



CELL INJURY

CELLULAR ADAPTATIONS

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FACULTY OF APPLIED SCIENCES SUMMER SEMESTER

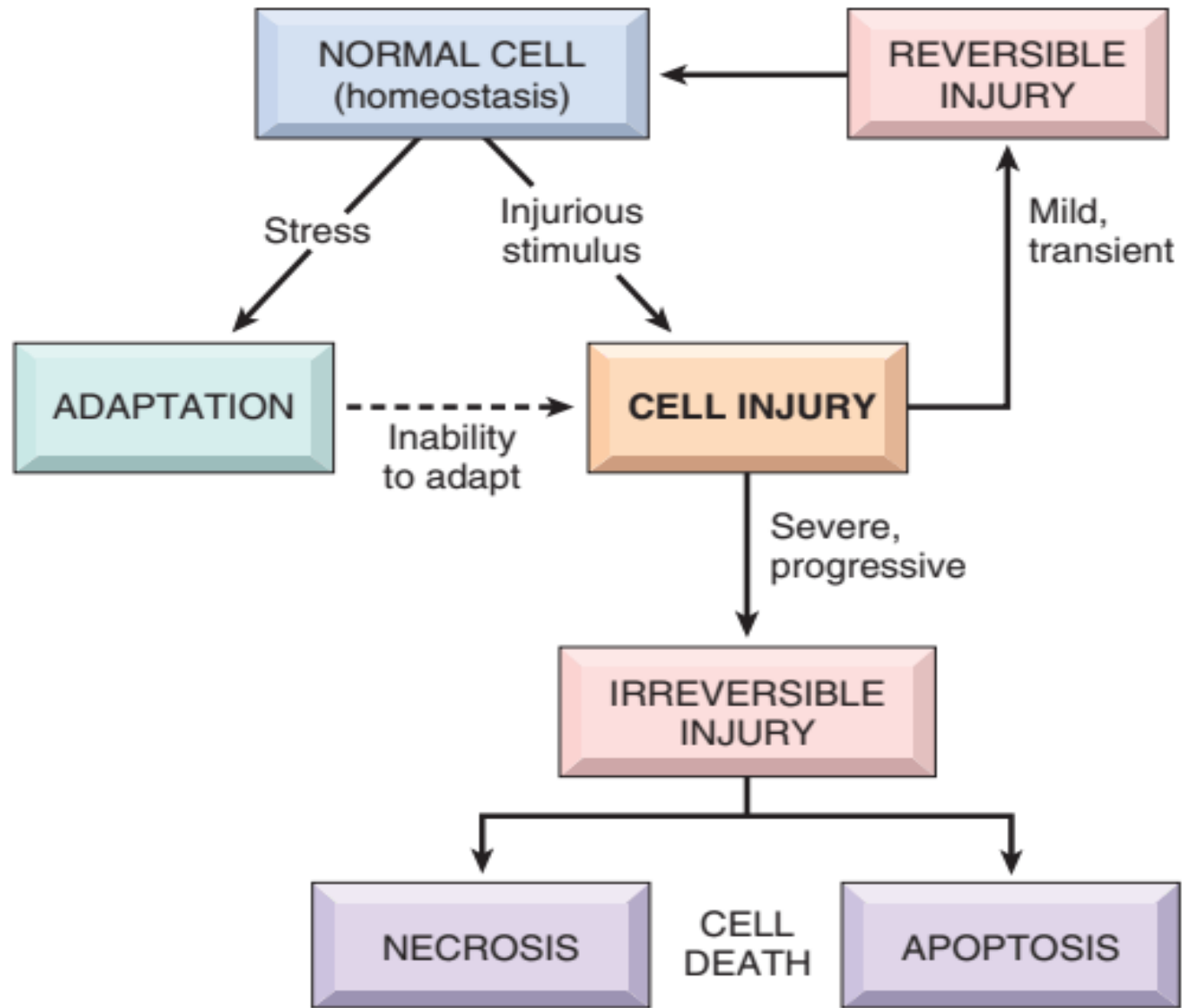
GENERAL PATHOLOGY GRADE - 4

WEEK – 2

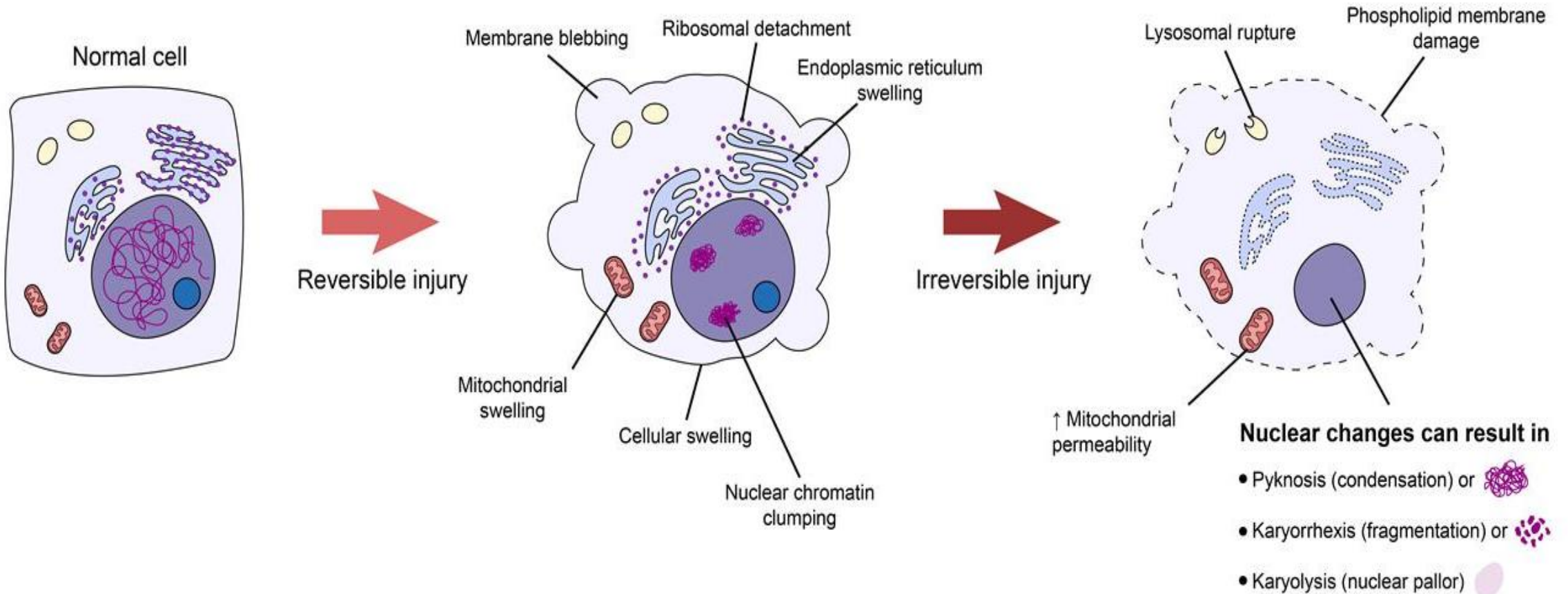
LEC. 2

CELL INJURY AND CELLULAR ADAPTATIONS

- **Homeostasis** – cell maintaining a steady state and handling the physiological demand
- Cells can alter their functional state in response to modest stress to maintain the steady state.
- More excessive physiologic stresses or adverse pathologic stimuli (injury), result in:
 1. Adaptation.
 2. Reversible injury.
 3. Irreversible injury and cell death.



Cell Injury



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- **Adaptations** – A new altered steady state with structural and functional changes in cell to handle the severe physiologic stress and some pathologic stimuli
 - **Cell adaptations** are reversible and cell can revert back to normal when the stimuli is removed

CELL INJURY AND CELLULAR ADAPTATIONS

Cellular responses to stress & injurious stimuli

Normal cell (homeostasis)

Altered physiologic stimuli and non lethal injurious stimuli



CELL ADAPTATIONS

- HYPERPLASIA
- HYPERTROPHY
- ATROPHY
- METAPLASIA
- DYSPLASIA

Injurious stimuli like reduced oxygen supply, chemical injury and microbial infection



CELL INJURY



Acute and transient



REVERSIBLE CELL INJURY



Progressive and severe



IRREVERSIBLE CELL INJURY



CELL DEATH

Necrosis and apoptosis

CELL ADAPTATIONS

HYPERPLASIA

- Increase in the number of cells in an organ or tissue resulting in increased volume of organ
- Hyperplasia takes place if the cells are capable of synthesizing DNA , thus permitting mitotic activity
- Hyperplasia can be
 - a) Physiological
 - b) Pathological

MECHANISM OF HYPERPLASIA

Activation of particular intracellular signaling pathways



Increased transcription of genes encoding for the GF, GF receptors & cell cycle regulators



Increased production of growth factors



Increased level of growth factor receptors



CELL PROLIFERATION

CELL ADAPTATIONS

HYPERPLASIA

PHYSIOLOGICAL HYPERPLASIA

This can be divided into

a) Hormonal hyperplasia – increase in functional capacity of a tissue when needed

Eg – proliferation of glandular epithelium of female breast (puberty and during pregnancy).

b) Compensatory hyperplasia – increase in tissue mass after damage or partial resection

