CELLULAR ADAPTATIONS

CELLULAR RESPONSES TO HARMFUL STIMULI

- Each cell in the body is designed to carry a specific function or functions, which is dependent on its machinery and metabolic pathways.
- ability of all parts of the cell to maintain a dynamically stable state is referred to as homeostasis.
- Should the cells encounter more severe external changes (physiological or pathological);they can modify the homeostatic state and achieve a new steady state to counteract the noxious effects of these external stresses. These changes are referred to as adaptations. The aim behind these adaptations is to avoid cell injury & death.

CELLULAR RESPONSES TO HARMFUL STIMULI

- The morphological & functional changes induced by the injury may be reversible, i.e. the cells return to a normal state on the removal of the offending agent, or irreversible i.e. there is no possibility of making turn to normal state . Irreversible changes ultimately eventuate in cell death.

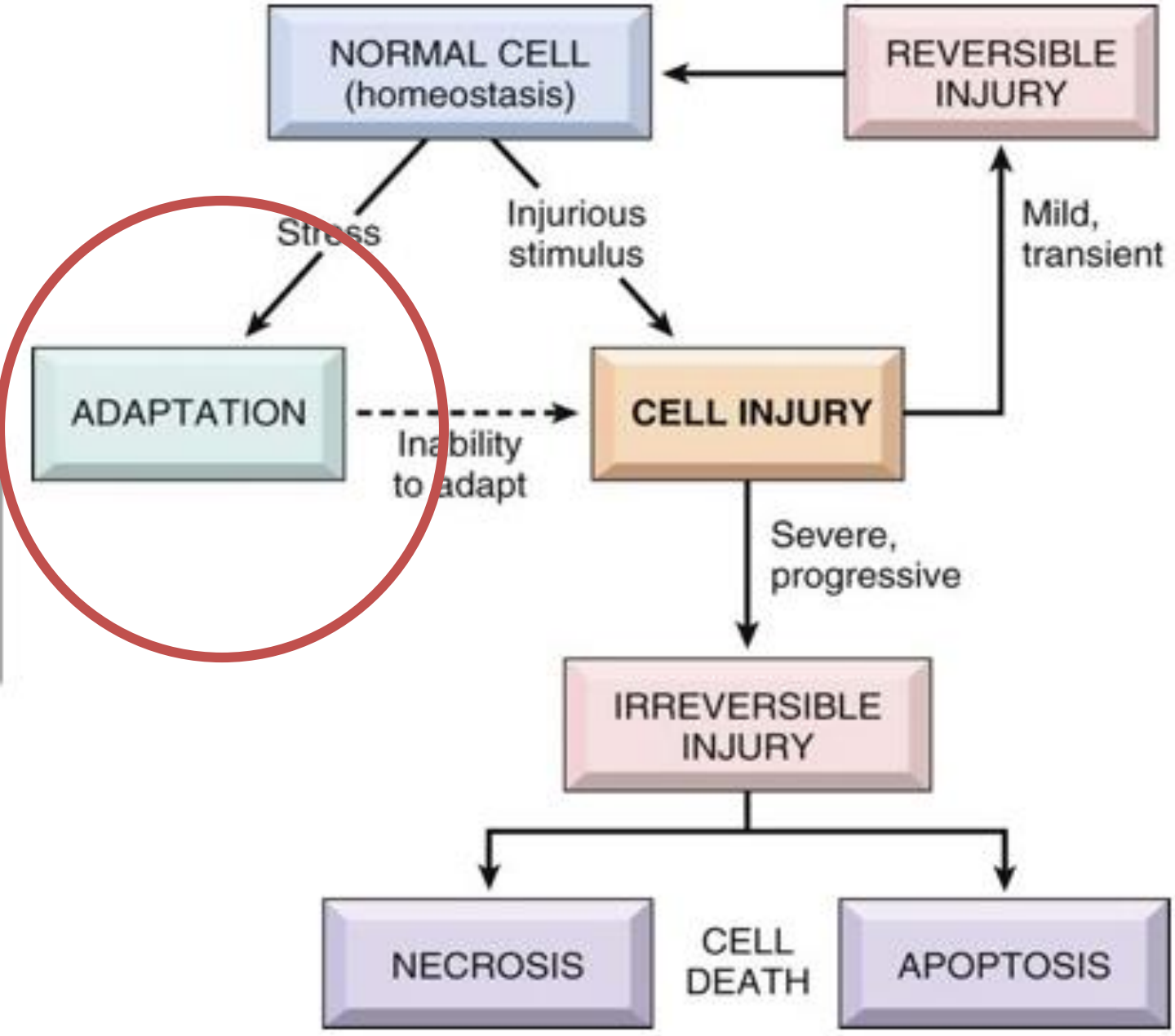
CELLULAR ADAPTATIONS

- Adaptations: reversible changes in the number, size, phenotype, metabolic activity, or functions of cells in response to changes in their environment.
- Physiologic Adaptations: responses of cells to normal stimulation
- Pathologic Adaptations: responses to stress that allow cells to modulate their structure and function and thus escape injury

Causes of cell injury

1. Oxygen Deprivation (***Hypoxia****, due to restriction of blood "**ischemia**")*
2. *Chemical, physical agents*
3. *Infectious*
4. *Genetic defects,*
5. *Nutritional imblances,*
6. *aging.*

Figure 1–1 Stages in the cellular response to stress and injurious stimuli.



Principal Adaptive Responses

- Hypertrophy: increase in size of the cells
- Hyperplasia: increase in the number of cells
- Atrophy: reduce or shrinkage in the size of the cell
- Metaplasia: one adult cell type is replaced by another adult cell type

