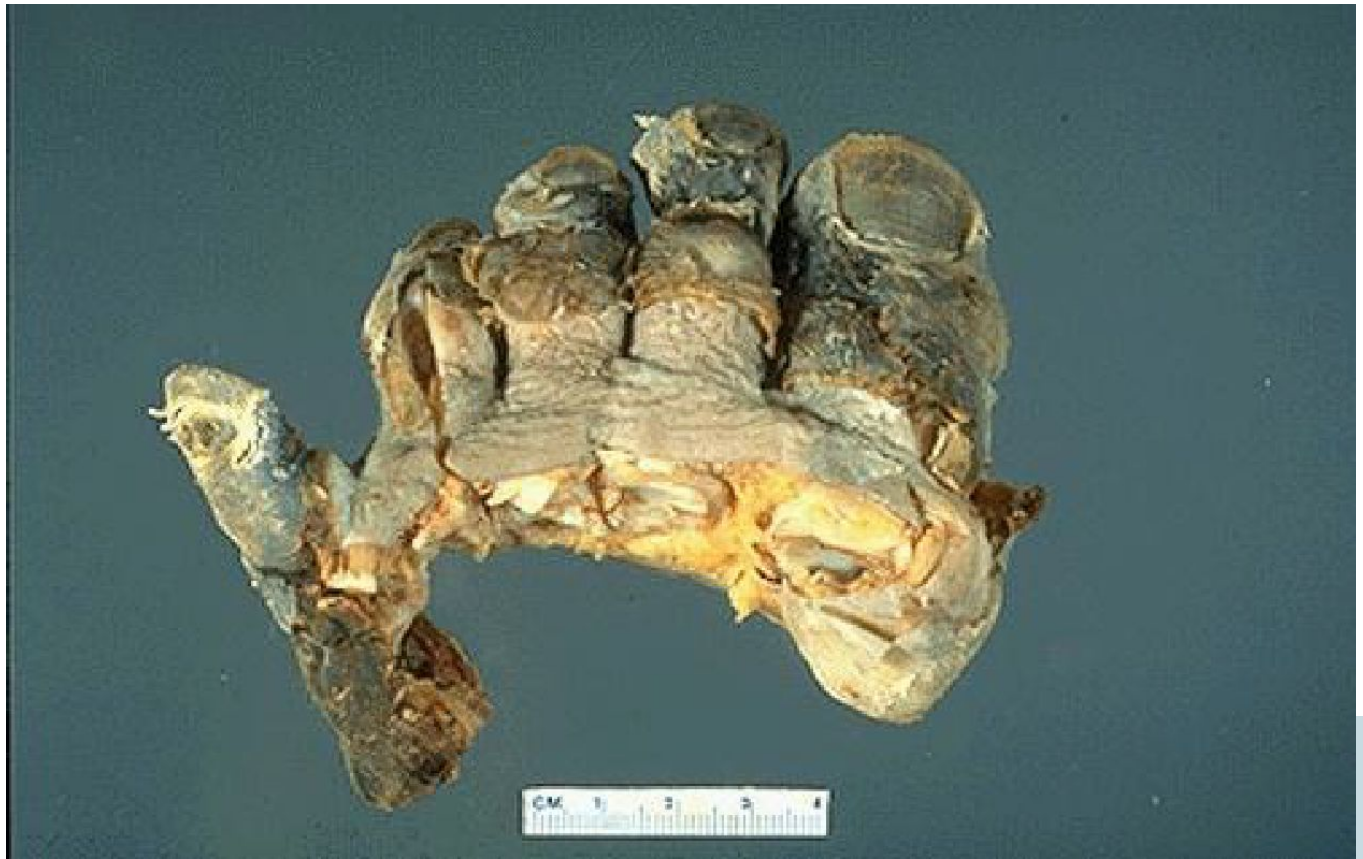
4. Fat Necrosis :- Lipids auto digested by lipases, E.g. acute pancreatitis

