CELL INJURY
CELLULAR ADAPTATIONS

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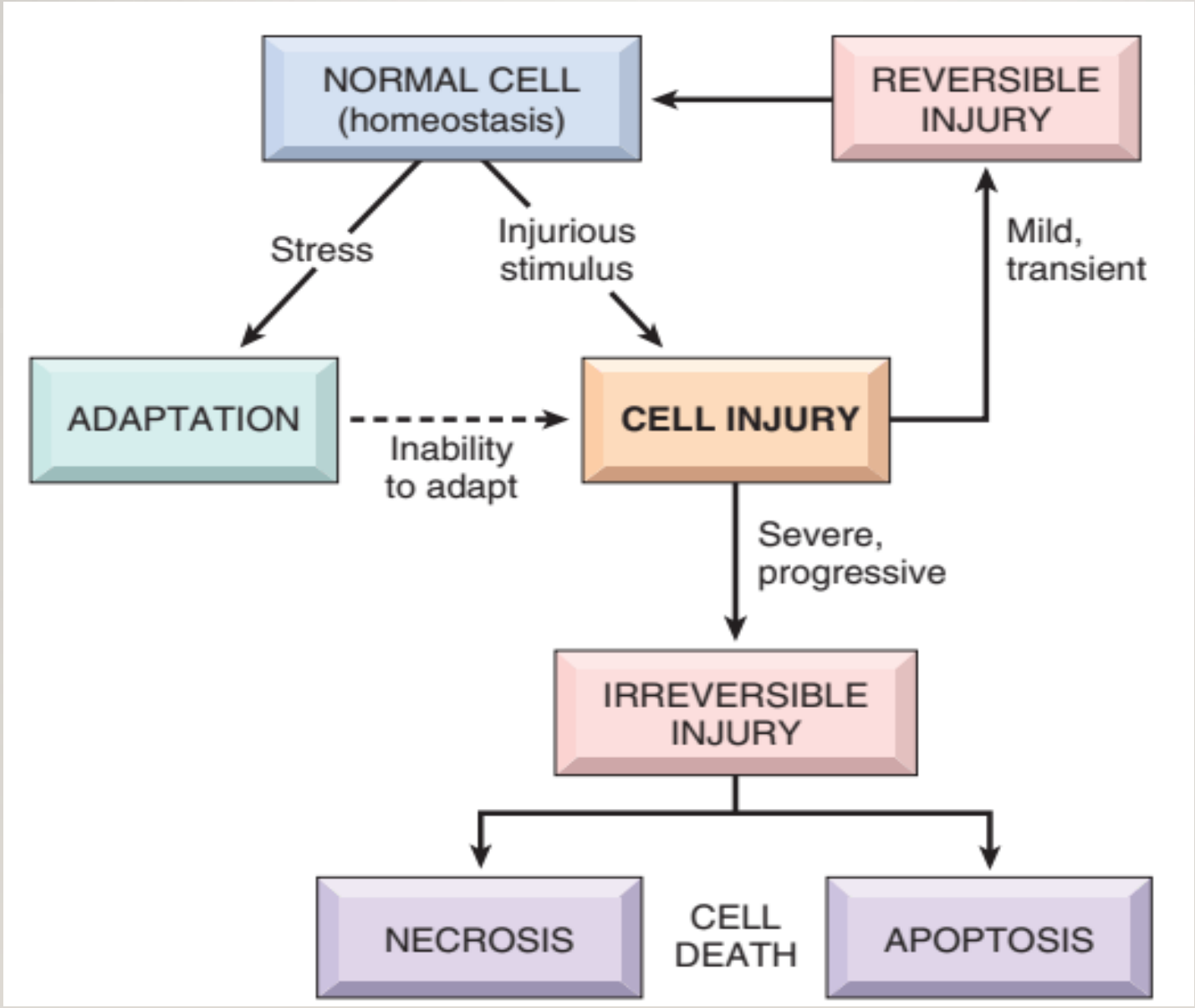
GENERAL PATHOLOGY GRADE - 4
WEEK – 2
LEC. 2

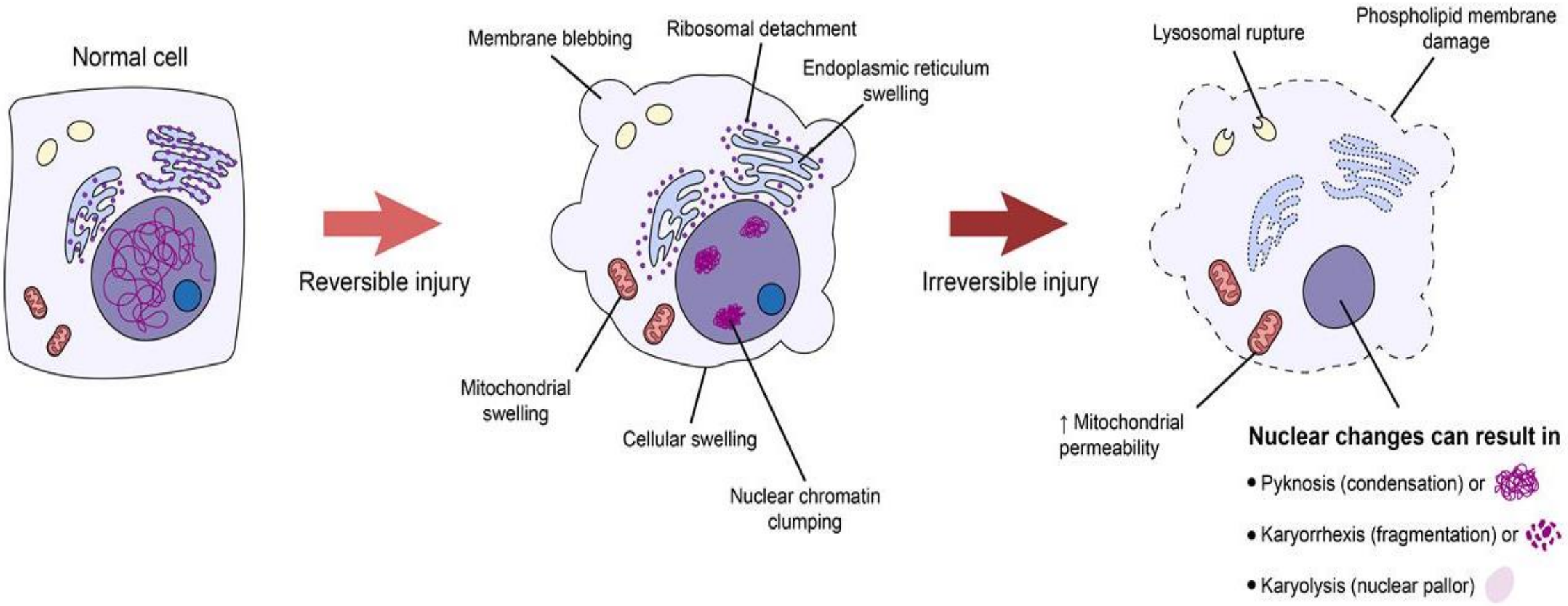
CELL INJURY AND CELLULAR ADAPTATIONS

- **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.


NORMAL CELL
(homeostasis)
REVERSIBLE
INJURY
Stress
Injurious
stimulus
Mild,
transient
ADAPTATION
Inability
to adapt
CELL INJURY
Severe,
progressive
IRREVERSIBLE
INJURY
NECROSIS
CELL
DEATH
APOPTOSIS

Cell Injury


Normal cell
Reversible injury
Membrane blebbing
Ribosomal detachment
Endoplasmic reticulum swelling
Mitochondrial swelling
Cellular swelling
Nuclear chromatin clumping
Irreversible injury
Lysosomal rupture
Phospholipid membrane damage
↑ Mitochondrial permeability
Nuclear changes can result in
• Pyknosis (condensation) or
• Karyorrhexis (fragmentation) or
• Karyolysis (nuclear pallor)