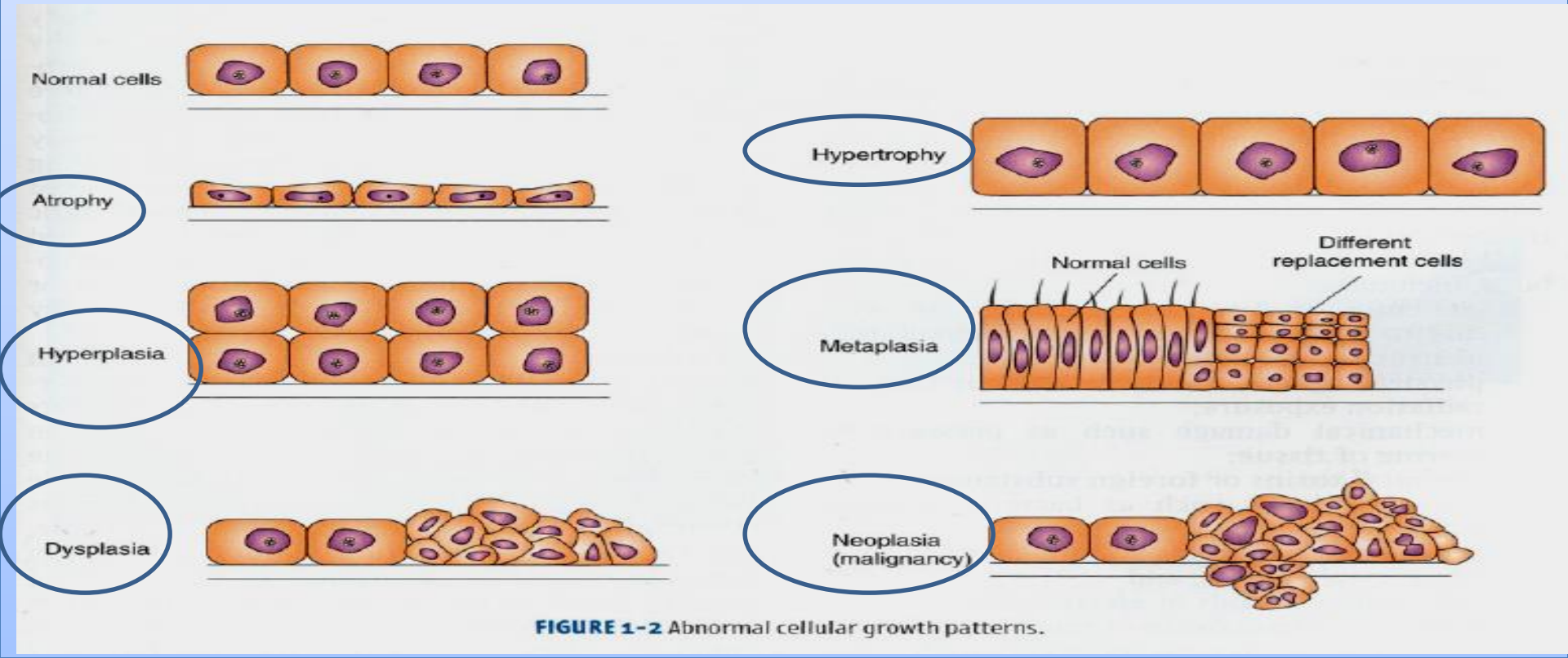


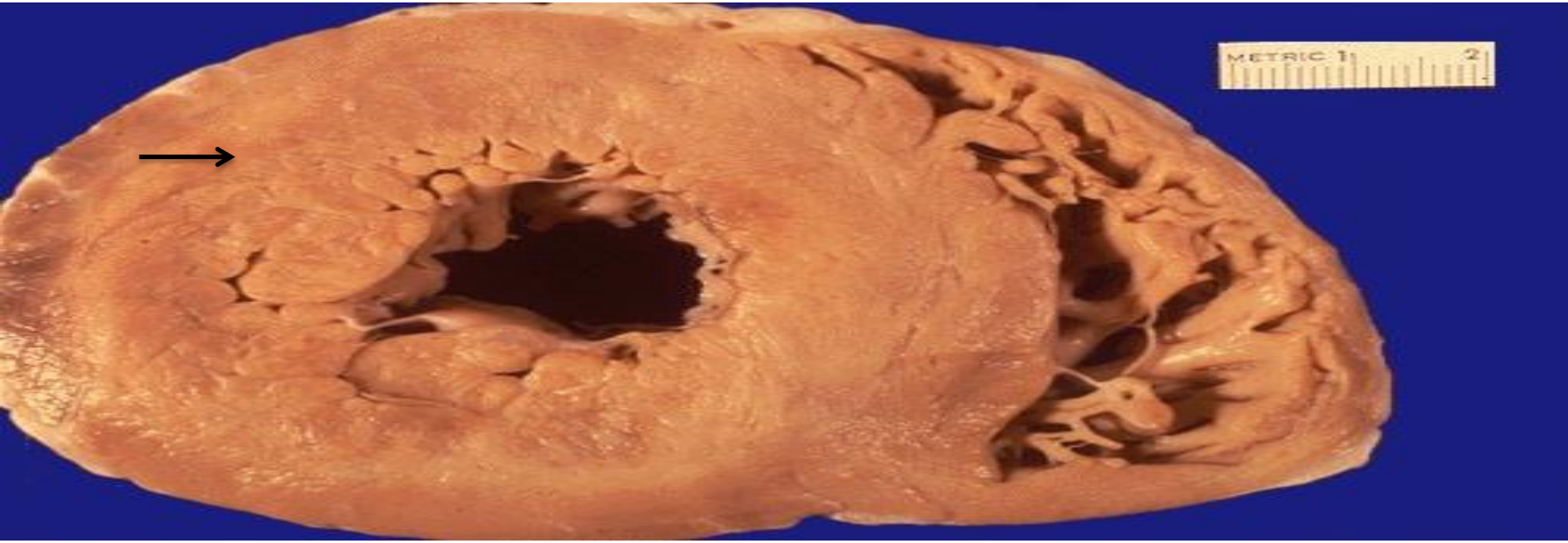
FIGURE 1-2 Abnormal cellular growth patterns.

Hypertrophy

- refers to an increase in the size of cells that results in enlargement of their relevant organ.
- Hypertrophy can be physiologic or pathologic and is caused either by increased functional demand or by specific hormonal stimulation.
- Examples of physiologic hypertrophy
  - hypertrophy of skeletal muscles in athletes and mechanical workers

Mechanisms of Hypertrophy

- **Hypertrophy is the result of increased production of cellular**
- **proteins**
- Example of Pathologic hypertrophy:
  - ventricular enlargement of the heart with chronic hypertension

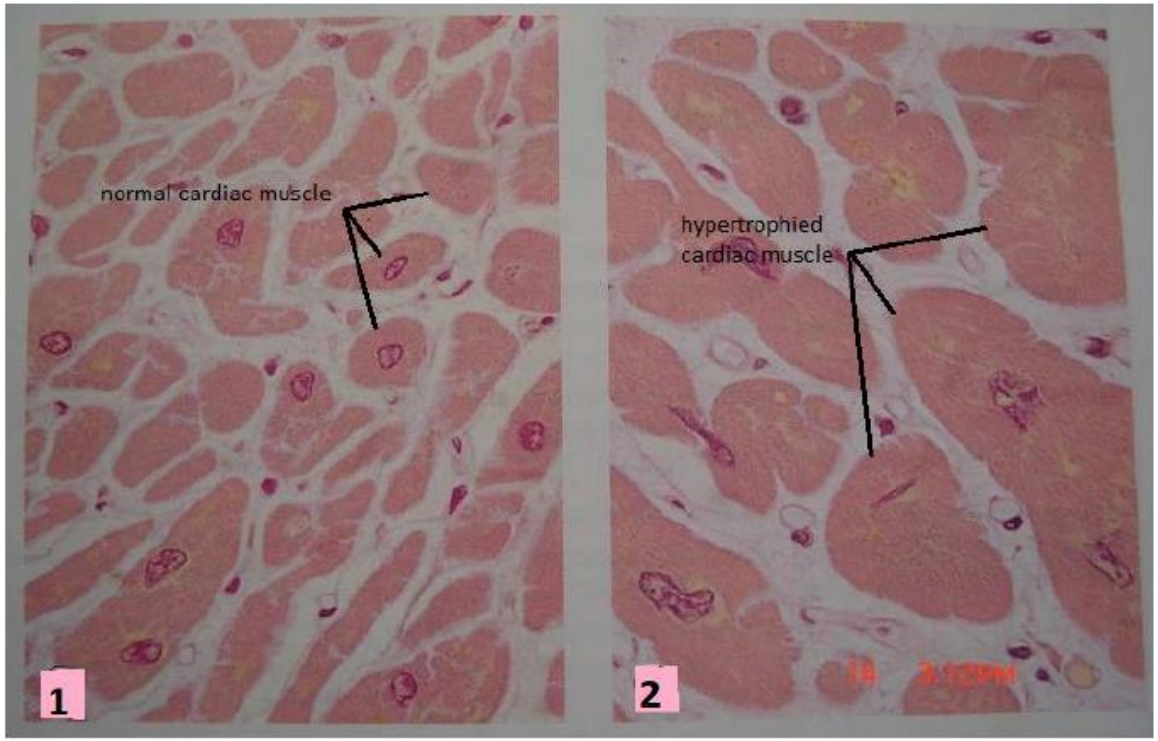


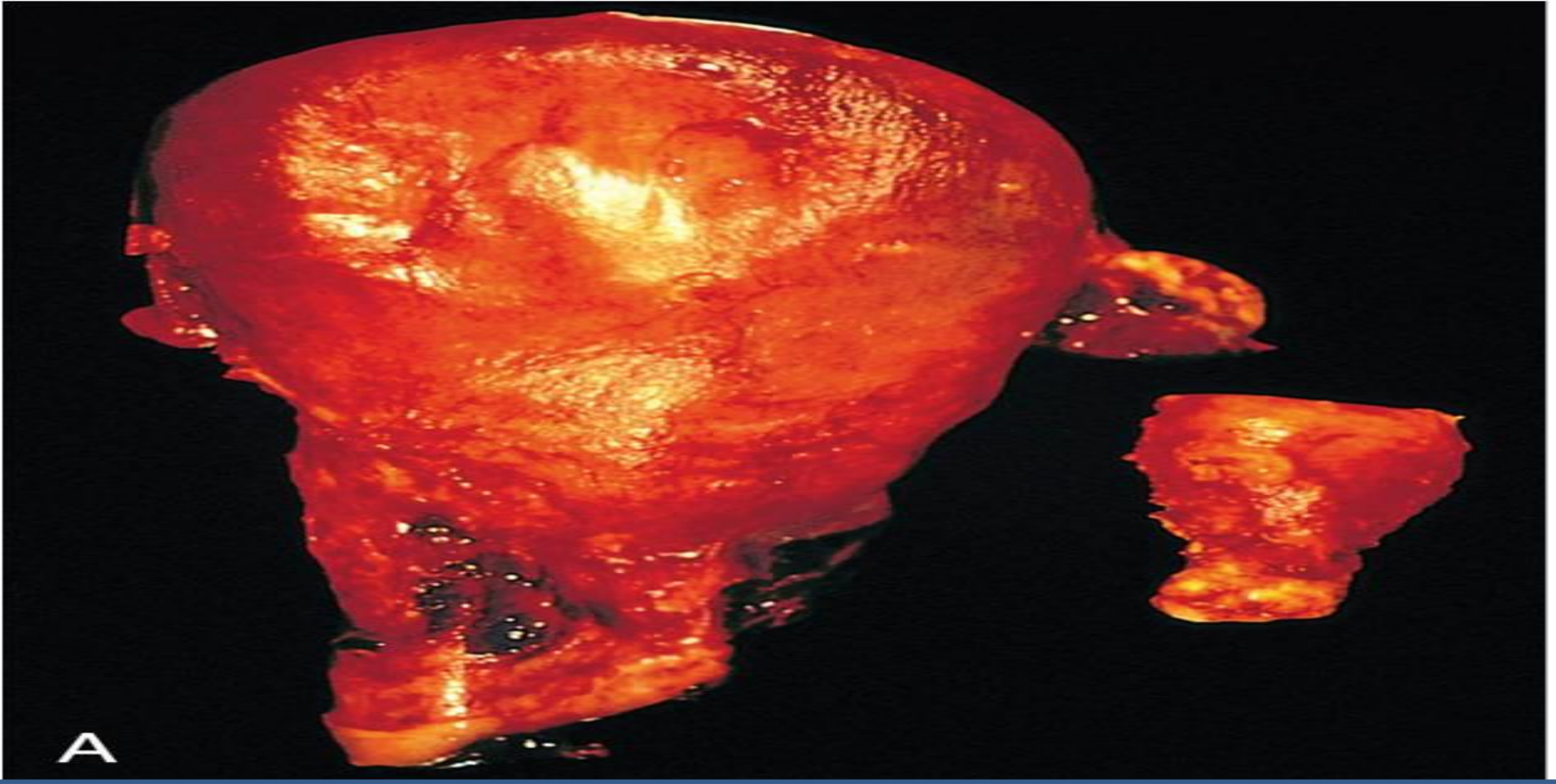
This is cardiac hypertrophy involving the **left ventricle**. The number of myocardial fibers does not increase, but their size can increase in response to an increased workload, leading to the marked thickening of the left ventricle in this patient with systemic hypertension.

