Cellular Adaptations PA 2.6

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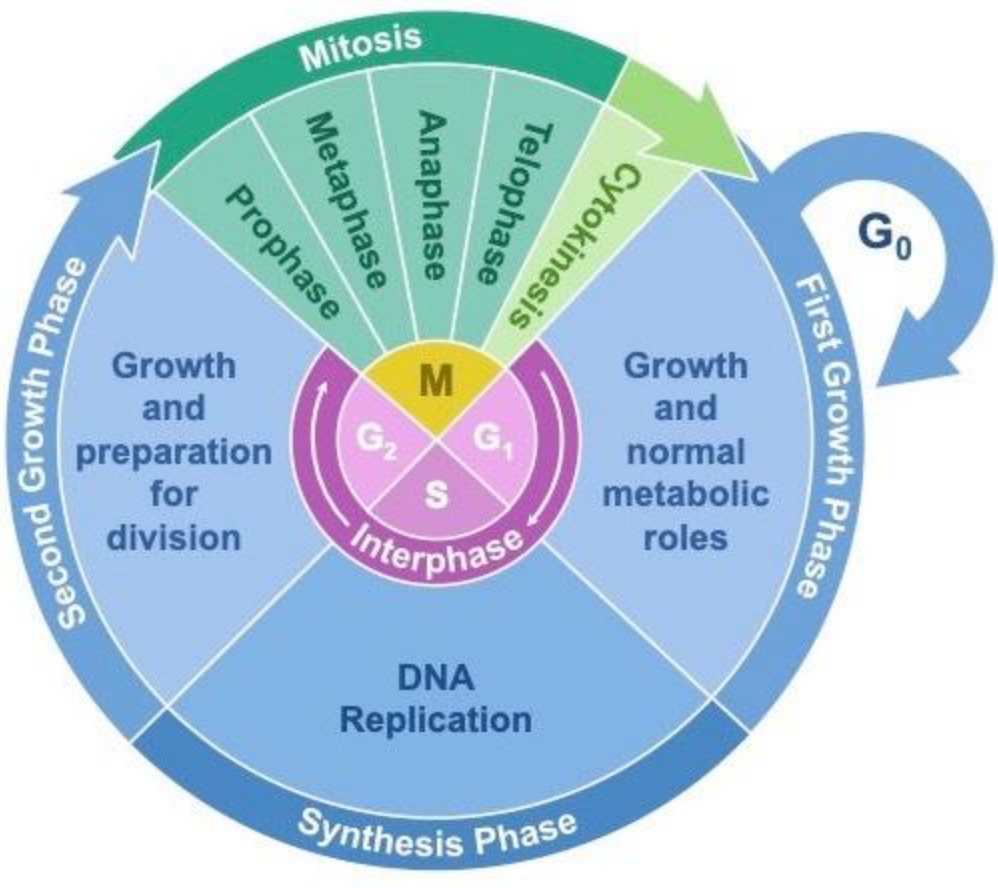
Cell Cycle



STAGES OF THE CELL CYCLE

INTERPHASE:

G_1 – Growth and metabolic roles
S – Replication of DNA occurs
G_2 – Growth and more preparation

MITOSIS:

P – Chromosomes are condensed
M – Chromosomes align at cell centre
A – The duplicated DNA segregates
T – Chromosomes are decondensed

CYTOKINESIS

Cell splits into two daughter cells

RESTING PHASE (G_0)

