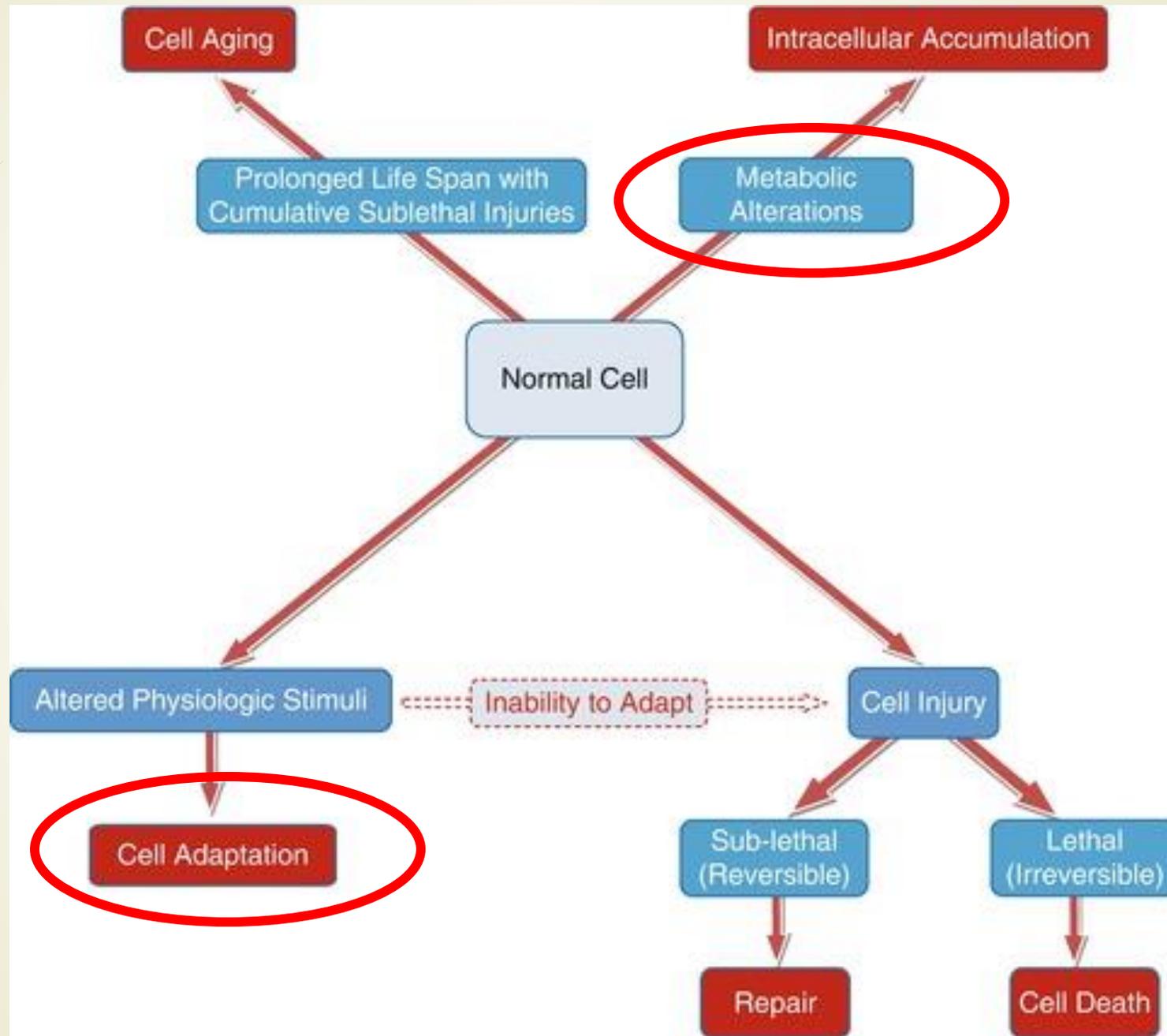


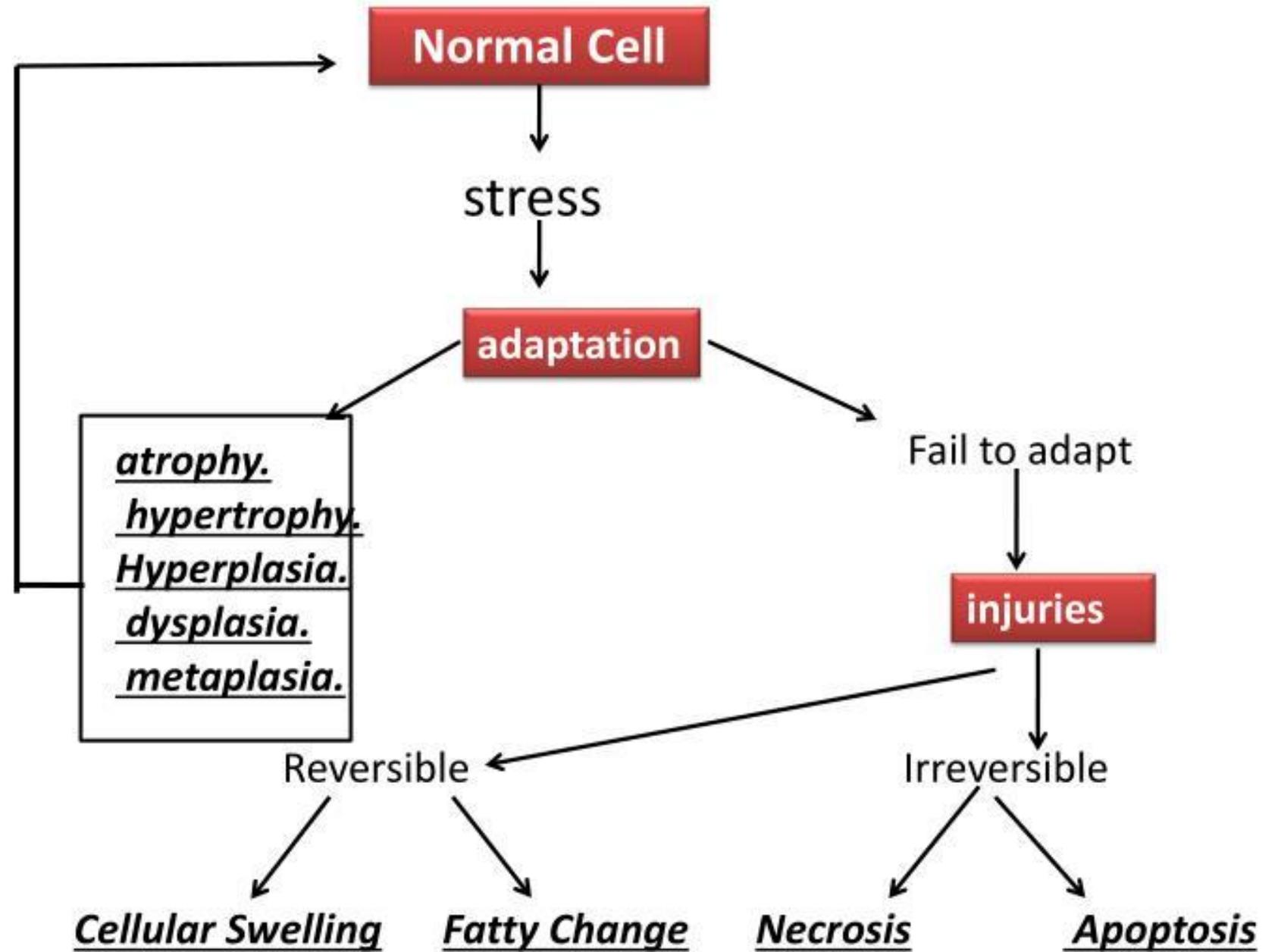
Cellular Adaptations and accumulations



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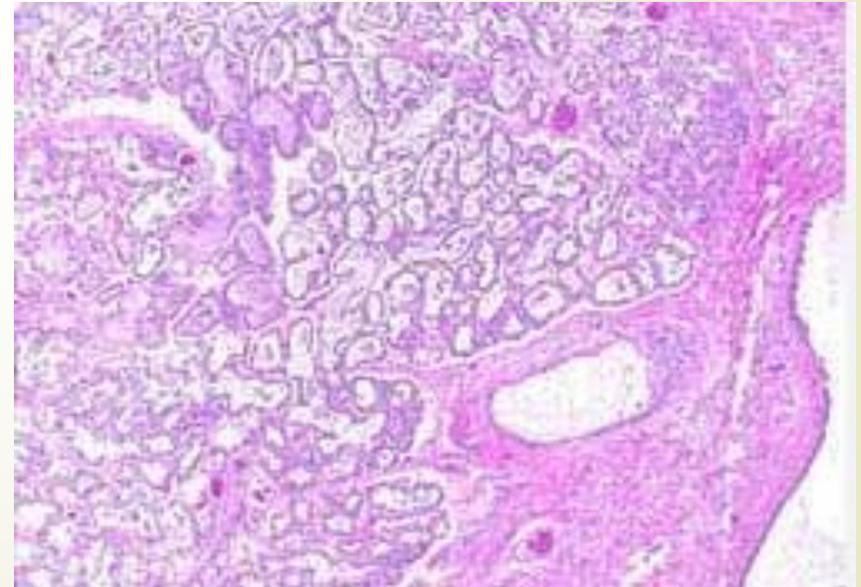
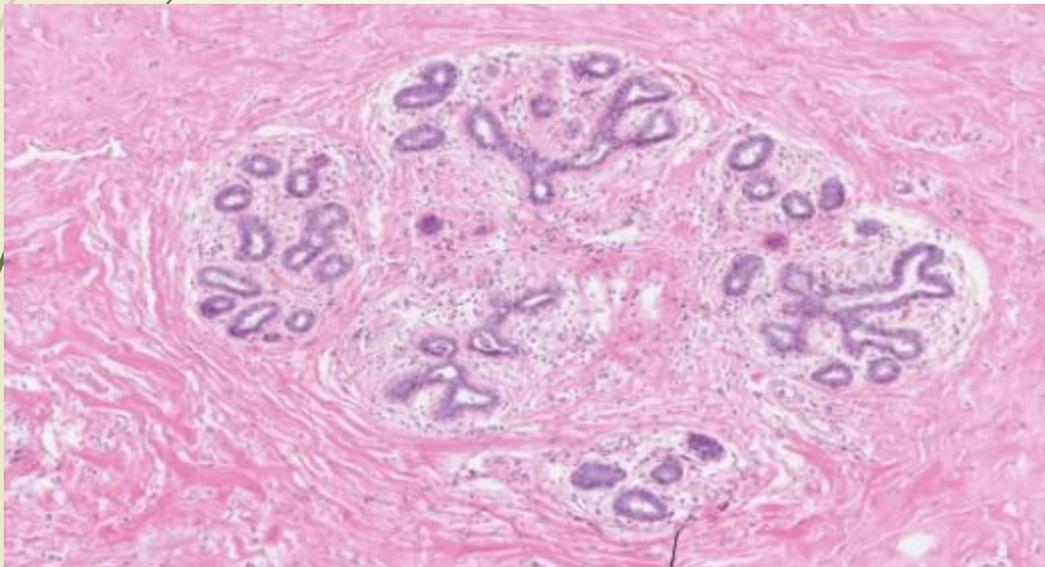




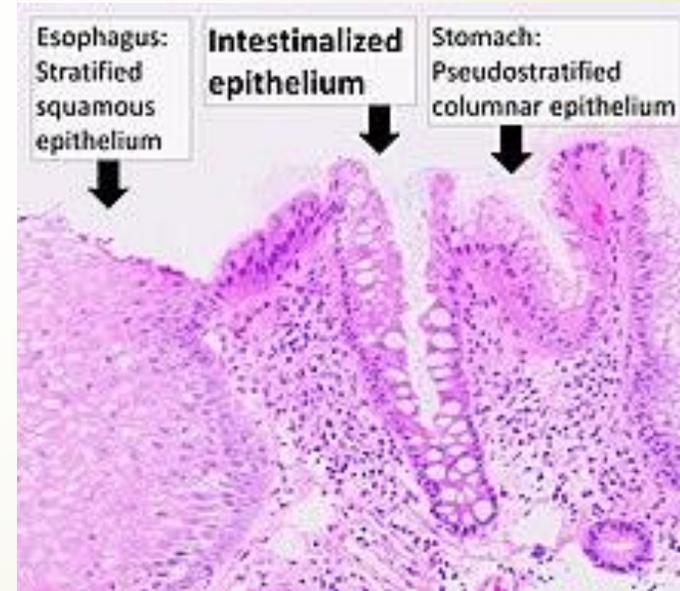
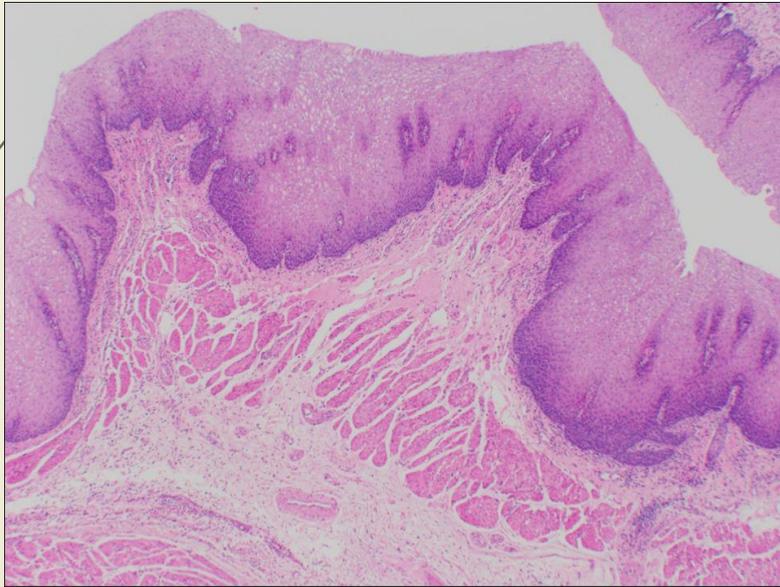
Cellular adaptation

- ▶ Cellular adaptation is the ability of cells to respond to various types of stimuli and adverse environmental changes.
 - ▶ Tissues adapt differently depending on the replicative characteristics of the cells that make up the tissue.
 - ▶ These changes usually make it easier for cells to tolerate adverse environments.
 - ▶ Persistent stress can lead to cell injury.
- 

- ▶ Changes experienced by cells in response to physiological stimuli such as:
 - increased muscular mass after exercising.
 - increased number of epithelial breast cells during pregnancy.