LV hypertrophy:
under microscope

1: cross section shows normal cardiac muscle fiber

2: cross section shows hypertrophy in cardiac muscle fiber increase in nuclear and cytoplasmic size





The massive physiologic enlargement of the uterus during pregnancy due to estrogen-stimulated smooth muscle hypertrophy

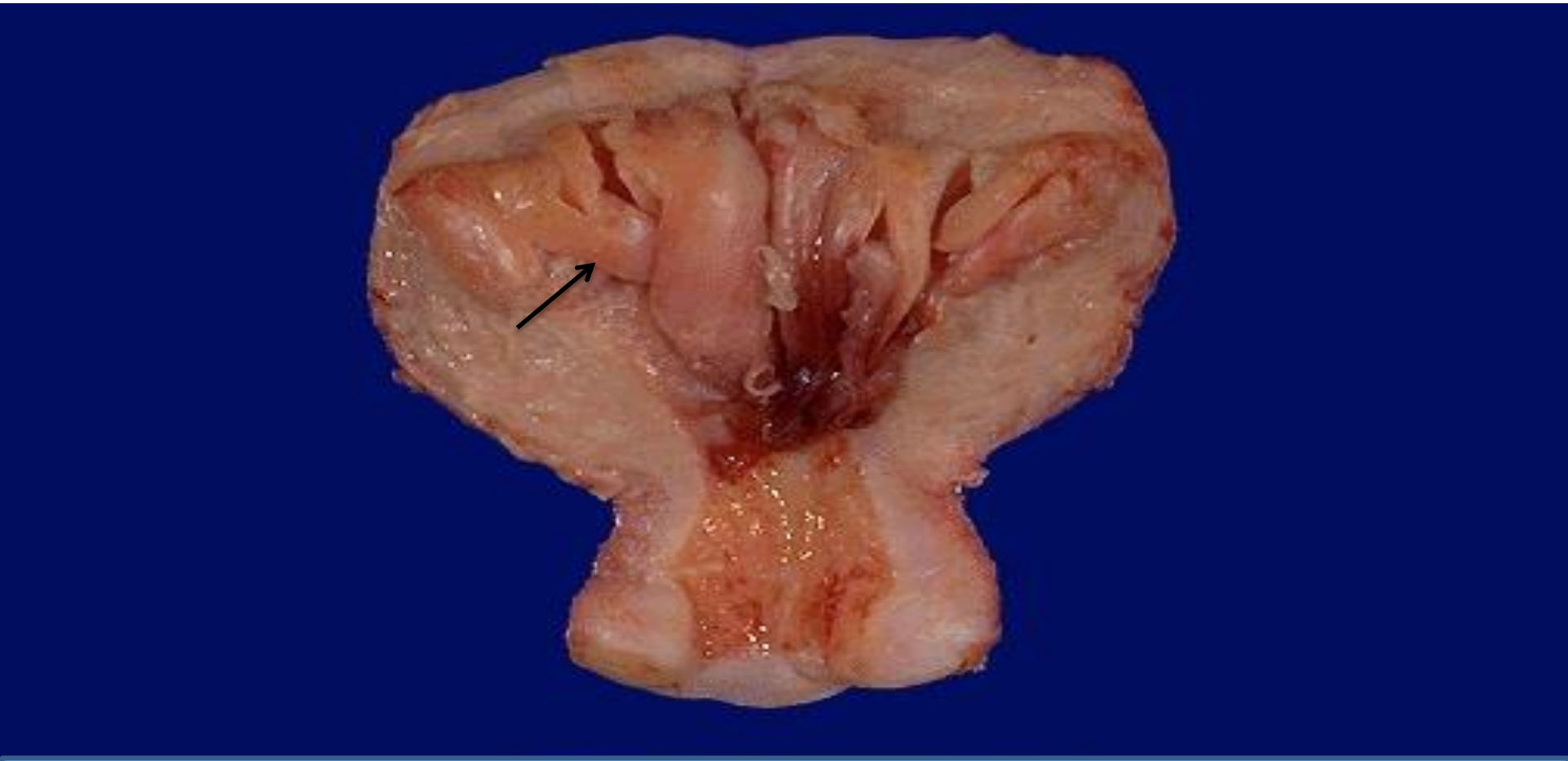
Hyperplasia

Hyperplasia refers to an increase in the number of cells. It takes place only if the cells are capable of replication; it may occur with hypertrophy and often in response to the same stimuli. Hyperplasia can be physiologic or pathologic.

- Physiologic hyperplasia: this is of two types
- 1. Hormonal hyperplasia: The enlargement of the gravid uterus is due to a combination of hypertrophy & hyperplasia.
- Compensatory: liver restoring itself to pre-surgical mass after a portion is removed.

Pathologic Hyperplasia

- Example:**Pathologic hyperplasia:** is mostly caused by excessive hormonal or growth factor stimulation. Examples include
- Endometrial hyperplasia: this results from excessive estrogen stimulation of the endometrium. This hyperplasia is a common cause of abnormal uterine bleeding.



Endometrial hyperplasia: this results from excessive estrogen stimulation of the endometrium. This hyperplasia is a common cause of abnormal uterine bleeding

Atrophy

- refers to shrinkage in the size of the cell,due to Loss of cell substance --> ↓ in size of cell,Function is diminished.
- Atrophy is of 2 types:

•**Physiological atrophy:** (normal programmed reduction of cell size) e.g. : thymus gland.

• **Pathological atrophy :** related to diseases.

1-Starvation atrophy: there is reduction in CHO, fat, followed by protein. There is general weakness, anemia (emaciation) e.g. Cancer, chronic illness.

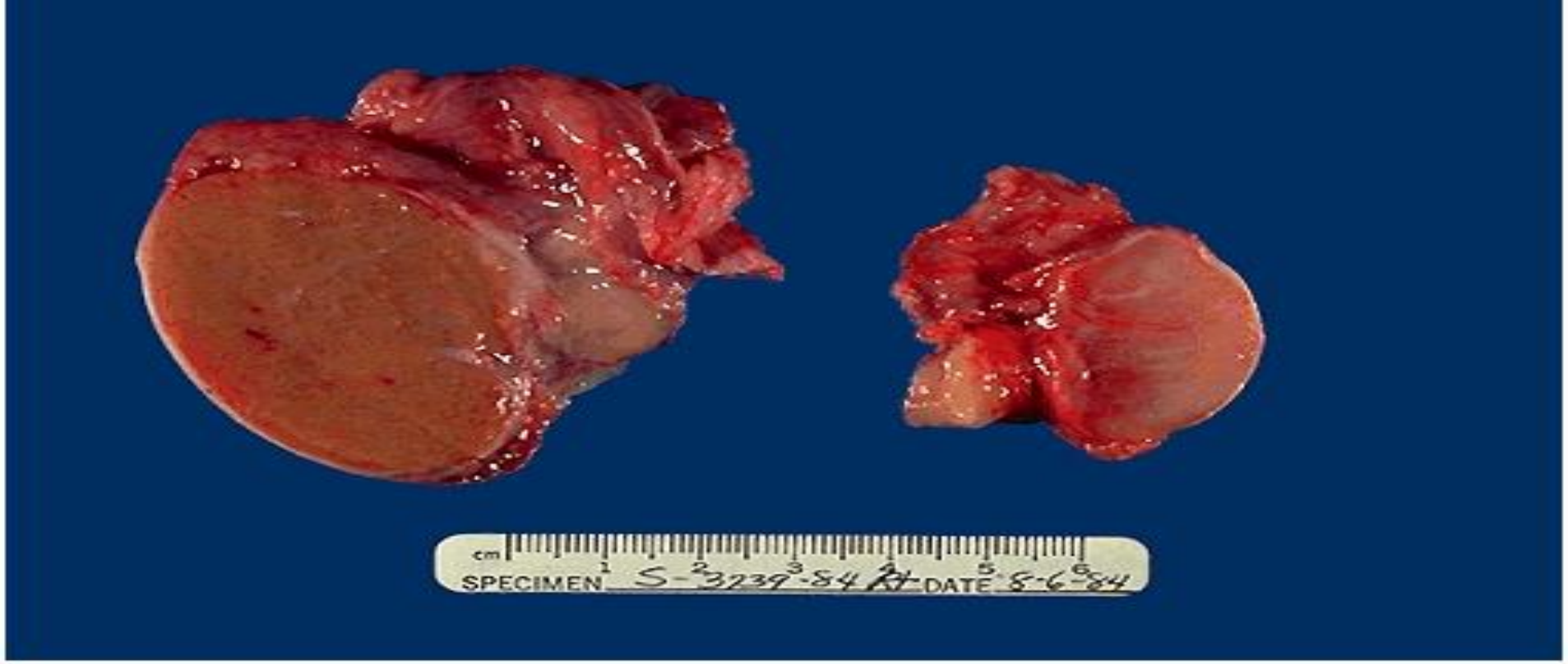
2-Ischaemic atrophy : Due to decrease in blood supply which leads to shrinkage of the affected organ. Gradual obstruction of the renal artery leads to ischaemic atrophy of the kidney , brain atrophy in cerebrovascular diseases.

