CELL INJURY

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Introduction to pathology

By end of this session; you should be able to:

- Define cell injury and identify its etiology
- Identify main types of cell injury with examples.
- Mention etiology, mechanism and describe morphology and fate of fatty change of liver.
- Identify types and pathological changes of necrosis
- Define apoptosis and identify its types
- Describe differences between necrosis and apoptosis

Cell injury

- ***Definition:*** Cell injury is damage of the cells due to exposure to insult (injurious agents)

- ***Causes***:

1. Hypoxia: the main cause of cell injury is decrease oxygen supply to the cells.
2. Infectious agents: Bacteria, viruses, rickettsia, fungi and parasites.
3. Physical agents: Trauma, heat, cold and radiation.
4. Chemical agents: Acids, alkalies and poisons
5. Immunologic reactions as allergy
6. Nutritional deficiencies.
7. Genetic defects

Cell injury

Effect of cell injury:

Based on **type of injured cells**, **nature of injurious agents** and **severity of injurious agents**; cell injury is classified **into two main types**:

CELL INJURY

- **Reversible (Degeneration)**
- **Irreversible (Cell death)**

Cell injury

Reversible (Degeneration)

Induced by: mild injury or injury of short duration with no damage of nucleus.

Affects: commonly active cells with high rate of metabolism.

Examples:

1. Cell swelling (cloudy and hydropic swelling).
2. Fatty change.

Irreversible (Cell death)

Induced by: severe injury or injury of long duration results in damage of nucleus

Affects: commonly active cells with high rate of metabolism.

Examples:

1. Necrosis
2. Apoptosis

Cell injury

Reversible cell injury (Degeneration)

1. Cell swelling (cloudy and hydropic swelling)
2. Fatty change

Cell injury

Fatty change:

- ***Definition:*** intracellular accumulation of neutral fat within parenchymal cells
- ***Sites***: Mainly affect liver and less commonly involve cardiac muscle and kidney.
- ***Fatty liver***:
  - **Etiology:** Fatty change of liver occurs through two main pathways:
    1. Excess fat transport to liver that exceed capacity of the liver to metabolise fat.
    2. Liver cell damage; so hepatocytes can`t metabolise fat

Cell injury

Fatty change:

- ***Fatty liver:***
  - **Etiology:**
    1. Excess fat transport to liver: occurs in cases of obesity, diabetes mellitus and congenital hyperlipidaemia

    2. Liver cell damage; so hepatocytes can`t metabolise fat: occurs in
       - Chronic hepatitis (common in Egypt)
       - Alcoholic liver disease (most common in Western societies)
       - Drug-induced liver cell injury: long standing administration of methotrexate, steroids and other drugs