- ▶ Or pathological:
- Barrett esophagus due to chronic gastric acid exposure stimuli

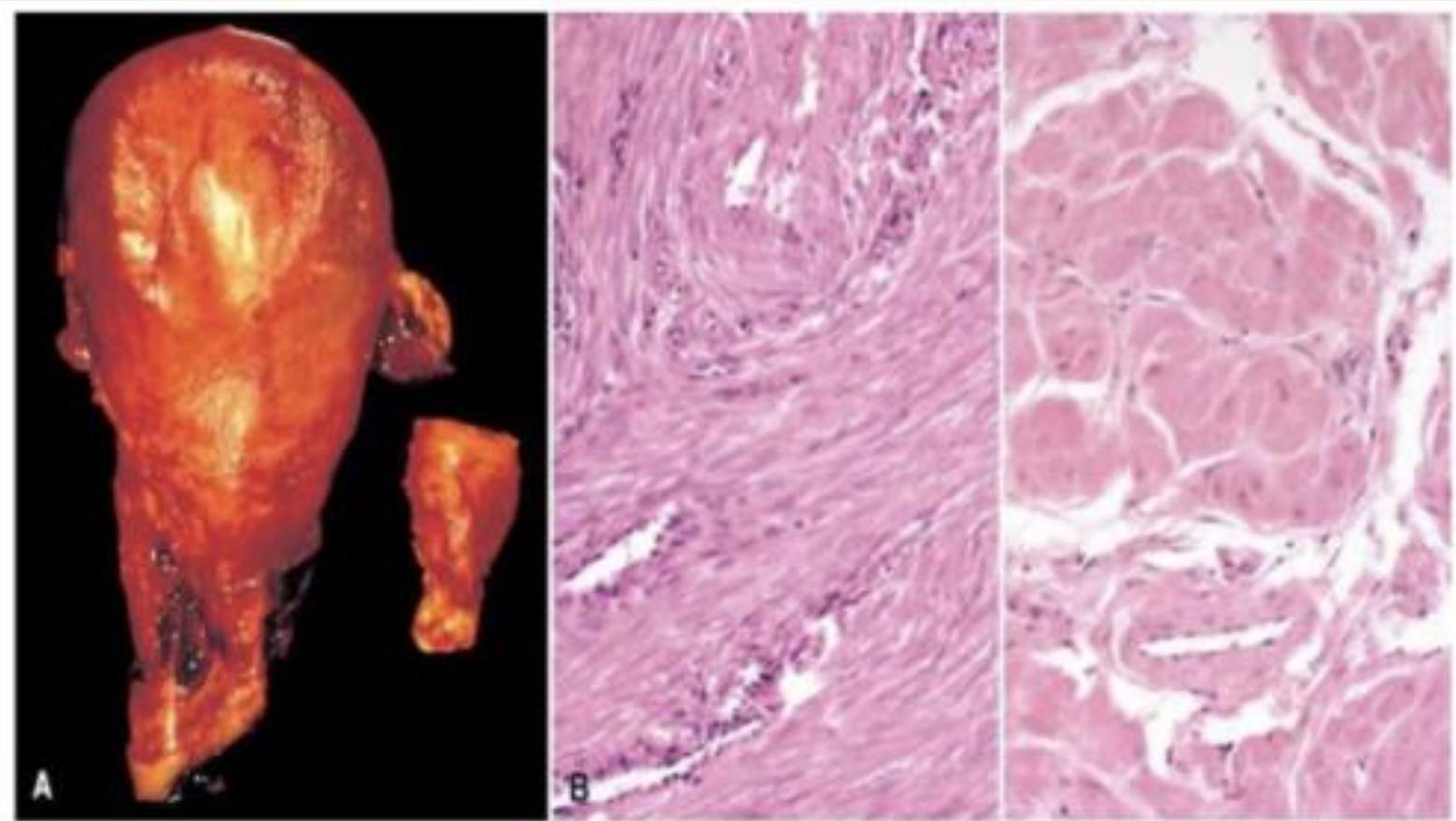




1. Hypertrophy

- ▶ Increased tissue size via enlargement of cells (due to an increase in organelles and structural proteins).
- ▶ Physiological hypertrophy
 - Increased muscle mass through sport
 - Uterus enlargement due to hormonal changes
- ▶ Pathological hypertrophy:
 - hypertrophic cardiomyopathy due to arterial hypertension

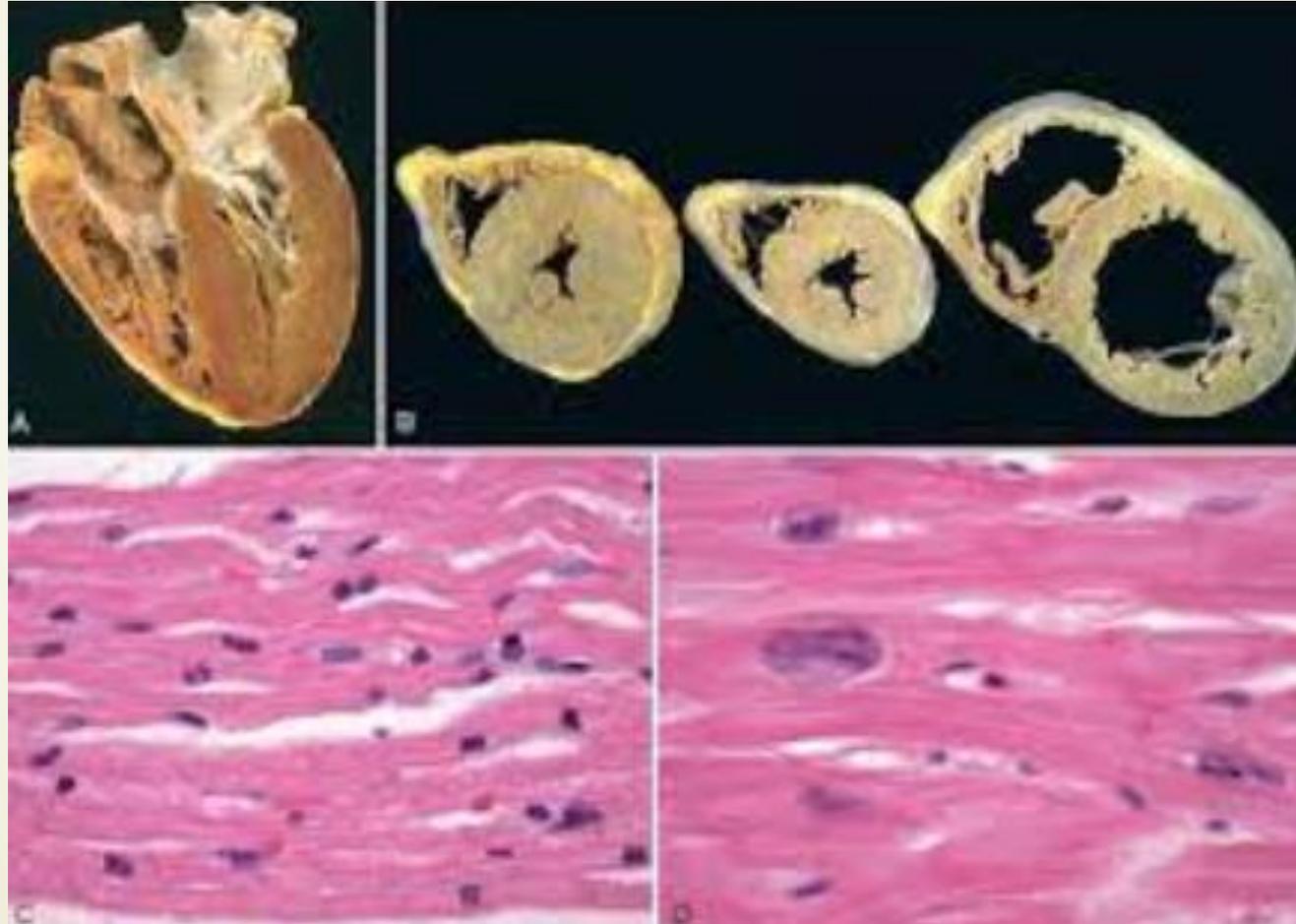
- Uterus enlargement due to hormonal changes



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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*).