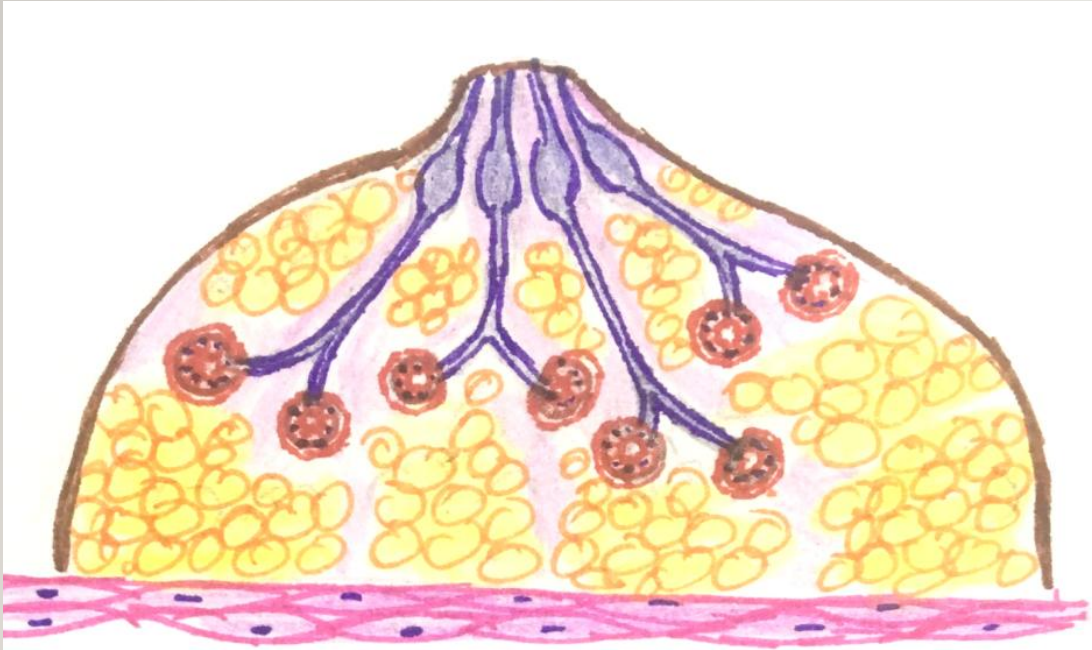
Eg – Liver after partial resection



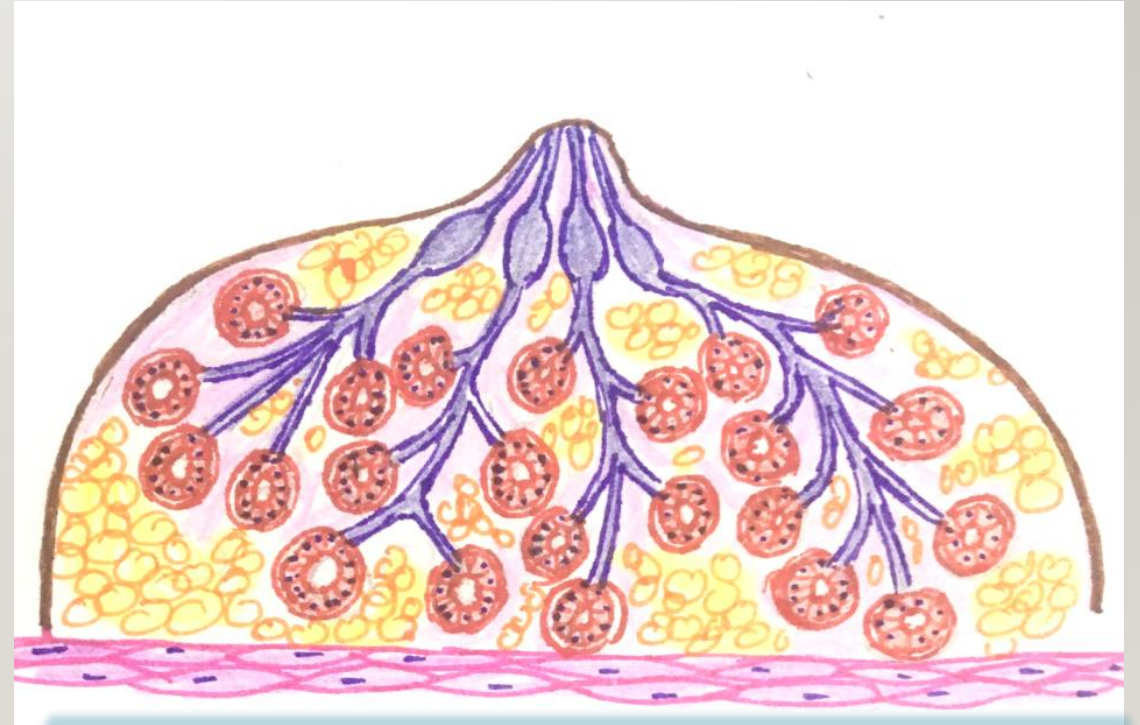
PHYSIOLOGICAL HYPERPLASIA

Action of hormones or growth factors

Mammary gland hyperplasia in pregnancy and lactation



Normal mammary tissue

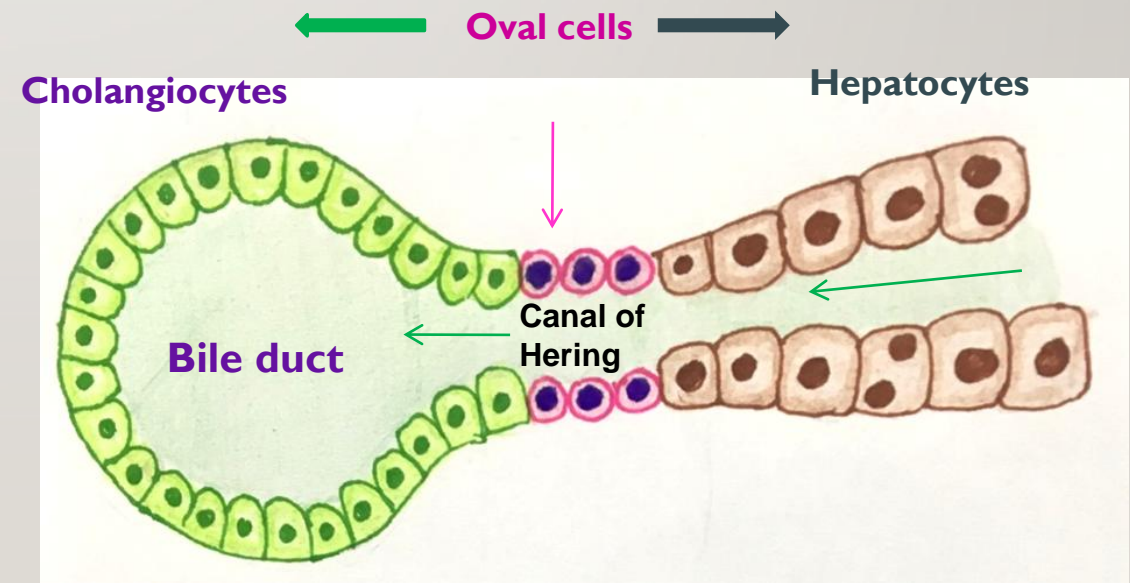
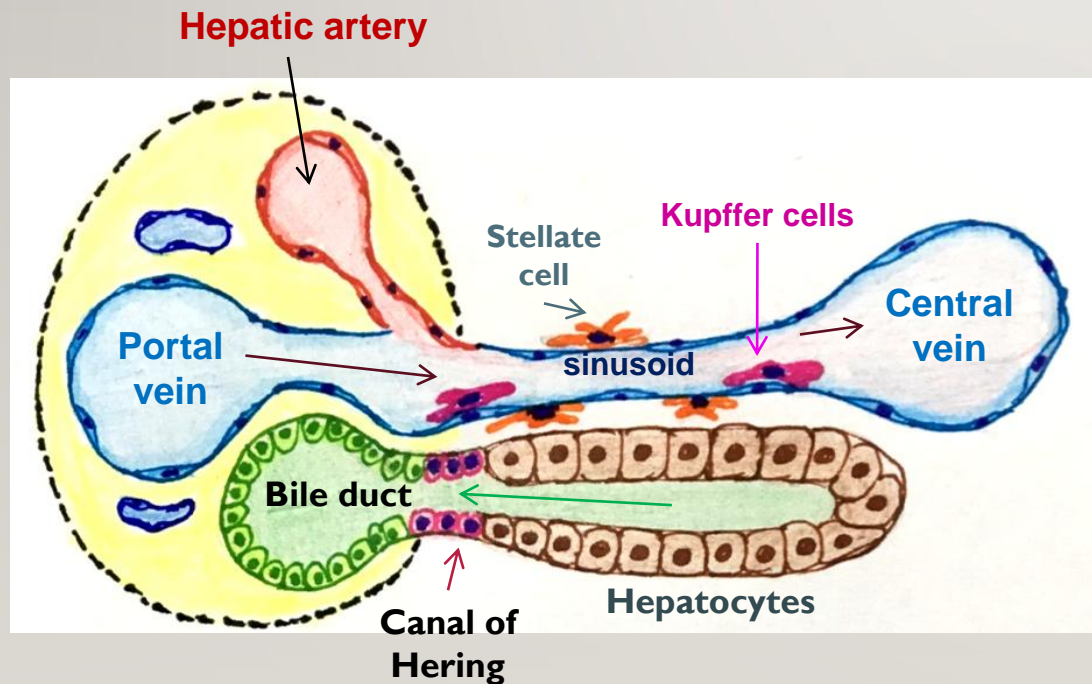


Mammary gland hyperplasia under the influence of estrogen and progesterone

PHYSIOLOGICAL HYPERPLASIA

Compensatory increase after damage or resection of tissue (stem cells)

Hepatic regeneration after resection



CELL ADAPTATIONS

HYPERPLASIA

PATHOLOGICAL HYPERPLASIA

- It is caused by excessive hormonal stimulation or GF acting on target cells

Eg – Endometrial hyperplasia because of estrogen

- Benign prostatic hyperplasia because of growth factors

- Pathologic hyperplasia however constitutes a fertile soil in which cancerous proliferation may eventually arise
- In pathologic hyperplasia if the stimulus removed the hyperplasia disappears.



