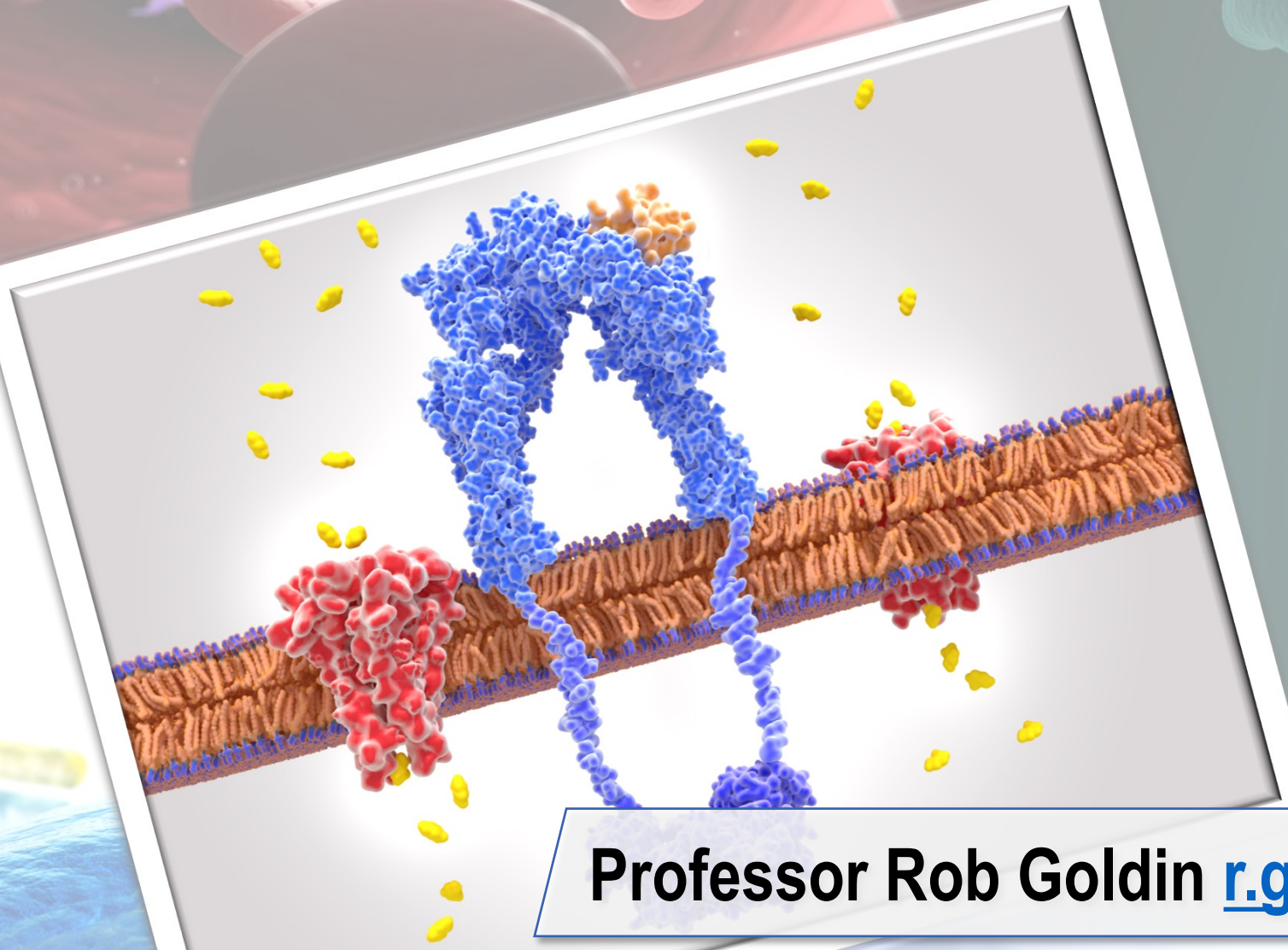
IMPERIAL

Cell injury and fate



Professor Rob Goldin r.goldin@imperial.ac.uk

Session Plan

Part 1

- List the causes of cell injury.
- List the mechanisms of cell injury.
- To be able to distinguish lethal and sublethal injury

Part 2

- Define (and give examples of) hyperplasia, hypertrophy, atrophy, metaplasia and dysplasia.
- List the morphological changes associated with reversible and irreversible injury.
- Compare apoptosis and necrosis.

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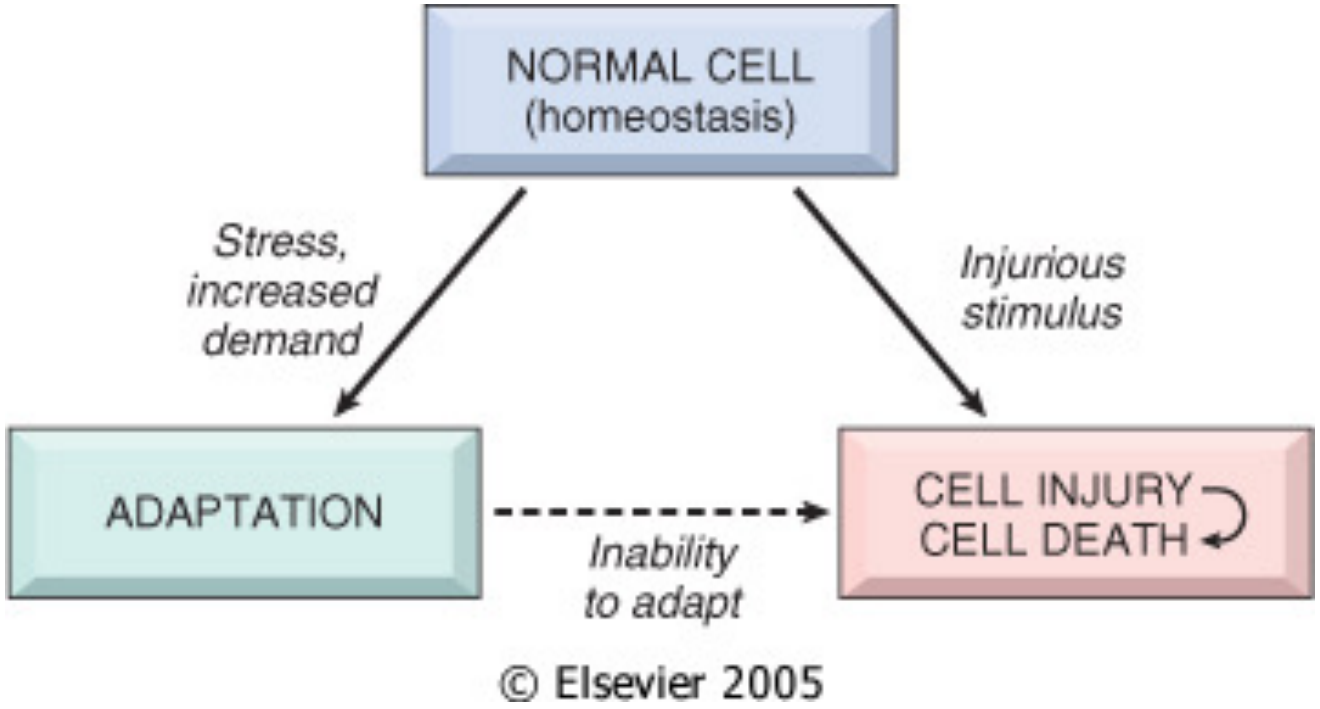


POM-1-5: Cell injury: List the causes and mechanisms of cell injury, recall the morphological changes associated with reversible and irreversible injury and explain how cell injury generates useful biomarkers of disease.