- hypertrophic cardiomyopathy due to arterial hypertension





2. Hyperplasia

- ▶ Controlled proliferation in form of elevated reproduction rate of stem cells and differentiated cells → increased cell number → increased tissue mass.
- ▶ Hyperplasia takes place if the tissue contains cell populations capable of replication.
- ▶ may occur concurrently with hypertrophy
- ▶ Hyperplasia can be physiologic or pathologic; in both situations, cellular proliferation is stimulated by growth factors that are produced by a variety of cell types.

Types of physiologic hyperplasia are

(1) **Hormonal** hyperplasia:

the proliferation of the glandular epithelium of the female breast at puberty & during pregnancy.

(2) **Compensatory** hyperplasia:

residual tissue grows after damage or resection of part of an organ. (part of a liver is resected → mitotic activity in the remaining cells begins as early as 12 hours later, eventually restoring the liver to its normal size.

- ▶ This process is stimulated by growth factors produced by uninjured hepatocytes. After restoration of the liver mass, various growth inhibitors turn off cell proliferation.

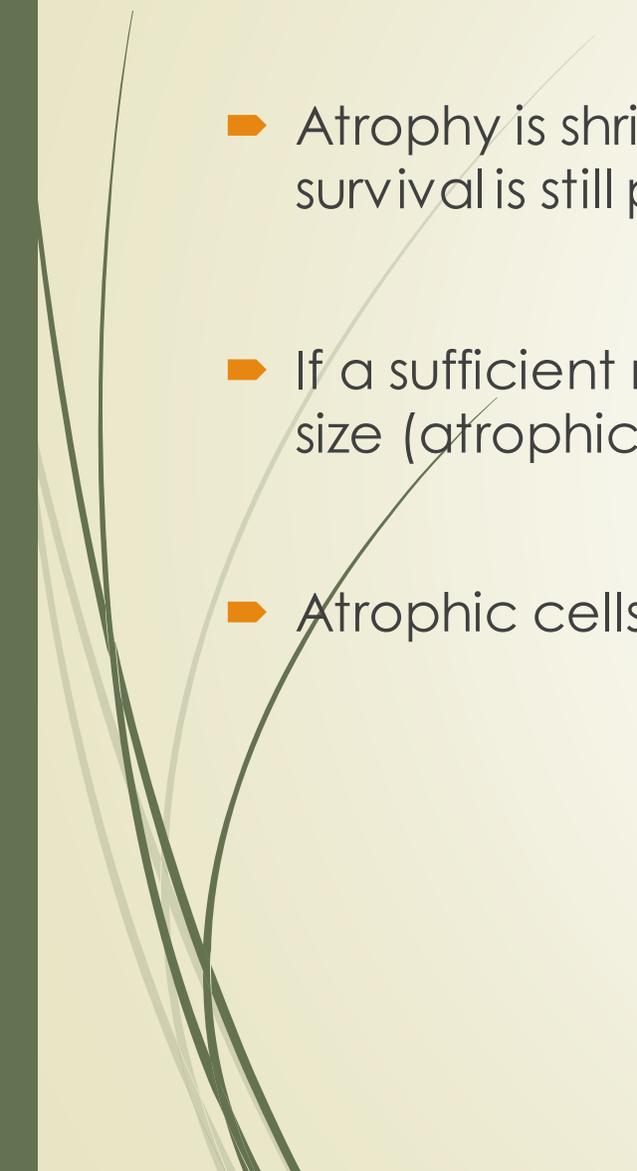
Pathologic hyperplasia

- ▶ Caused by **excessive** hormonal or growth factor stimulation.
- ▶ E.g. **Normally**, after a normal menstrual period there is a burst of uterine epithelial proliferation (tightly regulated by the stimulatory effects of pituitary hormones and ovarian estrogen and the inhibitory effects of progesterone)

A **disturbance** in this balance → increased estrogenic stimulation → endometrial hyperplasia, (a common cause of abnormal menstrual bleeding).



3. Atrophy

- ▶ Atrophy is shrinkage in the size of cells by the loss of cell substance, at which survival is still possible.
 - ▶ If a sufficient number of cells are involved, the entire tissue or organ is reduced in size (atrophic).
 - ▶ Atrophic cells may have diminished function, they are not dead.
- 



3. Atrophy

- ▶ Atrophy may be caused by physiological stimuli:
 - loss of hormone stimulation in menopause:

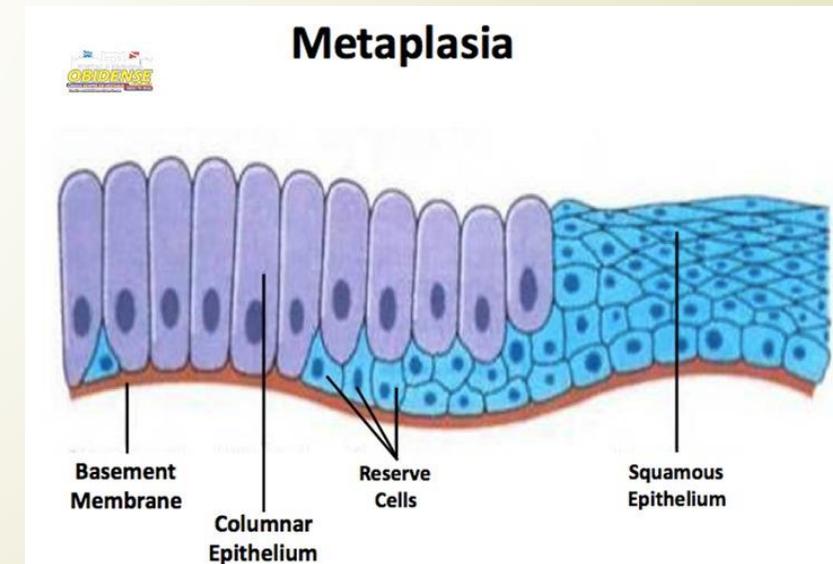
- ▶ OR pathologic :
 - denervation.
 - decreased workload during immobilization of a limb to permit healing of a fracture.
 - diminished blood supply
 - inadequate nutrition

- ▶ but the fundamental cellular changes are similar.