- **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

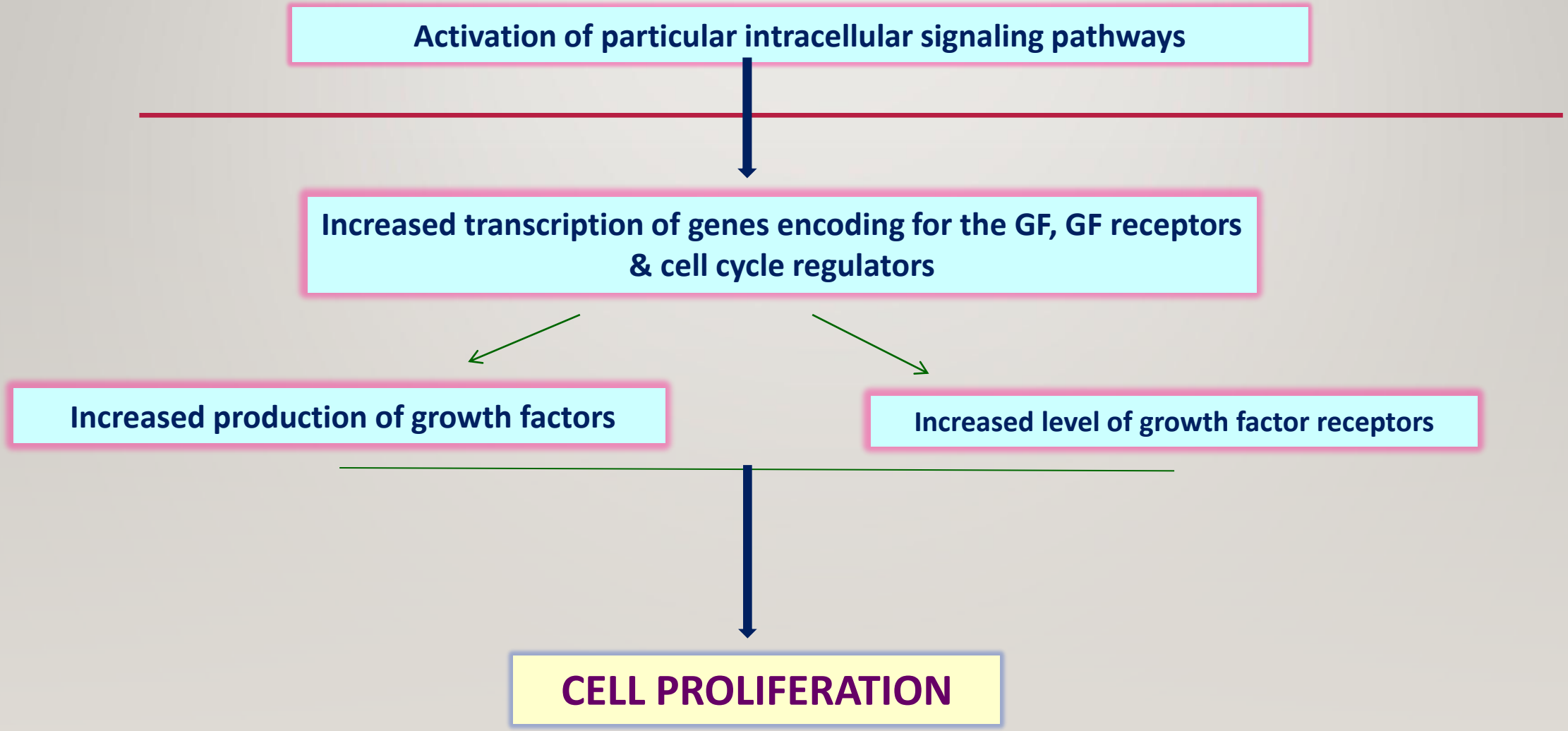
HYPERPLASIA

- 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



CELL ADAPTATIONS
HYPERPLASIA

PHYSOLOGICAL 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).**

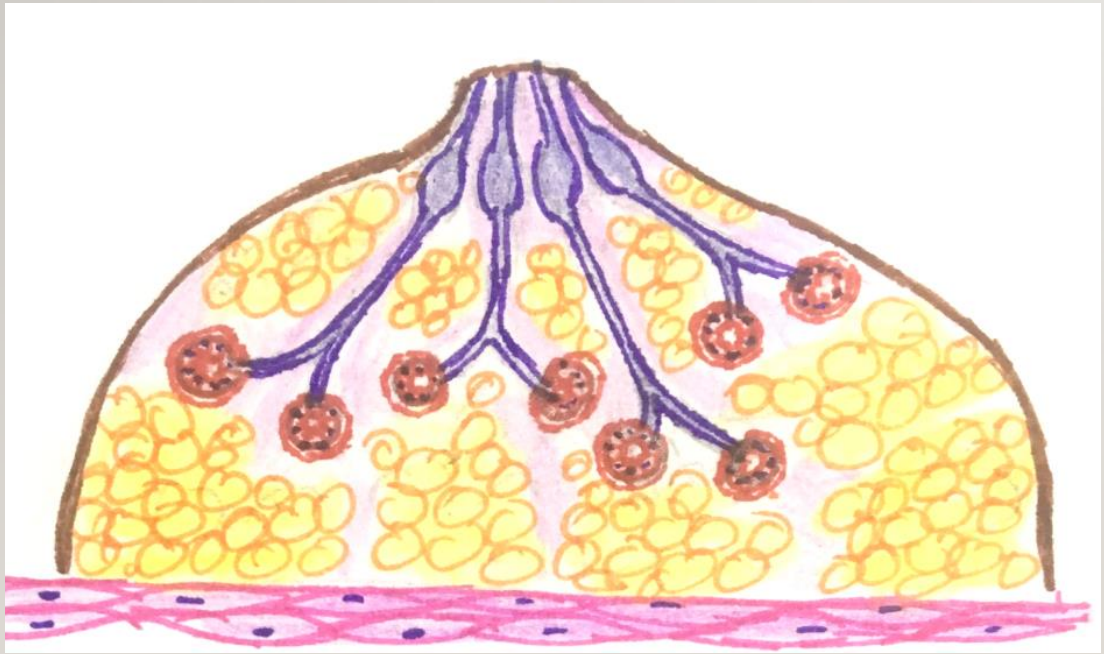
b) Compensatory hyperplasia – increase in tissue mass after damage or partial resection

Eg – Liver after partial resection

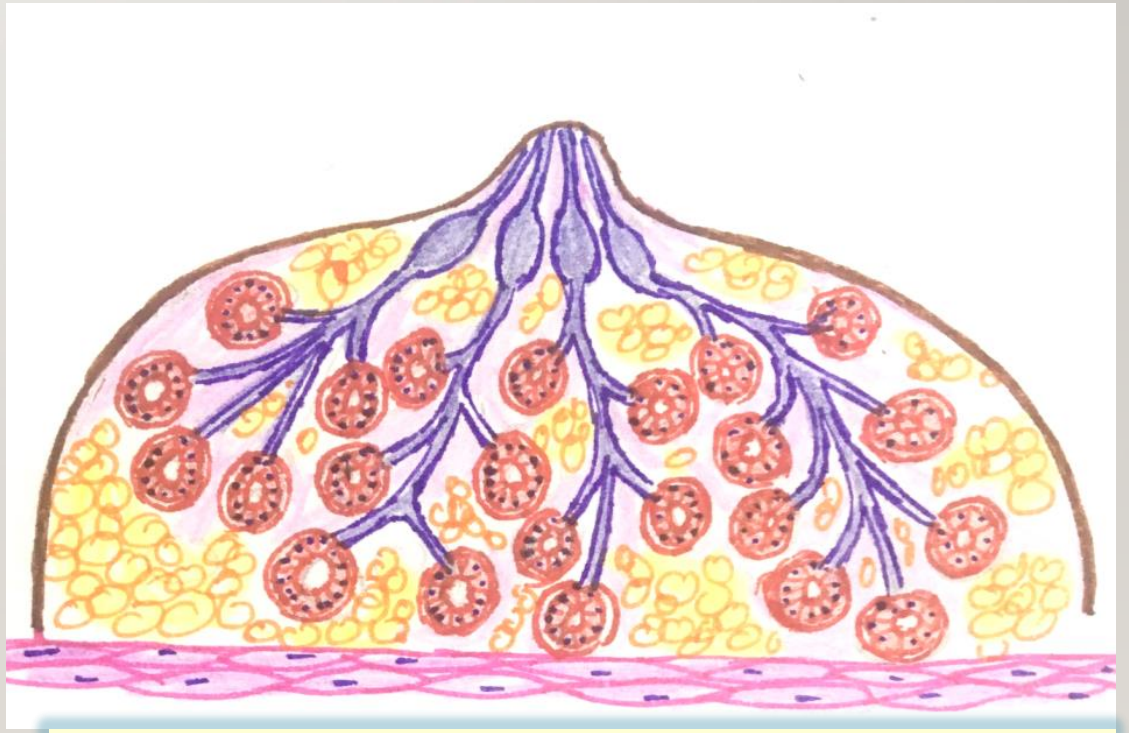
PHYSIOLOGICAL HYPERPLASIA

Action of hormones or growth factors

Mammary gland hyperplasia in pregnancy and lactation



Normal mammary tissue

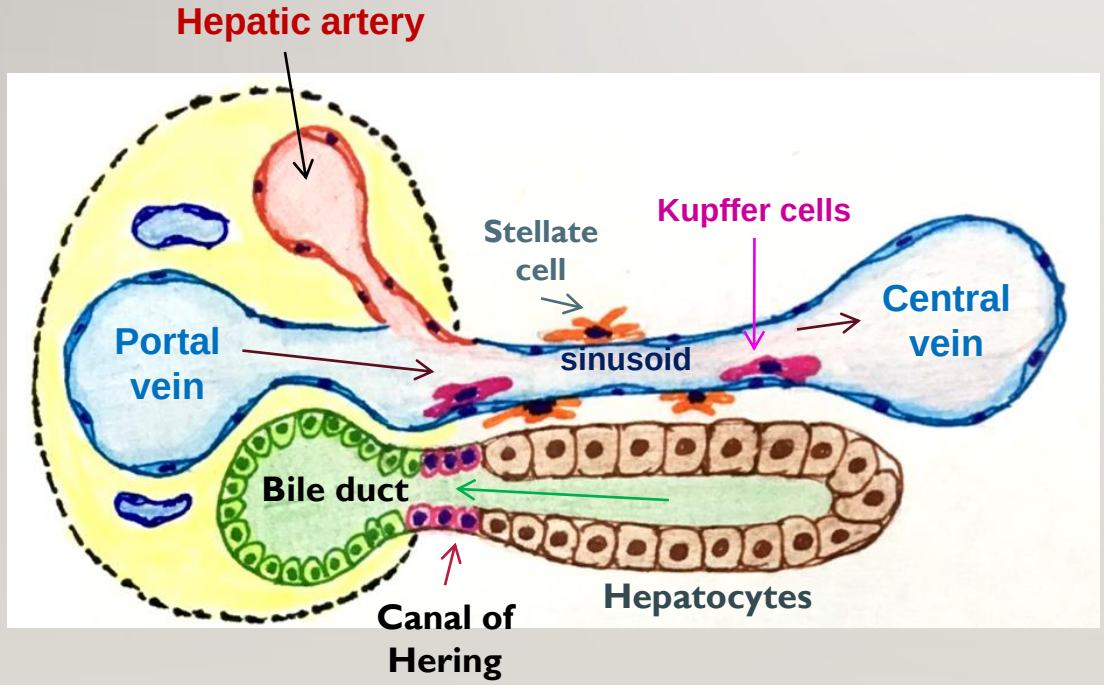


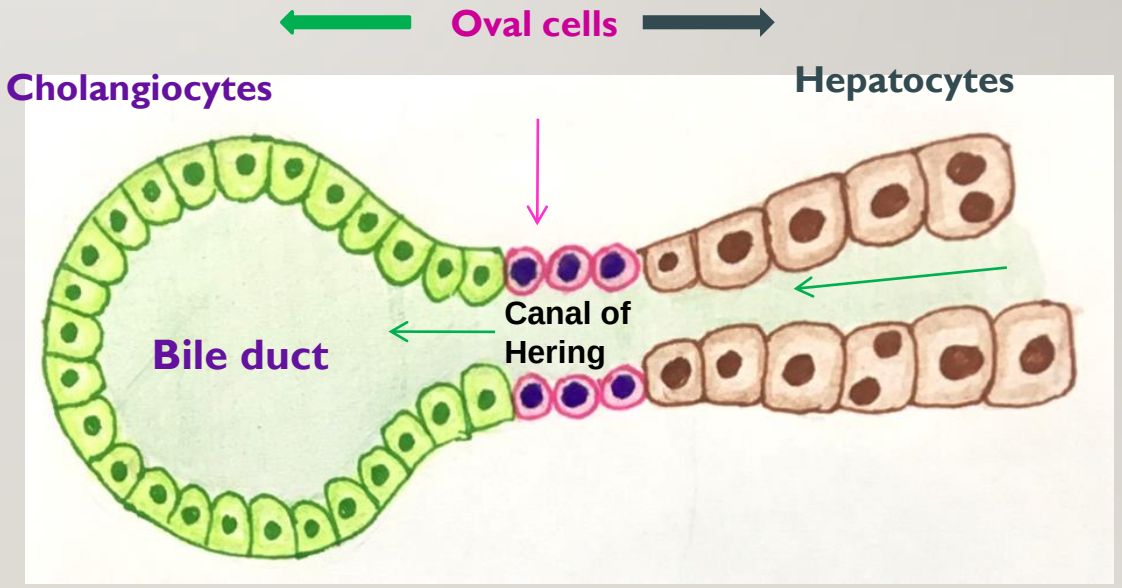
Mammary gland hyperplasia under the influence of estrogen and progesterone