Cell injury

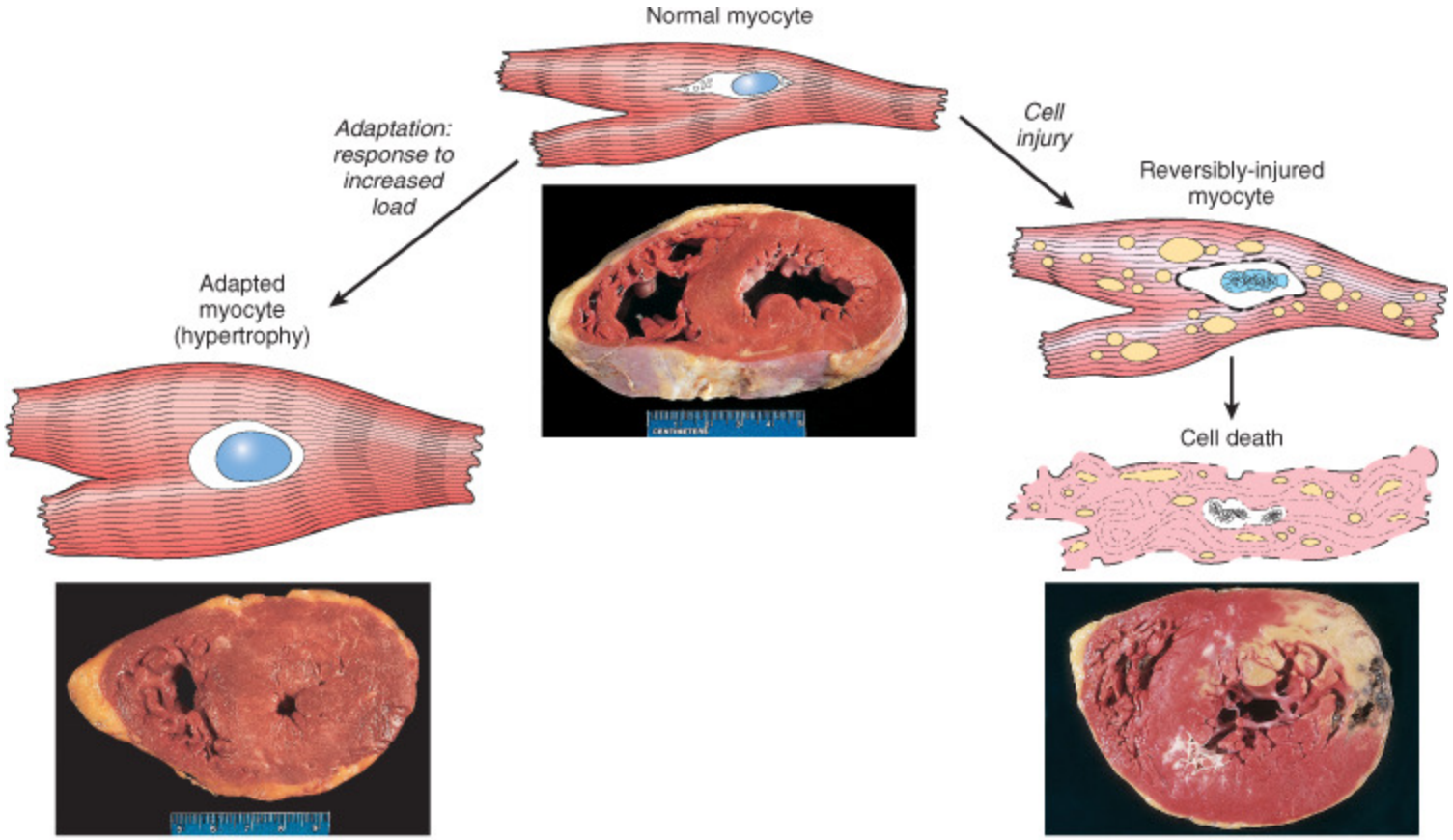
- **Lethal*:***

produces cell death

- **Sublethal:**

produces injury not amounting to cell death

may be reversible or progress to cell death



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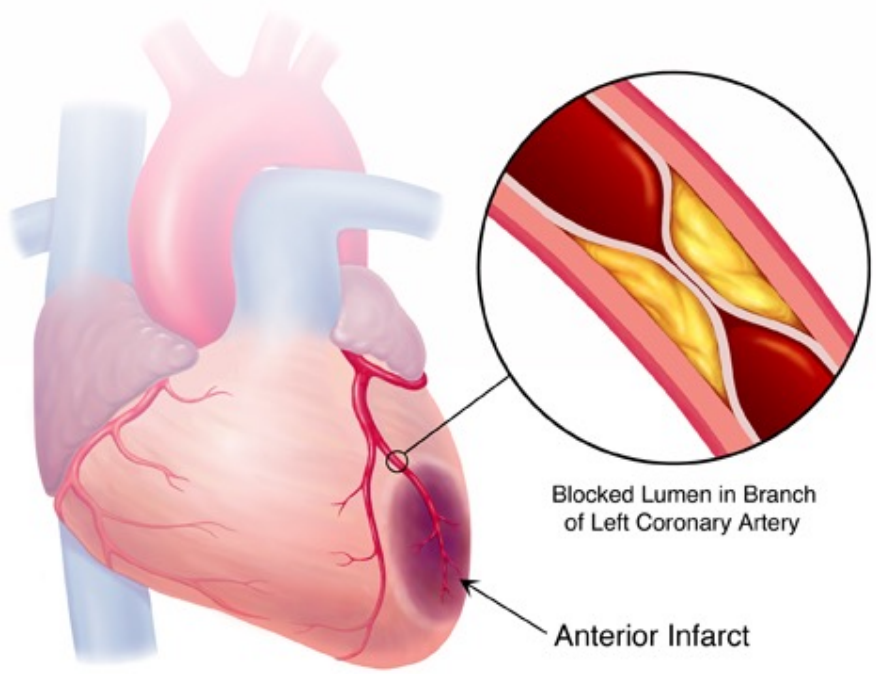
Causes of Cell Injury

1. Oxygen deprivation
2. Chemical agents
3. Infectious agents
4. Immunological reactions
5. Genetic defects
6. Nutritional imbalances
7. Physical agents
8. Aging

POM-1-5: Cell injury: List the causes and mechanisms of cell injury, recall the morphological changes associated with reversible and irreversible injury and explain how cell injury generates useful biomarkers of disease.

Oxygen deprivation: Myocardial infarction



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Mechanisms of Cell Injury

The cellular response to injurious stimuli depends on:

1. the type of injury,
2. its duration and
3. its severity

Mechanisms of Cell Injury

- The consequences of an injurious stimulus depend:

1. on the type of cell and

2. its status

Mechanisms of Cell Injury

- Four intracellular systems are particularly vulnerable:

1. cell membrane integrity,
2. ATP generation,
3. protein synthesis and
4. the integrity of the genetic apparatus

Mechanisms of Cell Injury

- The structural and biochemical components of a cell are so integrally related that multiple secondary effects rapidly occur.
- Cellular function is lost before cell death occurs which in turn occurs before the morphological changes are seen.

Progress check

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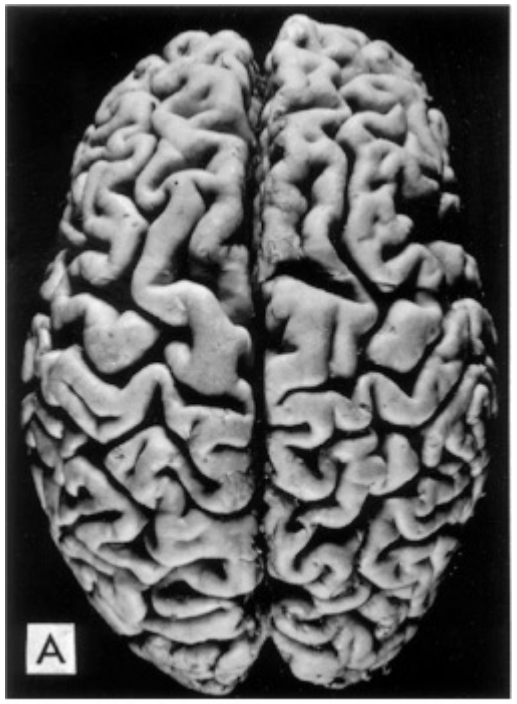
Cellular Adaptation to Injury: Atrophy

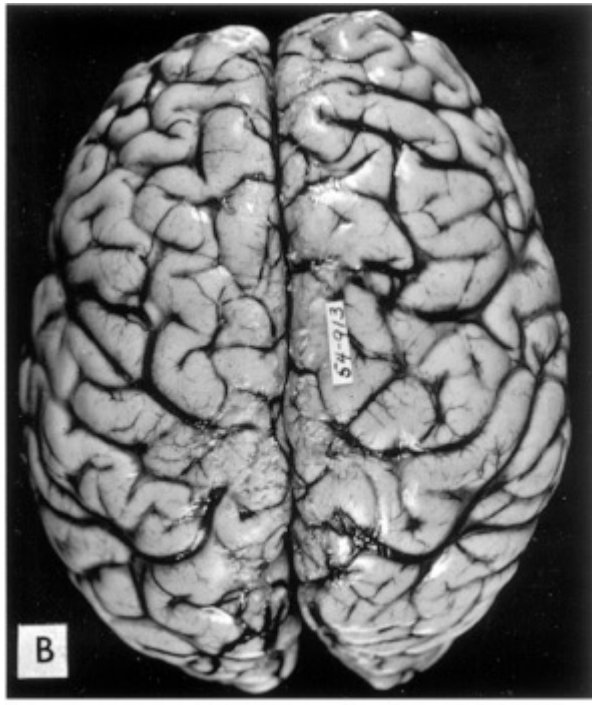
- Shrinkage in the size of the cell (or organ) by the loss of cell substance.

Dementia

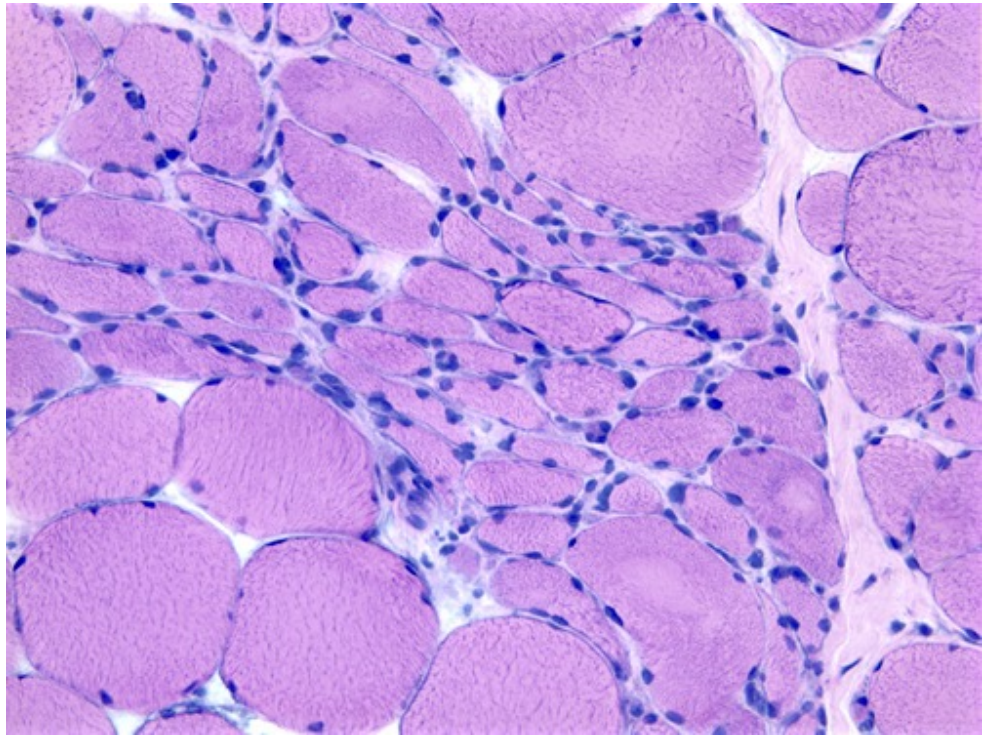
Atrophic brain



Normal brain



Muscle atrophy secondary to denervation



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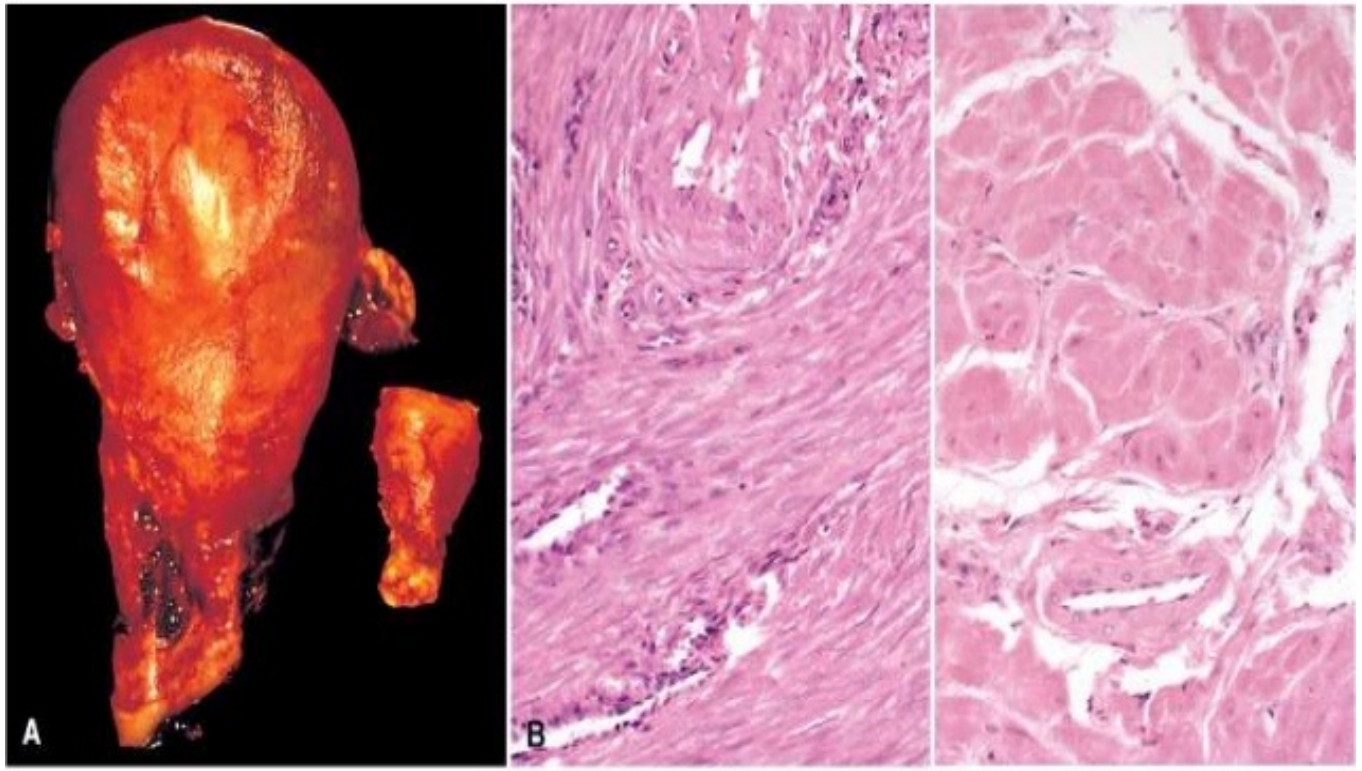
Cellular Adaptation to Injury: Hypertrophy