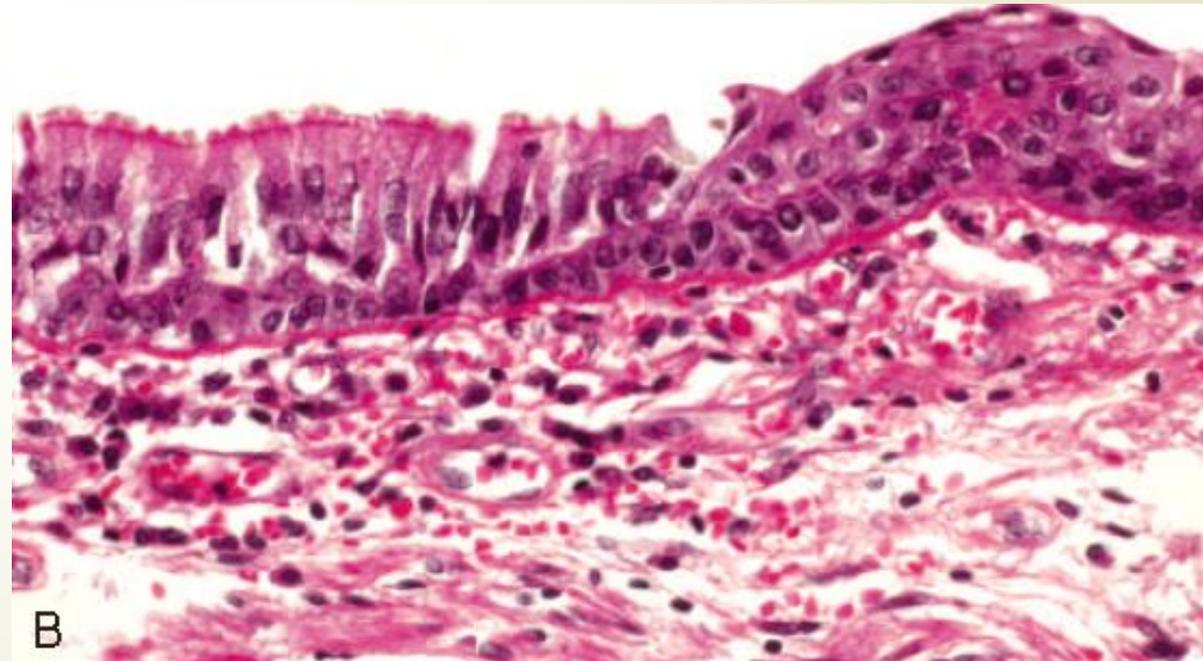
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- ▶ The process of cellular atrophy results from a combination of:
 - (1) decreased protein synthesis: reduced metabolic activity.
 - (2) increased protein degradation.

4. Metaplasia

- ▶ As a response to chronic stress, stem cells get reprogrammed into another type of epithelium (e.g., squamous metaplasia) that is more tolerable to the adverse environment.
- ▶ May completely regress or lead to a persistent insult and malignant transformation (dysplasia; considered precancerous)

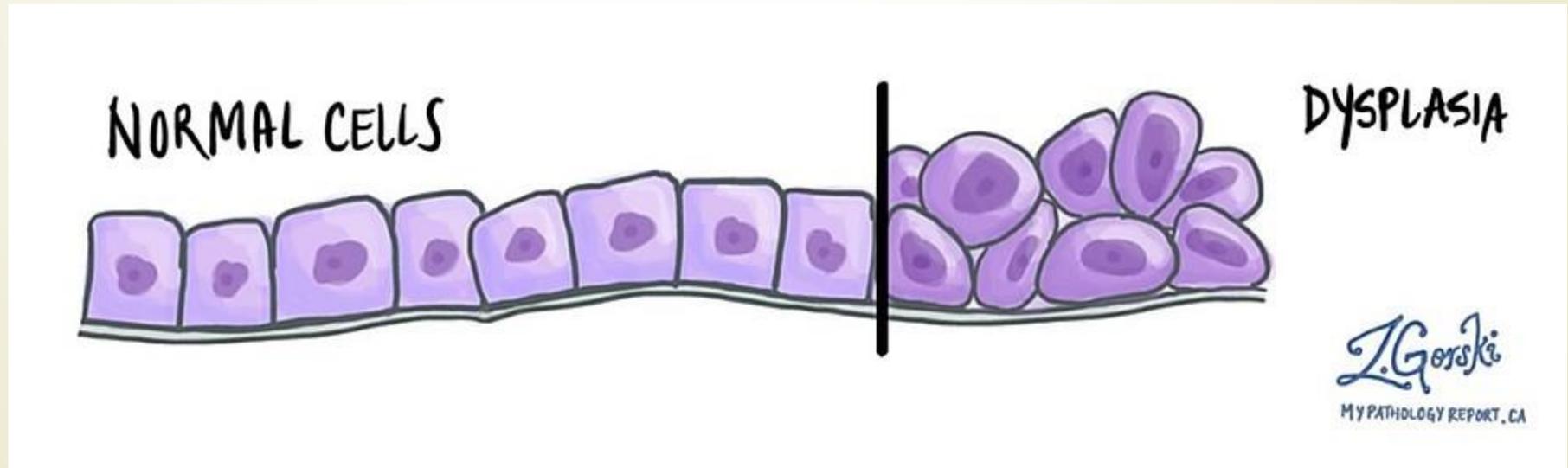


- ▶ In the respiratory epithelium of cigarette smokers the normal ciliated columnar epithelial cells of the trachea and bronchi → metaplasia → stratified squamous epithelial cells.
- ▶ The rugged stratified squamous epithelium can survive the noxious chemicals in cigarette smoke that columnar epithelium would not tolerate.
- ▶ Metaplasia here has survival advantages, but important protective mechanisms are lost, such as mucus secretion and ciliary clearance.



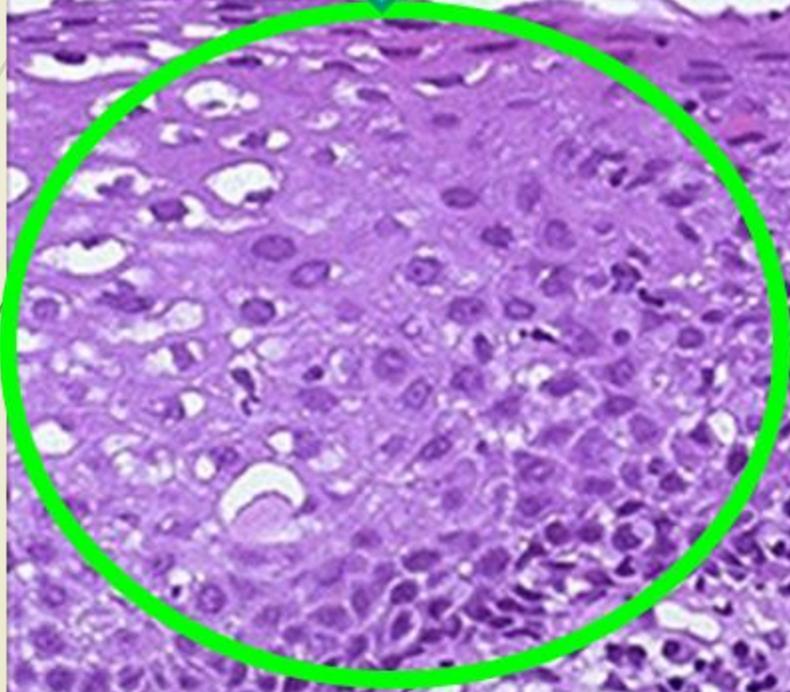
5. Dysplasia

- Dysplasia is an unequivocal neoplastic transformation of the epithelial cells that is confined within the basement membrane of the metaplastic glandular tissue within which it arises.
- Dysplasia is a precursor lesion to invasive carcinoma