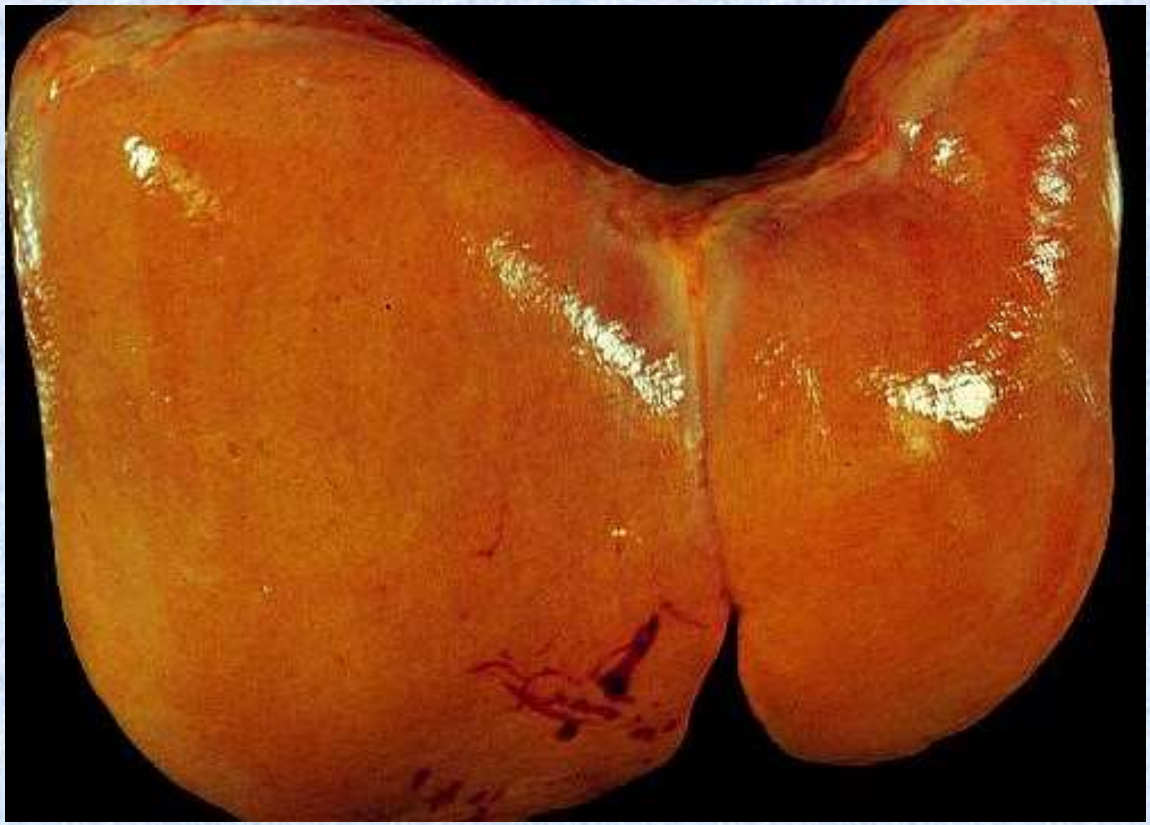
Cell injury

Fatty change:

- ***Fatty liver:***
  - **Morphology:**

***Grossly*: The liver has**

- Larger size
- Rounded borders
- Soft consistency.
- Pulging cut surface
- Pale-yellow color.



Cell injury

Fatty change:

- ***Fatty liver:***
  - **Morphology:**

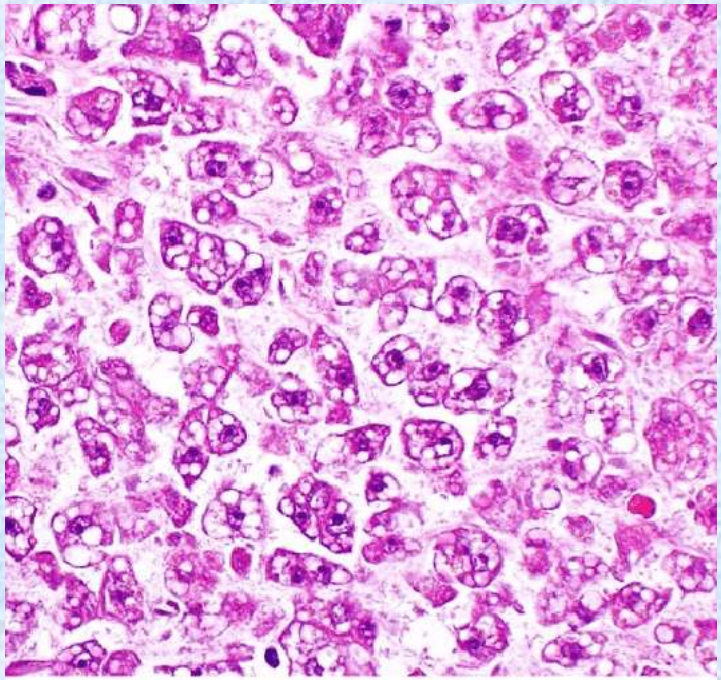
    Microscopically:
    - A characteristic feature is presence of numerous lipid vacuoles in the cytoplasm
    - Firstly; the vacuoles are small (micro-vesicular).
    - With disease progression, the vacuoles become larger pushing nucleus to periphery of the cells (macro-vesicular).
  - **Fate:** Usually regress after removal of causative factor but may lead chronic hepatitis in long standing cases