Cells may leave interphase and enter
Into a non-dividing quiescent phase

The Cell Cycle

Interphase

The cell grows and copies its DNA

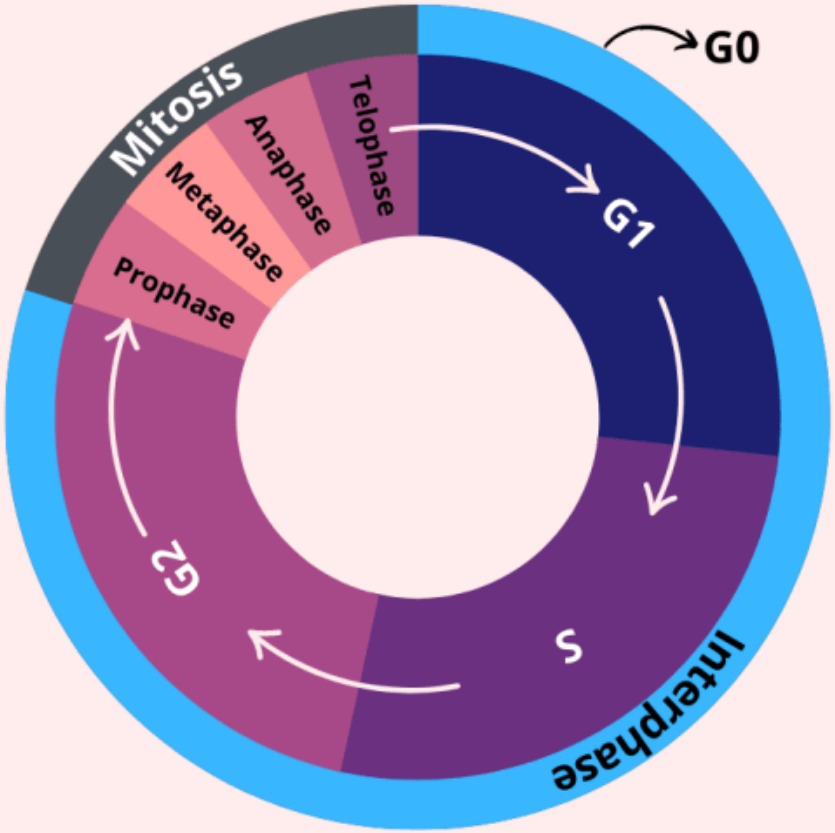
- **G_1**: Cell growth
- **S** : DNA synthesis
- **G_2:** More growth, preparation for mitosis

Mitosis

The cell divides its DNA and cytoplasm, forming two new cells

- **Prophase**
- **Metaphase**
- **Anaphase**
- **Telophase**

G_0: Resting state where the cell performs its functions and is not preparing to divide



Types of cells

- **Labile cells**
- **Stable cells**
- **Permanent cells**

- **<u>Continuously dividing/ Labile Cells:</u>**

  Proliferate throughout life, replacing those that are destroyed

  - Surface epithelium
  - Mucosal lining of glands , skin ,endometrium, haematopoietic tissue.

- **Quiescent/ Stable cells:**
  - Low levels of replication
  - Can undergo rapid division in respective to stimuli
  - In G_o → can be stimulated to G_1
  - Parenchymal cells - liver, kidney, pancreas
  - Mesenchymal cells – fibroblasts, smooth muscle
  - **Non dividing/ permanent cells:**
- Left the cell cycle & can not undergo mitotic division in post natal life
- Neurons, skeletal and cardiac muscle

Stages in cellular response to stress

Normal cell

↓

↑functional demand | Mild to moderate stress | severe persistent stress

↓ | ↓ | ↓

Cellular adaptations cell injury | **Reversible cell injury** | **Irreversible**

Atrophy, hypertrophy, hyperplasia, metaplasia, Dysplasia

Degeneration,subcellular alterations, intracellular accumalations

stress removed

stress removed

Normal cell restored | Repair & Healing | Cell death

(Necrosis,Apoptosis)

Cellular adaptations / Disorders of cell growth

1. Agenesis
2. Aplasia
3. Hypoplasia
4. Atrophy
5. Hypertrophy
6. Hyperplasia
7. Metaplasia
8. Dysplasia
9. Neoplasia

- **Agenesis –**
  - Without beginning total absence of organ or tissue, Eg. renal agenesis
- **Aplasia –**
  - Without complete formation, organ remains rudimentary. Mass of undifferentiated cells or fibrofatty tissue
  - E.g. anencephaly, aplasia of aorta, Incompatible with life
- **Hypoplasia –**
  - Defficient formation
  - Failure to reach normal size
  - Eg.-Renal hypoplasia

- Atrophy -
  - Reduction in number of parenchymal cells of organ which was once normal

Physiological atrophy:

- Gradual atrophy of lymphoid tissue from adolescence onwards
- Atrophy of ovaries after menopause
- Atrophy of brain in old age

Pathological atrophy:

1. Starvation atrophy –
   emaciation, wasting & atrophy
2. Ischaemic atrophy –
   gradual onset & longer duration
   seen in atherosclerosis

- 3.Disuse atrophy –

  e.g. wasting of muscles immobilized in plaster,cast.
- 4.Neuropathic atrophy –
  i. Poliomyelitis
  ii. Motor neuron disease
- 5.Endocrine atrophy –