3- Disuse atrophy: prolonged immobilization or decrease activity of the affected organ or tissue. e.g. wasting of the limb after fracture of the bone or after prolonged bed rest .

4-Neuropathic atrophy: damage to the nerve supply e.g.: denervation of limb as in poliomyelitis and traumatic spinal cord injury .

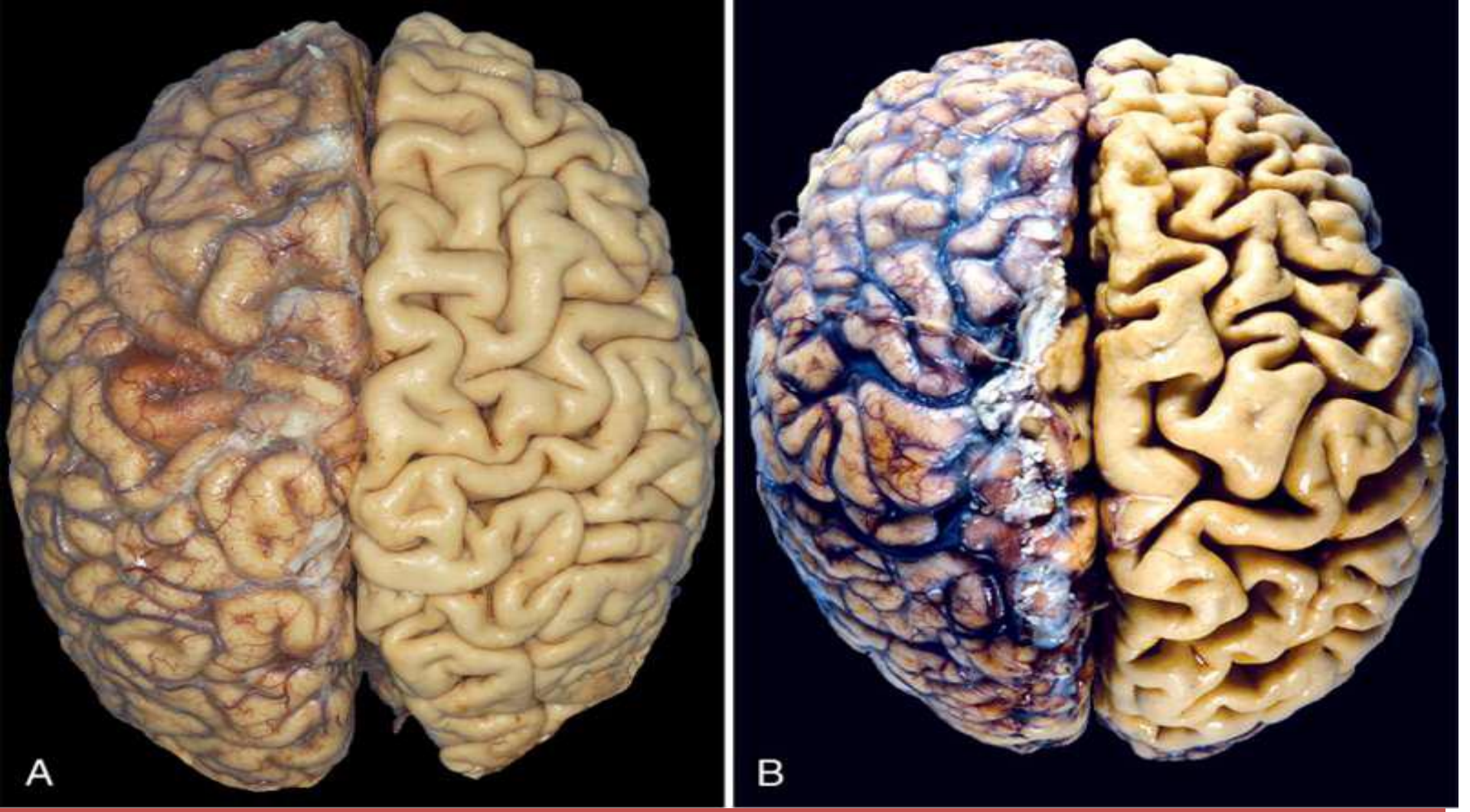
5-Endocrine atrophy: {hormonal atrophy}: Loss of endocrine regulatory mechanism.
e.g. postmenopausal endometrial atrophy.

6-Idiopathic atrophy: the cause is unknown e.g. myopathies.



The testis at the **right** has undergone atrophy and is much smaller than the normal testis at the **left**.

testicular atrophy (due to decrease in the production of LH as in hypopituitarism, **Bilateral atrophy may occur with a variety of conditions including chronic alcoholism, hypopituitarism, atherosclerosis,chemotherapy or radiation, and severe prolonged illness.**



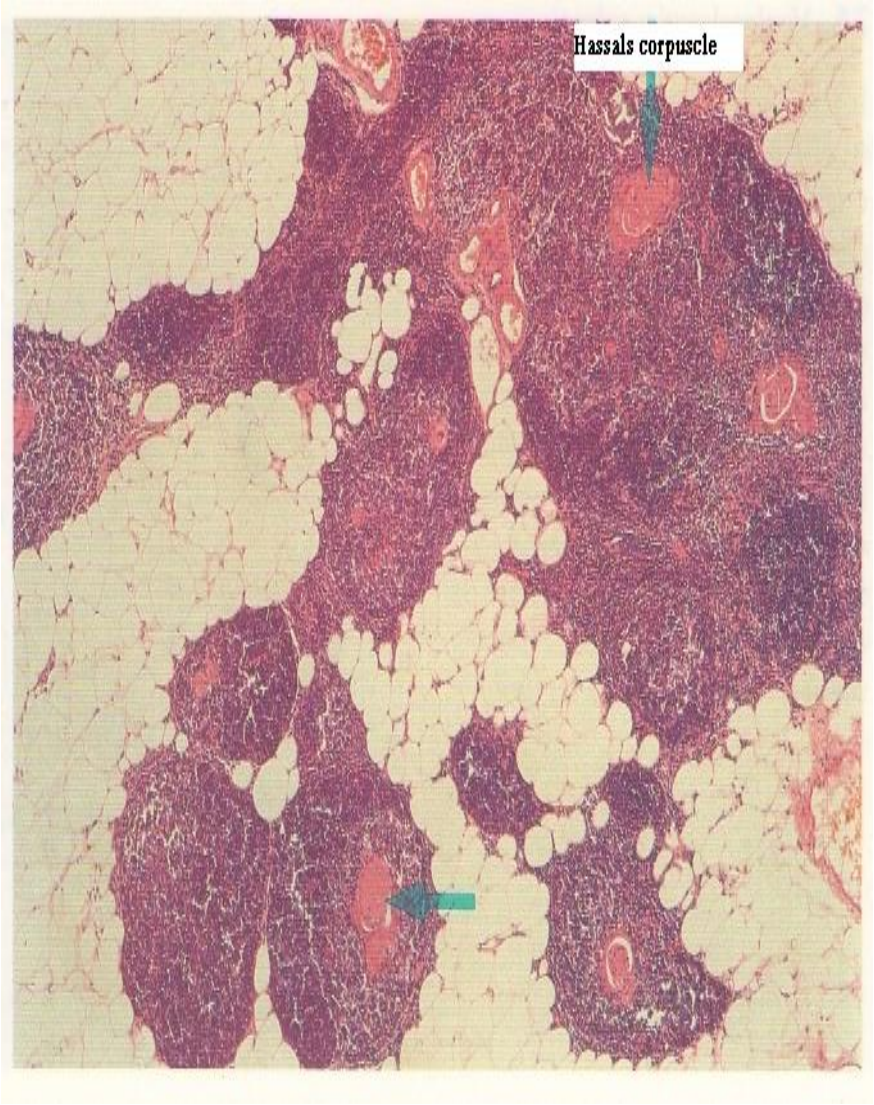
A. Normal brain of a young adult. B. Atrophy of the brain in an 82-year-old male with atherosclerotic disease. Atrophy of the brain is due to aging and reduced blood supply. Note that loss of brain substance narrows the gyri and widens the sulci.