Cell injury

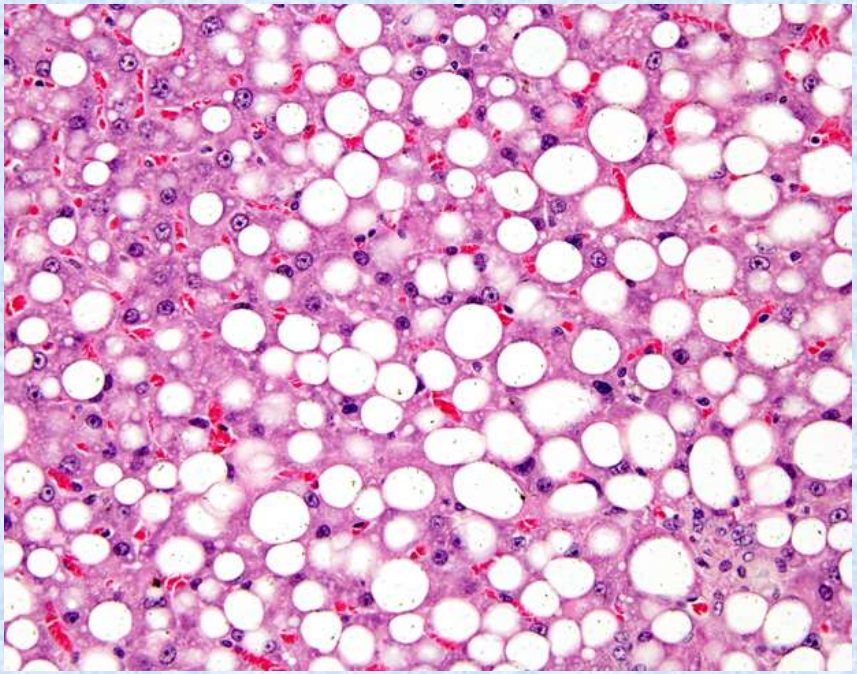
Fatty change:

- ***Fatty liver*:**
  - **Morphology:**

    ***Microscopically*:**



Micro-vesicular fat vacuoles



Macro-vesicular fat vacuoles

Cell injury

Irreversible cell injury (Cell death)

1. Necrosis
2. Apoptosis

Cell injury

Necrosis

- Definition
- Main features
- Morphology (gross and microscopic changes)
- Types and examples

Cell injury

Necrosis

- ***Definition:*** Local death of large number of adjacent cells or tissue within living body.

- ***Main pathogenic features:***
  - Loss of membrane integrity
  - Damage of the nucleus
  - Destruction of organelles especially lysosomes
  - Release of lysosomal enzymes from injured cells.
  - Local inflammation around necrosis.

Cell injury

Necrosis

❑ ***Morphology*:**

Grossly:

- Necrotic tissue appears opaque and pale white or yellow in color.
- The surrounding tissue appears red due to inflammatory hyperemia.