  Hypopituitarism causes atrophy of thyroid, adrenal & gonads
- 6.Pressure atrophy –
  i. Obstruction to flow of CSF → atrophy of brain tissue
  ii. Erosion of sternum by aneurysm of aorta

- 7.Irradiation atrophy – Atrophy of skin appandages, lymphoid tissue, bone marrow, spermatogonia & ova.
- 8.Idiopathic atrophy – testicular atrophy

Gross:

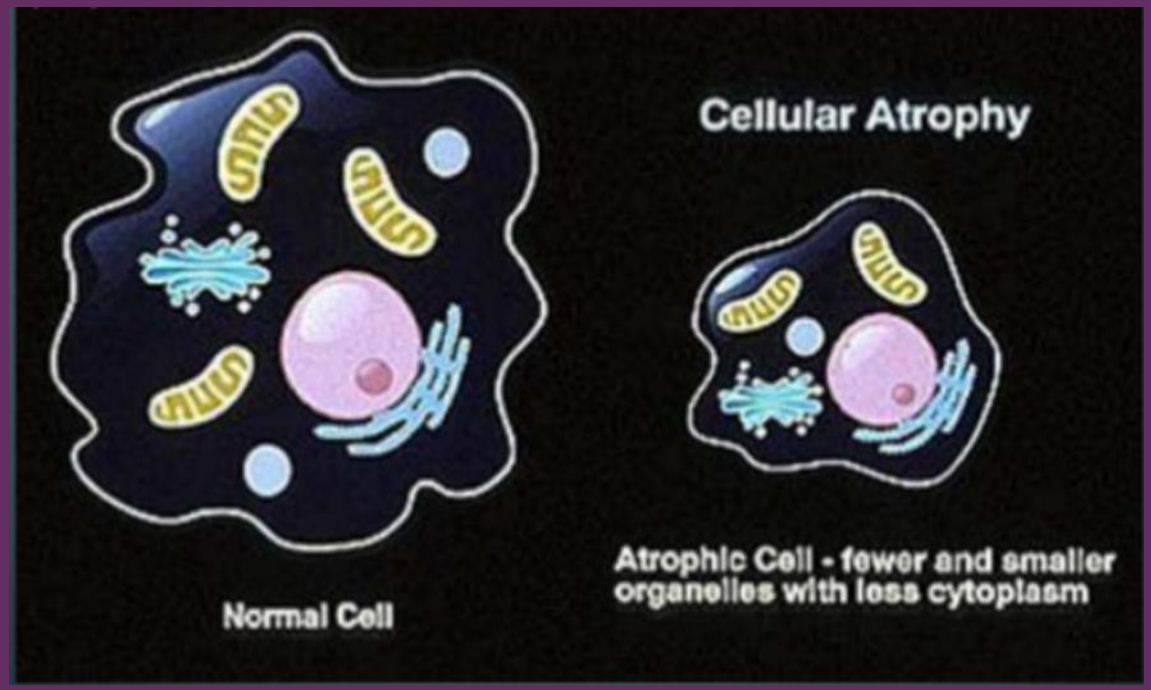
Small & shrunken

Microscopy:

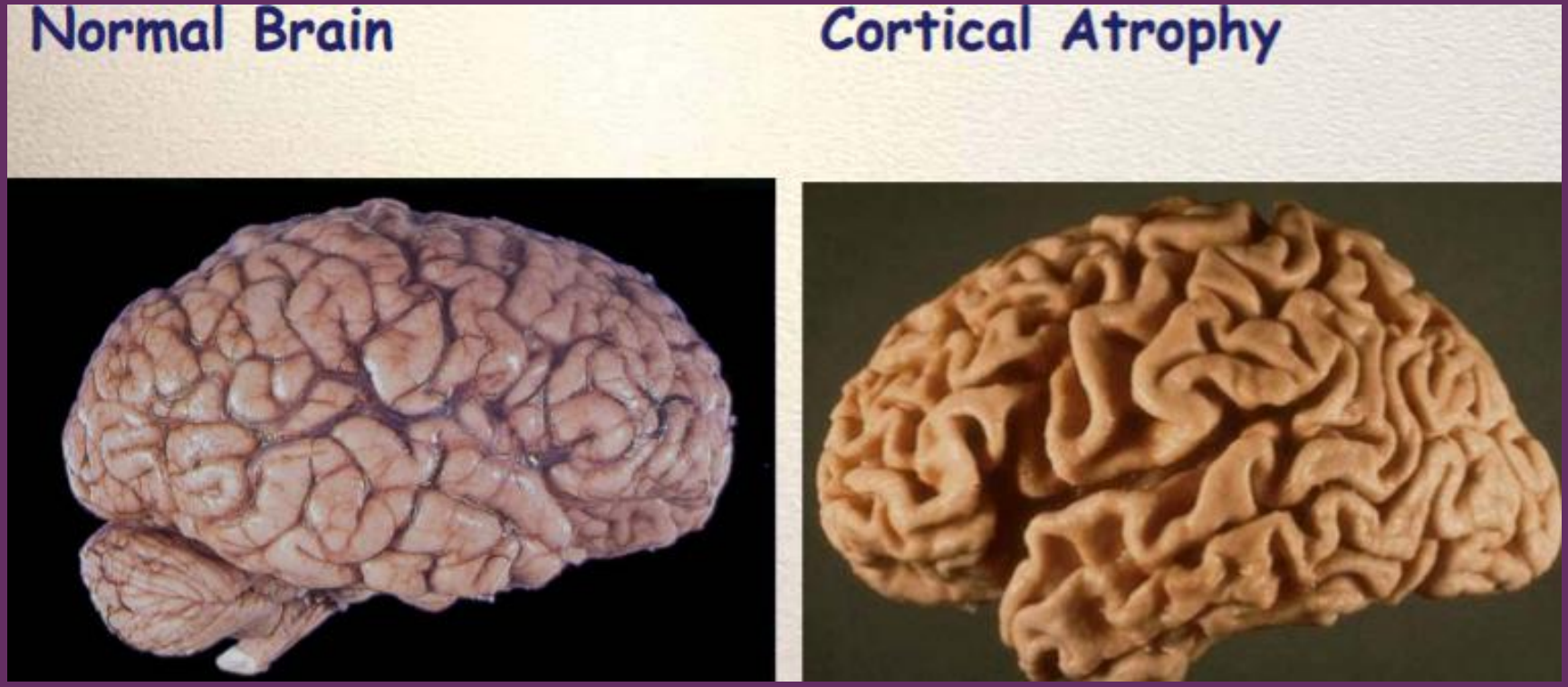
Cells are smaller in size but they are viable.

Decreased cell organelles e.g. mitochondria

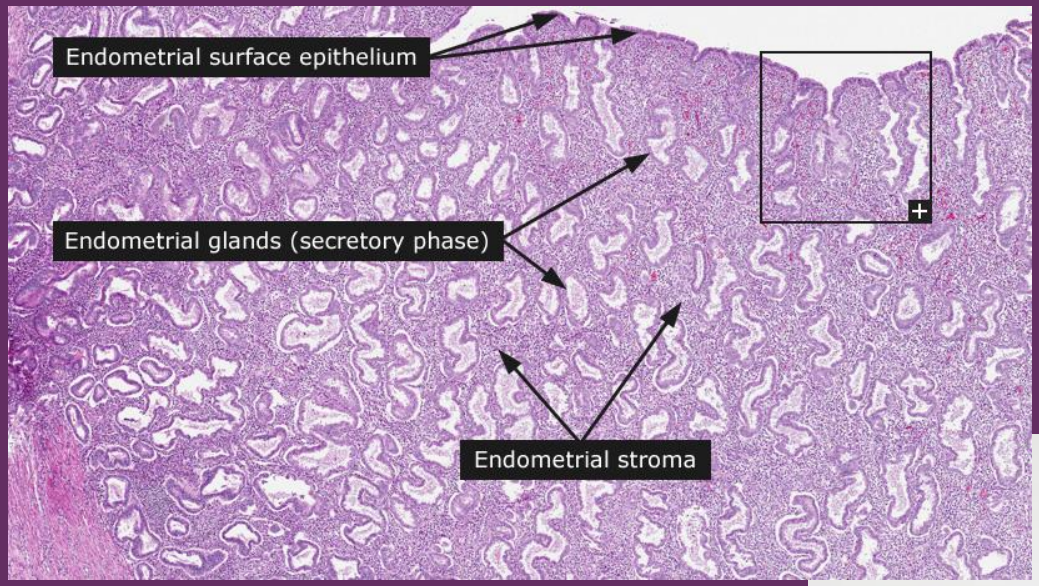
Myofilaments & E R.