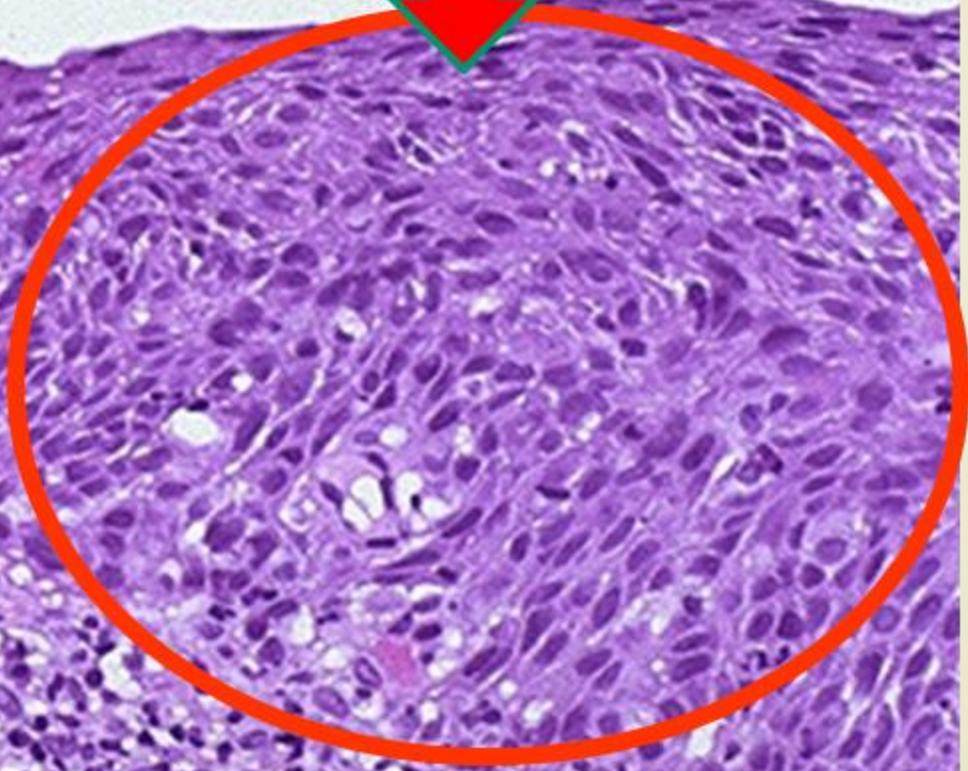
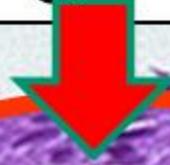




Normal

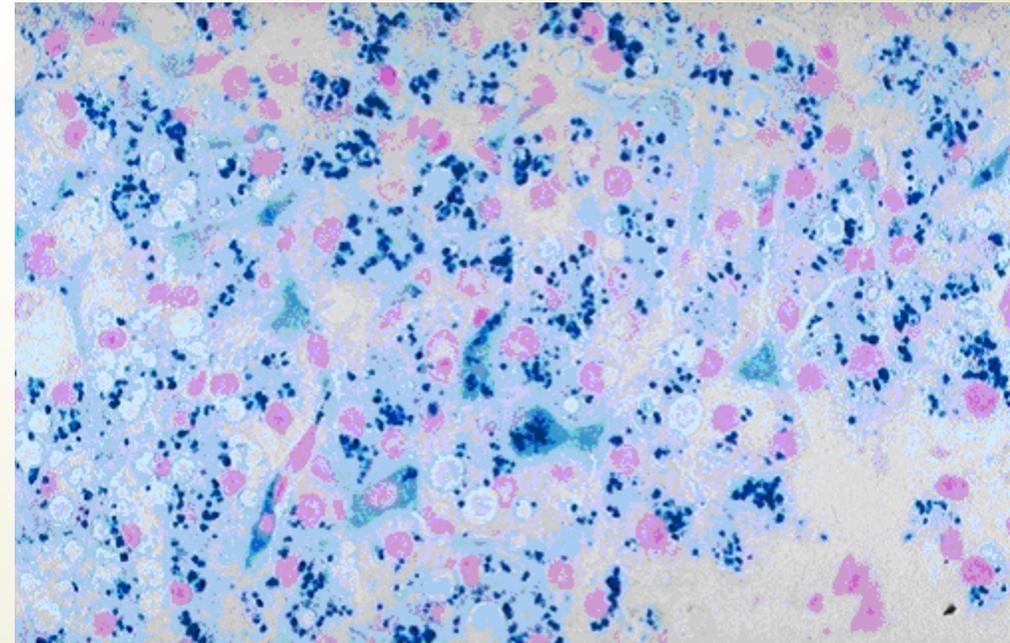


Abnormal architecture & arrangement



Intracellular Accumulations

- ▶ Accumulation of abnormal amounts of various substances under some circumstances, can be harmless or cause varying degrees of injury.
- ▶ Synthesized by the affected cells or it may be produced elsewhere



INTRACELLULAR ACCUMULATIONS

METABOLIC PRODUCTS

1. Lipid metabolism disorder products

- a. Fatty change
- b. Cholesterol metabolism
 - Atherosclerosis
 - Xanthomas
 - Cholesterosis
 - Neimann-Pick disease type C

2. Protein metabolism disorder products

- a. Resorption droplets in proximal renal tubules
- b. Russel Bodies
- c. Alpha 1 antitrypsin deficiency
- d. Cytoskeletal proteins
- e. Amyloidosis

3. Carbohydrate metabolism disorder products

- a. Glycogen storage disorders/Lysosomal storage disorders
- b. Diabetes Mellitus