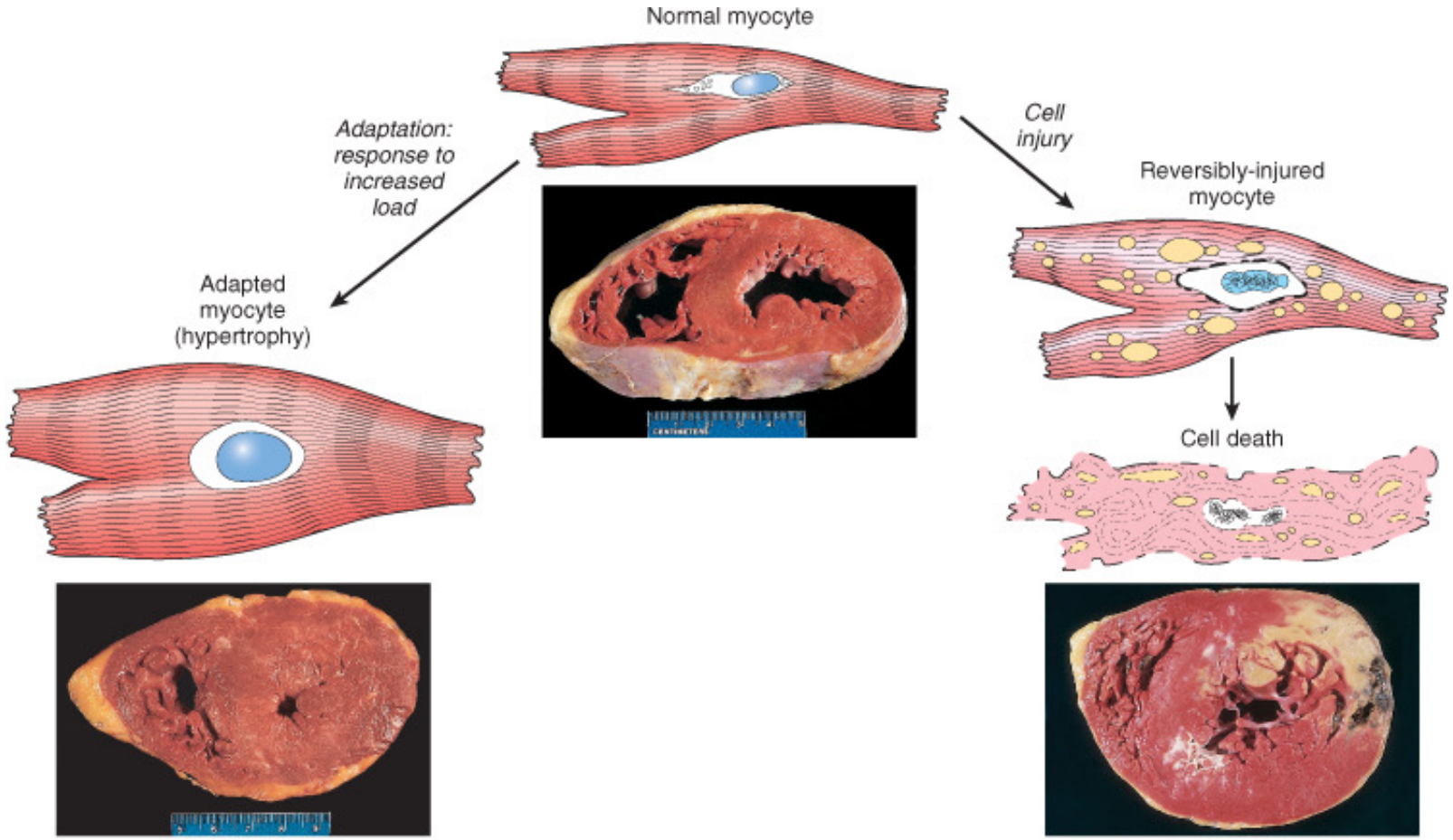
- Increase in the size of cells and consequently an increase in the size of the organ.
- Can be physiological or pathological.
- It is caused either by increased functional demand or specific hormonal stimulation.

Physiological Hypertrophy



Physiologic hypertrophy of the uterus during pregnancy. *A*, Gross appearance of a normal uterus *(right)* and a gravid uterus *(left)*. *B*, Small spindle-shaped uterine smooth muscle cells from a normal uterus *(left)* compared with large plump cells in gravid uterus *(right)*.

Pathological Hypertrophy



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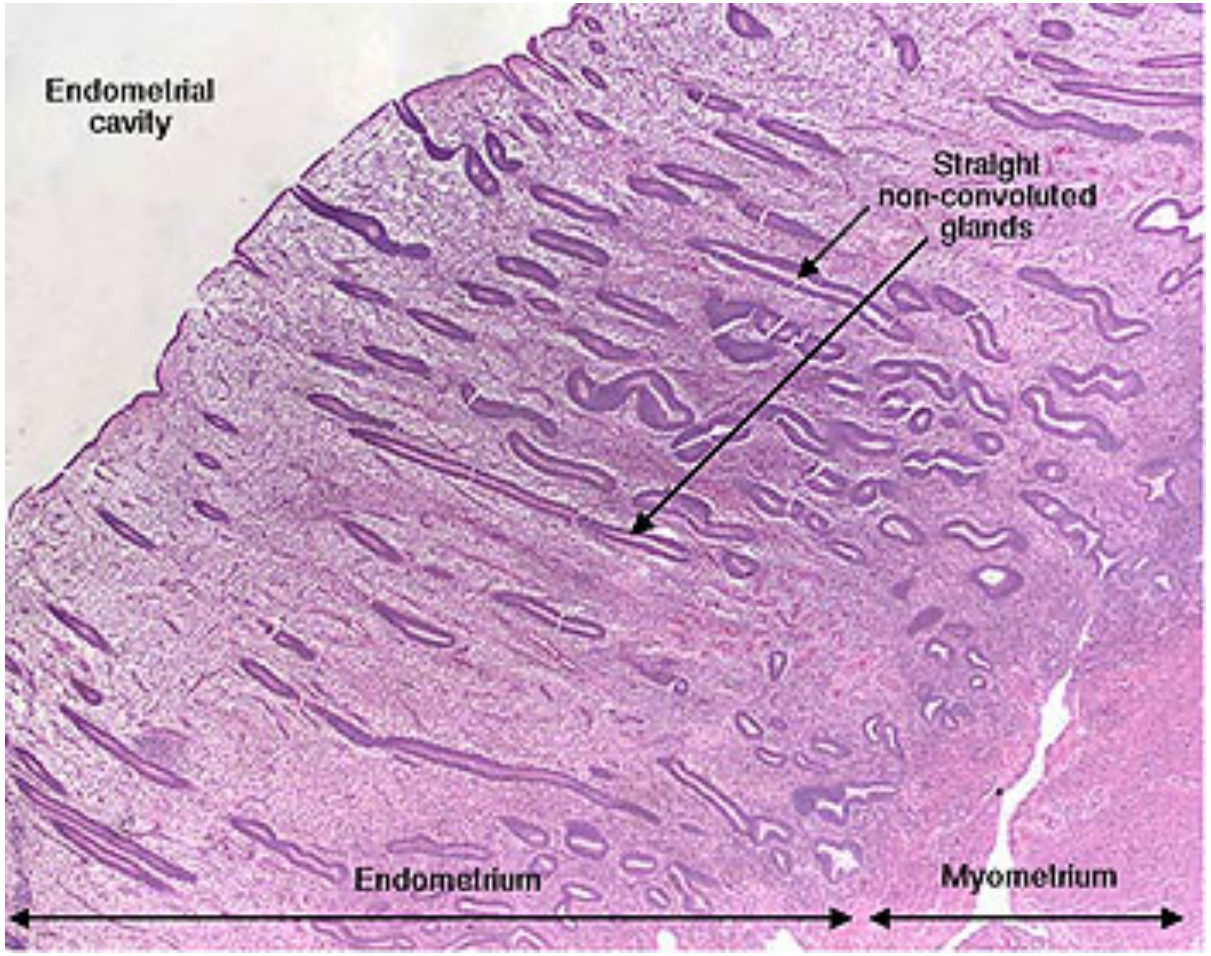
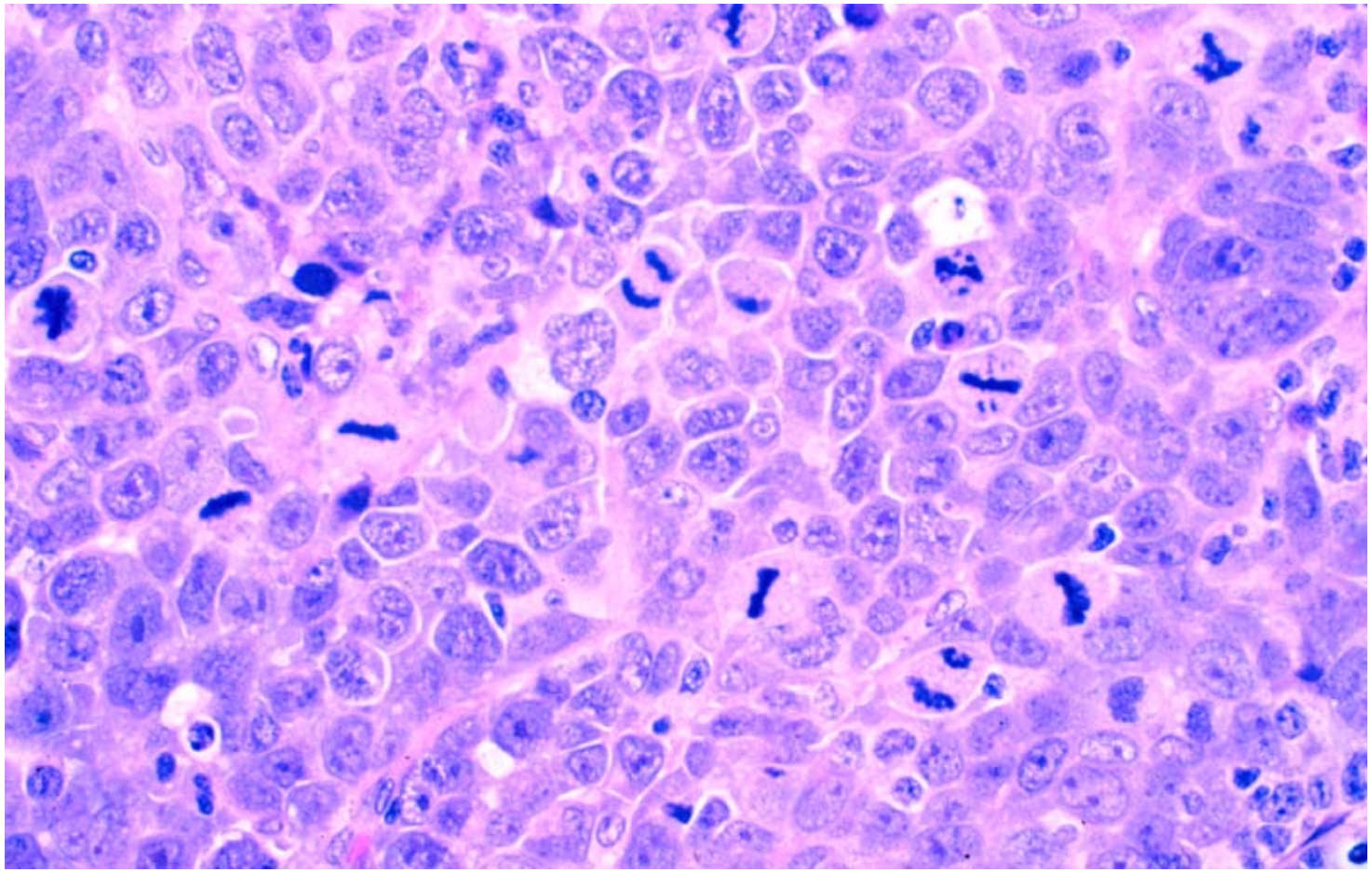
Cellular Adaptation to Injury: Hyperplasia

- An increase in the number of cells in an organ.
- Can be physiological or pathological.
- Physiological hyperplasia can be either hormonal or compensatory.
- Pathological hyperplasia is usually due to excessive hormonal or growth factor stimulation.