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

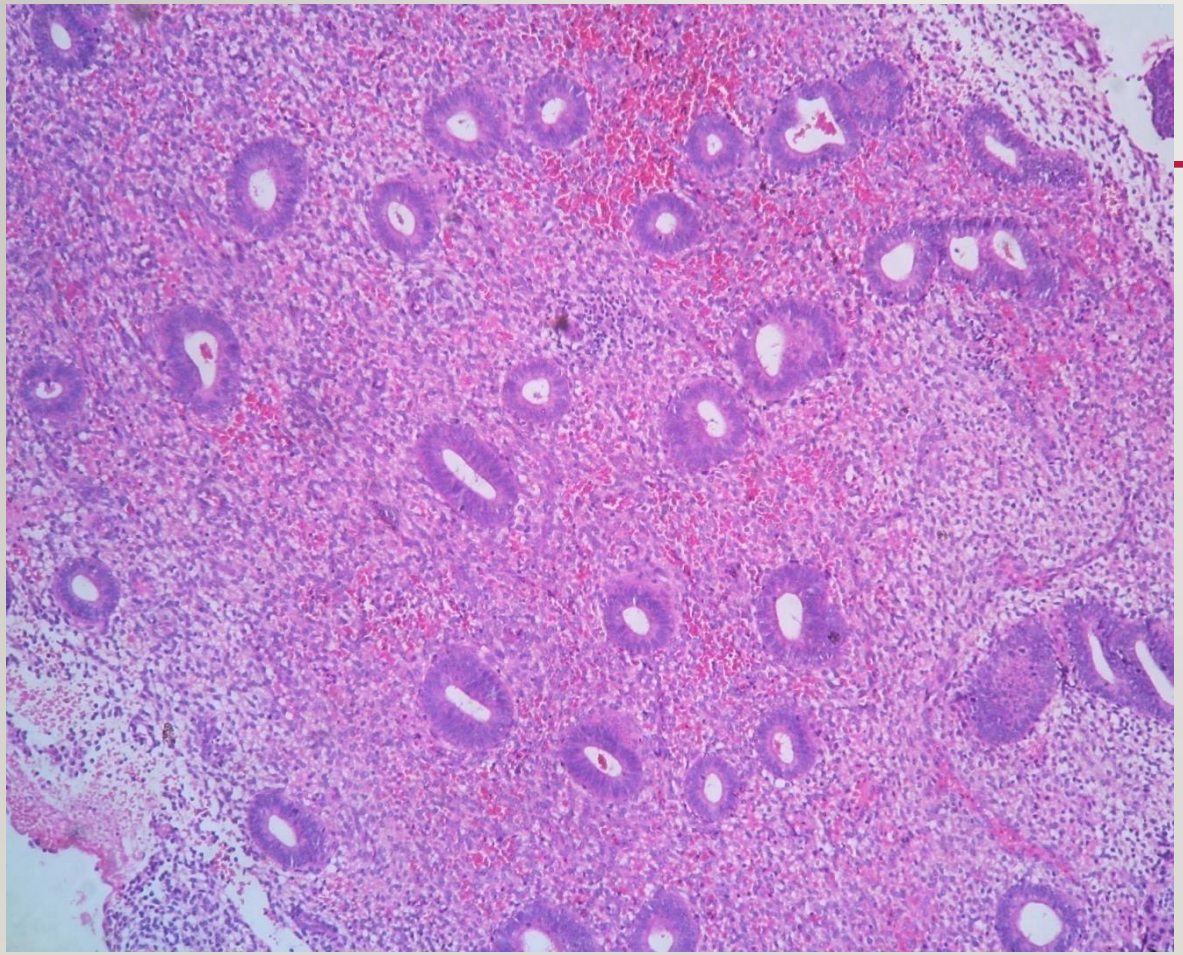
Endometrial hyperplasia

Crowded irregular glands with atypia

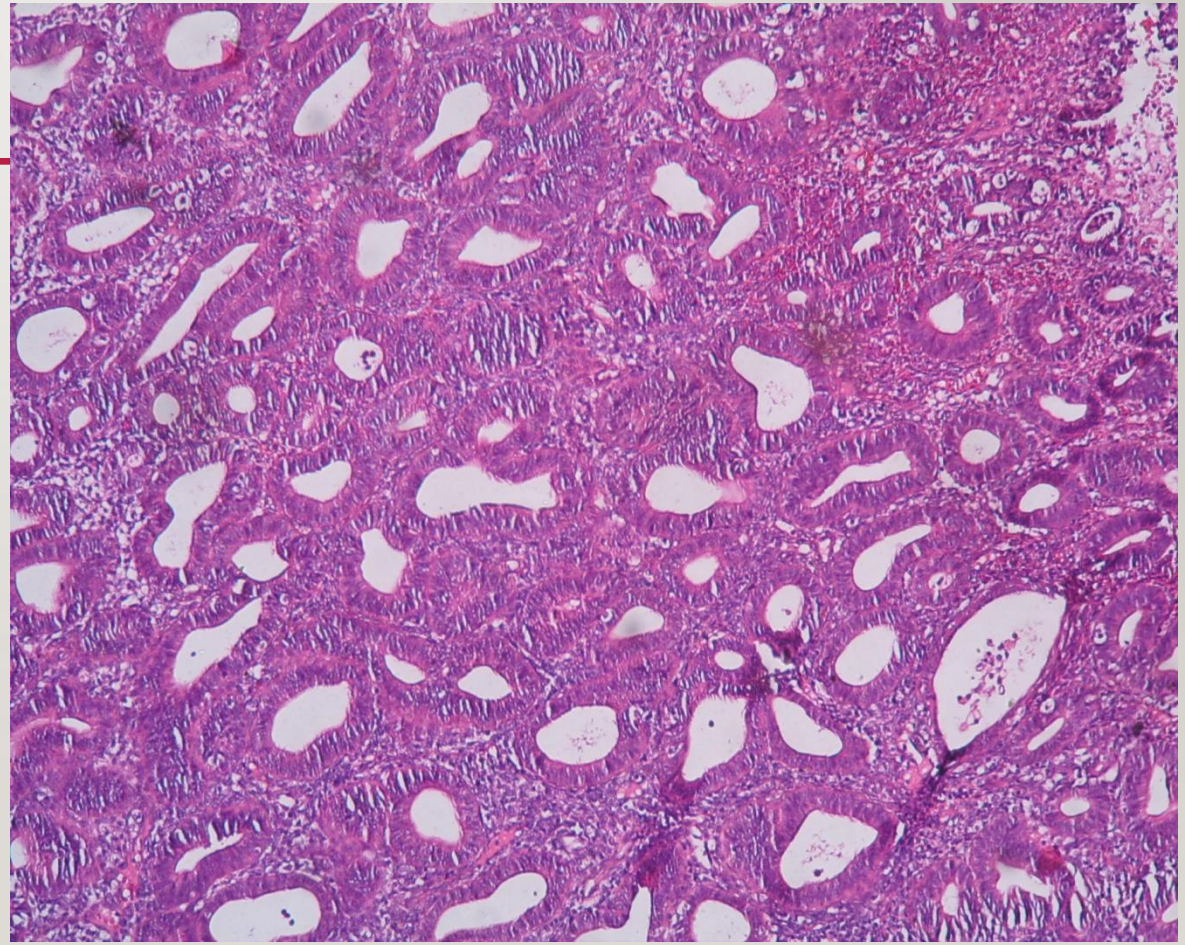
CAUSES OF HYPERESTROGENISM

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

HYPERPLASIA

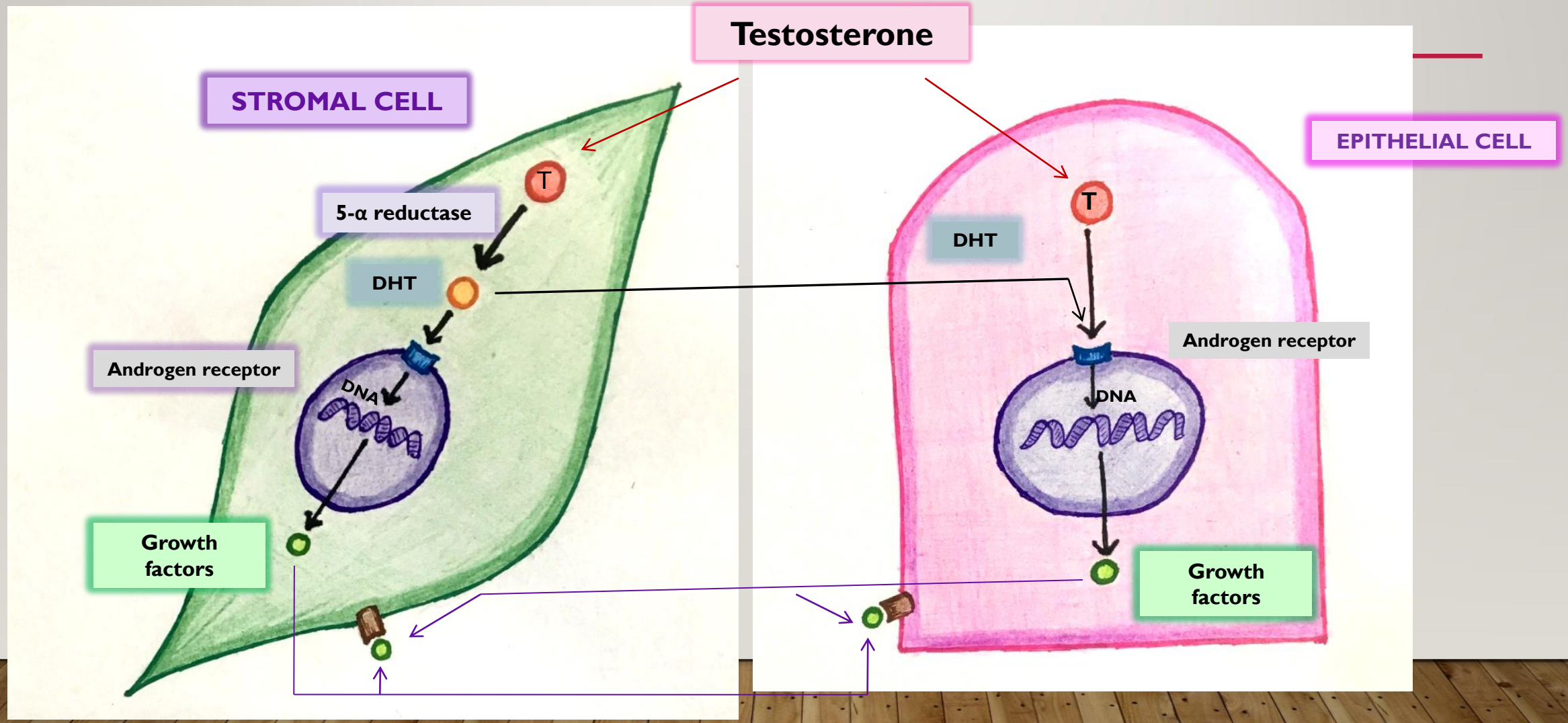


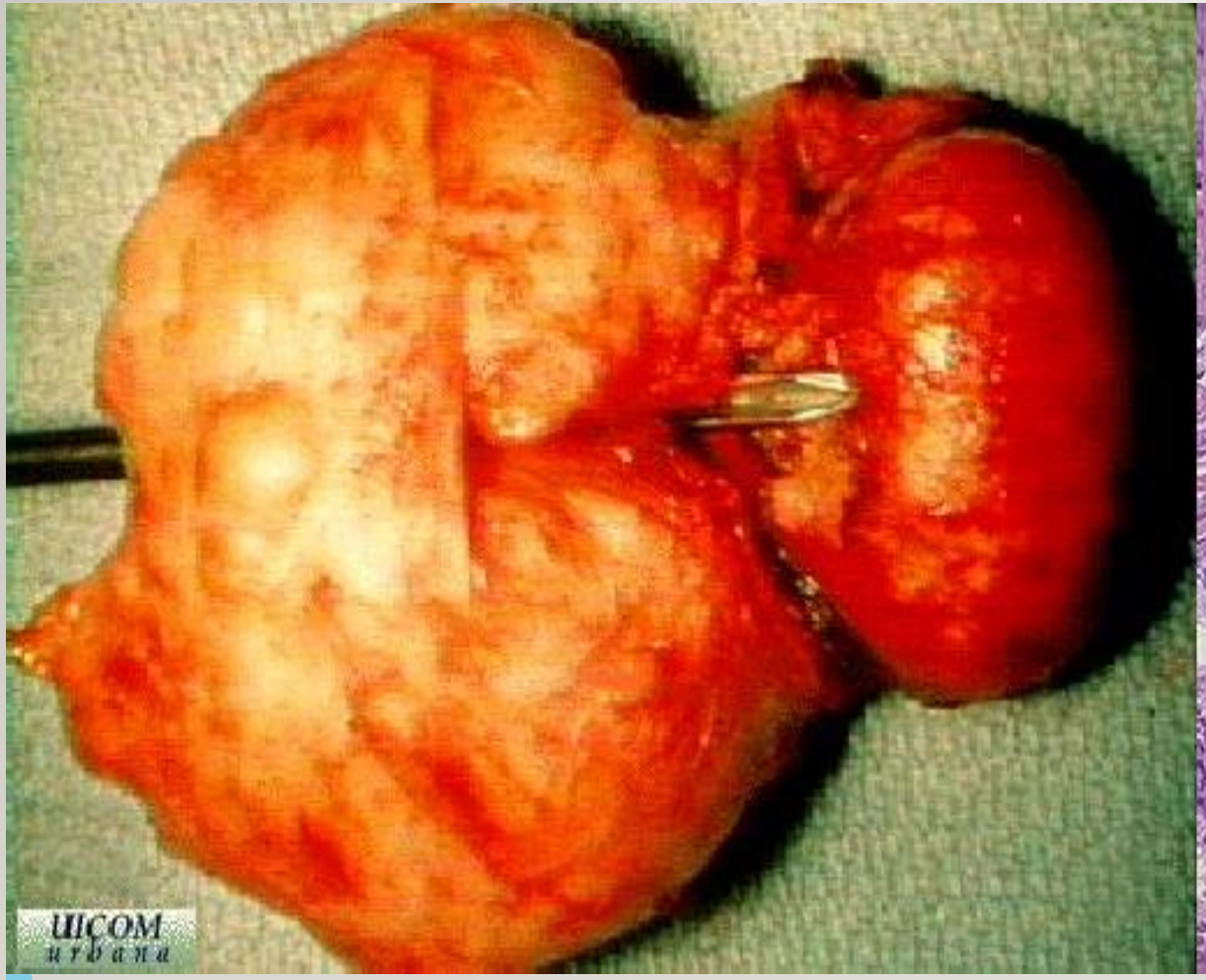
NORMAL ENDOMETRIUM