PIGMENTS

exogenous

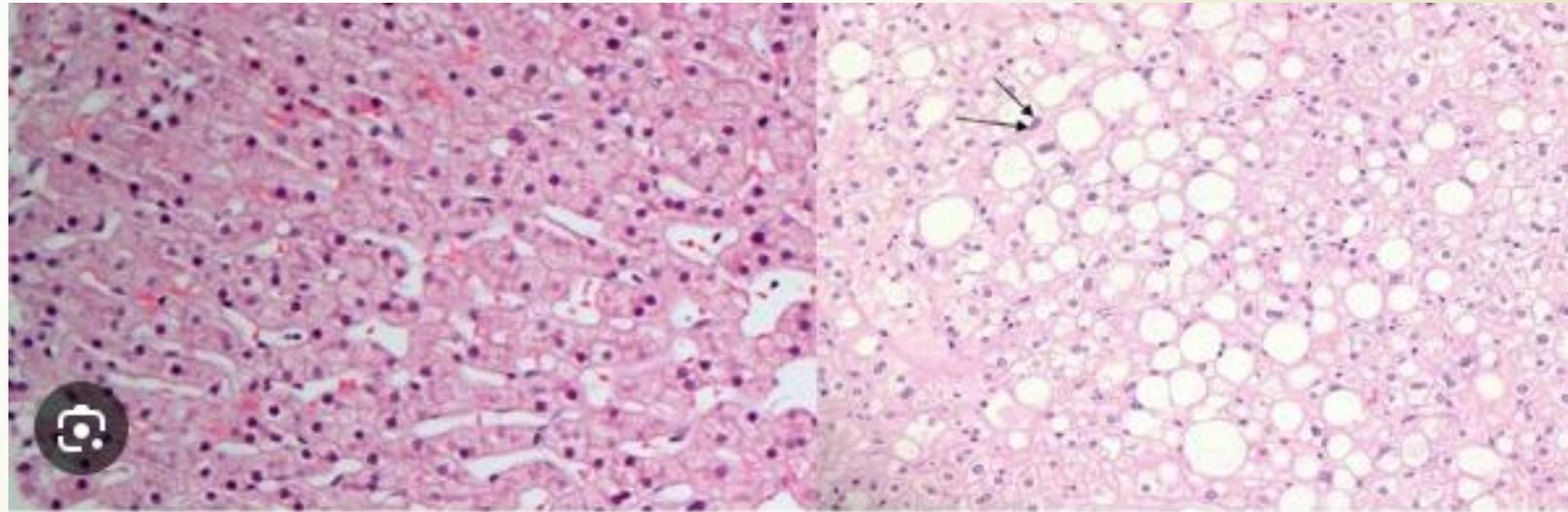
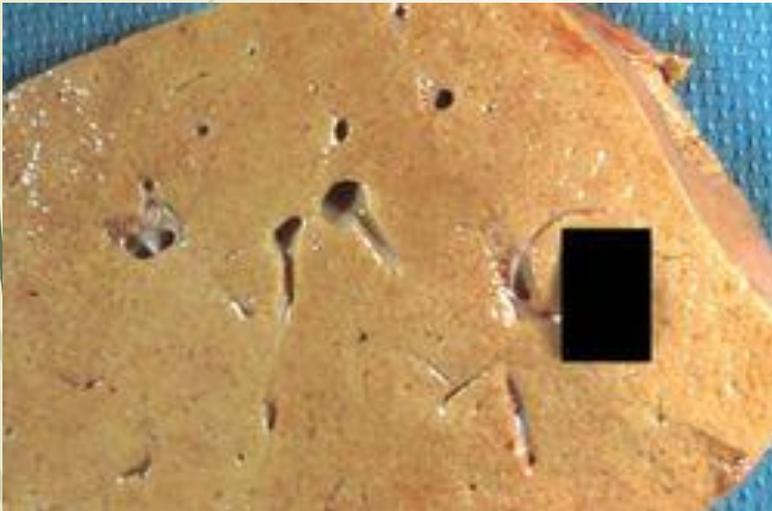
1. Coal
 - a. CWP
 - b. anthracosis
2. Tattooing

endogenous

1. lipofuscin
2. Hemosiderin
3. Melanin
4. Homogentisic acid
5. Bilirubin

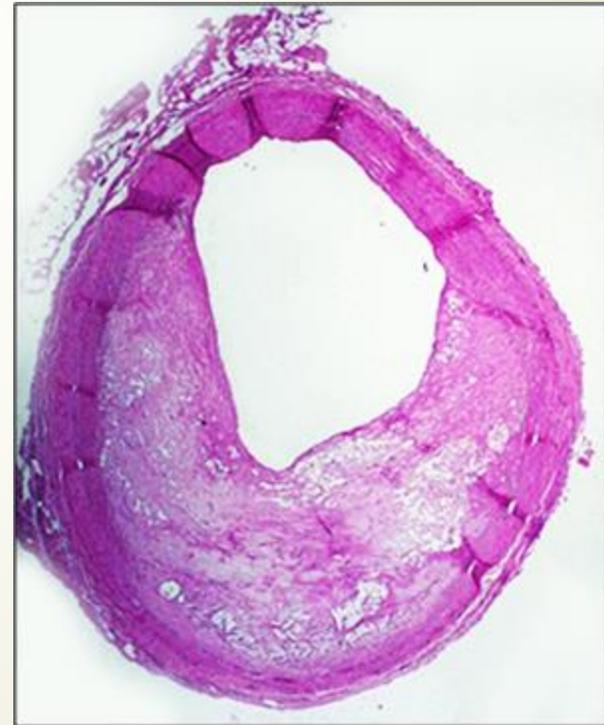
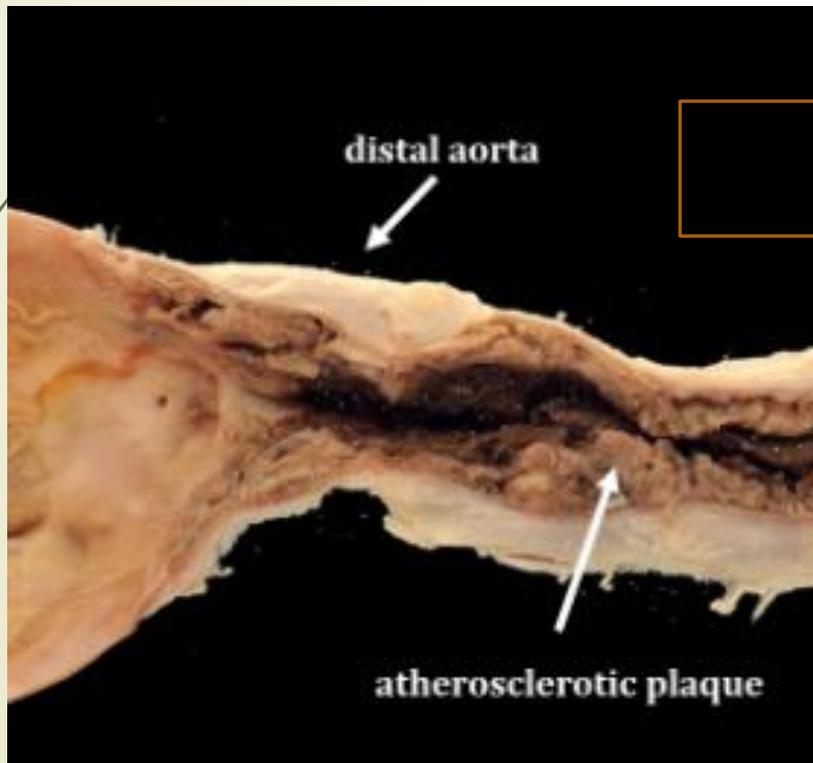
1. Fatty liver

- Caused by different causes like starvation or alcohol.
- Grossly: Greasy appearance.
- Microscopic: fat vacuoles accumulation.



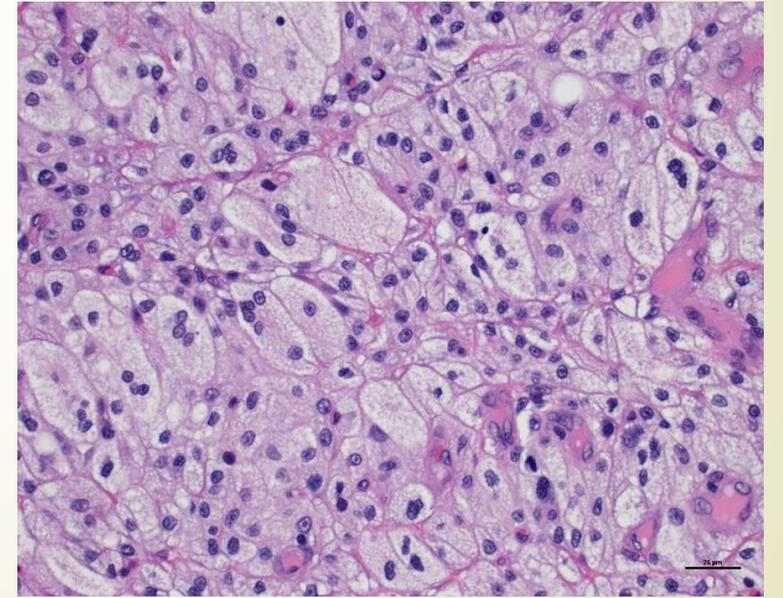
2. Atherosclerosis

- ▶ Accumulation of cholesterol plaques in intimal layers of aorta and large vessels.