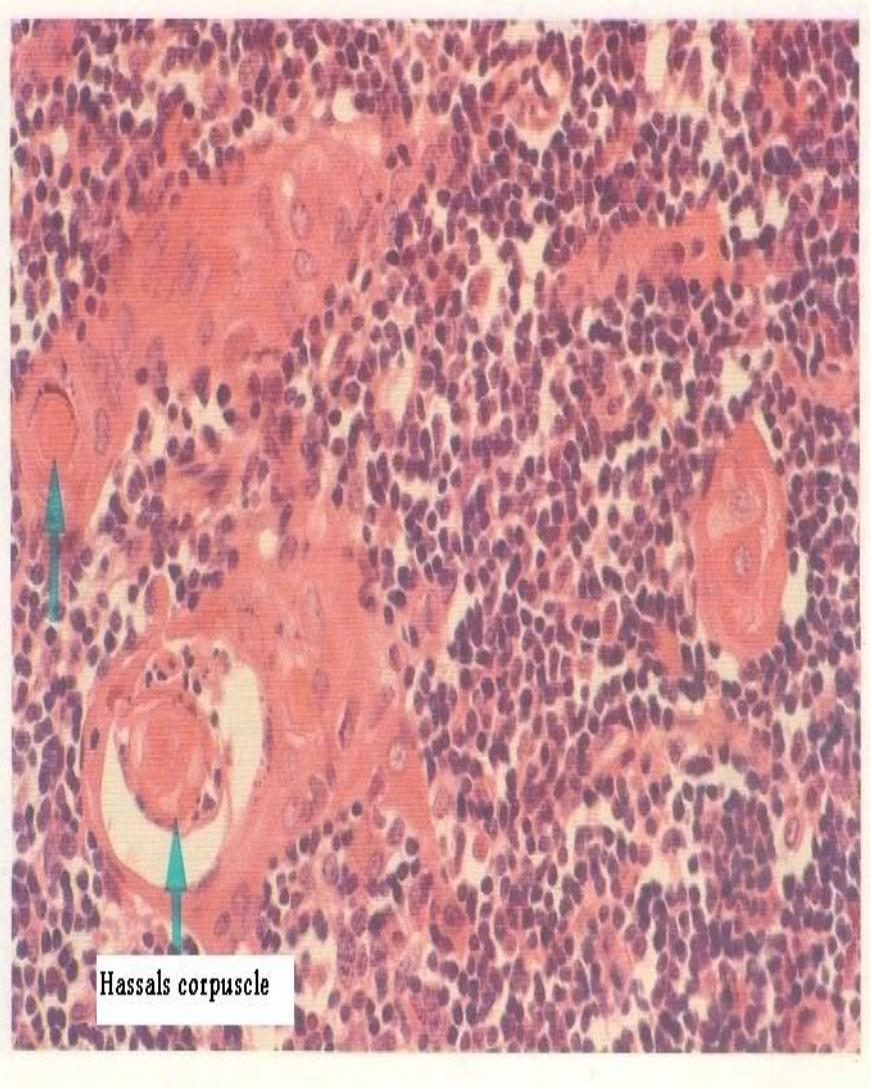
There are 2 special terms associated with atrophy:

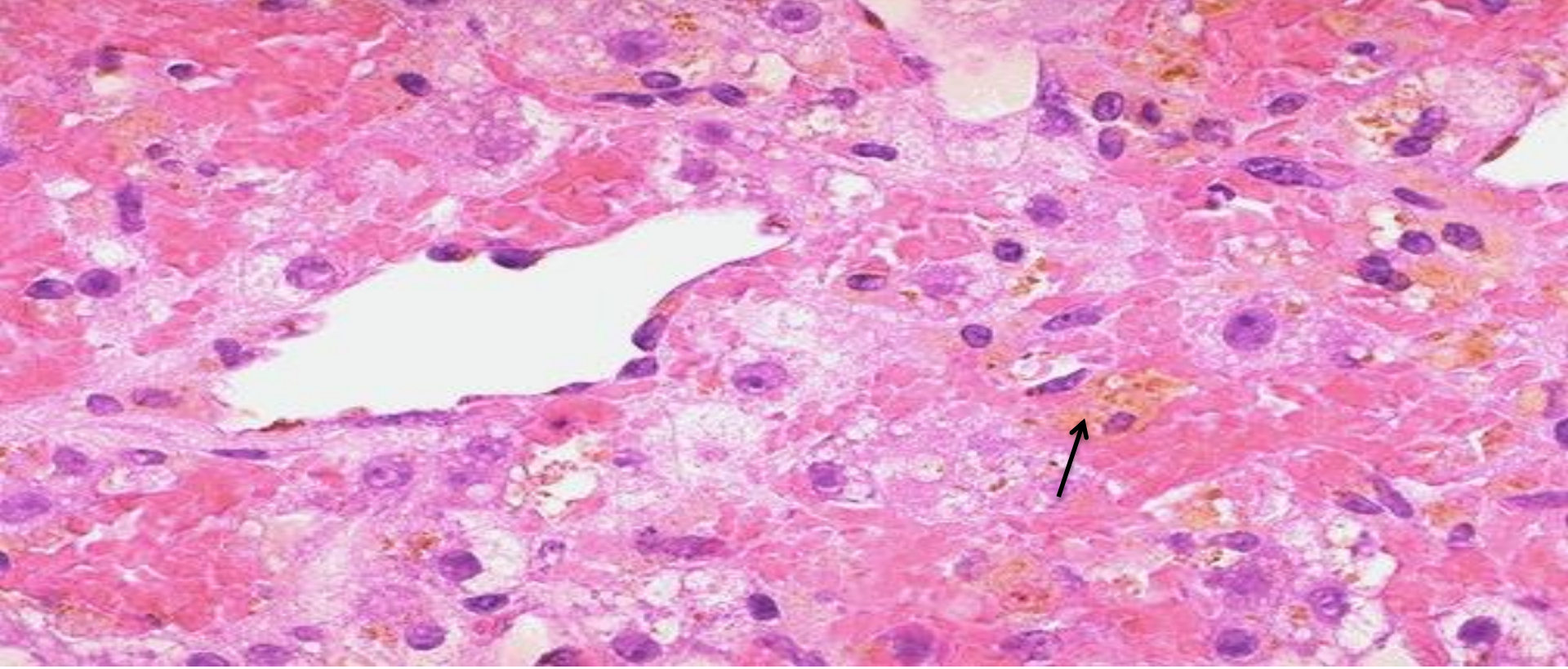
- **fatty atrophy:** the atrophic parenchyma is replaced with adipose tissue e.g. thymus , salivary glands.

- **Brown atrophy:** the atrophic cells accumulate brown pigment (lipofuscin) pigment, some time this accumulation is enough to be seen by naked eyes e.g. heart , liver.
  Under microscope this pigment can be seen close to the nuclei.