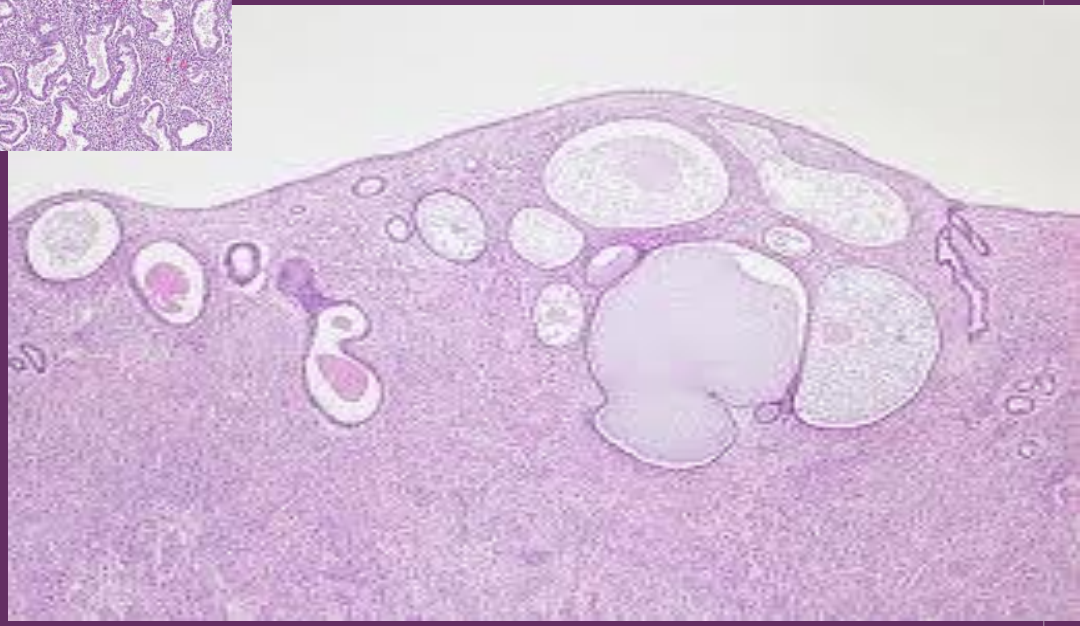

Cellular Atrophy
Normal Cell
Atrophic Cell - fewer and smaller organelles with less cytoplasm