Physiological Hyperplasia: Proliferative Endometrium



Pathological Hyperplasia: Carcinoma



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Cellular Adaptation to Injury: Metaplasia

- A **reversible** change in which one adult cell type is replaced by another
- May be physiological / pathological

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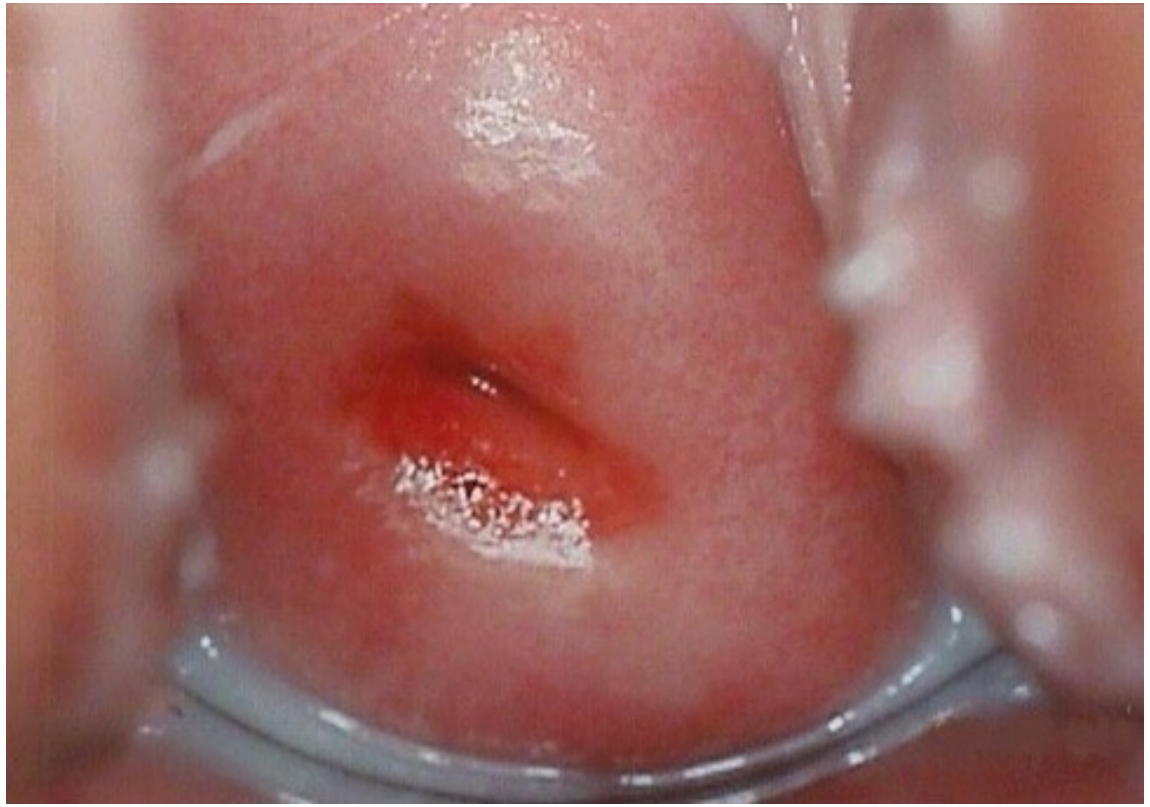
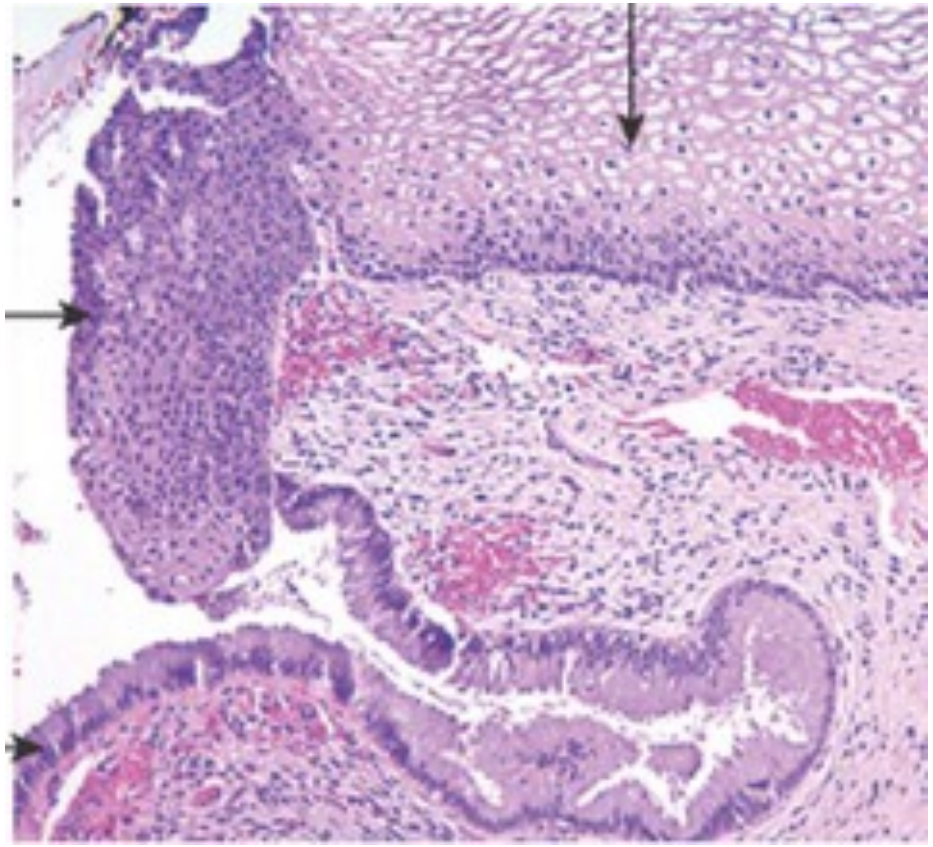
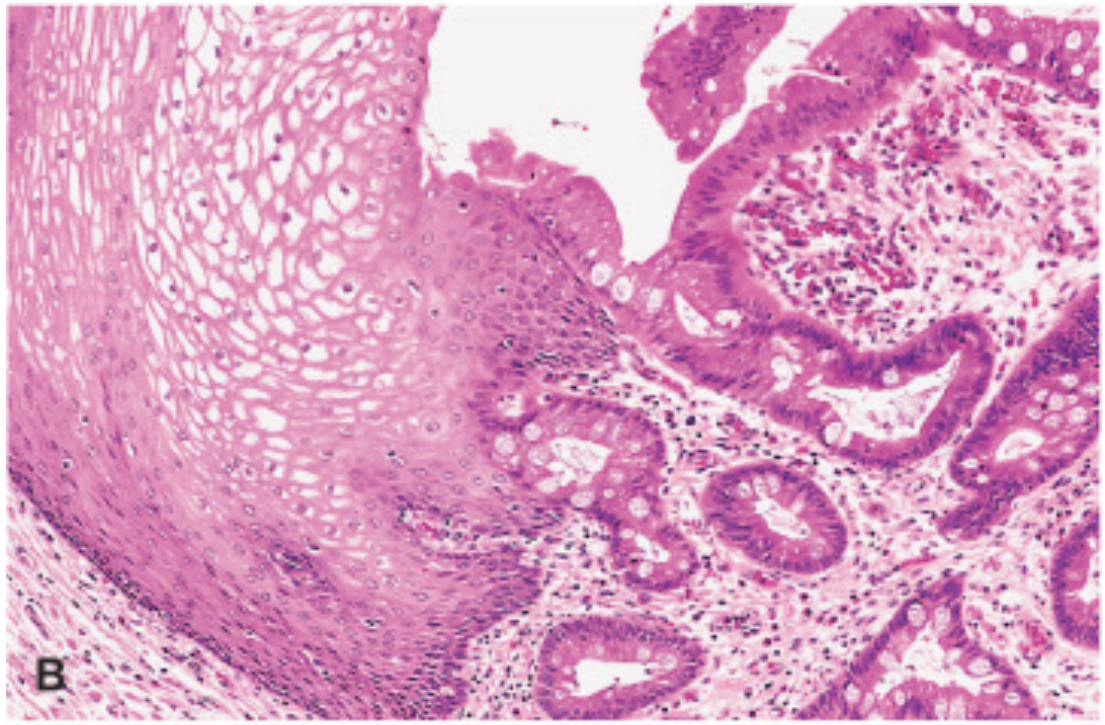
Physiological metaplasia: Cervix

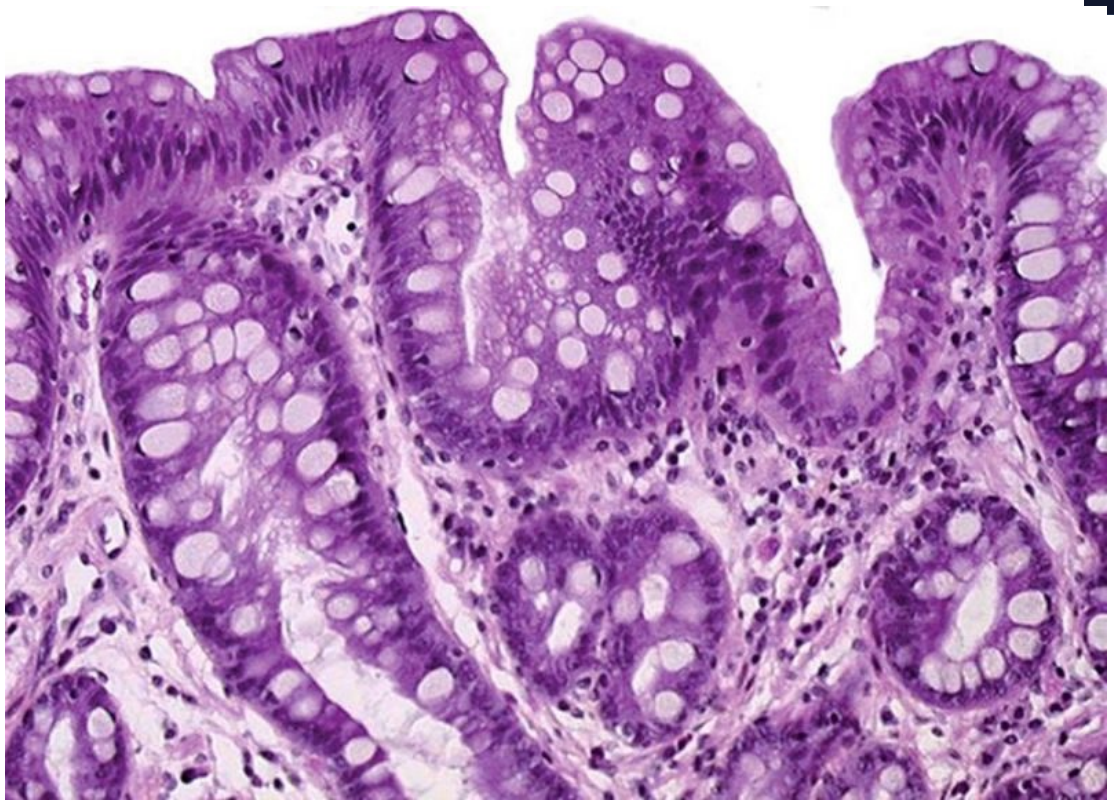




POM-1-6: Cell fate: Define and recall examples of hyperplasia, hypertrophy, atrophy, metaplasia and dysplasia; define and compare apoptosis and necrosis.