ENDOMETRIAL HYPERPLASIA

Occurs due to prolonged stimulation by increased estrogen hormone

Normal endometrium

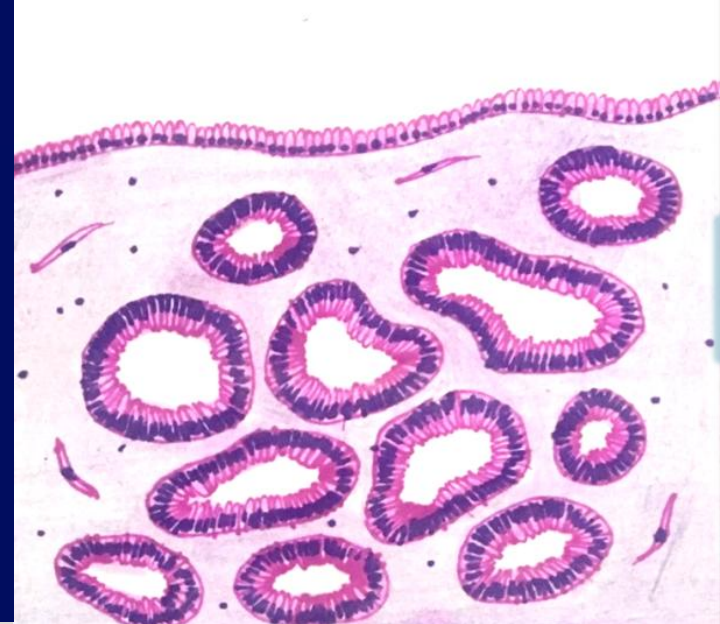


Round tubular glands with equal gland to stromal ratio

Estrogen



Endometrial hyperplasia

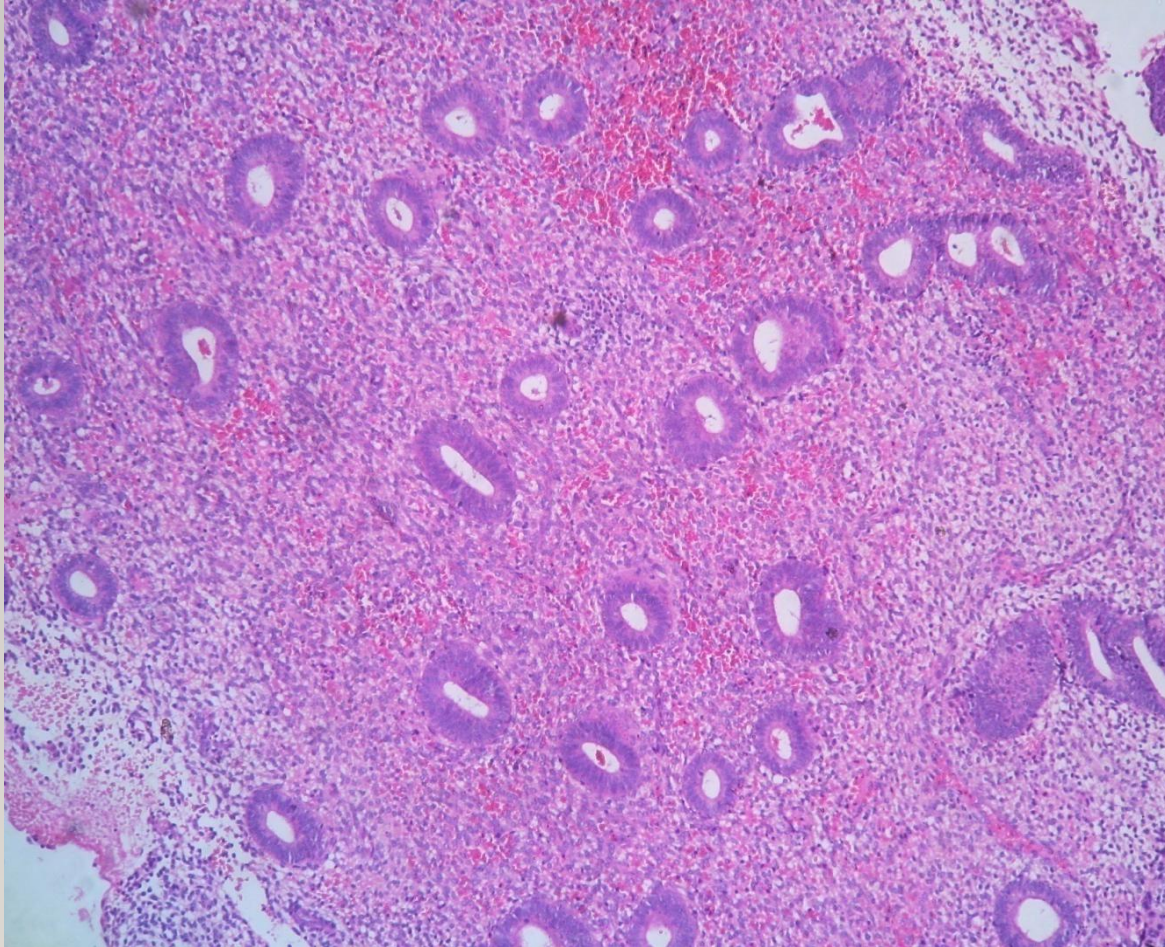


Crowded irregular glands with atypia

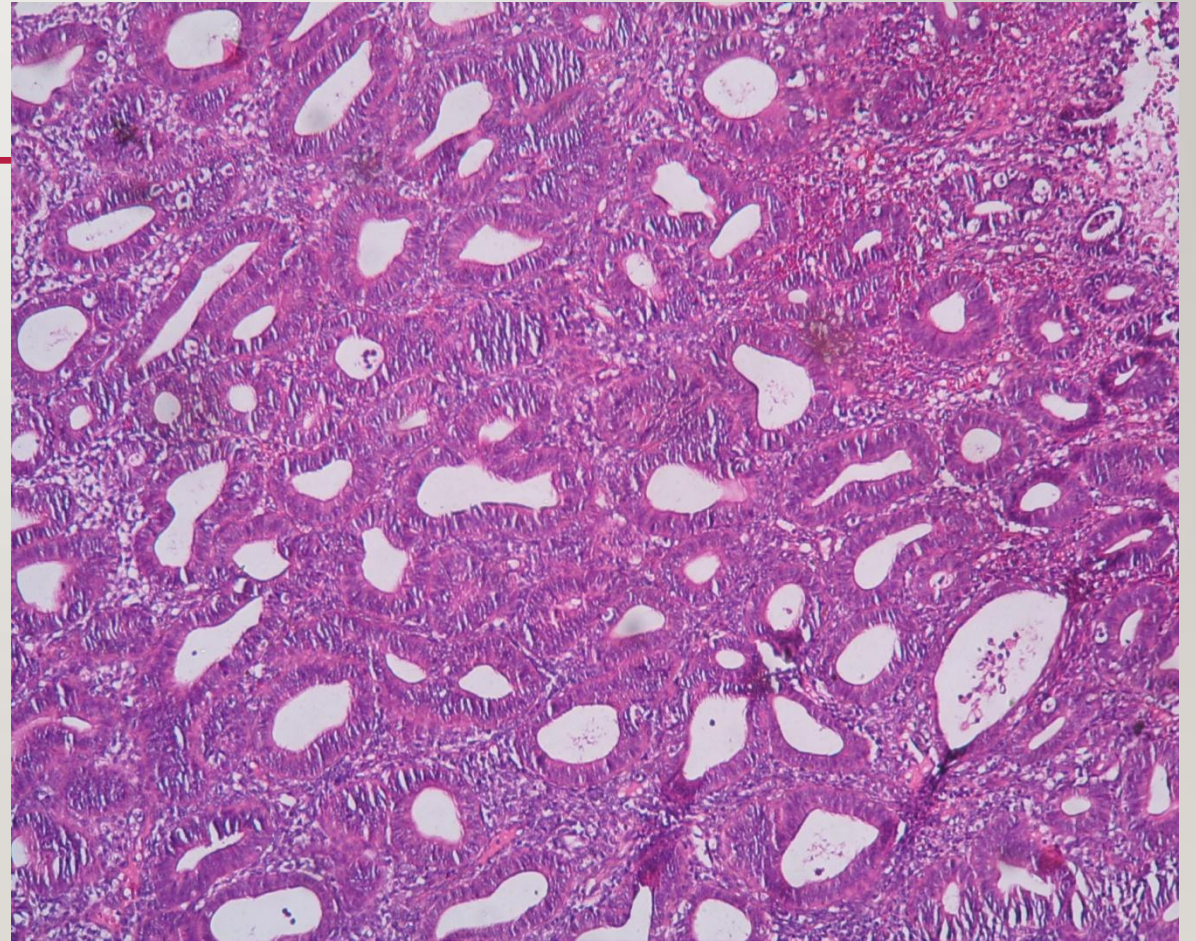
CAUSES OF HYPERESTROGENISM

Granulosa cell tumor, Estrogen replacement therapy, Polycystic ovarian disease, anovulation and obesity