Cell injury

Necrosis

❑ ***Morphology*:**

Microscopic: Cytoplasmic and nuclear changes

Cytoplasmic changes

- **Cell swelling**
- **Loss of cell membrane**

Nuclear changes

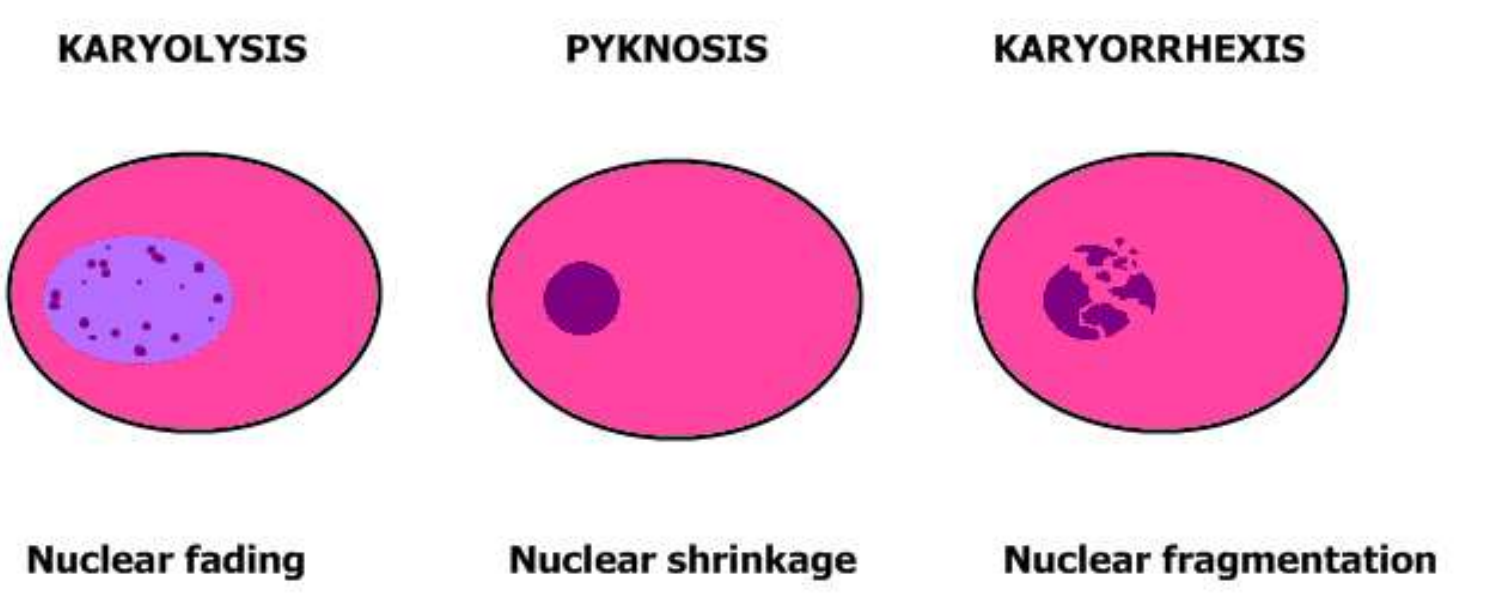
- **Pyknosis**: The nucleus shrinks and has dense and dark stain.
- **Karyorrhxis**: The nucleus breaks down into multiple small fragments.
- **Karyolysis**: The nucleus dissolves.

Cell injury

Necrosis

❑ ***Morphology*:**

Microscopic: Cytoplasmic and nuclear changes



Cell injury

Necrosis

- ***Types of necrosis*:**

1. **Coagulative necrosis**
2. **Liquifactive necrosis**
3. **Caseation necrosis**
4. **Fat necrosis**

Cell injury

Necrosis

1. ***Coagulative necrosis*:**

Main features:

- A type of necrosis in which necrotic area appear firm and opaque white.
- It is the most common type of necrosis
- Commonly affected organs are: heart, kidney and spleen
- Caused mainly by sudden cut of blood supply