Barrett's (Columnar lined) Oesophagus



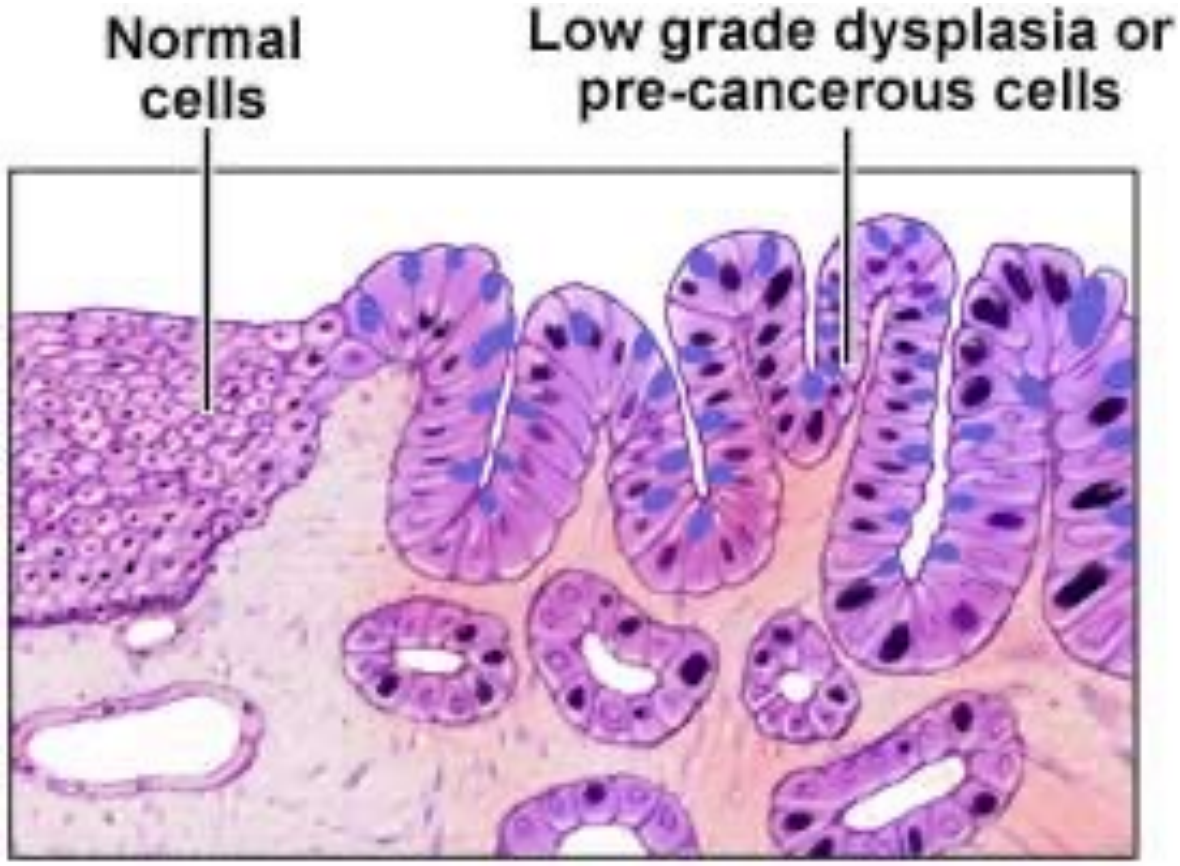


POM-1-6: Cell fate: Define and recall examples of hyperplasia, hypertrophy, atrophy, metaplasia and dysplasia; define and compare apoptosis and necrosis.

Dysplasia

- Precancerous cells which show the genetic and cytological features or malignancy but not invading the underlying tissue

Dysplasia



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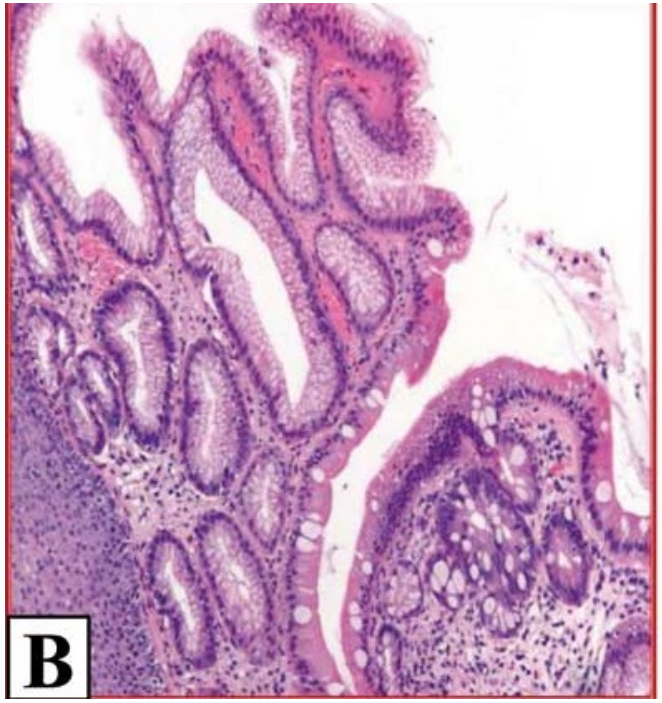
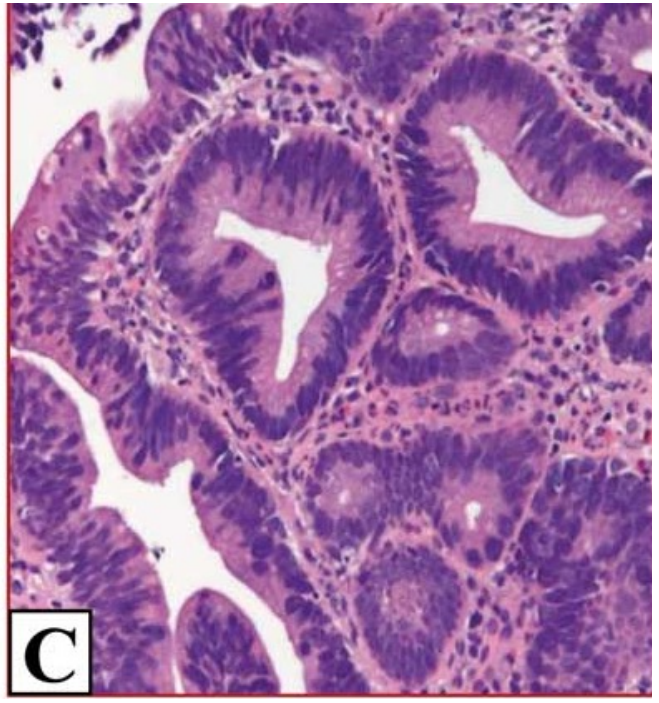
Dysplasia associated with Barrett's oesophagus



B. Metaplasia



C. Dysplasia

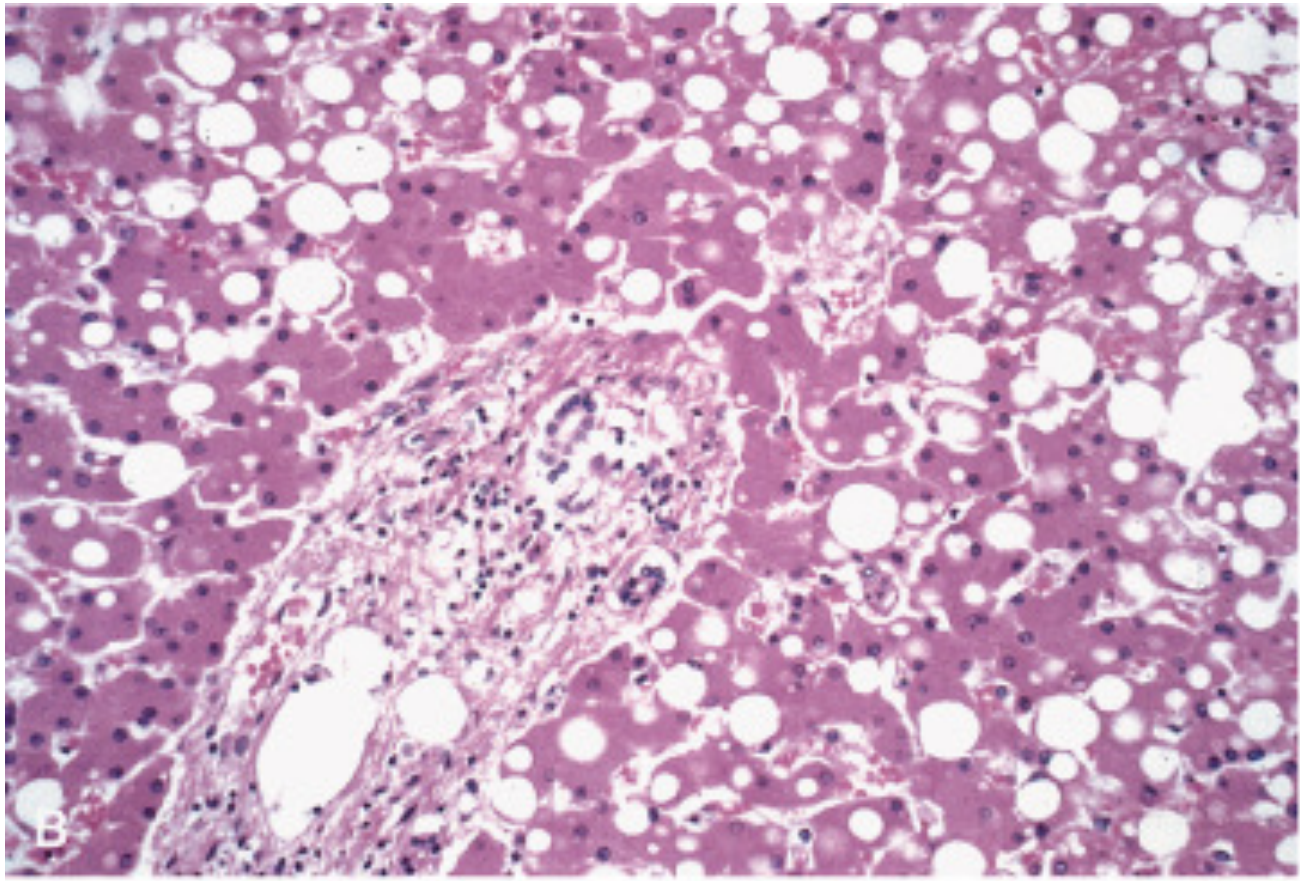
The Light Microscopic Changes Associated with Reversible Injury