HYPERPLASIA

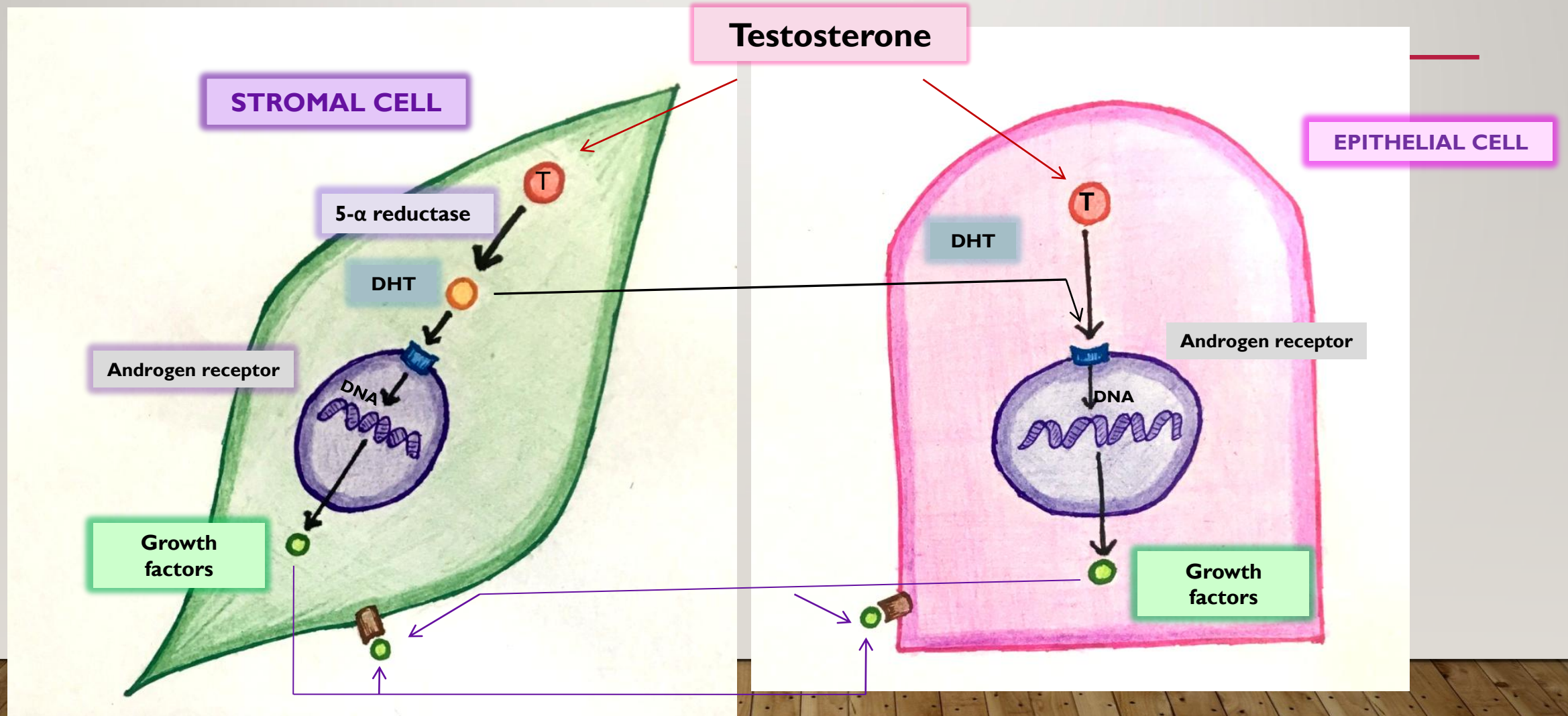


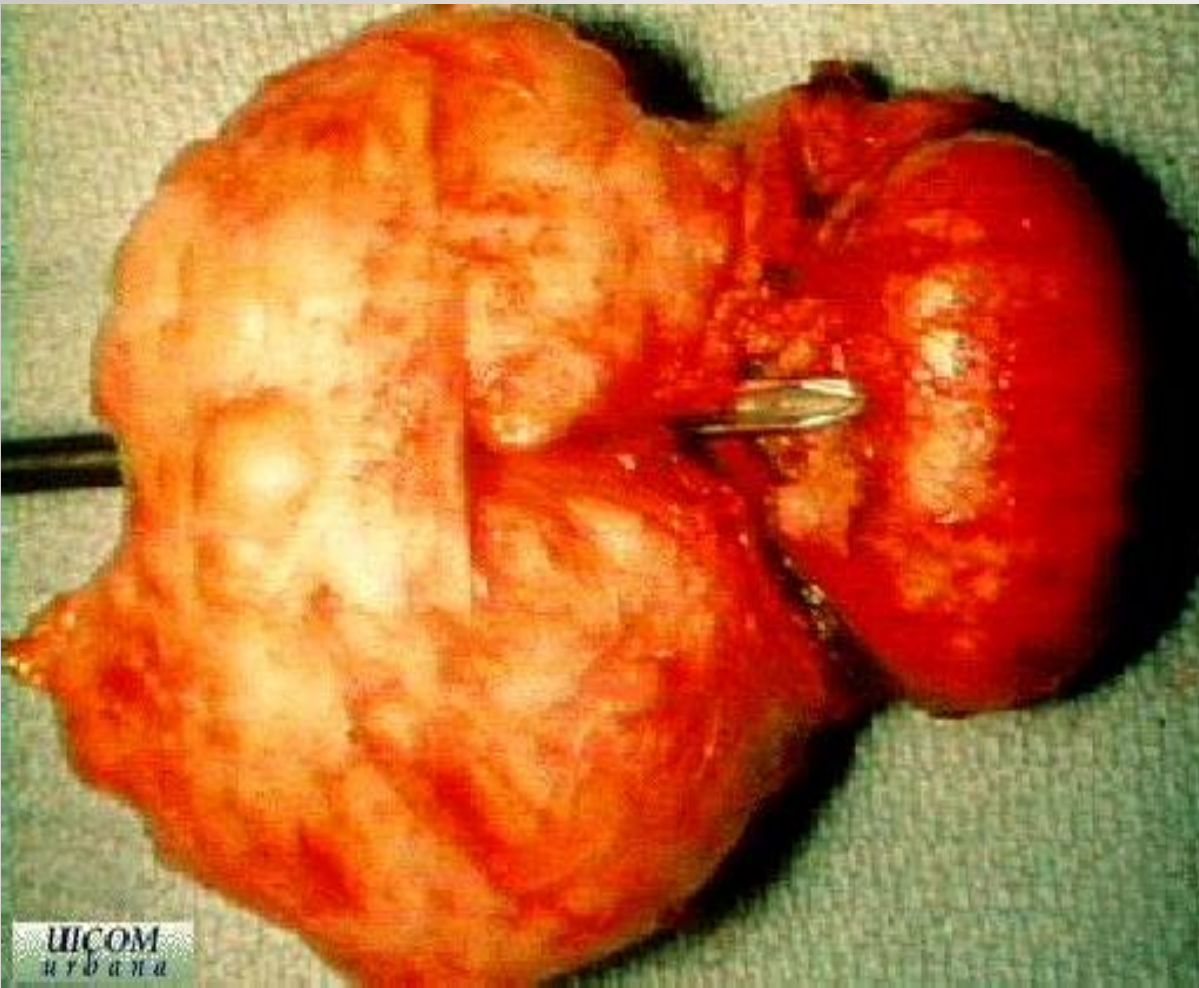
NORMAL ENDOMETRIUM



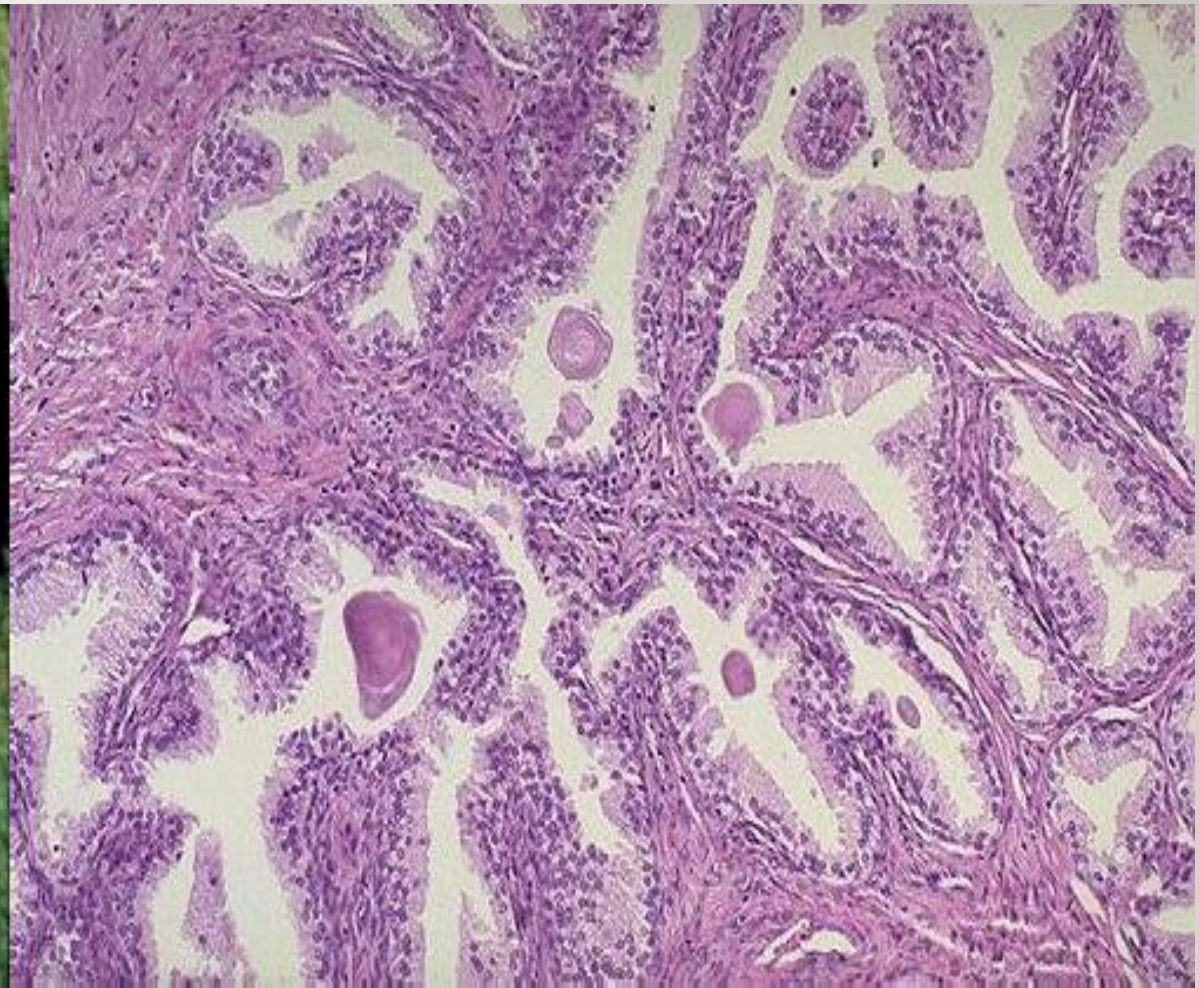
ENDOMETRIAL HYPERPLASIA

BENIGN PROSTATIC HYPERPLASIA





Benign prostatic hyperplasia
Pathologic hormonal hyperplasia



Microscopical appearance of BPH

CELL ADAPTATIONS

HYPERTROPHY

- Hypertrophy refers to **an increase in the size of cells** , resulting in an increase in the size of the organ (no new cells but larger cells)
- This is more common in non-dividing cells

eg. Myocardial fibers

- It can be physiologic or pathologic & is caused by increased functional demand or by specific hormonal stimulation

CELL ADAPTATIONS

HYPERTROPHY

Some of the examples of hypertrophy are

- a) Bulging of **muscles in body builders**
- b) Massive physiological growth of the **uterus during pregnancy** – hormone induced increase in size of an organ
- c) Hypertrophy of **myocardium**