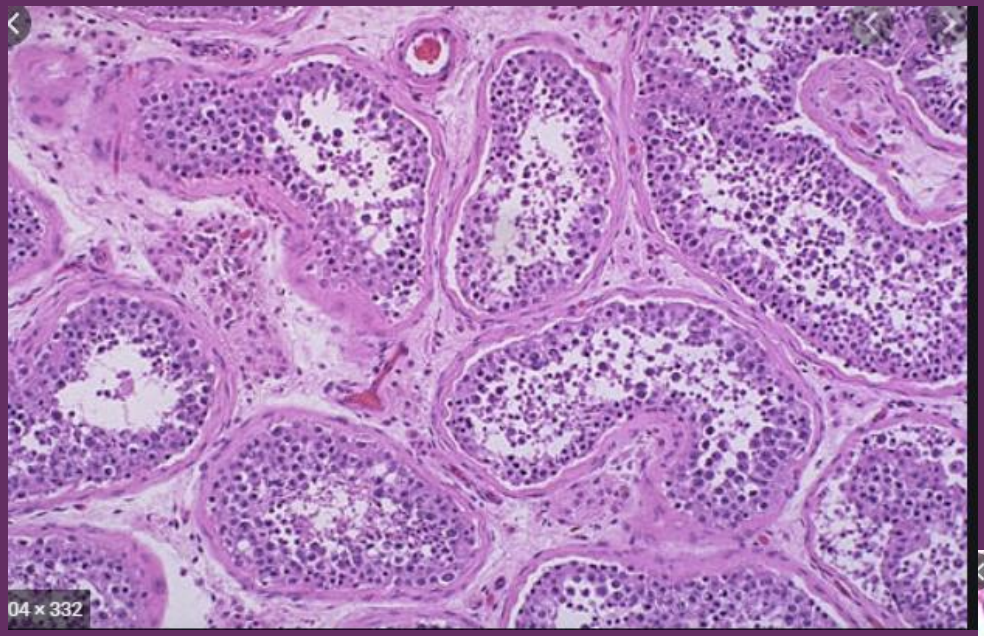
Cerebral Atrophy



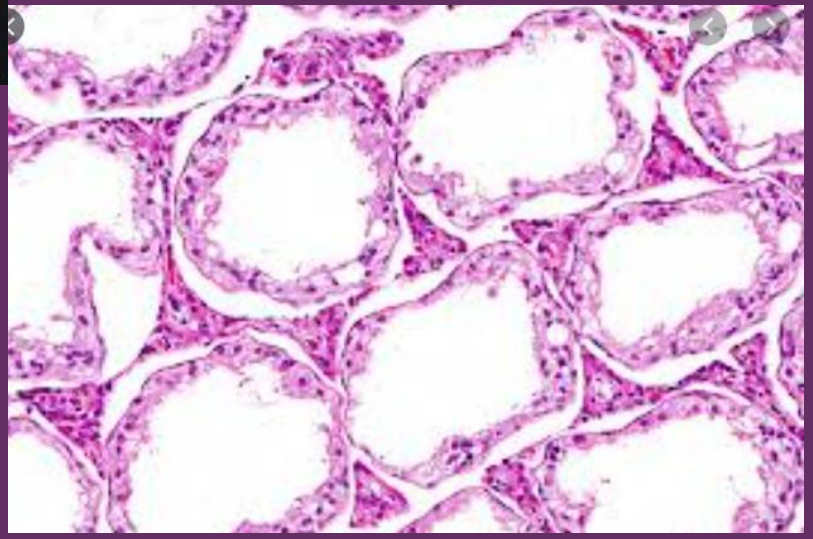
Cystic atrophy of Endometrium



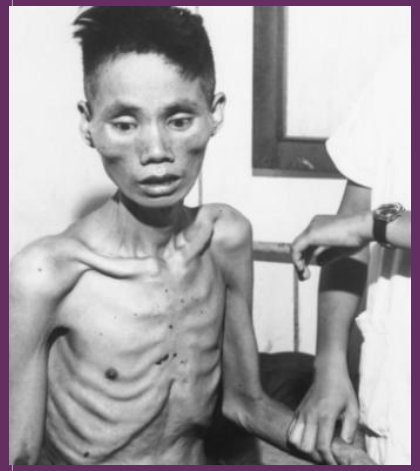




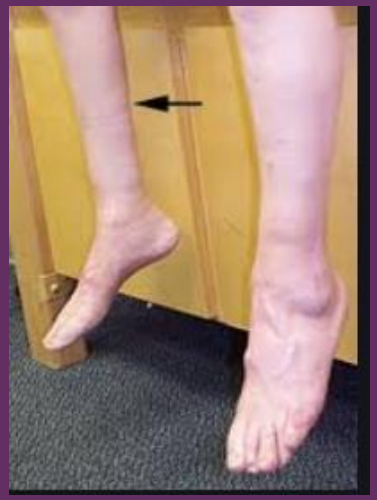
Normal semininferous tubules



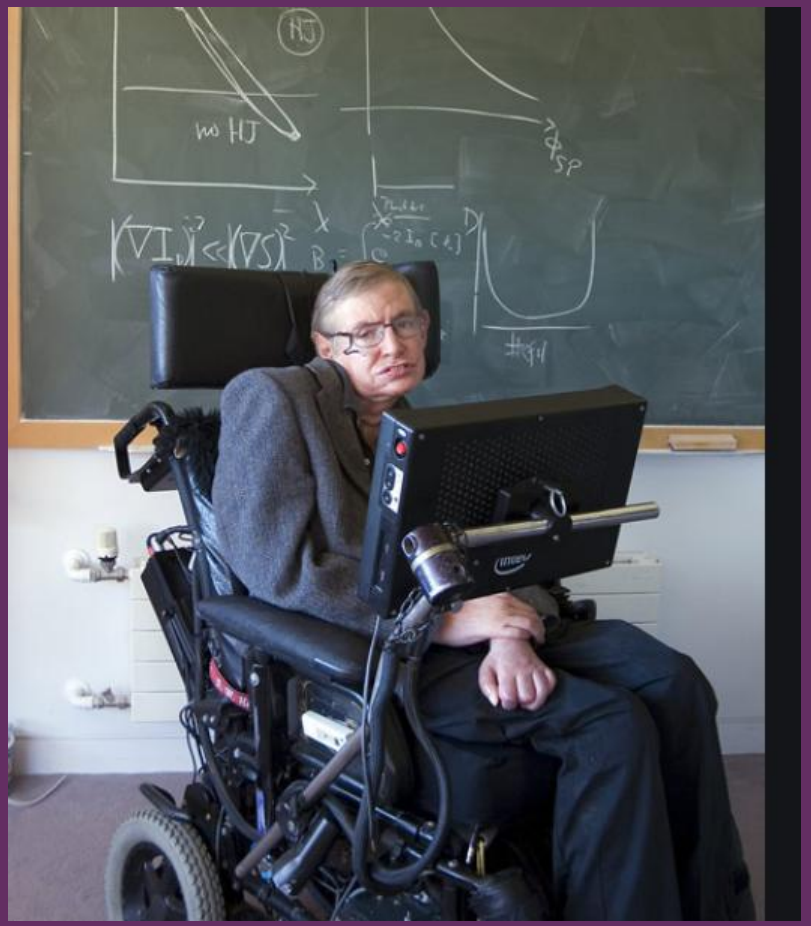
Atrophic seminiferous tubules



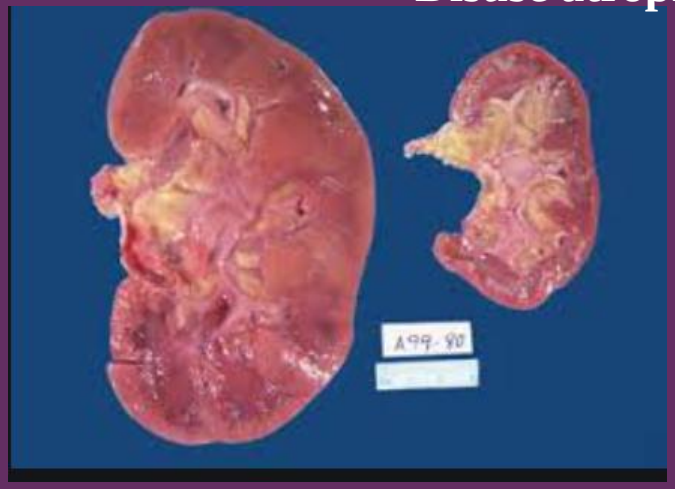
Starvation atrophy



Disuse atrophy



Neuropathic atrophy – motor neuron disease



Ischemic atrophy-kidney

- **Hypertrophy –**
  - Increase volume of tissue or organ
  - Enlargement of cells