5. Hemorrhagic Necrosis: is due to blockage of the venous drainage of an organ or tissue (e.g. in testicular torsion).

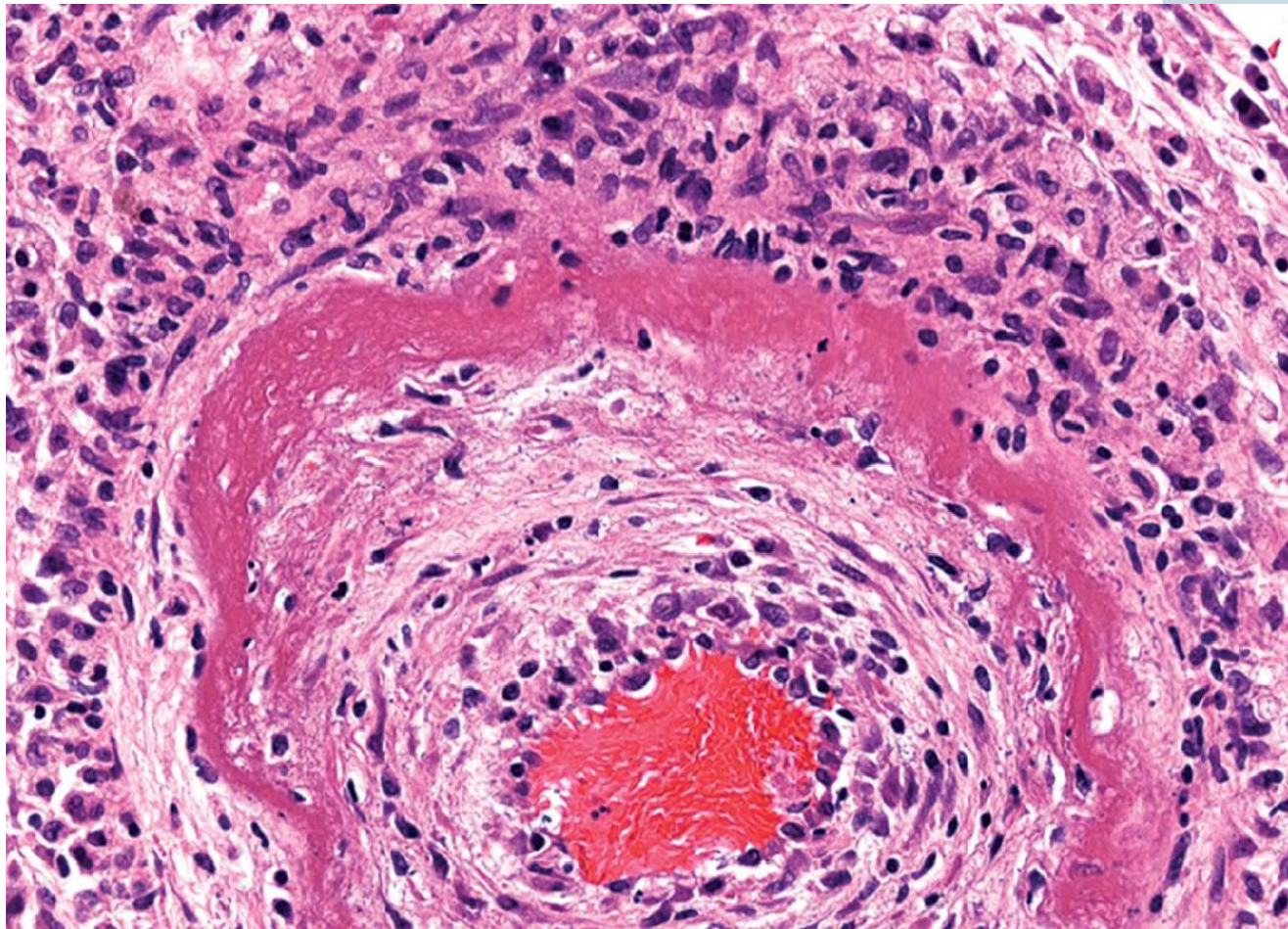


A tuberculous lung(Caseous necrosis) with a large area of caseous necrosis containing yellow-white and cheesy debris

6. Gangrenous Necrosis: Necrosis (secondary to ischemia) , usually with superimposed infection. Example: necrosis of distal limbs, usually foot and toes in diabetes. In this case, the toes were involved in a frostbite injury. This is an example of "dry" gangrene in which there is mainly coagulative necrosis from the anoxic injury



7. Fibrinoid necrosis: is caused by immune-mediated vascular damage. It is marked by deposition of fibrin-like proteinaceous material in arterial walls, which appears smudgy and eosinophilic on light microscopy.



fibrinoid necrosis of an artery in polyarteritis nodosa. the wall of the artery shows a circumferential bright pink area of necrosis with protein deposition and inflammation (dark nuclei of neutrophils)

References

1. Kumar, V., Abbas, A. K., & Aster, J. C. (2023). Robbins & Cotran Pathologic Basis of Disease (11th ed.). Elsevier.

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3. New England Journal of Medicine. (2022). Cellular Responses to Stress and Toxic Insults.

Any questions?