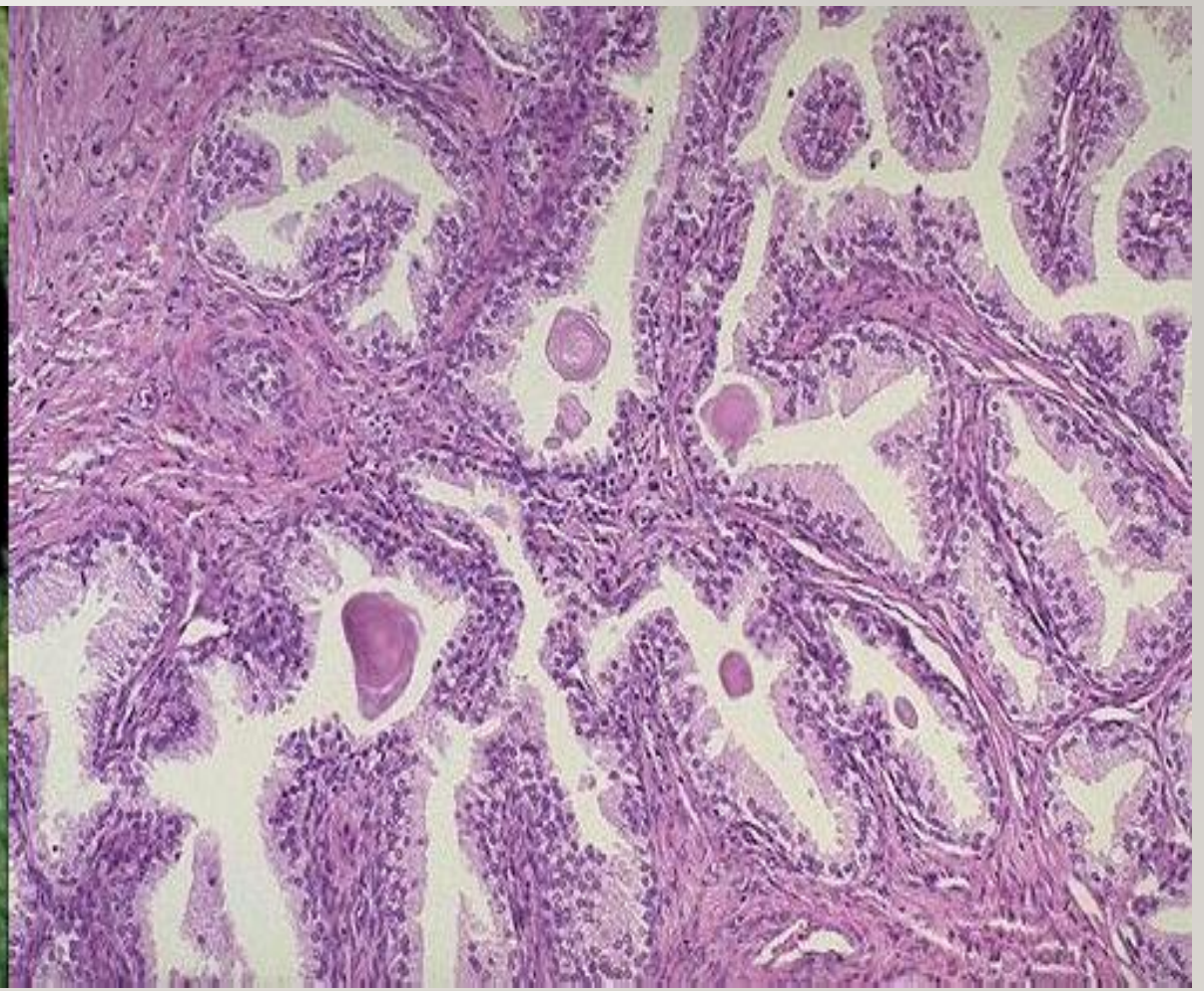


ENDOMETRIAL HYPERPLASIA

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

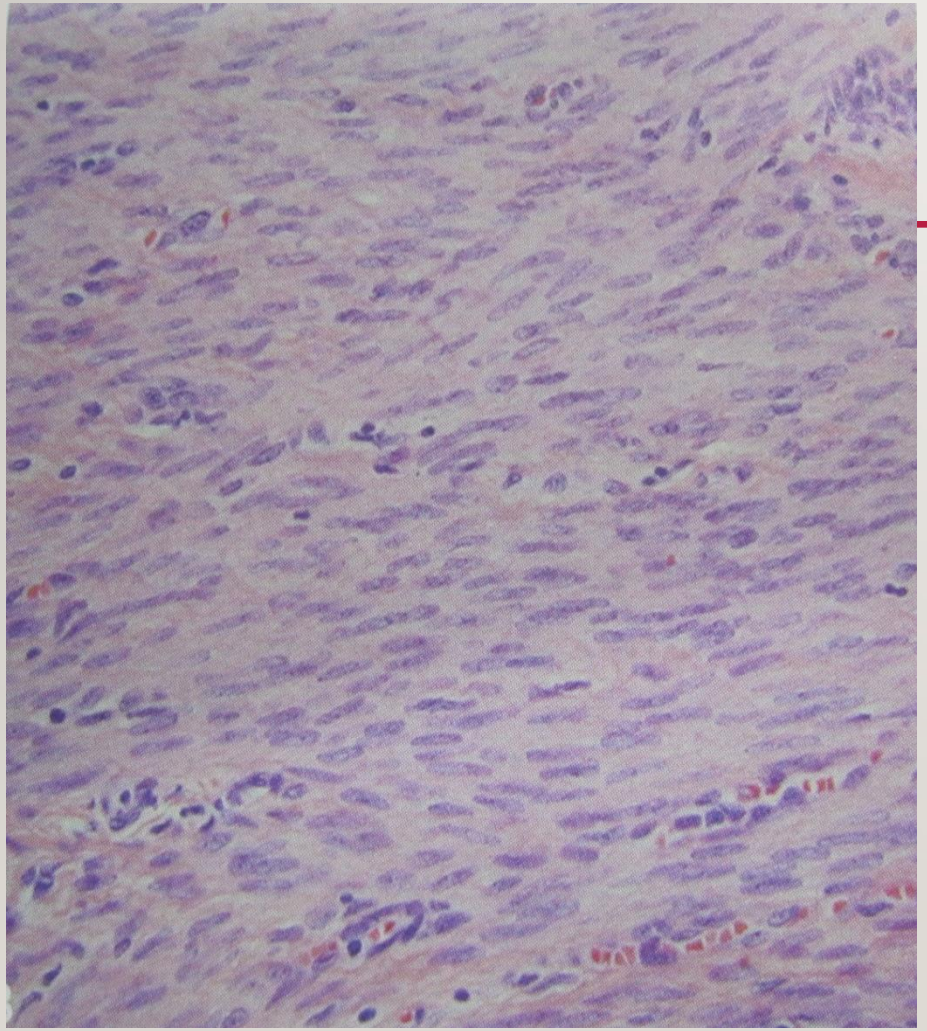
CELL ADAPTATIONS
HYPERTROPHY

- 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

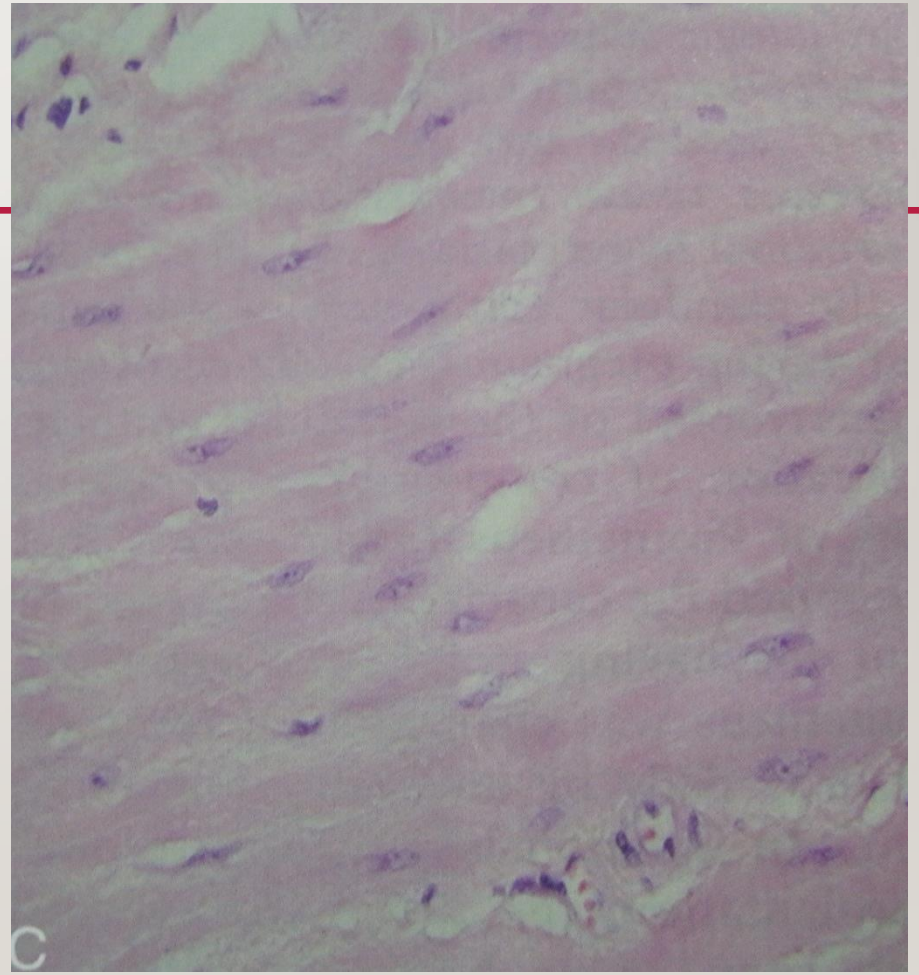
  eg – Individuals taking barbiturate drugs show hypertrophy of smooth muscle ER in hepatocytes