CELL ADAPTATIONS

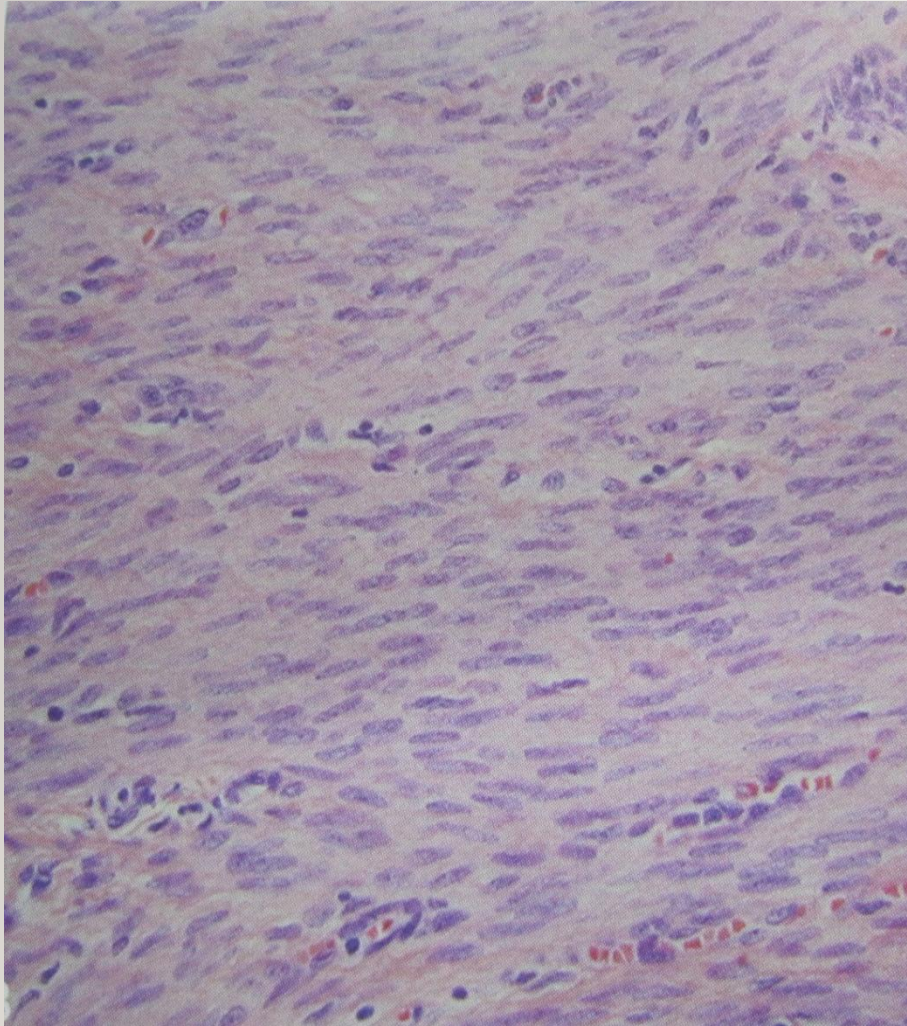
HYPERTROPHY

- Hypertrophy results from **increased production of cellular proteins**
- Mechanical stress and growth factors induce increased production of proteins which causes hypertrophy
- Selective hypertrophy can occur at the **subcellular organelle level** also
eg – Individuals taking barbiturate drugs show hypertrophy of smooth muscle ER in hepatocytes

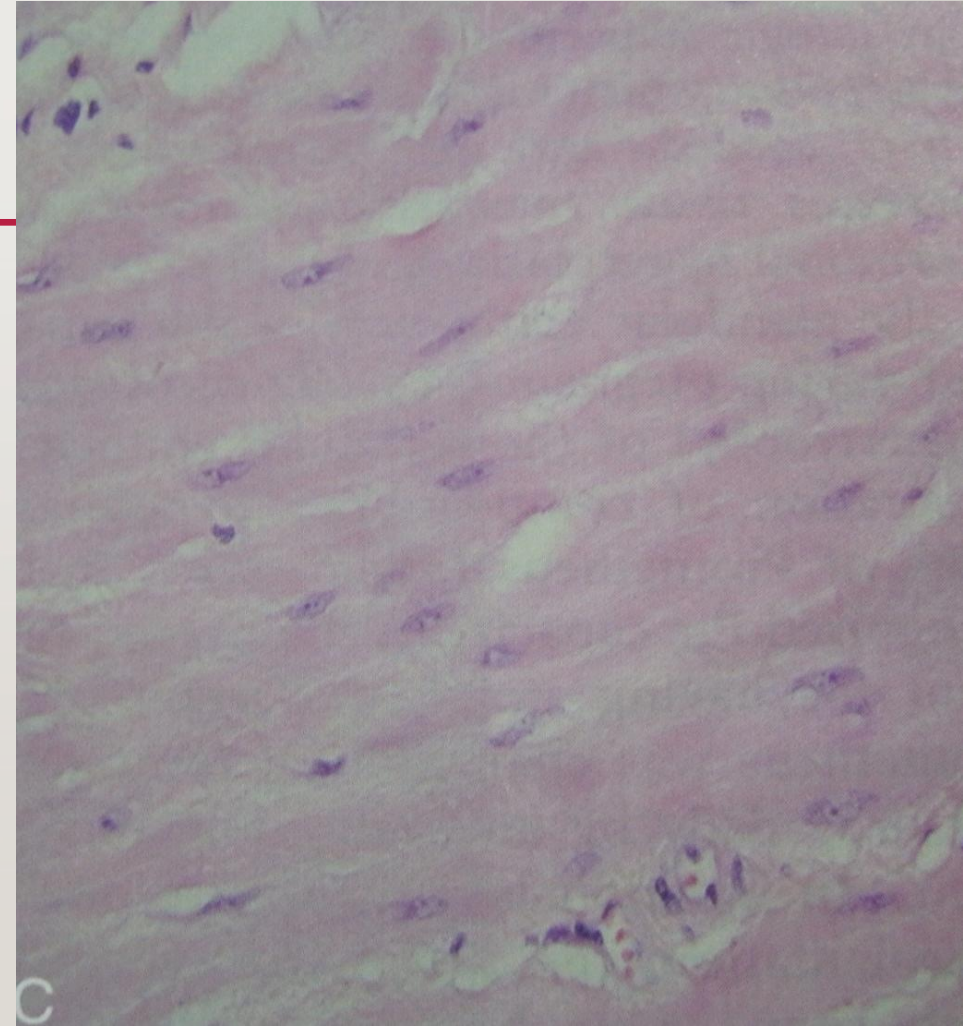
HYPERTROPHIED UTERUS



HYPERTROPHY OF MYOMETRIUM IN UTERUS

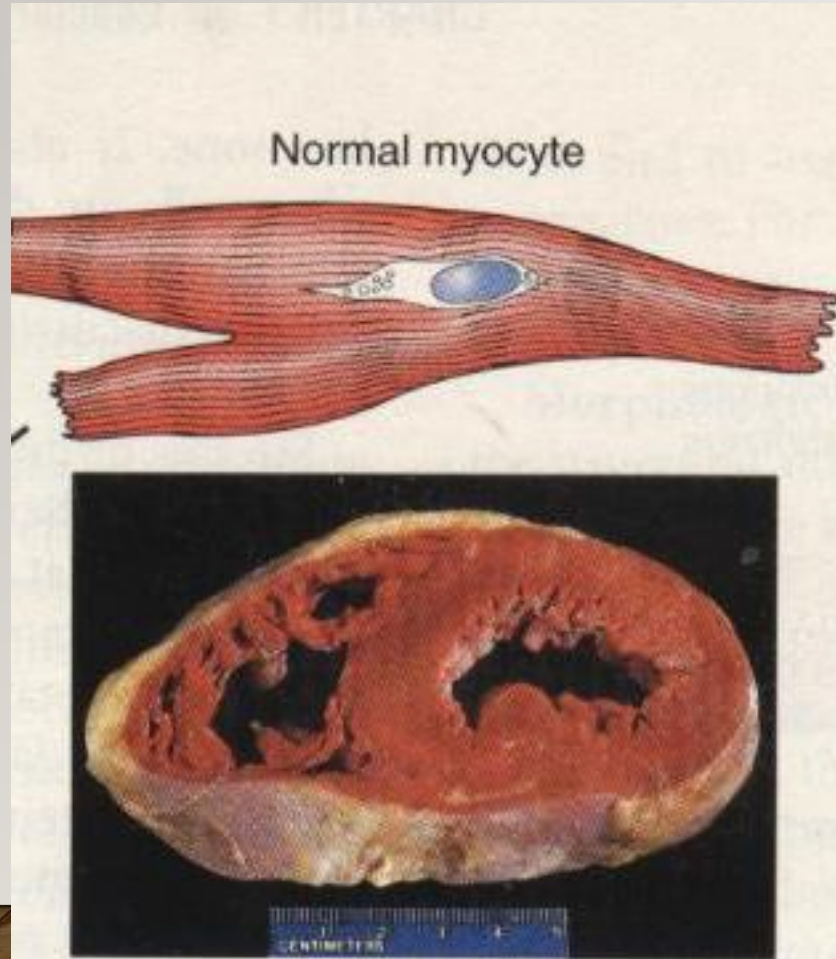


NORMAL MYOMETRIUM

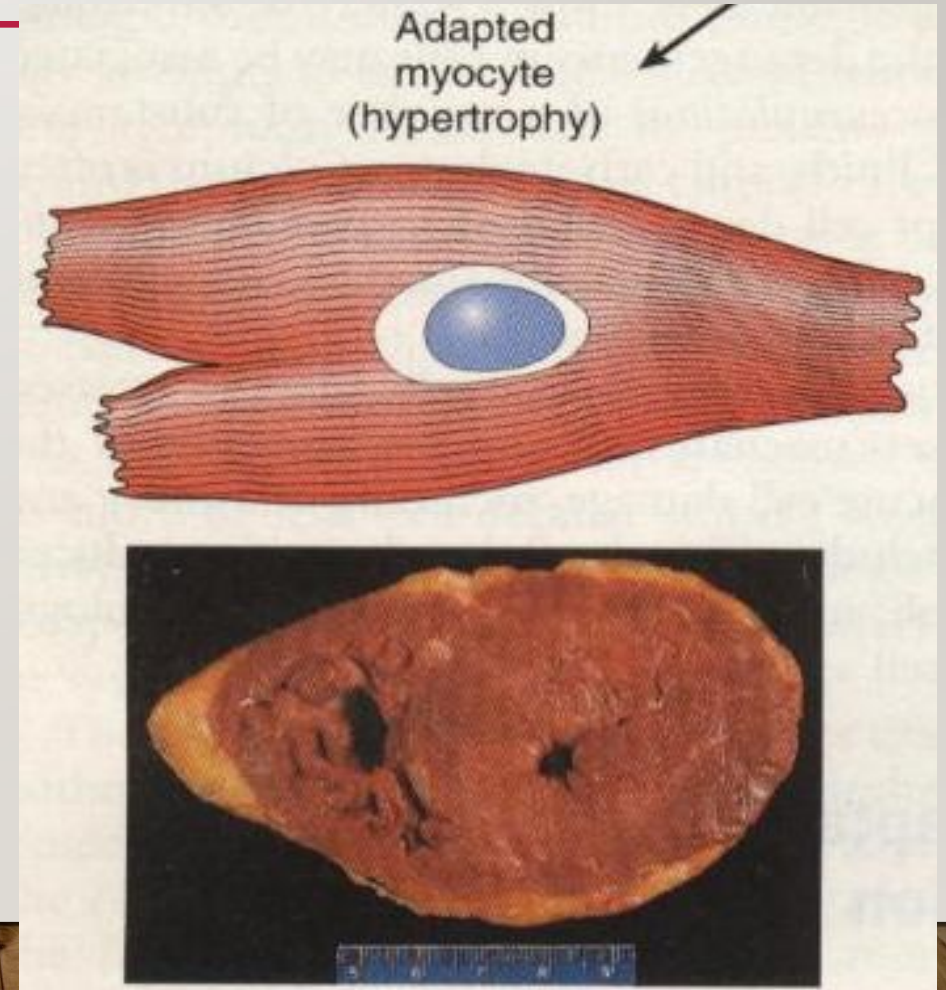
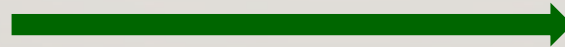