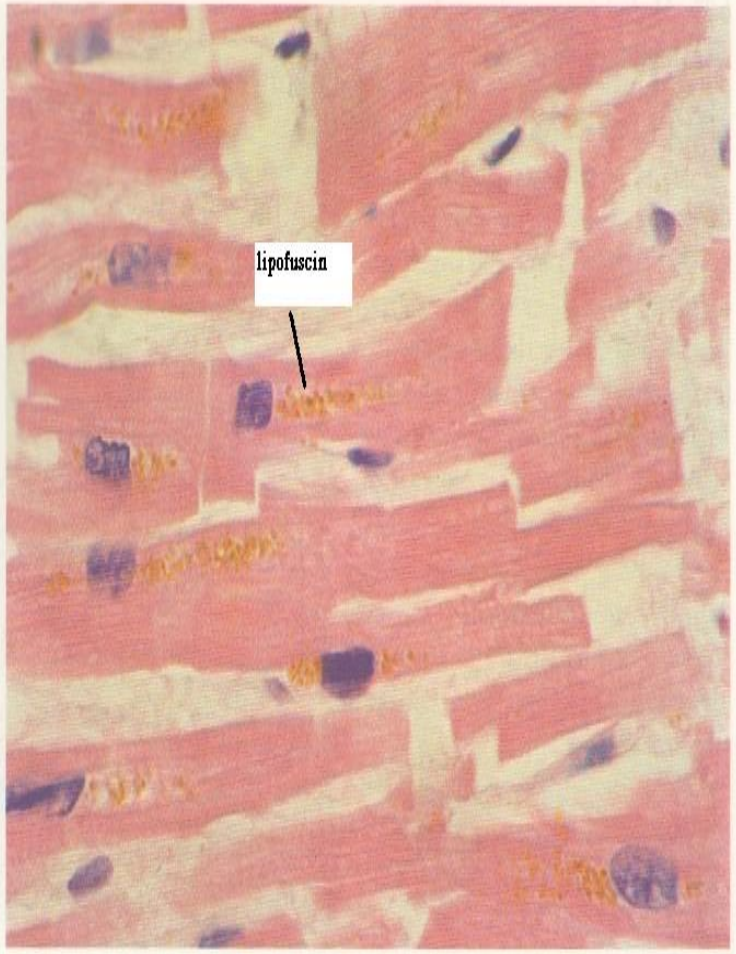
Atrophy: Thymus

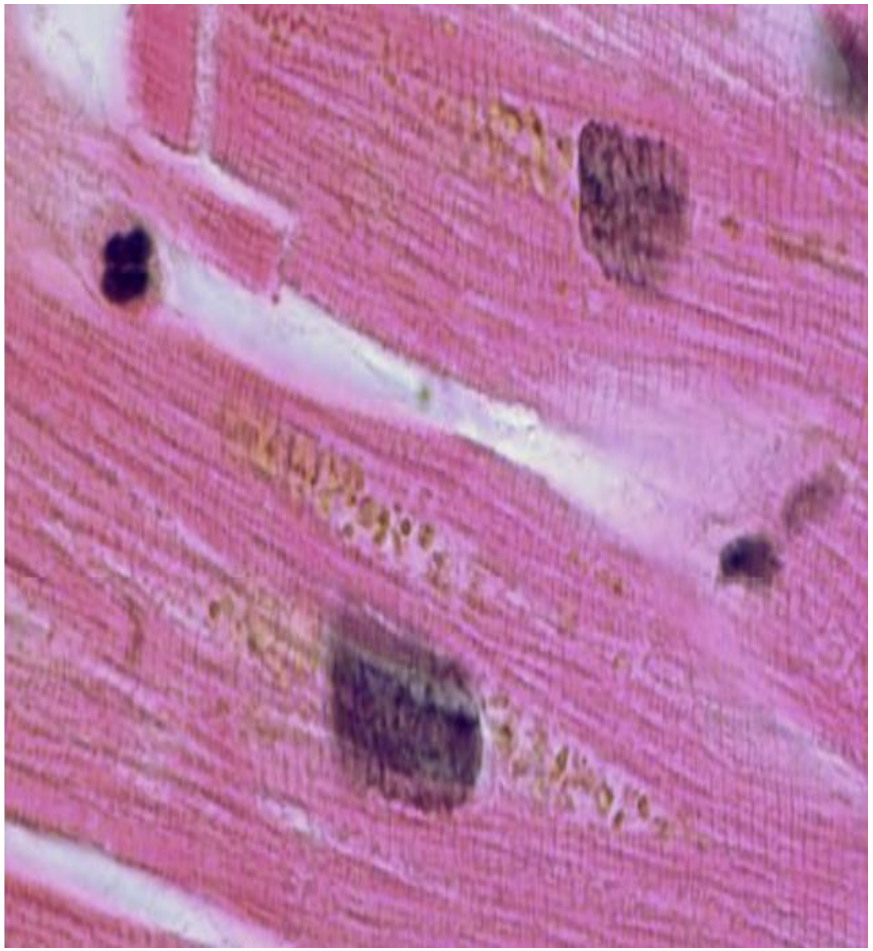






The cells have reduced in size or been lost from hypoxia.
The pale brown-yellow pigment is **lipochrome** that has accumulated as the atrophic and dying cells undergo autophagocytosis.





Lipofuscin, microscopic

The stippled, finely granular, intracytoplasmic, golden-brown pigment ( ) that lies primarily in a perinuclear location within these myocytes is lipofuscin (lipochrome) pigment.

This “wear-and-tear” pigment represents the remnants of long-term autophagocytosis .

With the small amounts shown here,which increase with aging,

there is no significant pathologic effect.