HYPERTROPHIED UTERUS

HYPERTROPHY OF MYOMETRIUM IN UTERUS

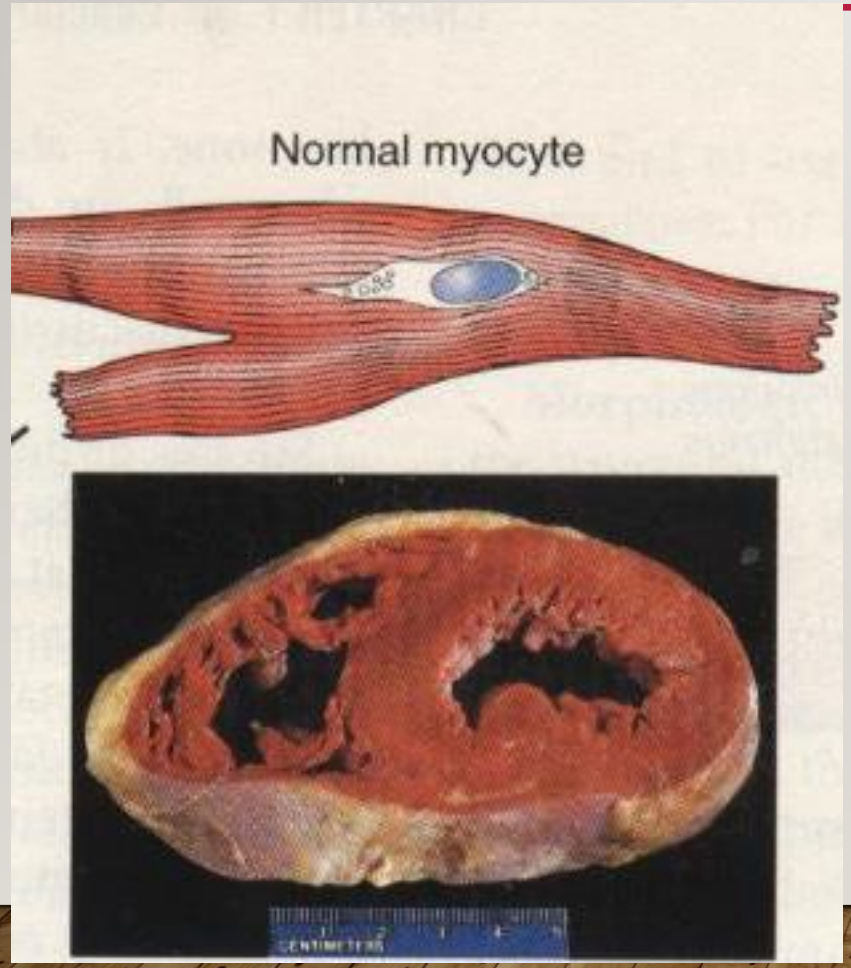


NORMAL MYOMETRIUM

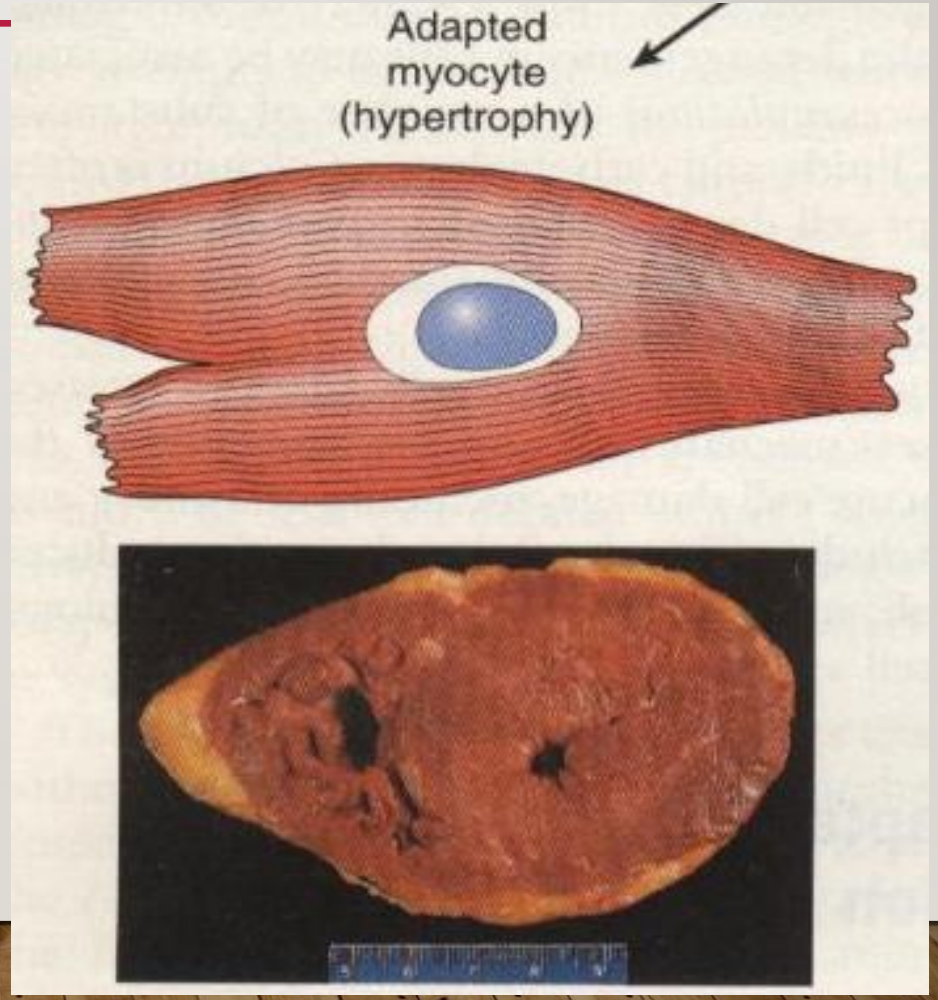


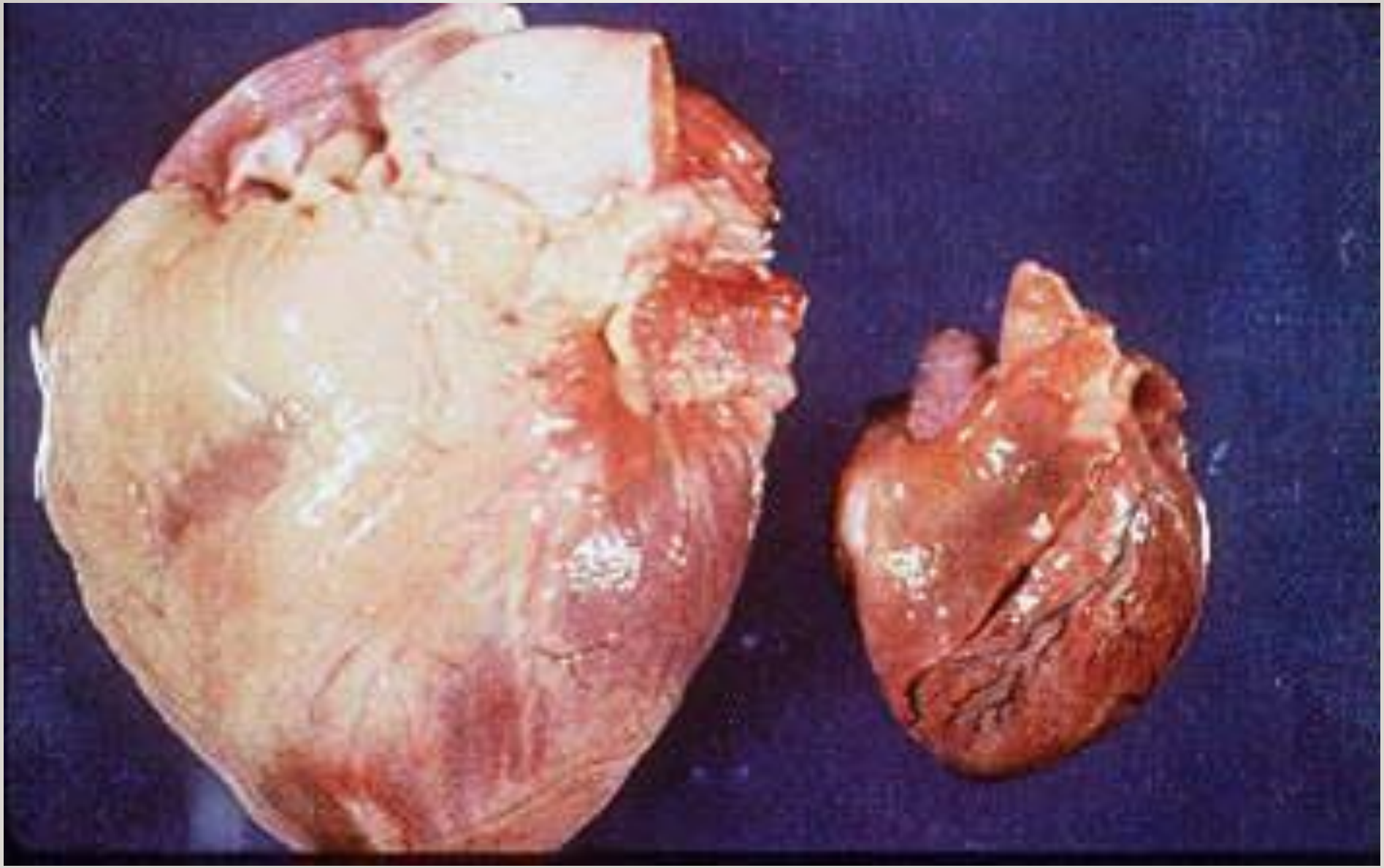
HYPERTROPHIED MYOMETRIUM

MYOCARDIAL HYPERTROPHY

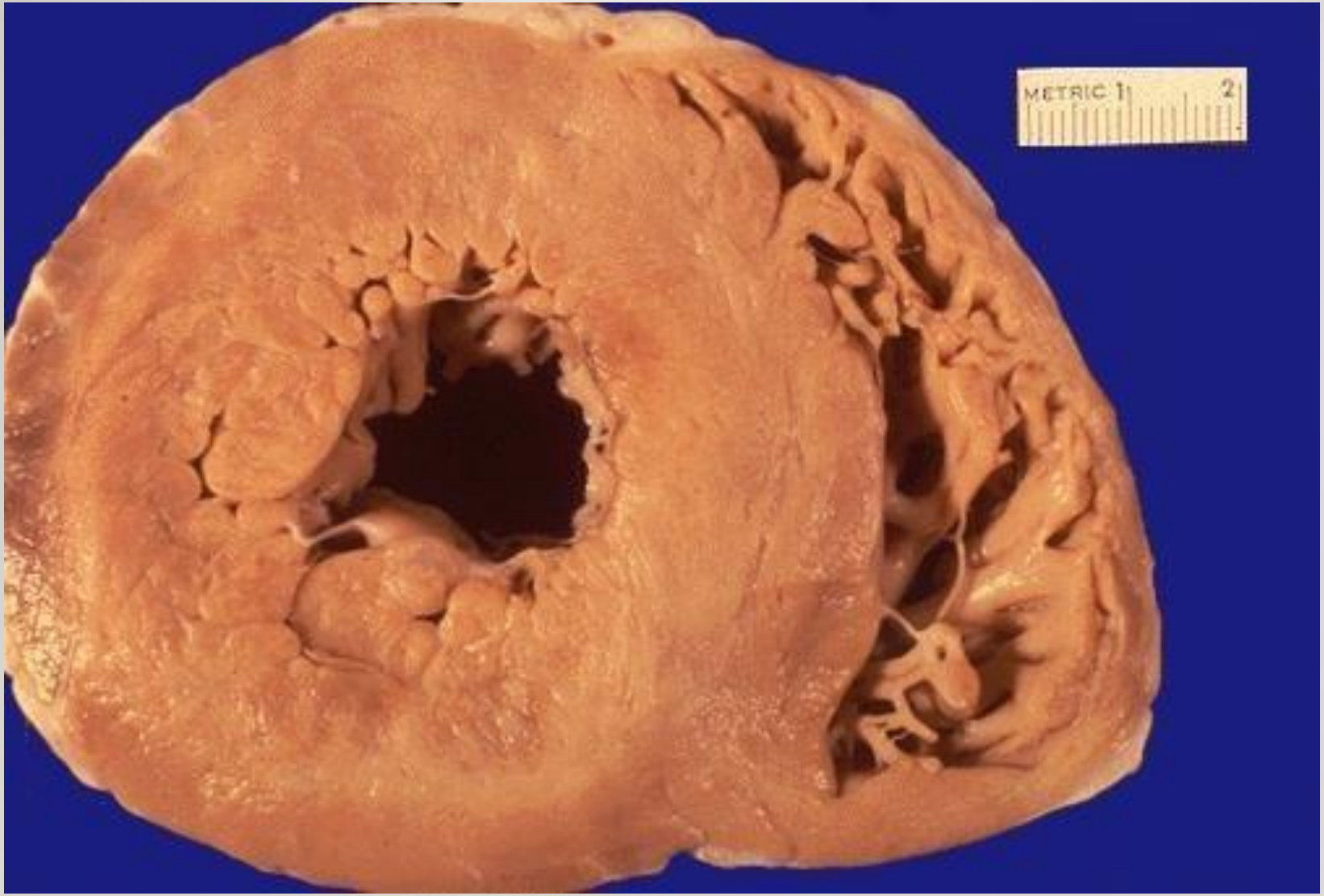


ADAPTATION TO INCREASED WORK LOAD





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**

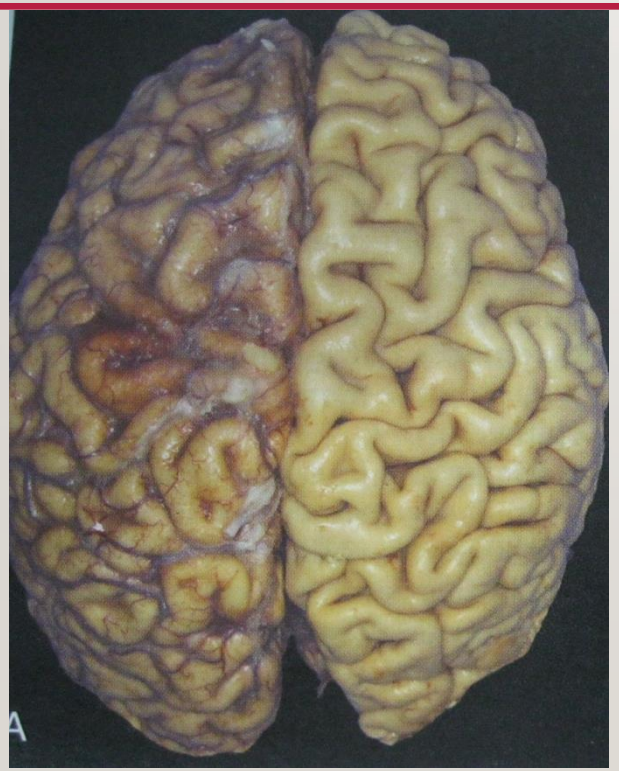
g) **Pressure – tissue compression for long time by enlarging benign tumor**