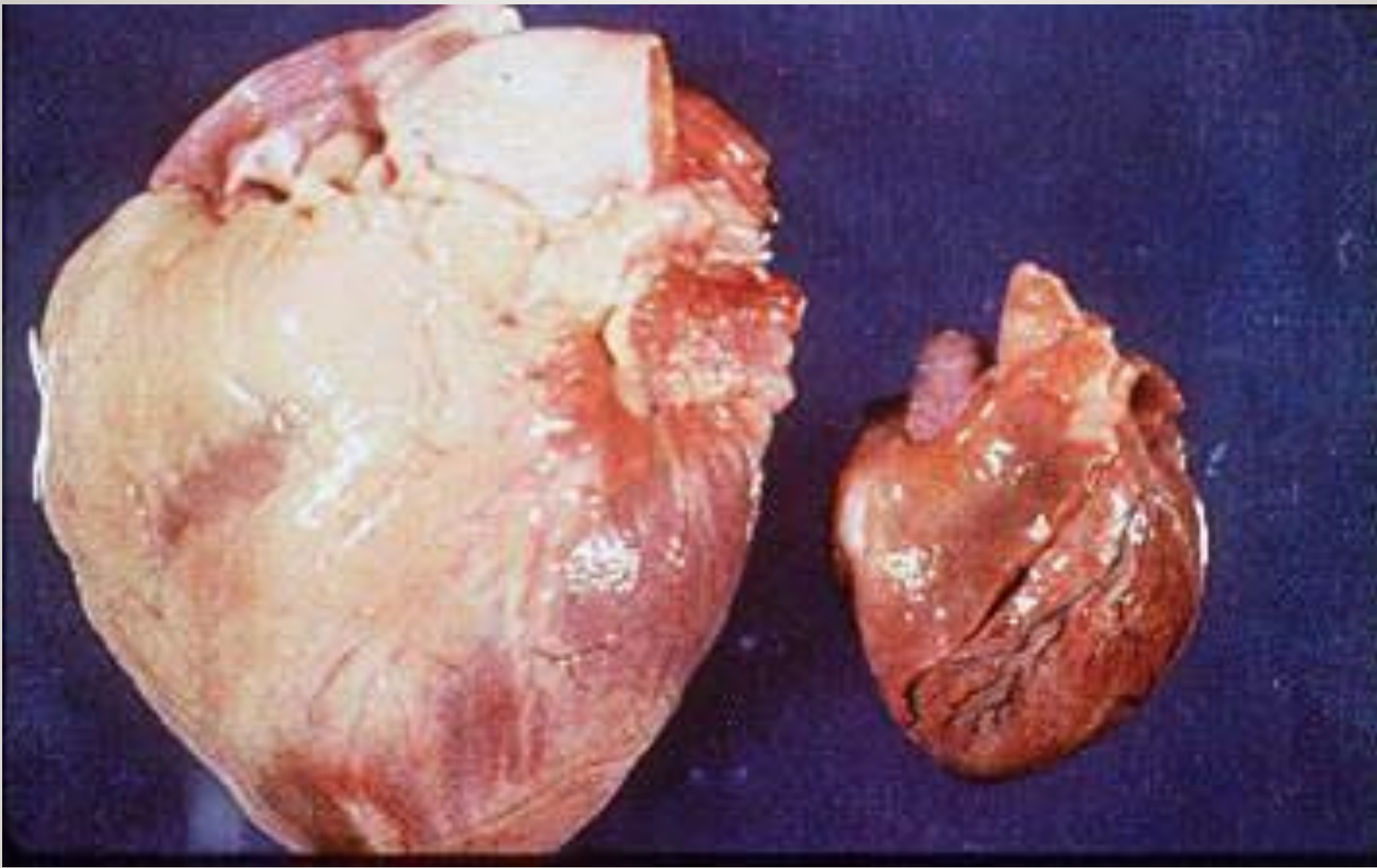
HYPERTROPHIED MYOMETRIUM

MYOCARDIAL HYPERTROPHY



ADAPTATION TO
INCREASED WORK
LOAD





Heart hypertrophy due to work overload (as in hypertension) compared with normal heart (Rt.side) for the same age & sex.



Left ventricular hypertrophy in patient with chronic hypertension

MYOCARDIAL HYPERTROPHY



NORMAL MYOCARDIUM



HYPERTROPHIED MYOCARDIUM

CELL ADAPTATIONS

HYPERTROPHY

- If the hypertrophied muscle mass cannot compensate for the increased work load , degenerative changes occur
- The limiting factors for continued hypertrophy may be –
 - a) Limitations of vascular supply to the enlarged fibers
 - b) Diminished oxidative capabilities of mitochondria
 - c) Alterations in protein synthesis & degradation
 - d) Cytoskeletal alterations

CELL ADAPTATIONS

ATROPHY

- Reduction in the size of the organ or tissue resulting from decrease in cell size and number is called atrophy
- This is divided into -
 - a) Physiologic
 - b) Pathologic

CELL ADAPTATIONS

ATROPHY

PHYSIOLOGIC ATROPHY

- Some embryologic structures like thyroglossal duct & Ductus arterioses
- Decrease in size of the uterus after parturition

CELL ADAPTATIONS

ATROPHY

PATHOLOGIC ATROPHY

This depends on the underlying cause –

- a) **Decreased work load** – immobilized broken limb in plaster cast
- b) **Denervation atrophy**
- c) **Diminished blood supply** – e.g. Brain in aged
- d) **Inadequate nutrition** – Marasmus and cachexia in cancer pts
- e) **Loss of endocrine stimulation**
- f) **Ageing (senile atrophy)** - in brain & heart
- g) **Pressure** – tissue compression for long time by enlarging benign tumor

CELL ADAPTATIONS

ATROPHY

MECHANISM OF ATROPHY

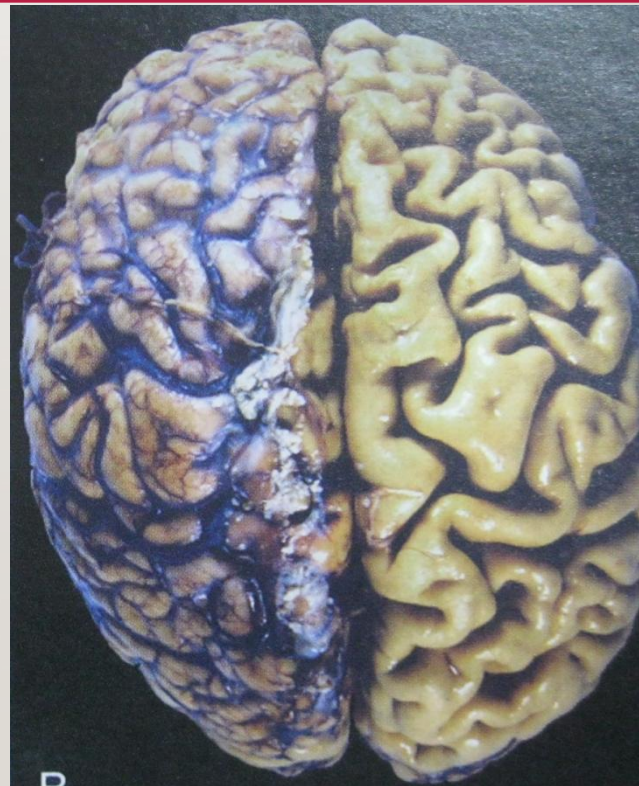
- Results from decreased protein synthesis and increased protein degradation by ubiquitin proteasome pathway
- Nutrient deficiency and disuse may activate ubiquitin ligases which attach the small peptide ubiquitin to cellular proteins and target these proteins for degradation in proteasomes
- In some cases atrophy is due to autophagy of cells own organelles

CELL ADAPTATIONS

ATROPHY



NORMAL BRAIN



SENILE ATROPHY



Testicular atrophy

CELL ADAPTATIONS

METAPLASIA

Metaplasia is a reversible change in which one adult cell type (epithelial or mesenchymal) is replaced by another adult cell type.

E.g. a) **Columnar to squamous** – In habitual smokers , the normal ciliated columnar epithelial cells of trachea & bronchi are replaced by squamous epithelium