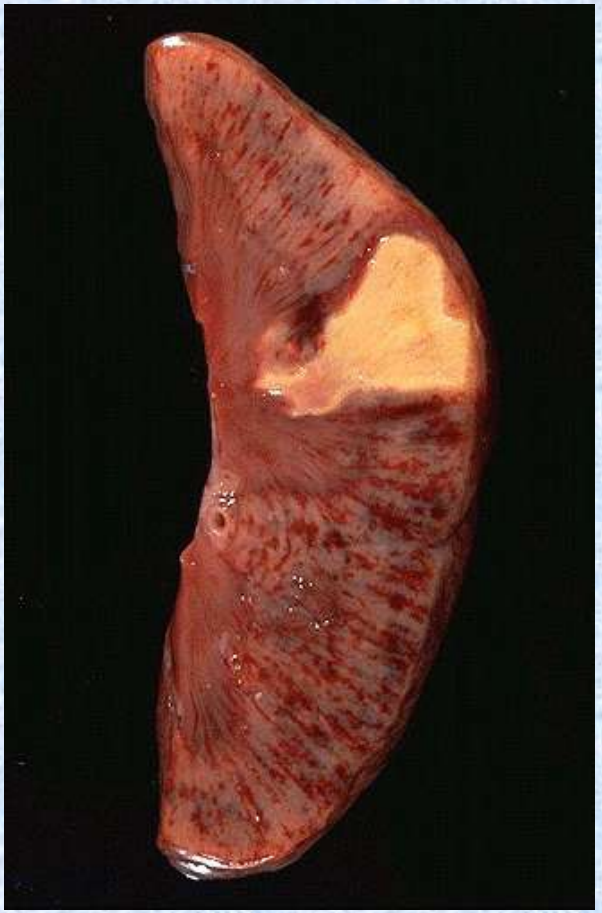
Cell injury

Necrosis

1. ***Coagulative necrosis*:**

Gross

- Early stage: necrotic area is pale, opaque, and slightly swollen.
- Late stage; the affected area becomes yellowish, soft, and shrunken.



Cell injury

Necrosis

2. ***Liquifactive necrosis*:**

Main features:

- A type of necrosis in which the necrotic area liquefies rapidly.
- It is a common type of necrosis
- Commonly affected organs are:

a. Infarction of brain and spinal cord: liquefaction is due to high fluid contents.

b. Pyogenic abscess

c. Amebic abscess

Cell injury

Necrosis

3. ***Caseation necrosis*:**

Main features:

- A type of necrosis in which the necrotic area showed partial liquefaction
- The necrotic tissue has a caseation or cheese-like appearance.
- It is a common type of necrosis
- Commonly occurs in tuberculosis

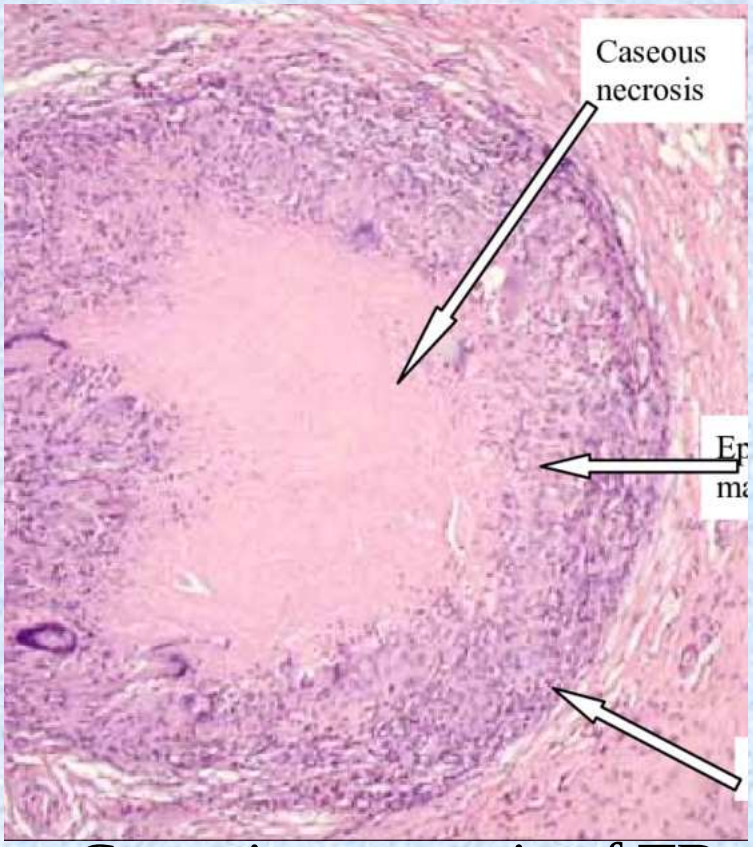
Cell injury

Necrosis

3. *Caseation necrosis*:

Gross

- Necrotic tissue appears dry, pale yellow and resembles creamy cheese or casein.