Metaplasia

Replacements of one mature cell type by another mature cell type

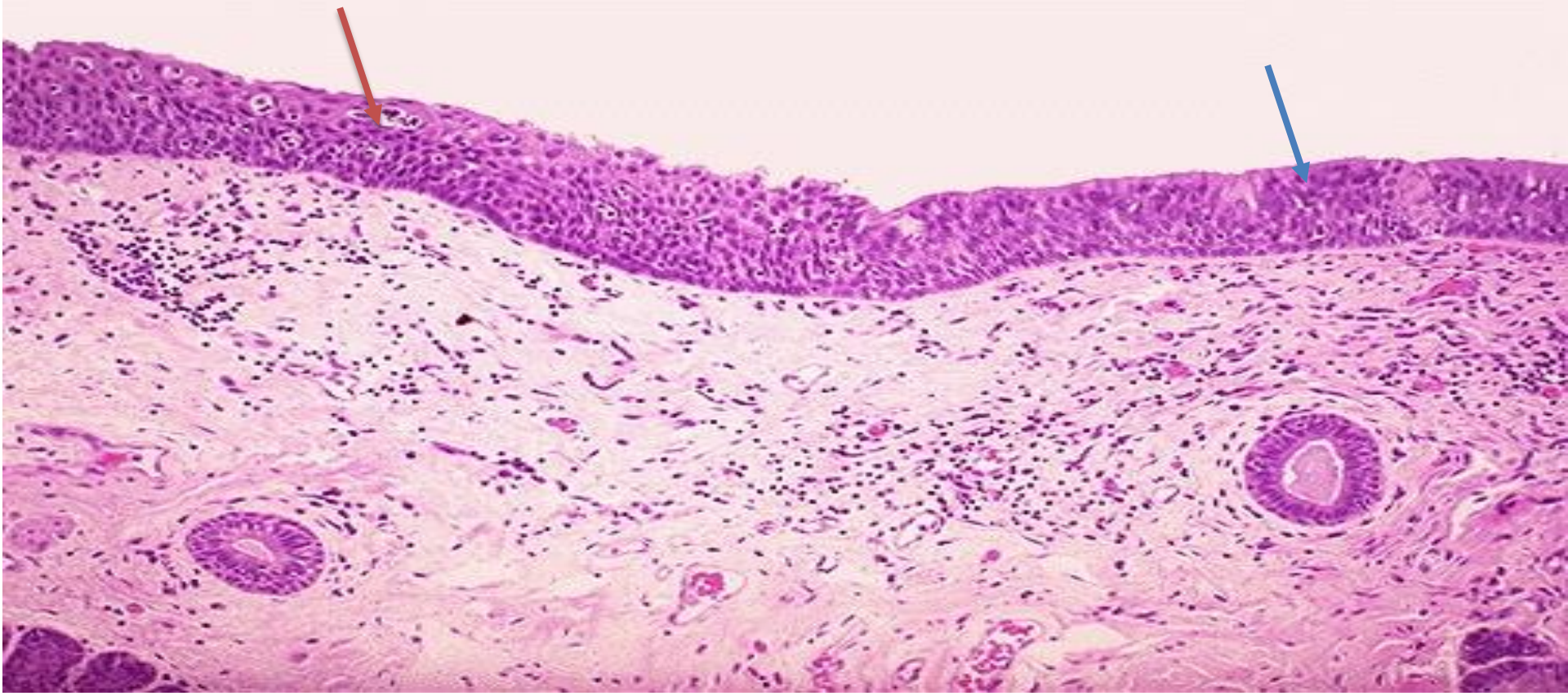
May represent an adaptation

Examples

1. Squamous metaplasia of the

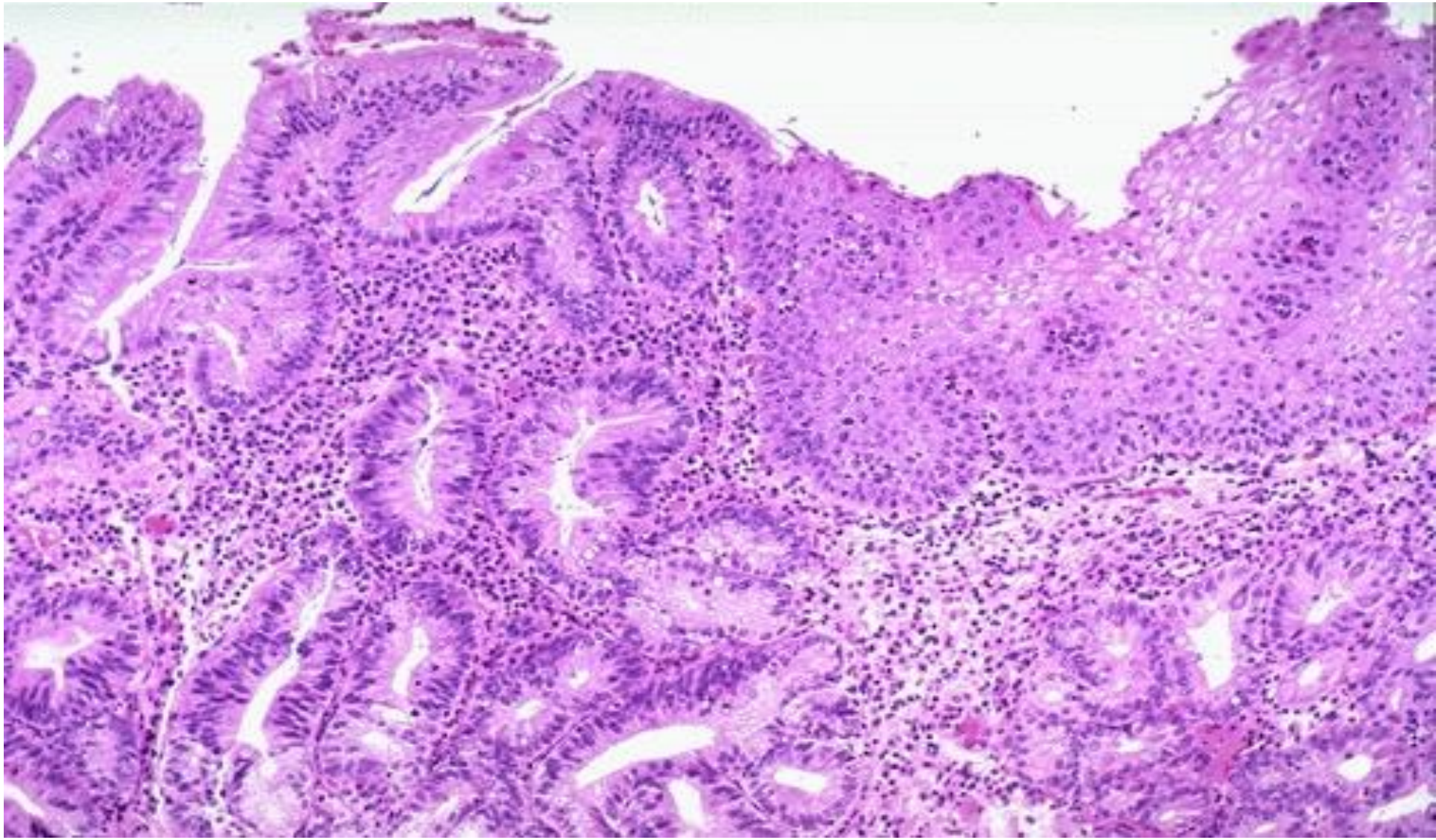
- laryngeal and bronchial respiratory epithelium.(squamous change that occurs in the respiratory epithelium in habitual cigarette smokers)
- urothelium in the urinary bladder

2. **Columnar metaplasia** of esophageal squamous epithelium



Metaplasia of laryngeal respiratory epithelium has occurred here in a smoker. The chronic irritation has led to an exchanging of one type of epithelium (the normal **respiratory epithelium** at the right) for another (the more resilient **squamous epithelium** at the left). Metaplasia is not a normal physiologic process and may be the first step toward neoplasia.

Q: Is metaplasia reversible?



- Metaplasia of the normal esophageal **squamous mucosa** has occurred here, with the appearance of gastric type **columnar mucosa**.

Cell injury

- Occurs
- 1. Limits of adaptive capability exceeded
- 2. No adaptive response is possible
- Cell injury divided
- 1. Reversible
- 2. Irreversible cell death

- **Categorization of injurious agents**
- Hypoxia ,Physical agents , , chemical agents
- Infectious agents ,Immunological reactions , Genetic derangement ,Nutritional imbalances ,Aging

Cell injury Morphological patterns of cell injury:

- Also it is called **degeneration** .It is accumulation of normal substances (glycogen, water) or abnormal (Amyloid) inside the cell due to injury agent. Classified into two main groups:
- 1- Those with primary change in the **cell.**
- 2- Those with interstitial accumulation compressing the cell.

Classification of degeneration

- **1-primary changes in the cell.**
- Intracellular accumulation of water (cloudy swelling, hydropic & vacuolar changes).
- Intercellular accumulation of fat.(fatty change)
- Intracellular accumulation of CHO.
- Intracellular accumulation of proteins.

Two patterns of morphologic change correlation to reversible injury can be recognized under light microscope

Intracellular accumulation of water :

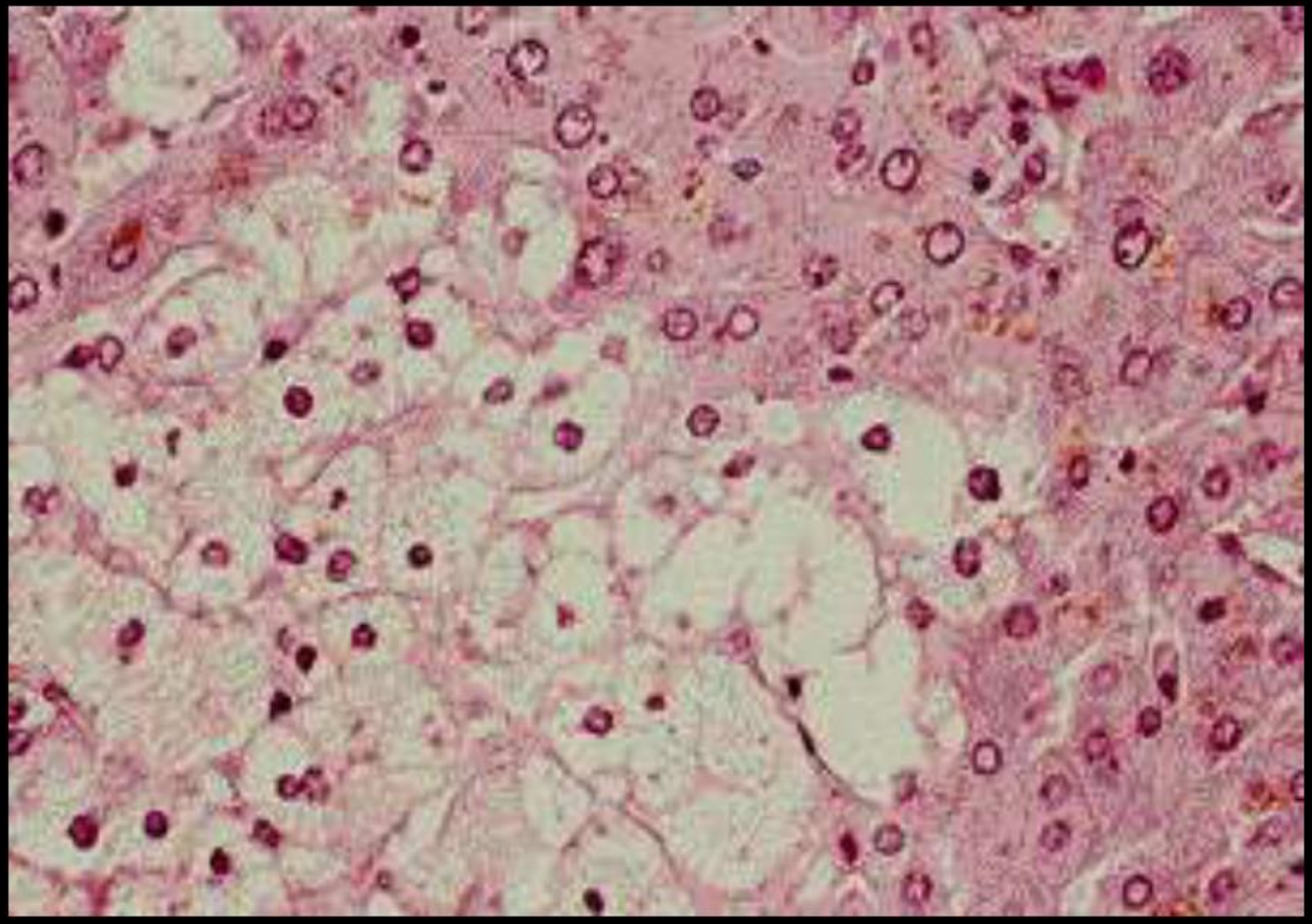
A.cloudy swelling and fatty change

Is the first manifestation of all forms of injury to cells ;it appear when ever cells are incapable of maintaining ionic and fluid homeostasis