CELL ADAPTATIONS
ATROPHY

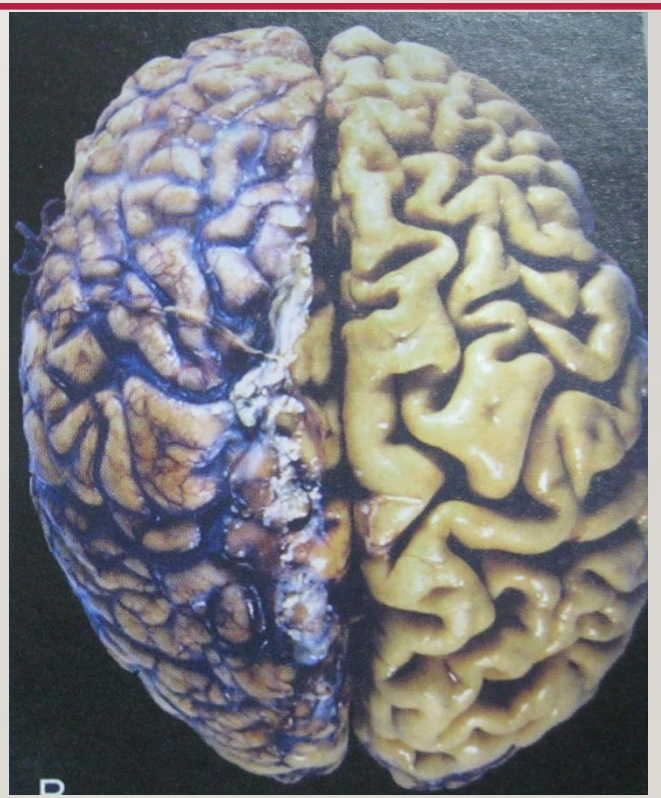
MECHANISM OF ATROPHY

- Results from decreased protein synthesis and increased protein degradation by ubiquitin proteosome 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 proteosomes
- 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

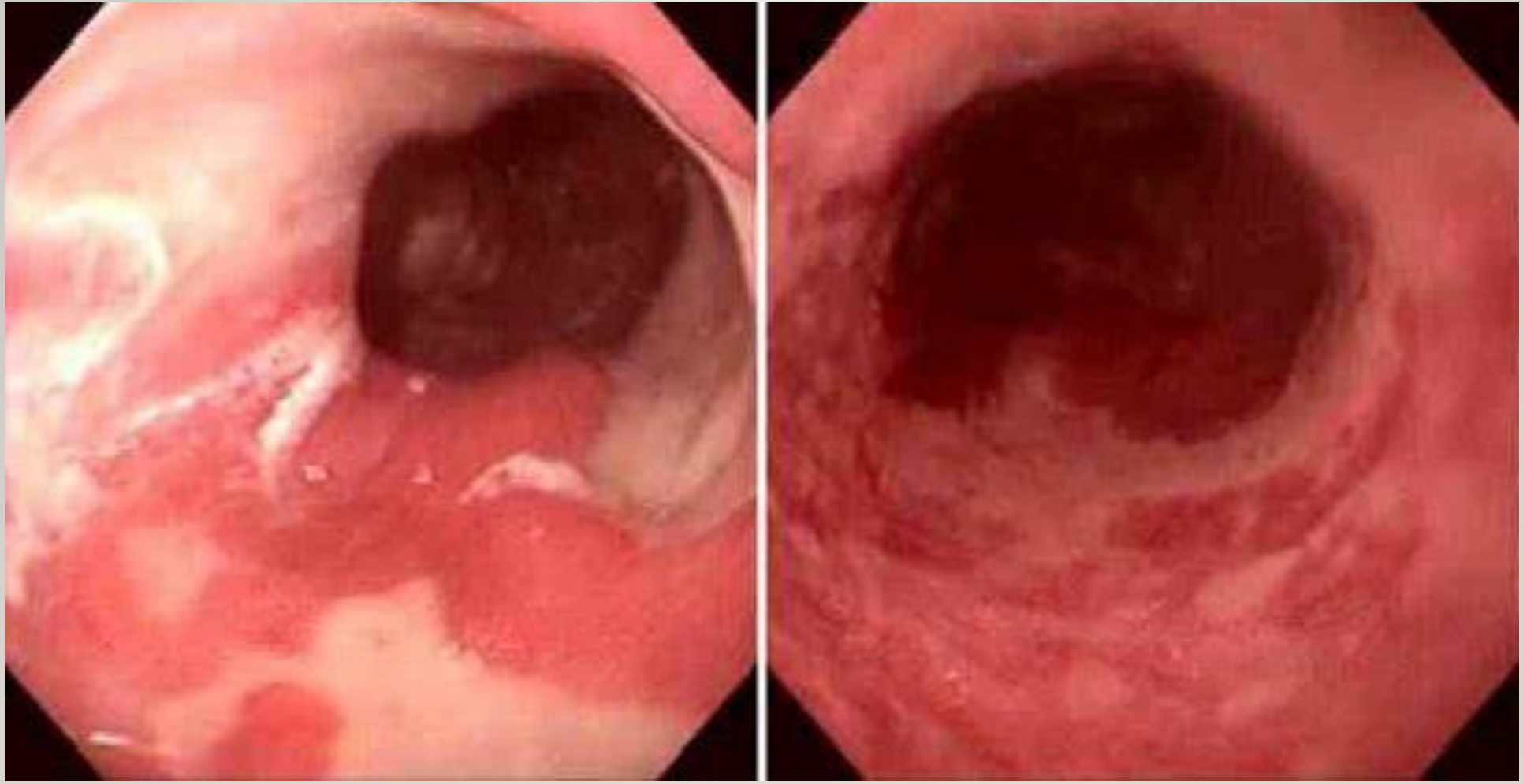
b) Squamous to columnar – Barrett's oesophagus