Caseation necrosis of TB

Cell injury

Necrosis

4. ***Fat necrosis*:**

<u>Two main types:</u>

- ***Enzymatic fat necrosis:*** occurs in pancreatitis. The pancreatic enzyme lipase escapes from ruptured pancreatic ducts and leads to liquefaction of omental and mesenteric fat.

- ***Traumatic fat necrosis:*** occurs as a result of trauma to the fatty tissue of breast and subcutaneous fat.

Cell injury

Necrosis

❑ ***Fate of necrosis***

1. ***Small area of necrosis:***
   - The necrotic tissue is removed by macrophages.

2. ***Large areas of necrosis***
   - The necrotic tissue is surrounded by a fibrous capsule.
   - They may show dystrophic calcification later on.

Cell injury

Apoptosis

- Definition
- Morphology (gross and microscopic changes)
- Examples
- Apoptosis versus necrosis

Cell injury

Apoptosis

- ***Definition:*** A programmed cell death affecting one cell or small group of cells.
- ***Morphology***

Gross

NO change

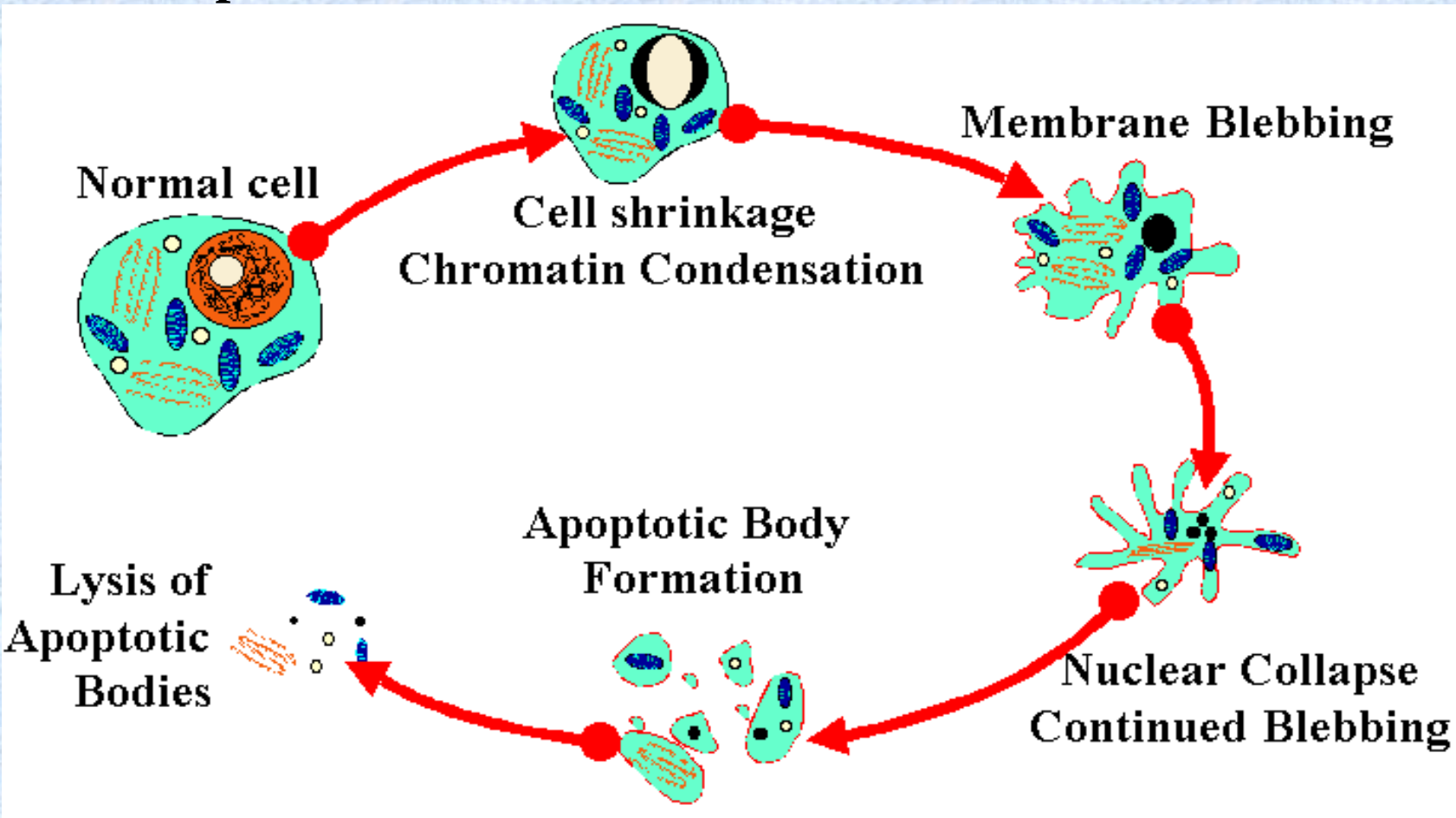
Microscopic

- Shrinkage of the cell.
- Loss of nuclear membrane
- Fragmentation of cell to form apoptotic bodies.
- Phagocytosis of apoptotic bodies by macrophages
- NO inflammation in surrounding tissues.

Cell injury

Apoptosis

- **Microscopic**:



Cell injury

Apoptosis

- *Examples of apoptosis.*

NOTE

Apoptosis:

- ***IS*** *an energy-dependent programmed cell death*
- ***FOR*** *removal of unwanted individual cells.*
- ***SO*** *occurs in both physiological and pathological conditions.*

Cell injury

Apoptosis

❑ ***Examples of apoptosis***.

Physiological apoptosis (apoptosis in normal tissue)