- Fatty change
- Cellular swelling

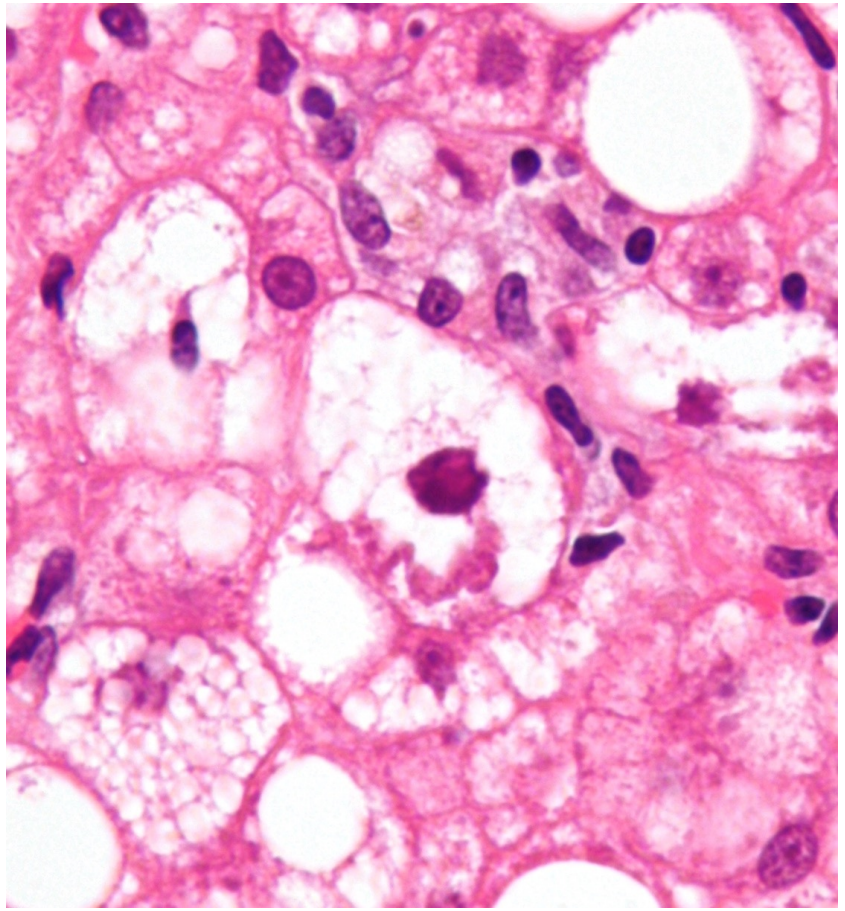
These are examples of degenerative changes

i.e. changes associated with cell and tissue damage.

Alcoholic fatty change



Ballooning degeneration



Necrosis

- Confluent cell death associated with inflammation

The Light Microscopic Changes Associated with Irreversible Injury

1. Coagulative necrosis
2. Liquefactive necrosis
3. Caseous necrosis
4. Fat Necrosis

The Light Microscopic Changes Associated with Irreversible Injury

1. **Coagulative necrosis**
2. Liquefactive necrosis
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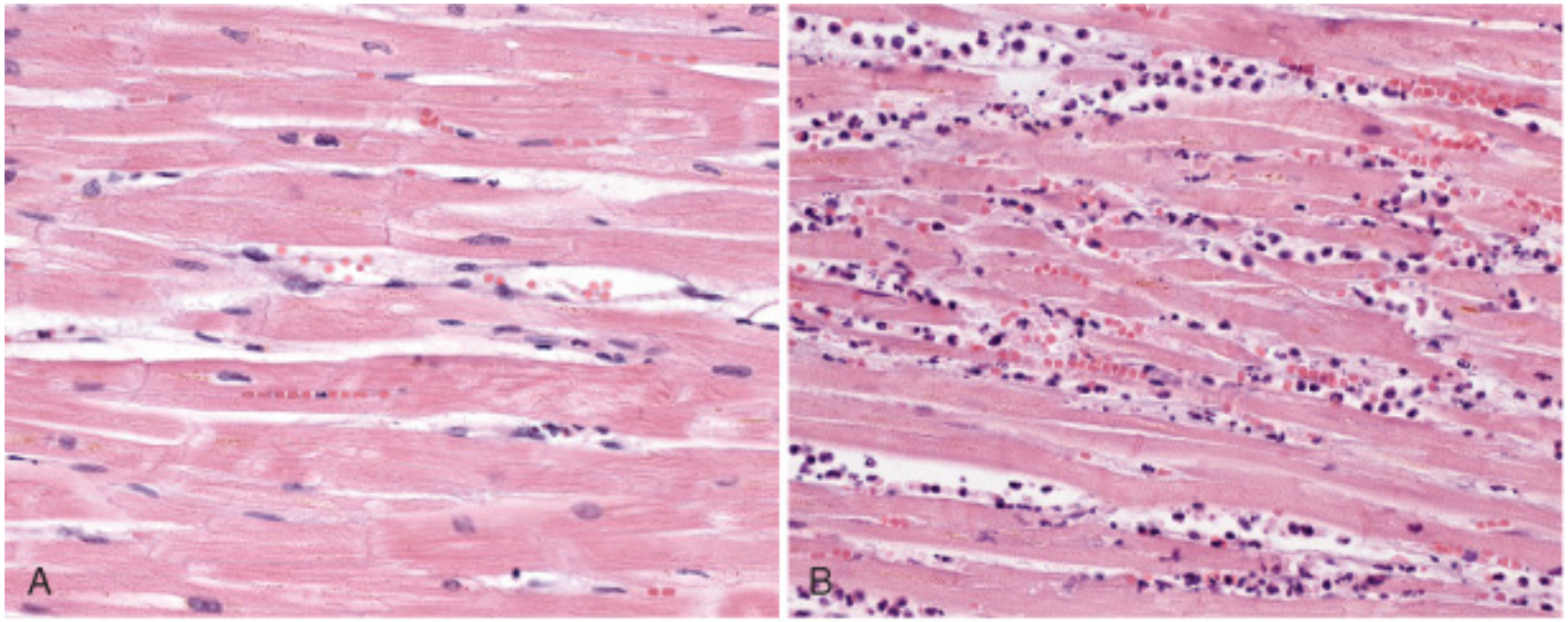
Myocardial infarct



The Light Microscopic Changes Associated with Irreversible Injury

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2. **Liquefactive necrosis**
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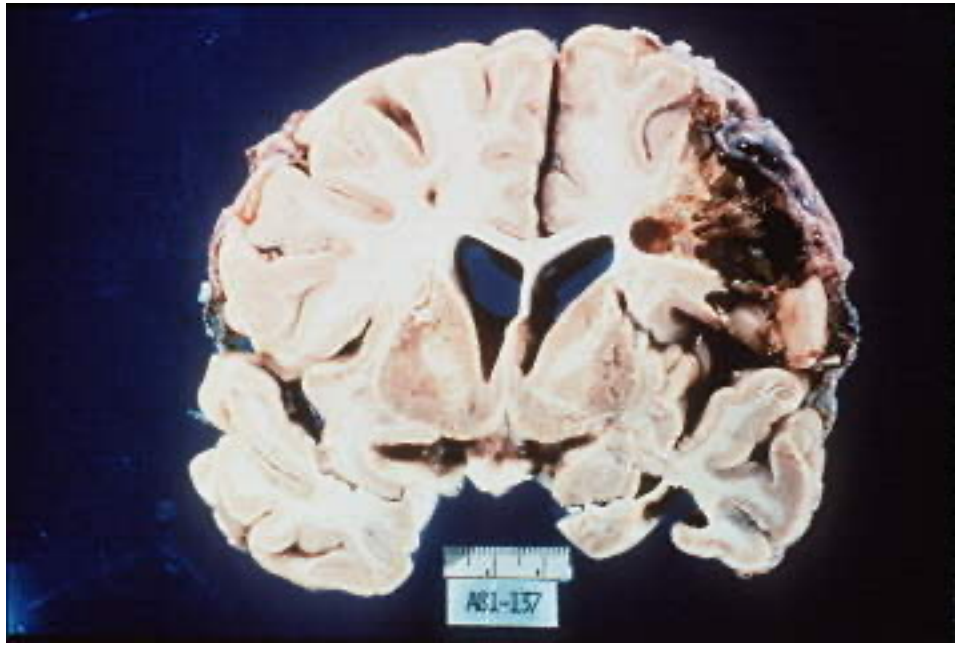
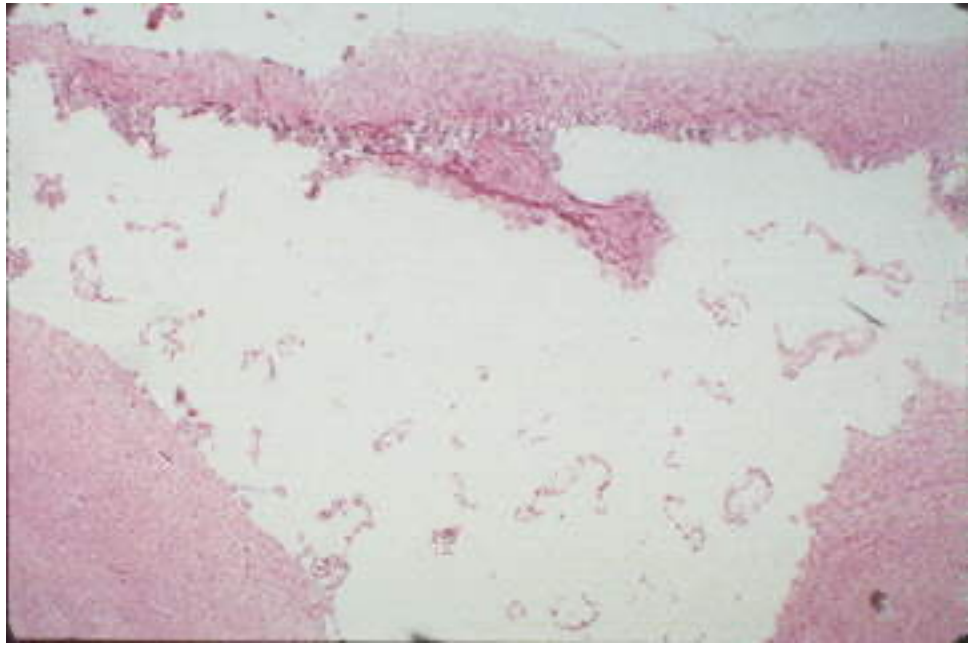
Old cerebral infarct





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The Light Microscopic Changes Associated with Irreversible Injury

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2. Liquefactive necrosis
3. **Caseous necrosis**
4. Fat Necrosis