CELL ADAPTATIONS
METAPLASIA

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

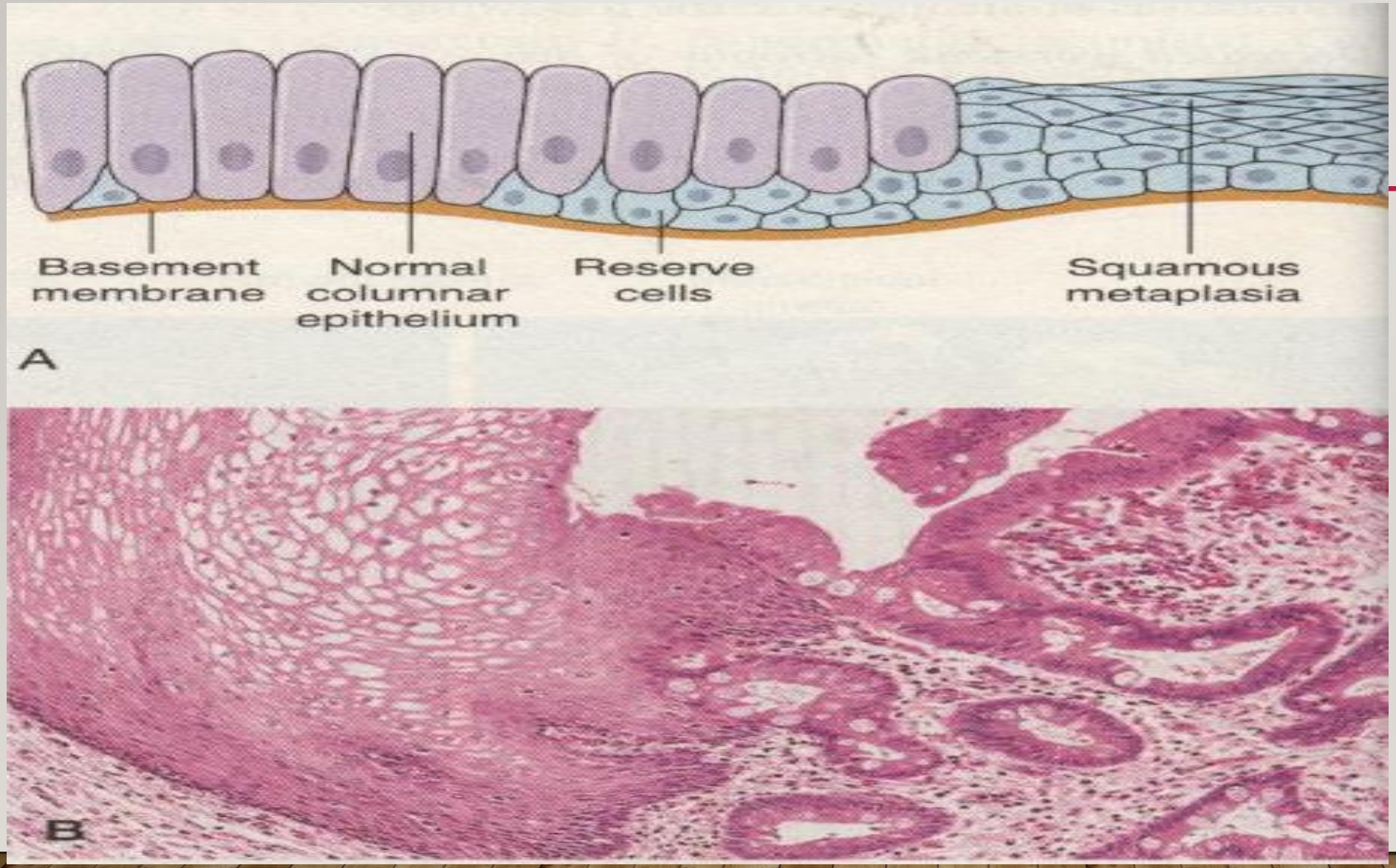
E.g. Myositis ossificans

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



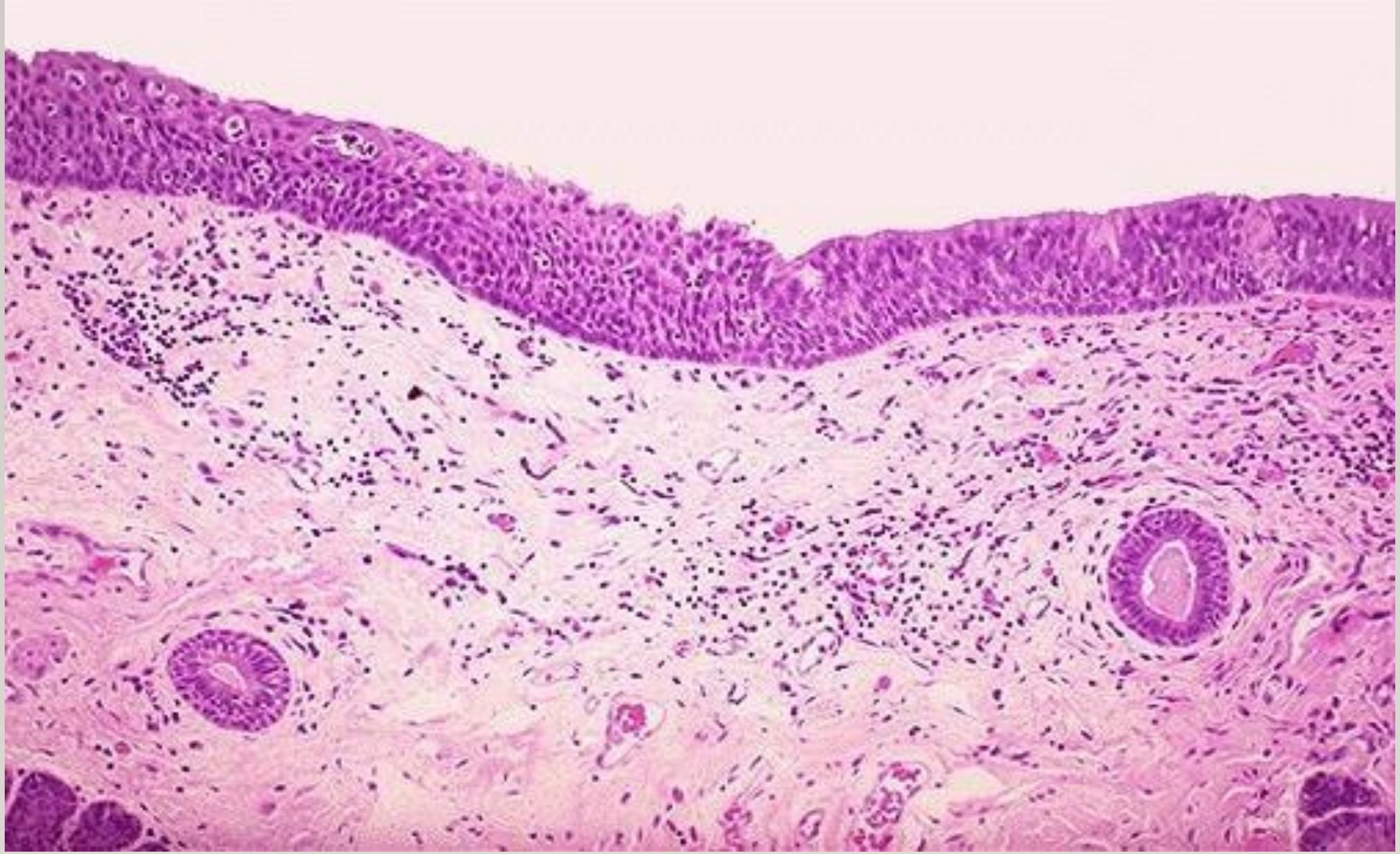
Endoscopical appearance of Barrett esophagitis Squamous epithelium white in color while columnar epithelium red-pink in color.

METAPLASIA



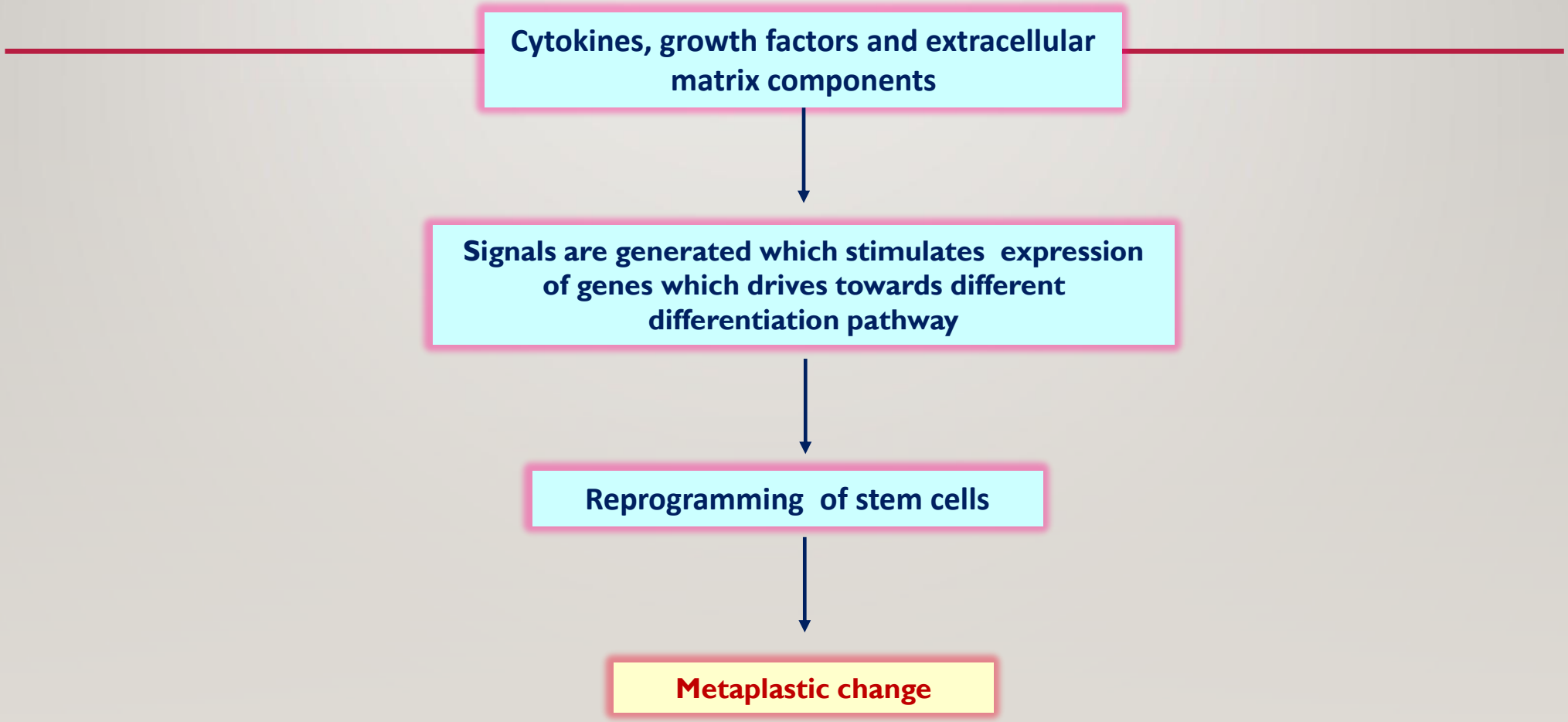
Barrett's esophagitis

(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



SUMMARY

ADAPTIVE CHANGES

HYPERPLASIA

Increased in number of cells