- In normal cell turnover: new cells replace aging (senescent) cells.
- Programmed cell destruction during embryonic development as shrinkage of thymus gland in adult life
- Endocrine dependent apoptosis:
  a. Monthly shedding of endometrium during the menstrual cycle.
  b. Regression of breast after weaning.
  c. Regression of breast size after menopause.
  d. Regression of size of uterus after menopause.

Cell injury

Apoptosis

- ***Examples of apoptosis***.

Apoptosis in pathological conditions (due to diseases)

a. Viral infection: as chronic hepatitis
b. Exposure to irradiation (radiation cell injury).
c. Drugs: as chemotherapy in cancer treatment
d. In degenerative disease: as Alzheimer's disease

Cell injury

	Apoptosis	Necrosis
• **Induction**	• Physiological and pathological.	• Only pathological (Hypoxia, toxins & chemical agents)
Cells affected	Single cell or small group of cells	• Large group or part of an organ.
• **Nuclei**	• Condensation and fragmentation of chromatin.	• Pyknosis, karyorrhexis and karyolysis.
• **Cytoplasm**	• Shrinkage of cells.	• Cytomegaly (cell swelling).
• **Cell membrane**	• Maintained.	• Lost
• **Tissue reaction**	• No inflammation.	• NO inflammation in surrounding tissue.
• **Fate of dead cells**	• Ingested (phagocytosed) by macrophages.	• Small lesions: phagocytosed by PML and macrophages and large lesions heal by fibrosis

Cell injury

❑ **Homework:**

- *Mention causes of cell injury.*
- *Mention etiology of causes of fatty liver.*
- *Mention types of necrosis.*
- *Give examples for physiological and pathological apoptosis.*
- *Compare between apoptosis and necrosis.*

Cell injury

GOOD LUCK