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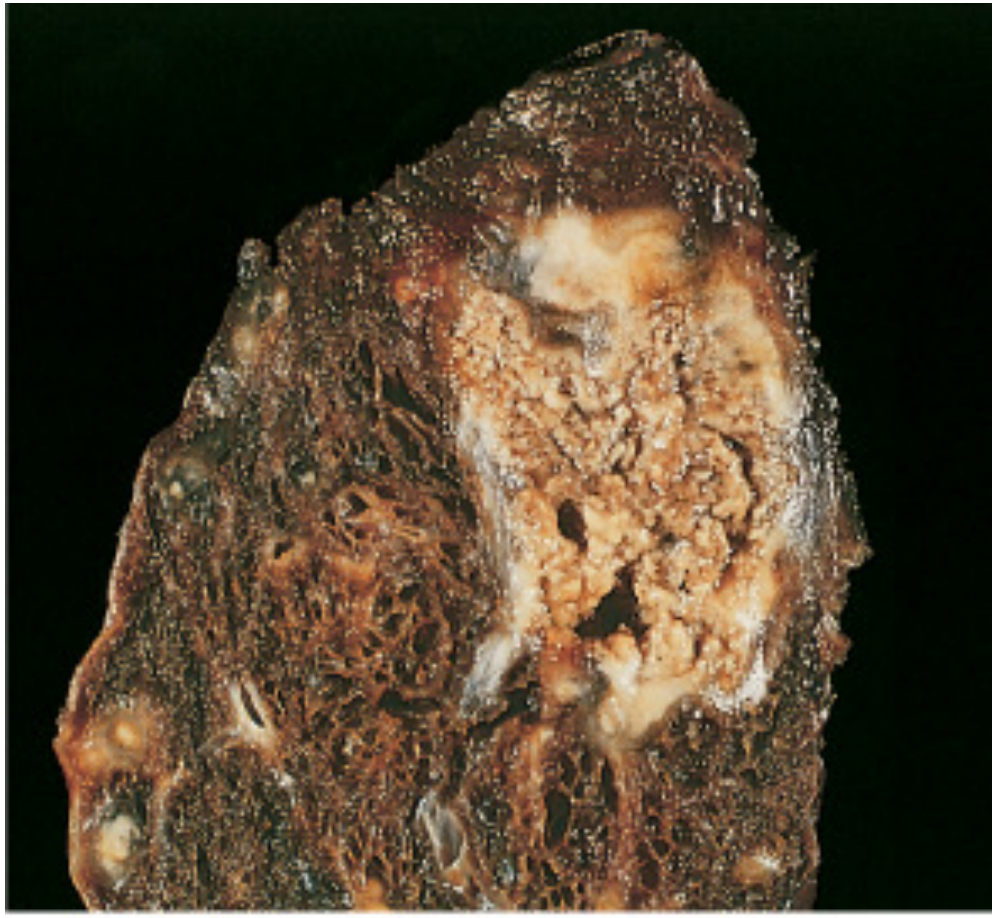
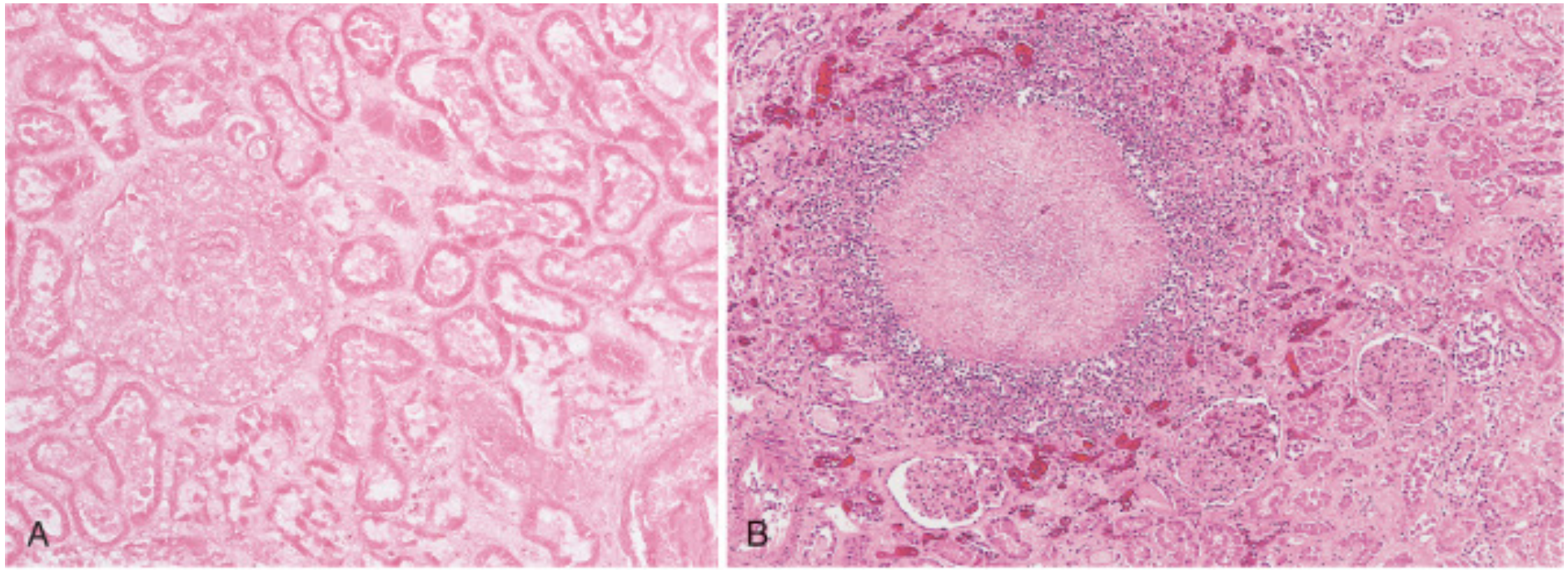
Pulmonary TB





The Light Microscopic Changes Associated with Irreversible Injury

1. Coagulative necrosis
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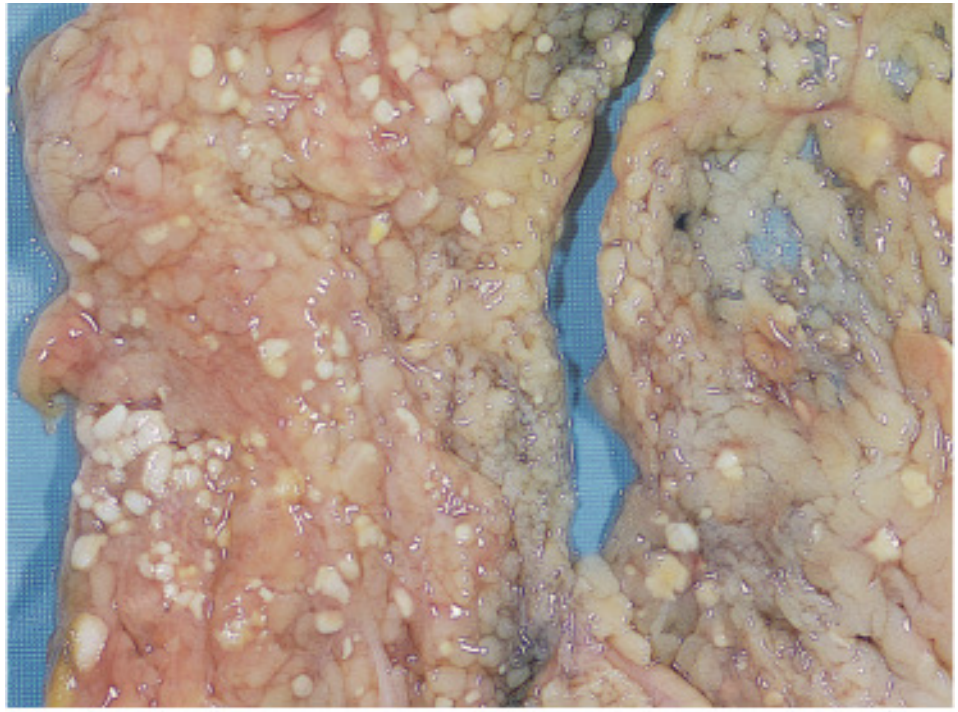
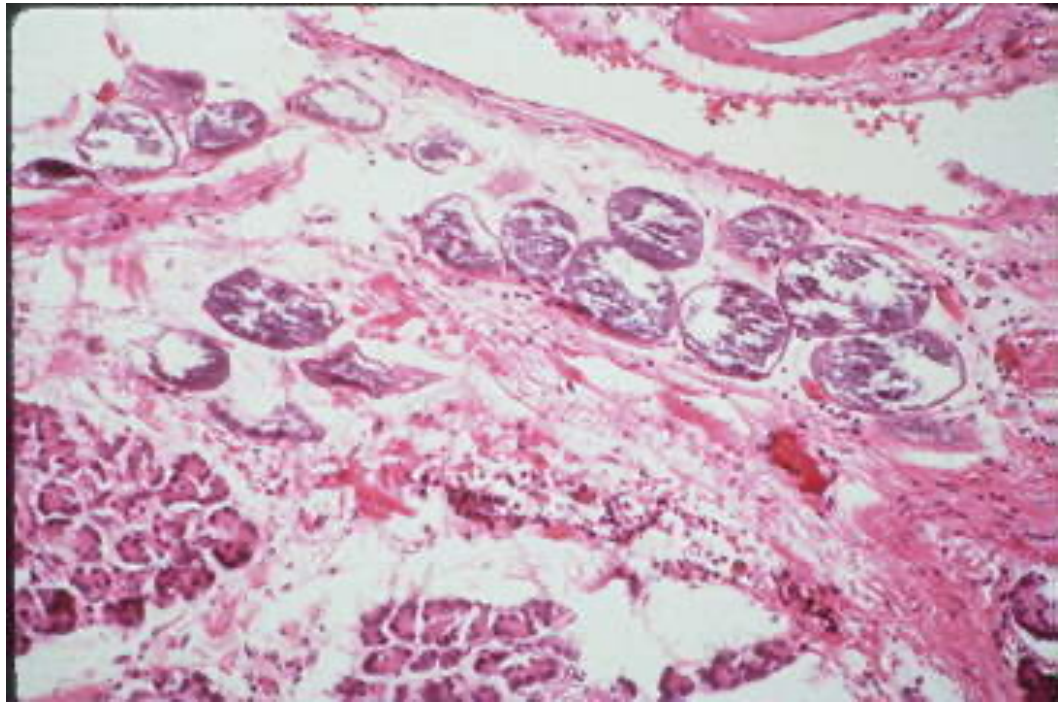
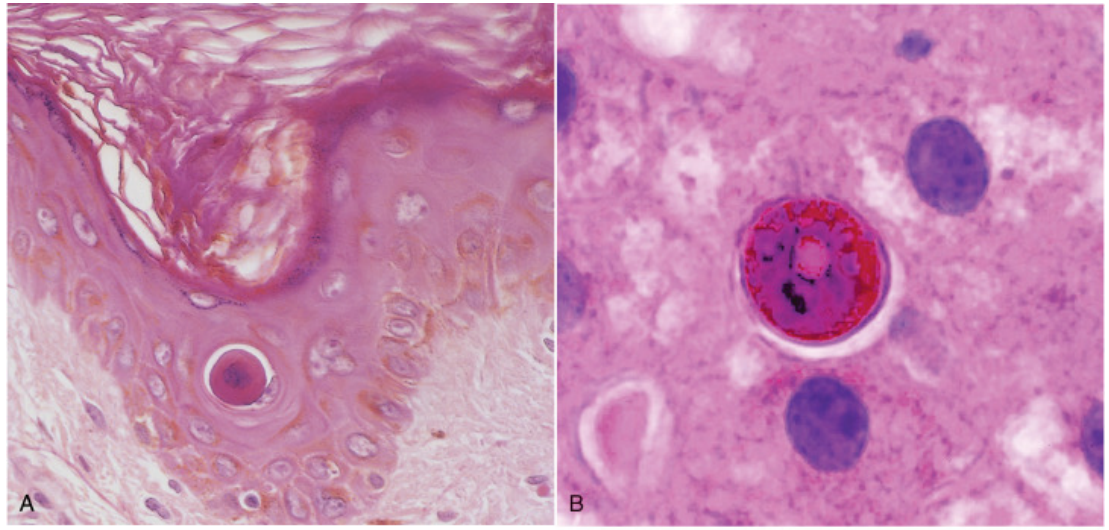
4. **Fat Necrosis**