- Physiological
  - Mammary gland
  - Liver
- Pathological
  - Endometrial hyperplasia
  - BPH

HYPERTROPHY

Increase in size of the cell

- Physiological
  - Skeletal muscle after exercise
  - Pregnant uterus
- Pathological
  - Cardiomyopathy

ATROPHY

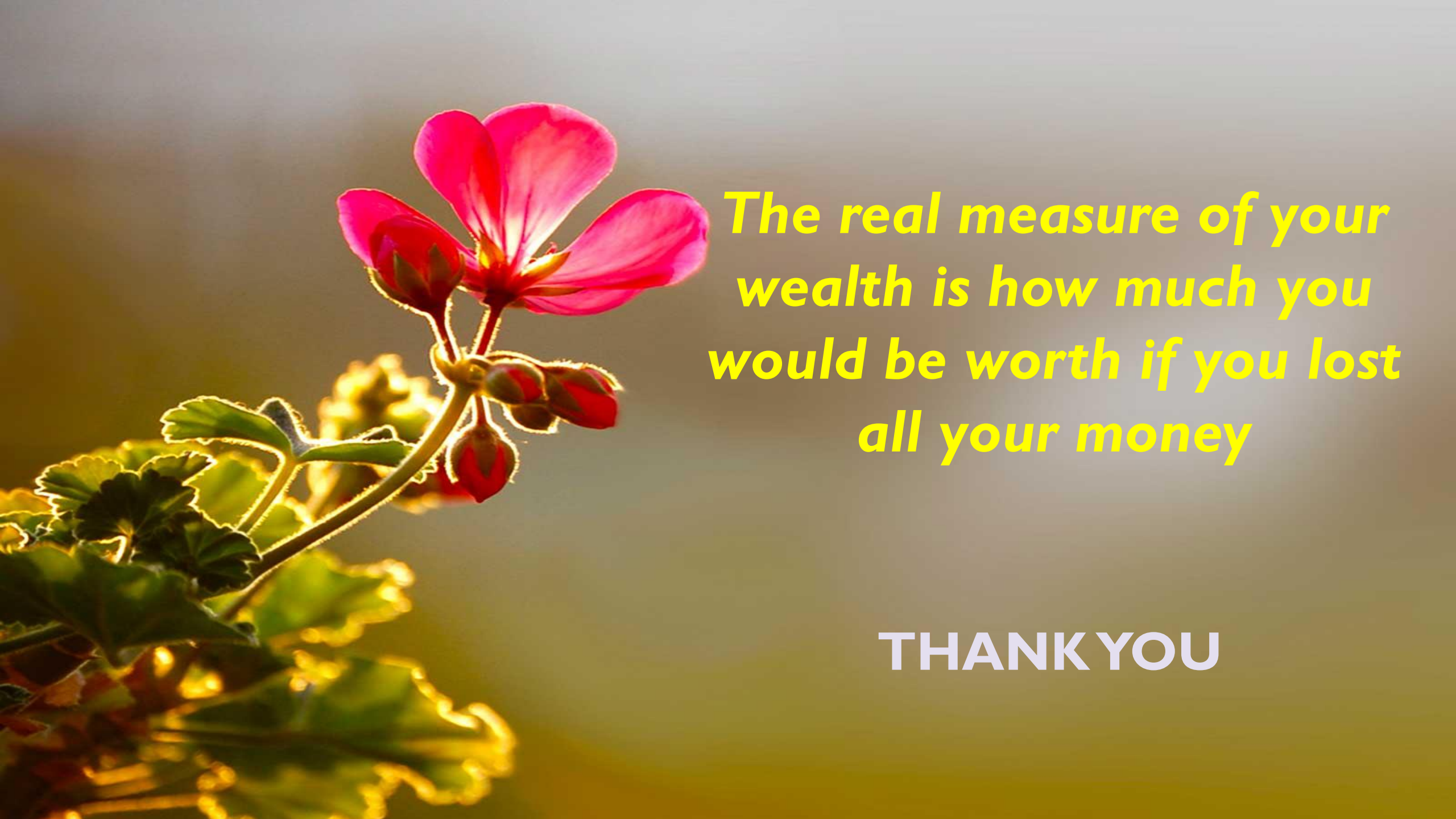
Decrease in number and size of the cell

- Physiological
  - Ductus arteriosus
  - Thyroglossal duct
- Pathological

METAPLASIA

Change of one type of tissue into other type

- Barrett's esophagus
- Myositis ossificans


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