b) **Squamous to columnar** – Barrett's oesophagus

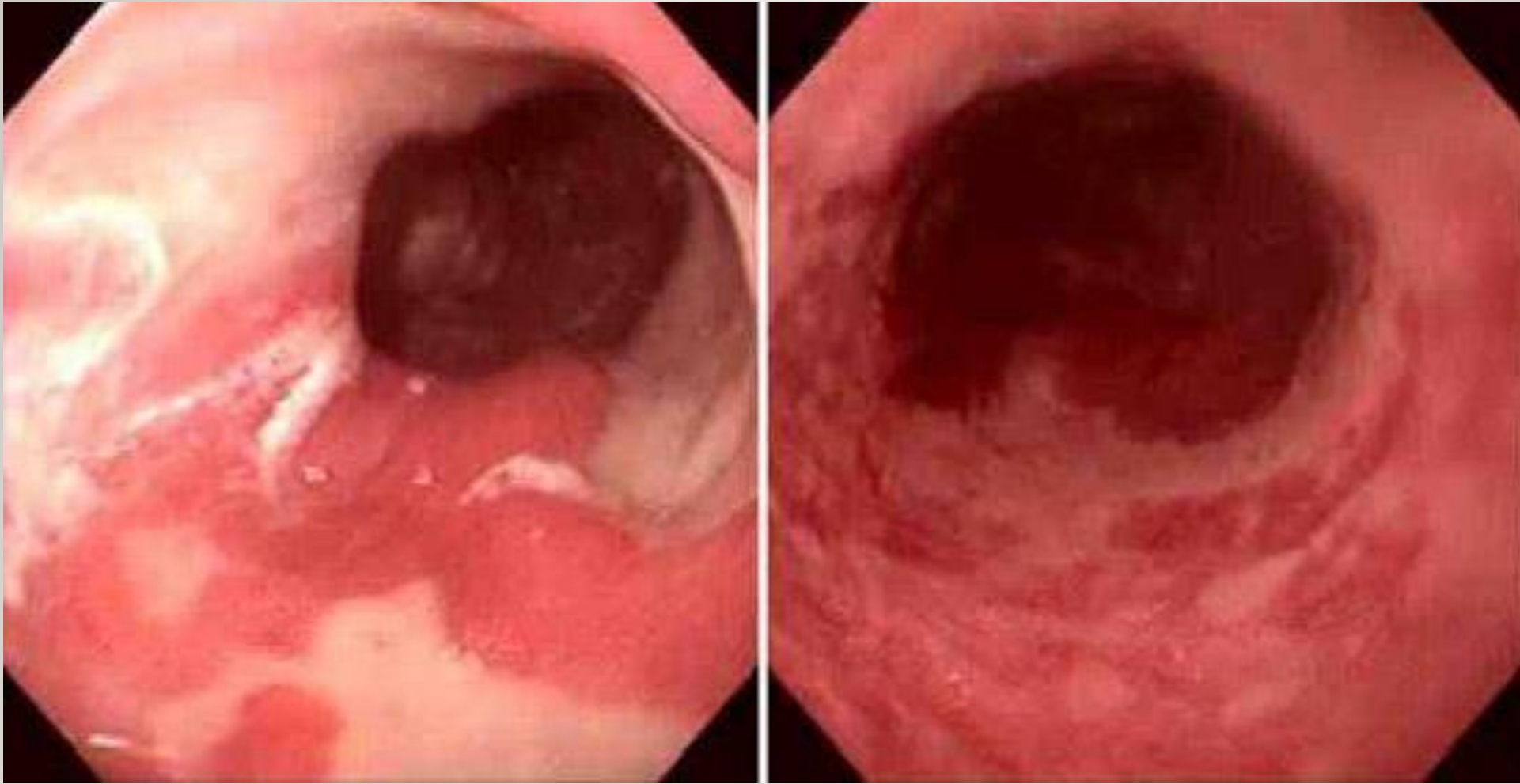
CELL ADAPTATIONS

METAPLASIA

Connective tissue metaplasia is the formation of cartilage, bone or adipose tissue in tissues that normally do not contain these elements

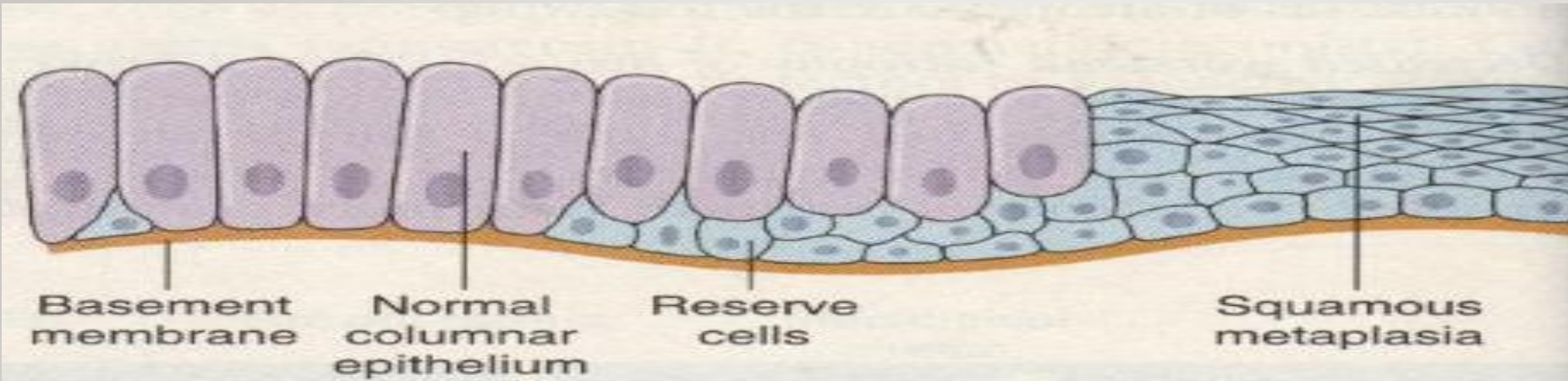
E.g. Myositis ossificans

The influences that predispose to metaplasia if persistent , may induce malignant transformation in metaplastic epithelium

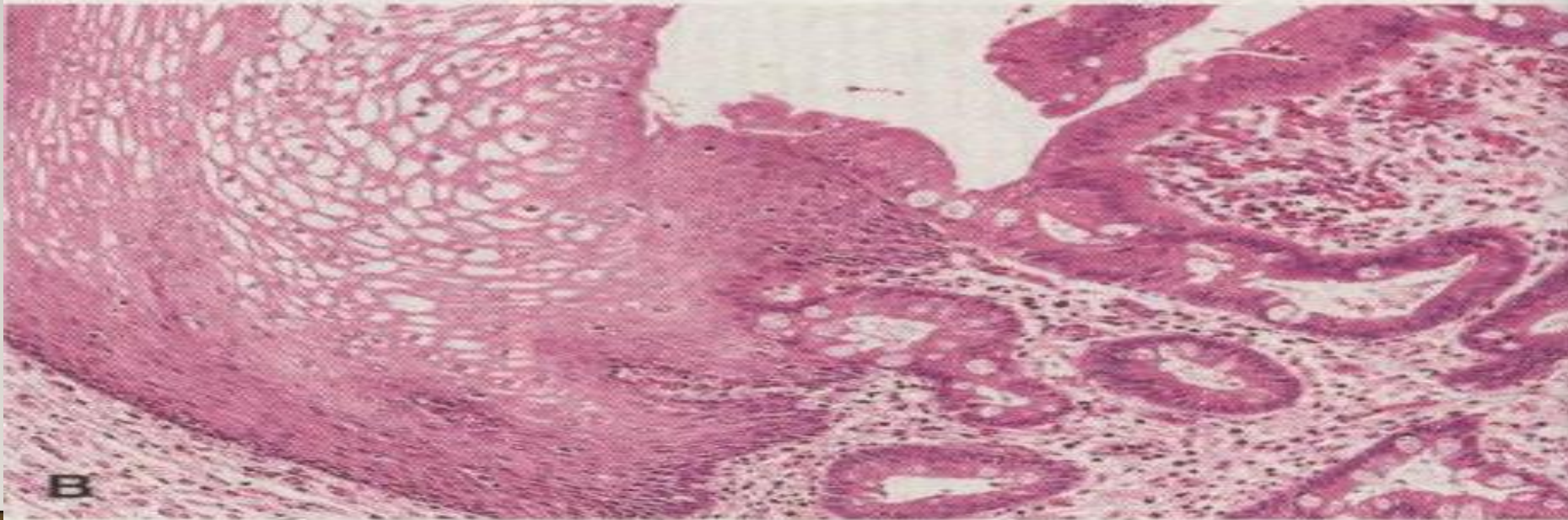


Endoscopic appearance of Barrett esophagitis Squamous epithelium white in color while columnar epithelium red-pink in color.