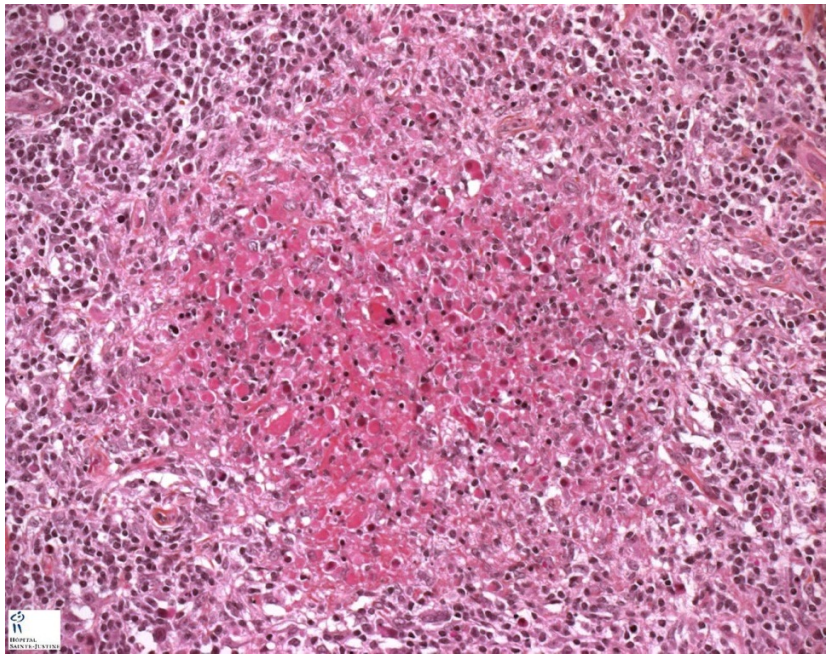
Acute pancreatitis





Apoptosis and necrosis





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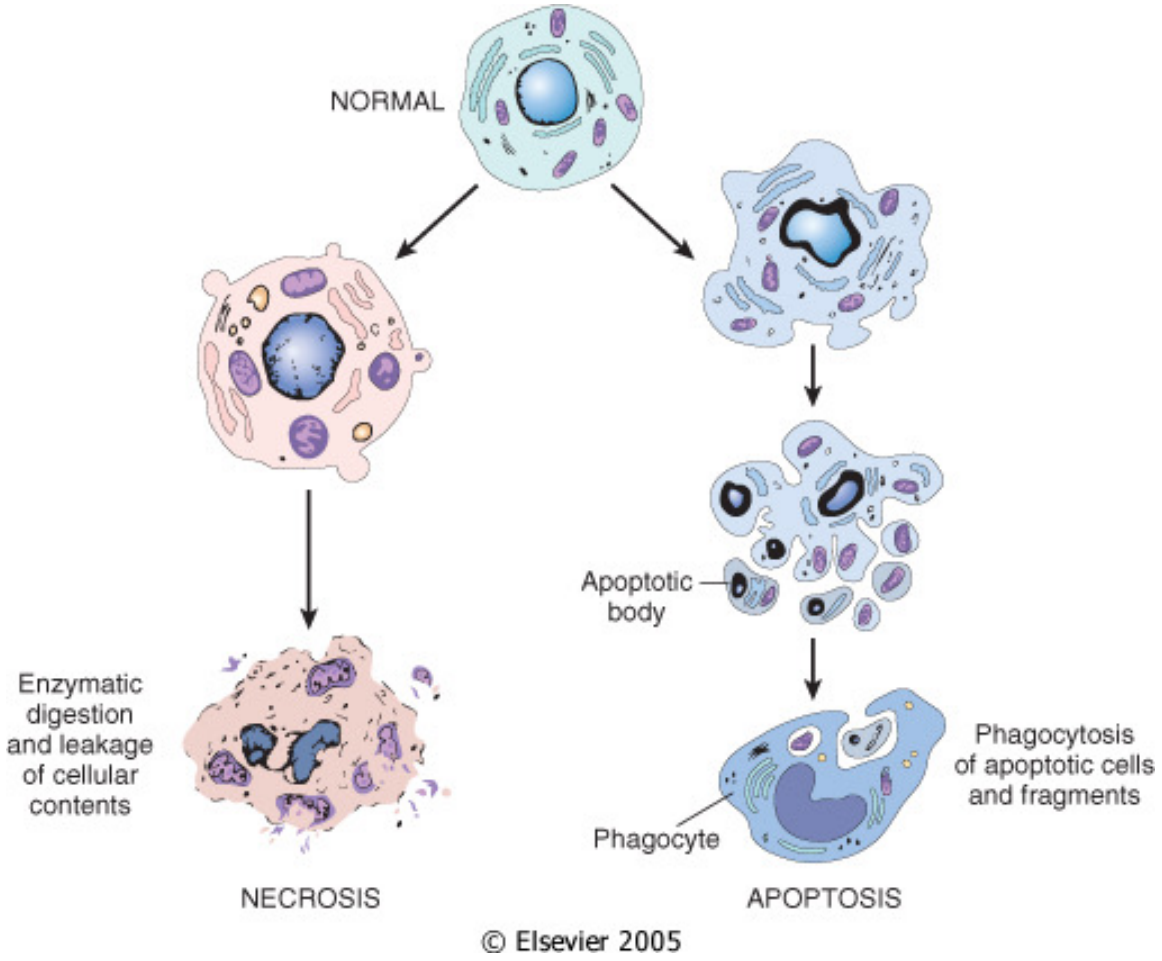

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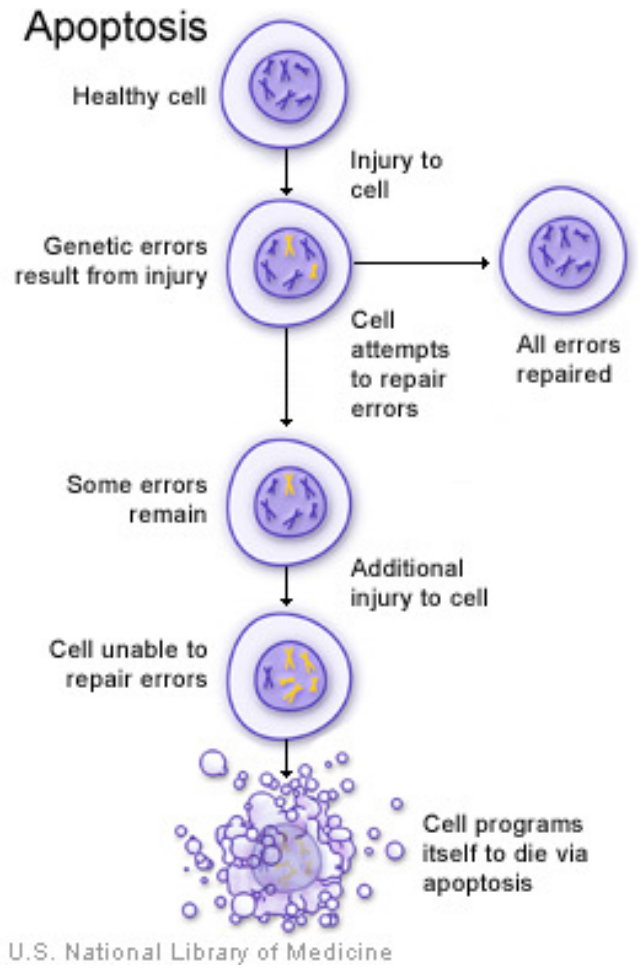
Apoptosis: Causes

1. Embryogenesis.
2. Deletion of auto-reactive T cells in the thymus.
3. Hormone-dependent physiological involution.
4. Cell deletion in proliferating populations.
5. A variety of mild injurious stimuli that cause irreparable DNA damage that, in turn, triggers cell suicide pathways.

Apoptosis: Programmed cell death



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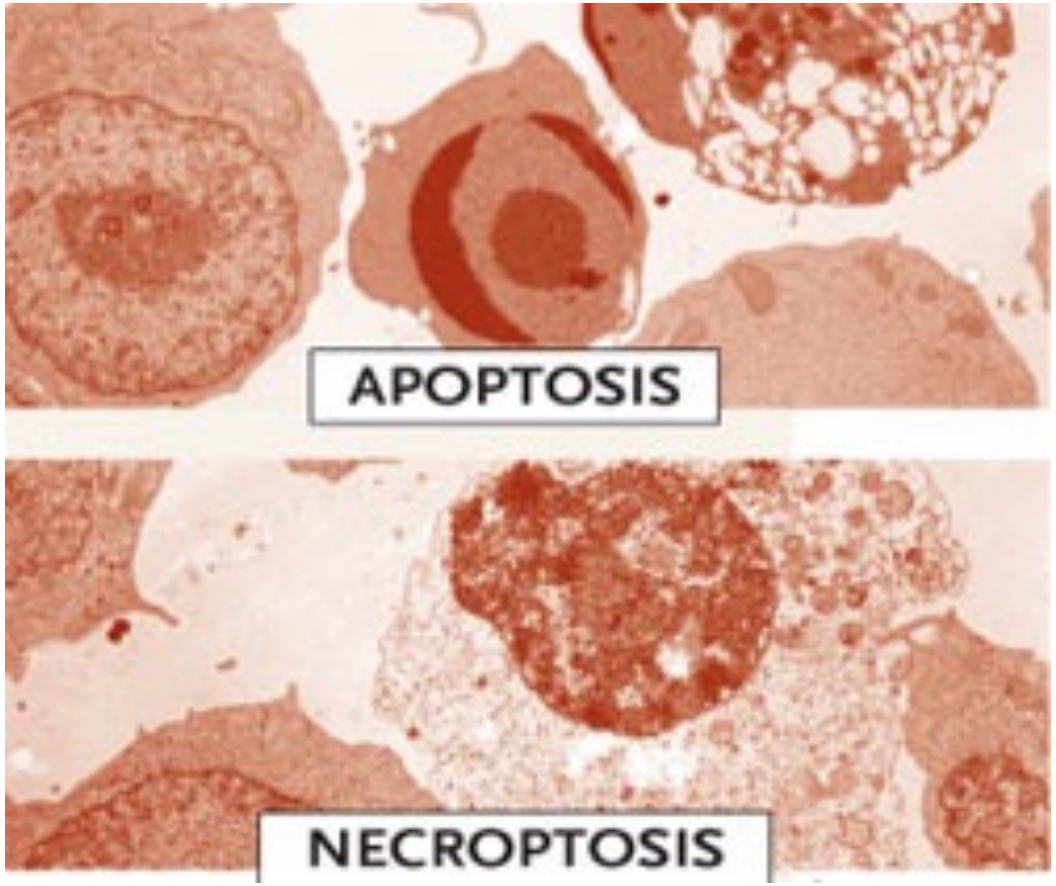
The differences between apoptosis and necrosis

1. Apoptosis may be **physiological**
2. Apoptosis is an **active** energy dependent process
3. **Not associated with inflammation**

But now there is another type of programmed cell death!



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Necroptosis

- Programmed cell death associated with inflammation
- Many causes e.g. viral infections

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