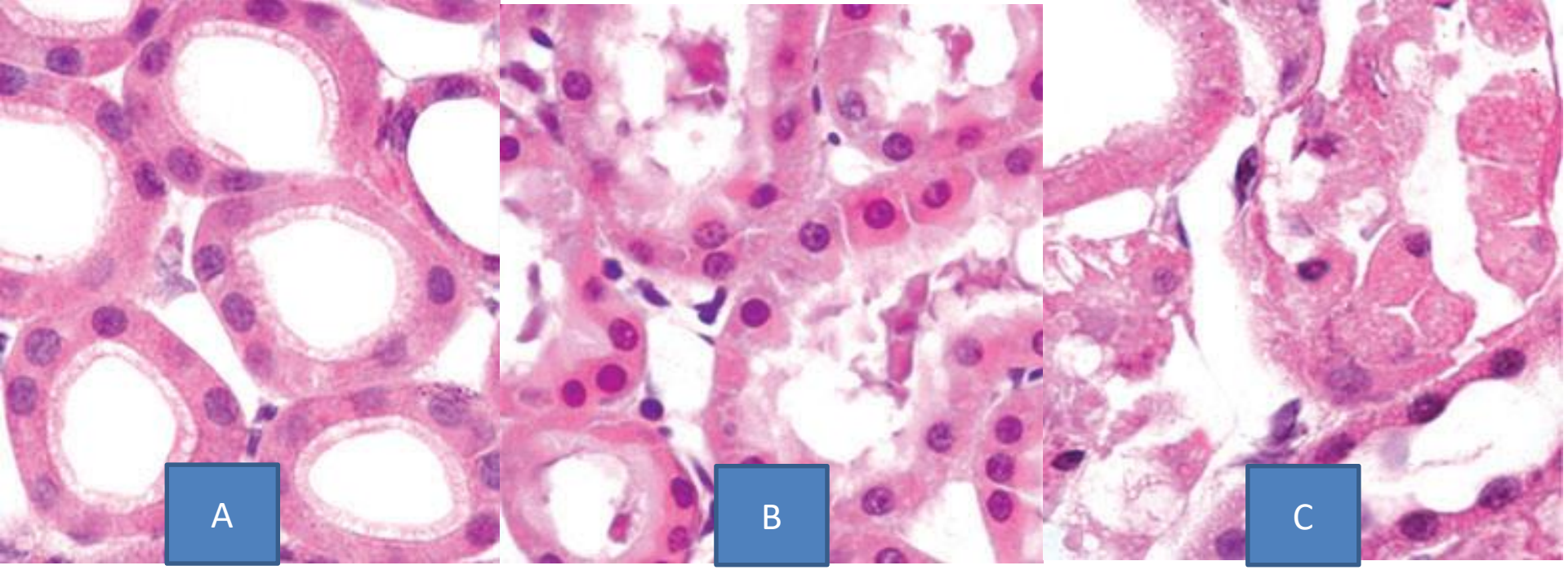
It cab be difficult morphological change to appreciate with LM . And may be more apperant at the level of whole organ .

Microscopically small, clear vacuoles My be seen within the cytoplasm;this pattern of non lethal reversible injury is called hydrpic change or vacuolar degeneration

Cellular swelling (hydropic change)



The affected hepatocytes are distended by accumulated water that imparts cytoplasmic pallor.



A, Normal kidney tubules with viable epithelial cells.

B, Early (reversible) ischemic injury showing surface blebs, increased eosinophilia of cytoplasm, and swelling of occasional cells.

C, Necrotic (irreversible) injury of epithelial cells, with loss of nuclei and fragmentation of cells and leakage of contents.

Intercellular accumulation of lipid :

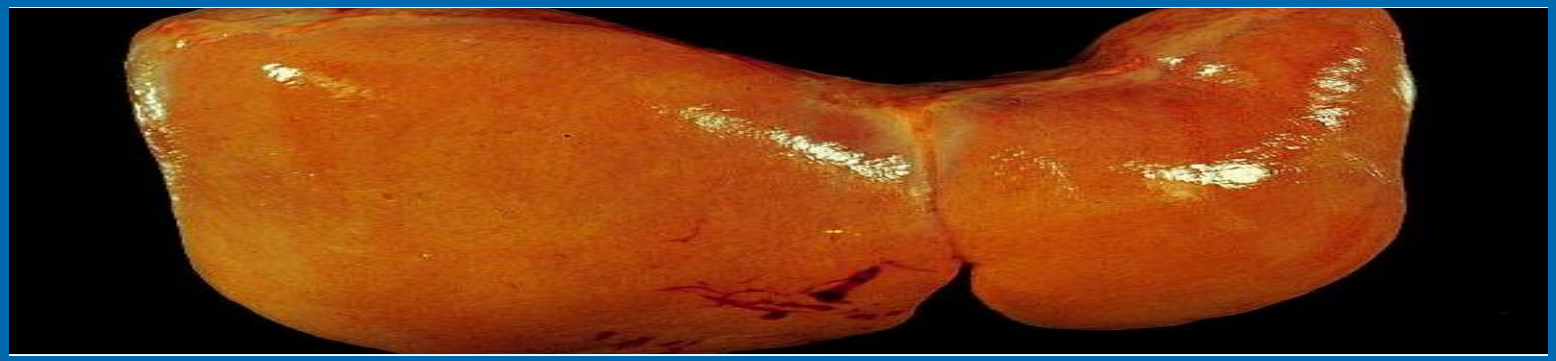
Fatty change: is the accumulation of neutral fat within parenchynal cells(lipid vacuoles). Seen in the liver, heart, skeletal muscle, kidney and others.

Etiology :

1. Starvation
2. Obesity
3. Malnutrition
4. Alcoholism
5. Diabetes mellitus
6. Chronic illness like T.B
7. Liver toxin

Grossly:

- Enlarged liver
- Waxy yellow surface
- Tense capsule
- The surface bulges on cut section /Greasy to touch



Organ: Liver.

Pathology or Lesion : Fatty Changes or Fatty Liver(. Gross: enlarged, greasy, yellow liver).

Etiology: abnormal accumulation of Triglycerides.

Important note: Recently proved, fatty change of liver predispose to cirrhosis &malignancy of liver

Microscopically:

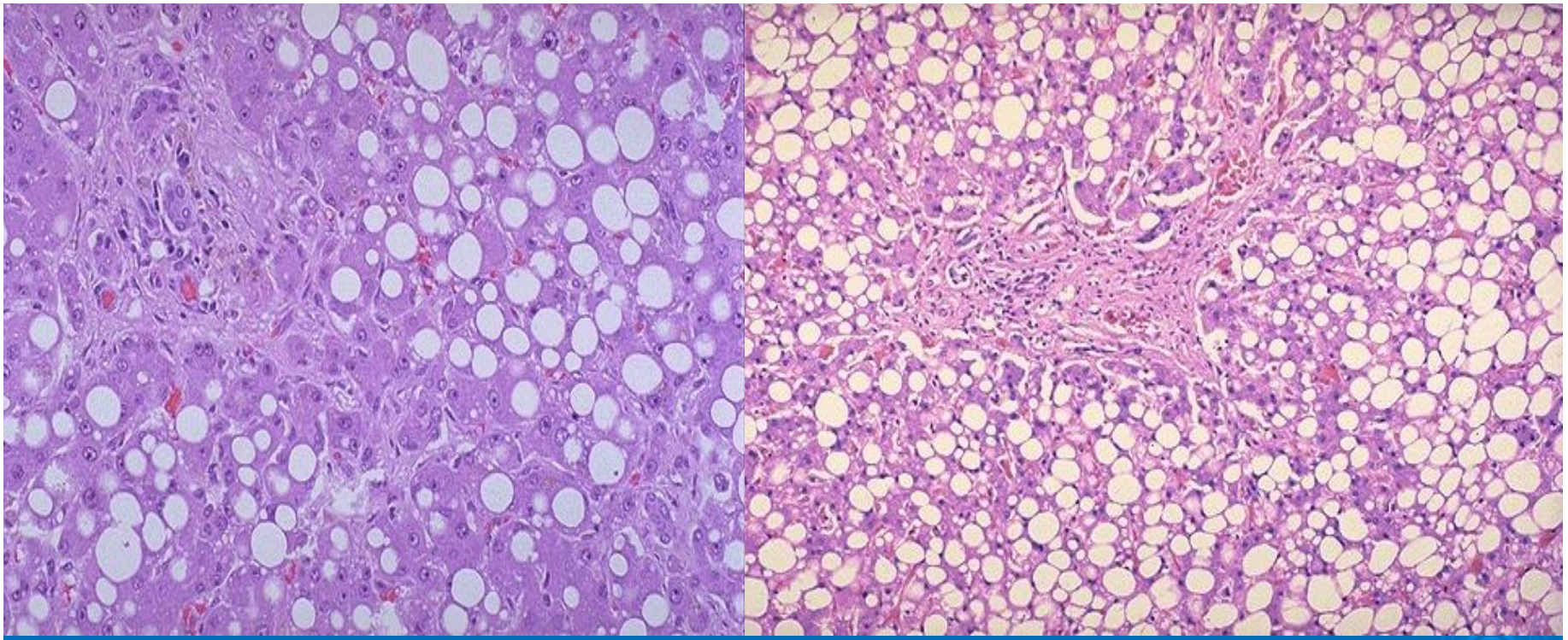
Many lipid vacuoles in the cytoplasm and around the nucleus (micro vesicular).

With progression, the vacuole become larger (macro vesicular) pushing the nucleus to the periphery.

Sometimes the hepatocytes filled with large lipid vacuoles may rupture and lipid vacuole coalesces to form fatty cyst.

Lesion: severe fatty change &hepatocytes atrophy

Diagnosis: liver cirrhosis



Organ: Liver.

Pathlogy or Lesion: Microscopical features of Fatty Liver (Intracytoplasmic fat or lipid vesicles).

Etiology: abnormal accumulation of Triglycerides.

Thanks