3. Xanthoma

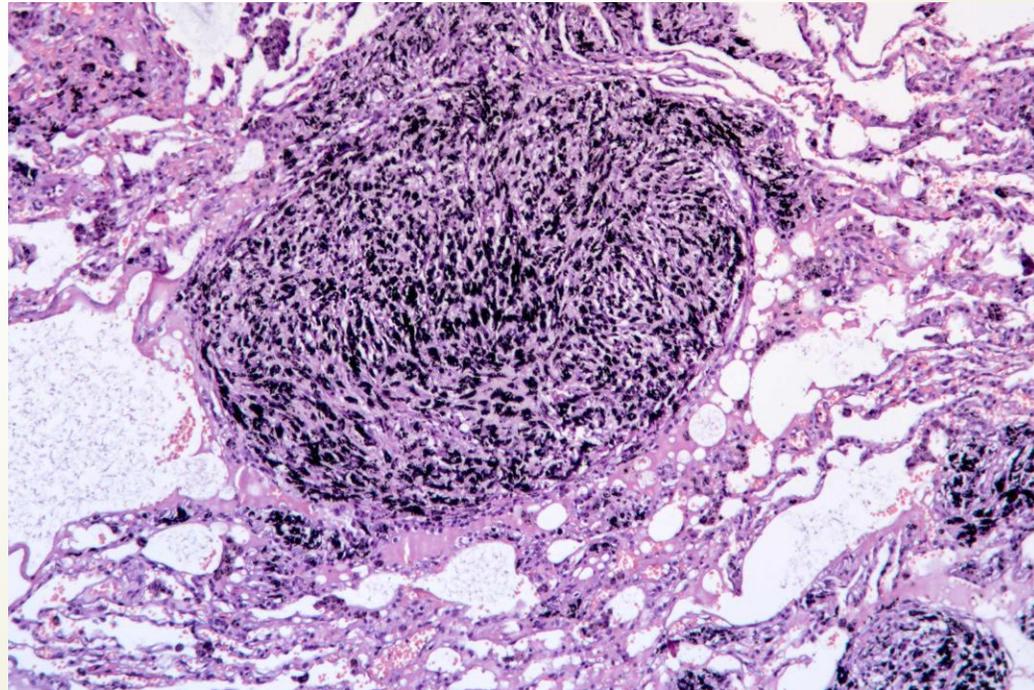
- Accumulation of fat in macrophages in the skin



Pigments:

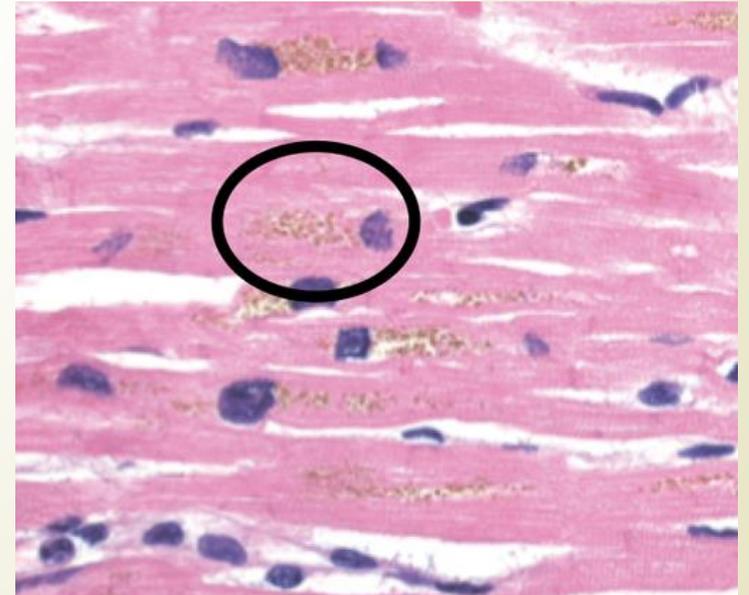
I. Exogenous pigment:

- ▶ Coal Workers' Pneumoconiosis:
 - CWP is defined as parenchymal lung disease secondary to the inhalation of coal dust, which includes both carbonaceous (coal) and noncarbonaceous minerals such as silica and silicates.



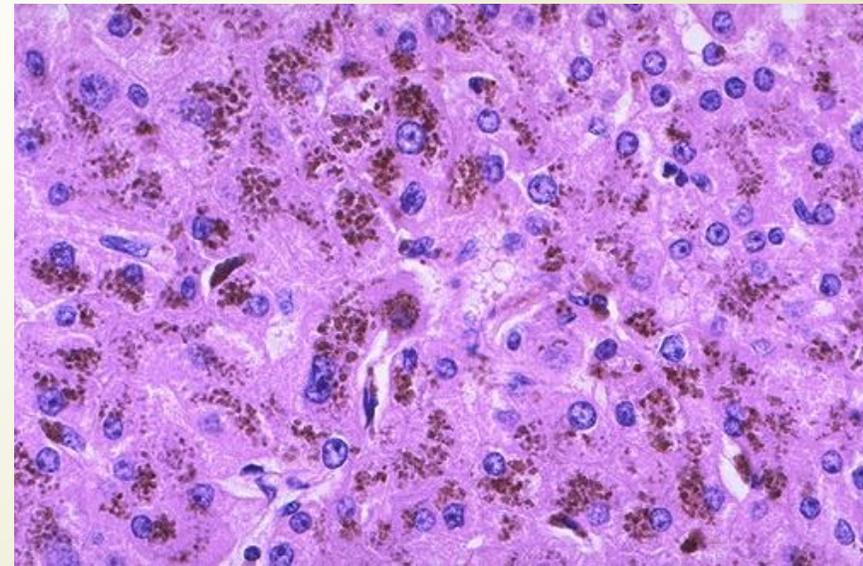
II. Endogenous : 1. Lipofuscin “wear-and-tear pigment”

- An insoluble brownish-yellow granular intracellular material that accumulates in a variety of tissues (heart, liver, and brain) with aging or atrophy.
- Lipofuscin represents complexes of lipid & protein that are produced by the free radical–catalyzed peroxidation of polyunsaturated lipids of subcellular membranes.



2. Hemosiderin.

- ▶ A hemoglobin-derived granular pigment that is golden yellow to brown.
- ▶ Accumulates in tissues when there is a local or systemic excess of iron.
- ▶ Iron is normally stored within cells in association with the protein apoferritin, forming ferritin micelles.
- ▶ Hemosiderin pigment represents large aggregates of these ferritin micelles, readily visualized by light and electron microscopy.



3. Melanin.

- An endogenous, brown-black pigment that is synthesized by melanocytes located in the epidermis.
- Acts as a screen against harmful UV radiation.
- Although melanocytes are the only source of melanin, adjacent basal keratinocytes in the skin can accumulate the pigment (e.g., in freckles), as can dermal macrophages.