METAPLASIA



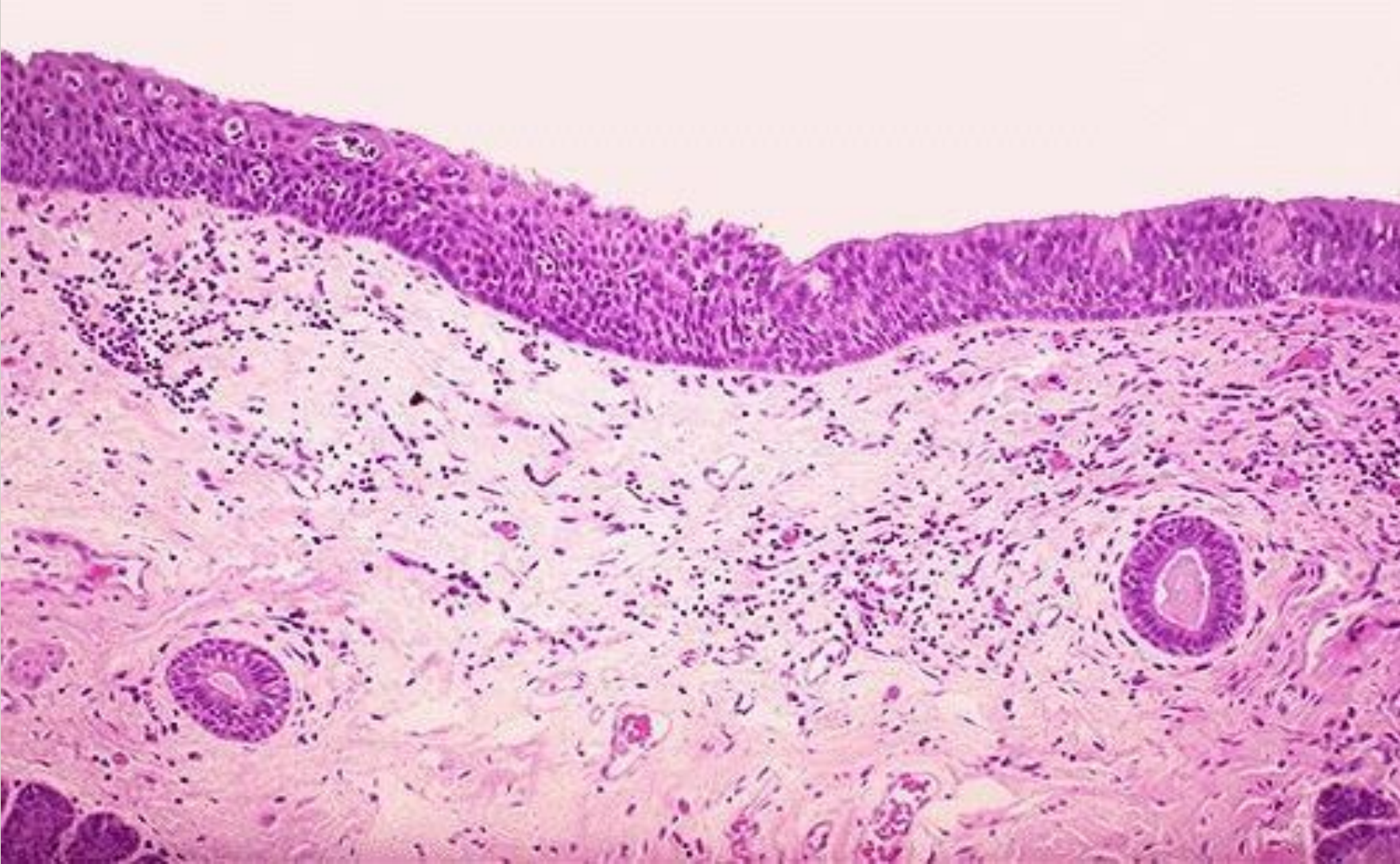
A



B

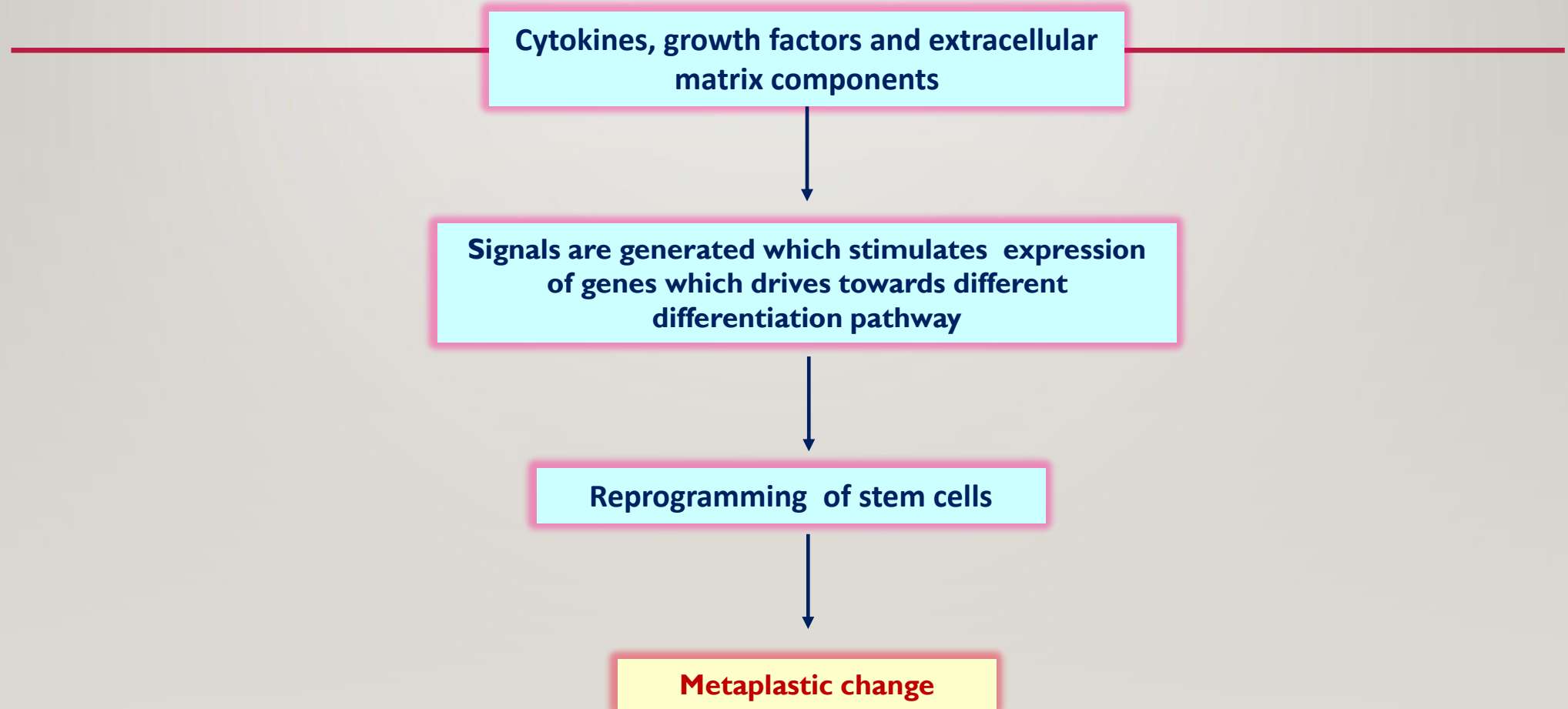
Barrett's esophagitis

**(squamous to columnar
metaplasia)**

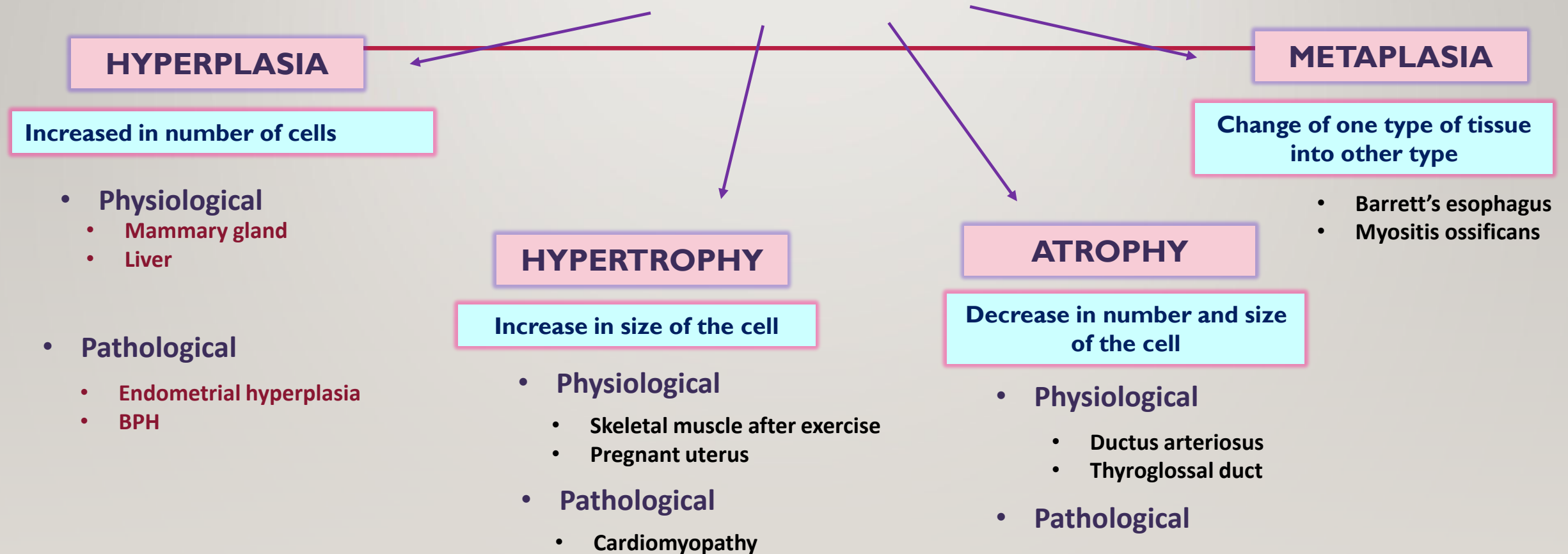


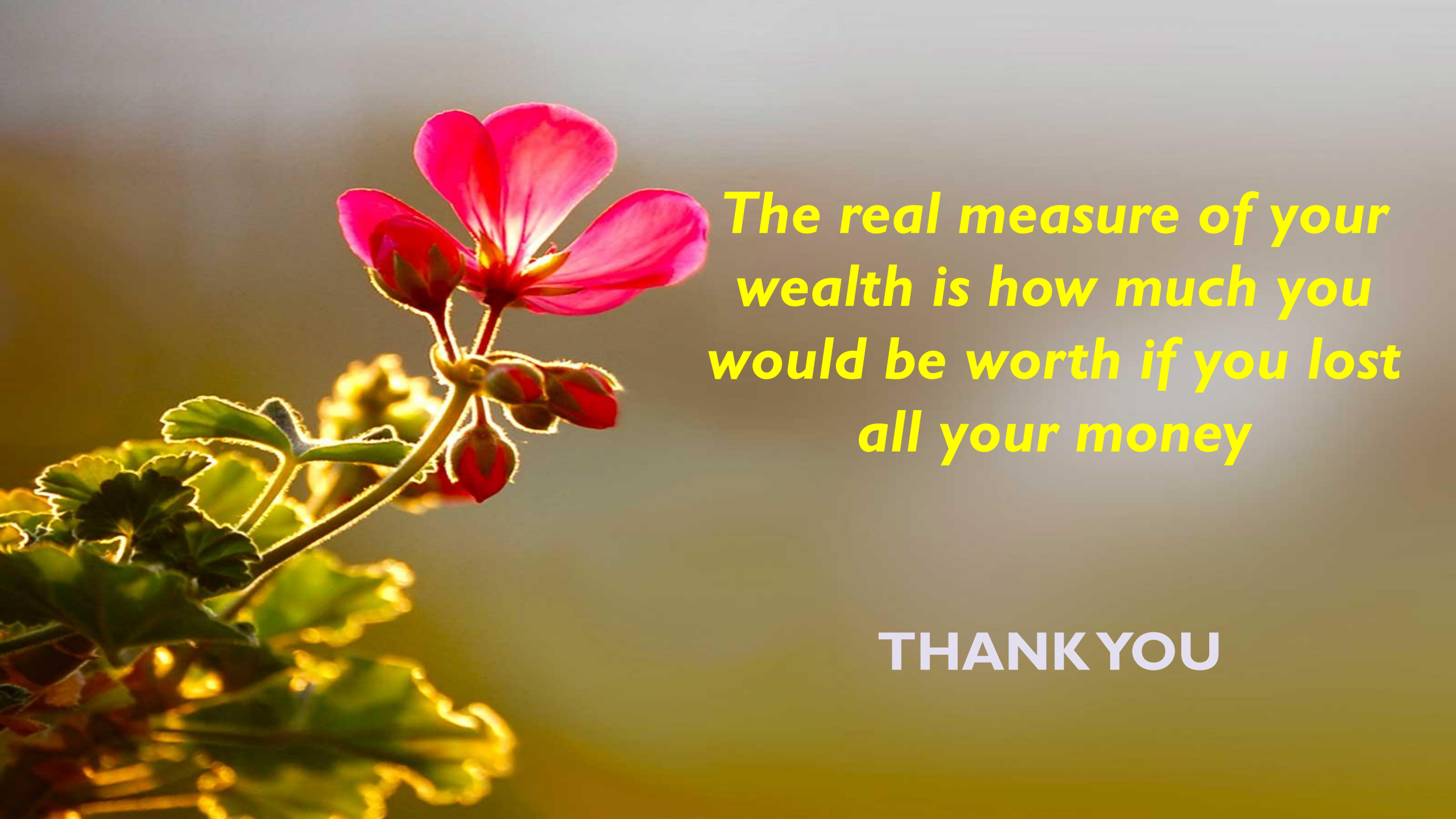
Squamous metaplasia of respiratory epithelium. Transformation of (pseudostratified ciliated columnar epithelium (Rt.side) to stratified squamous epithelium (Lt.side)

MECHANISM OF METAPLASIA



ADAPTIVE CHANGES





*The real measure of your
wealth is how much you
would be worth if you lost
all your money*

THANK YOU