  - Non dividing cells/ permanent cells
- **Hyperplasia –**
  - Formation of new cells (Proliferation of cells)
  - Size of the cells normal
  - Labile & stable cells

Hypertrophy

- **Physiologic:**
  Growth of uterus during pregnancy
- **Pathologic:**
- Hypertrophy of Left ventricles – in AS & hypertension
  Hypertrophy of Right ventricles – in pulmonary hypertension.
- Hypertrophy of Skeletal muscle with exercise
- Liver or one kidney if other is removed – Compensatory Hypertrophy

Hypertrophy

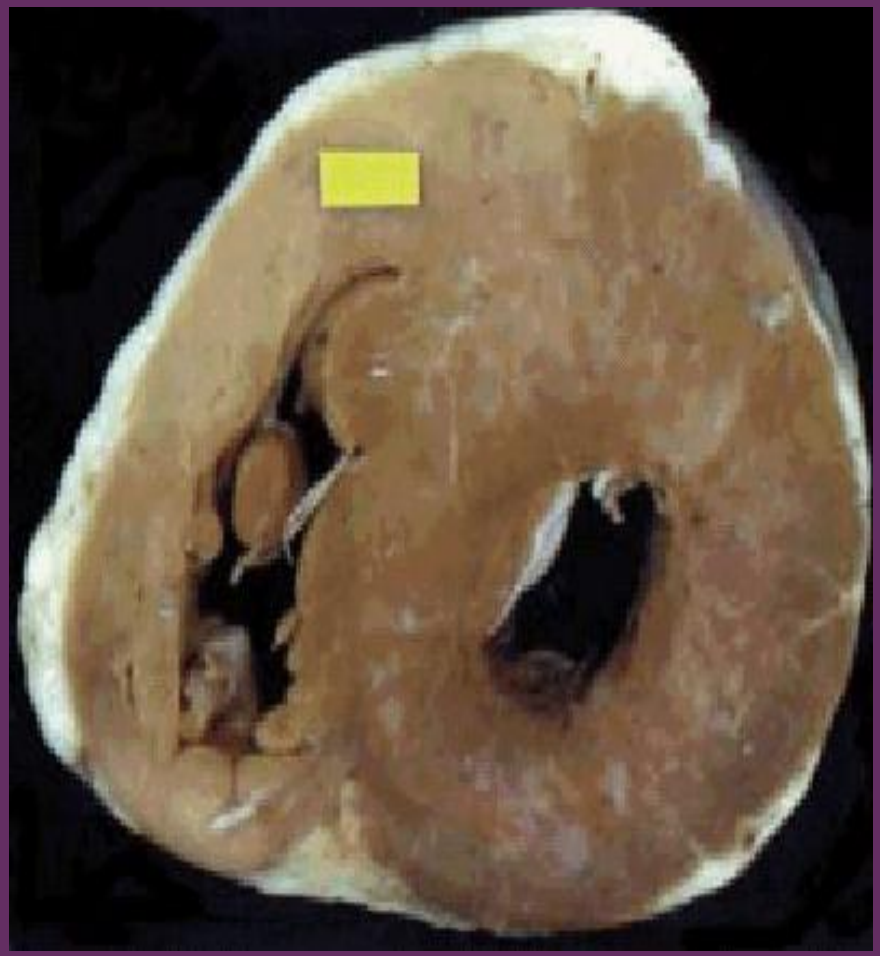
- Gross:

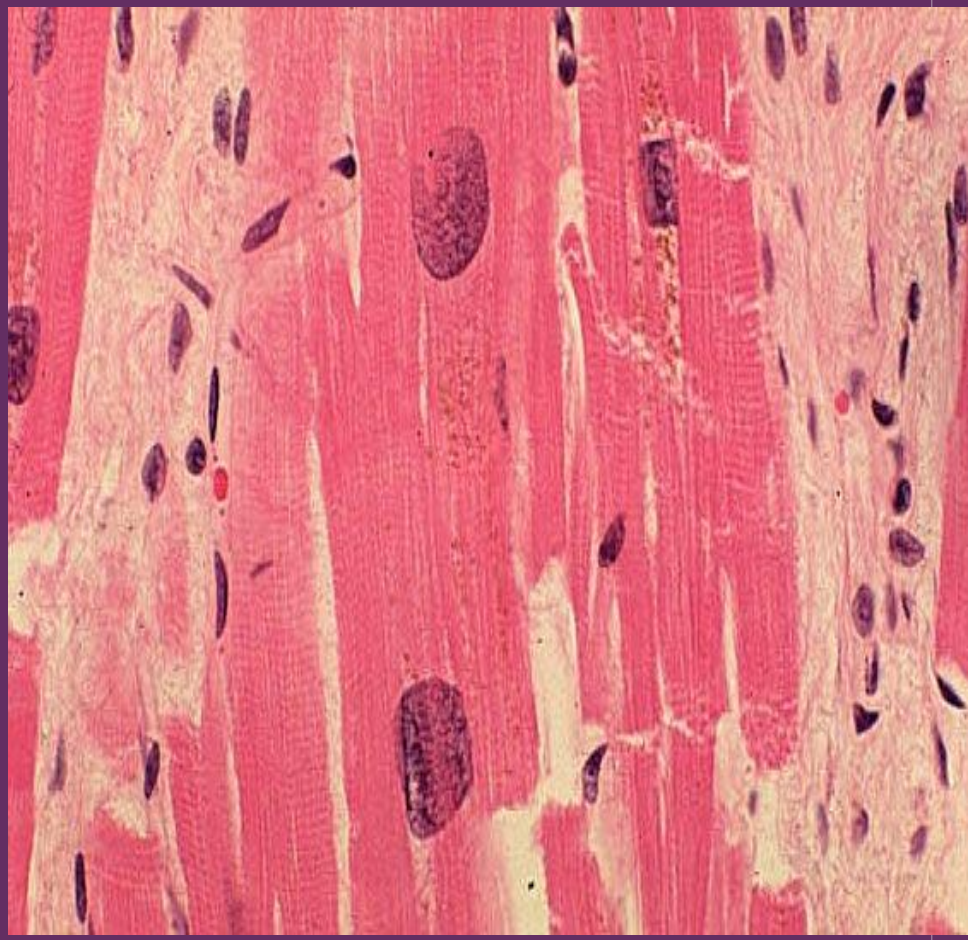
  Organs are enlarged & heavy. e.g. myocardial hypertrophy in patients of Hypertension 700 – 800 gm (250-350gm N)
- Microscopy:

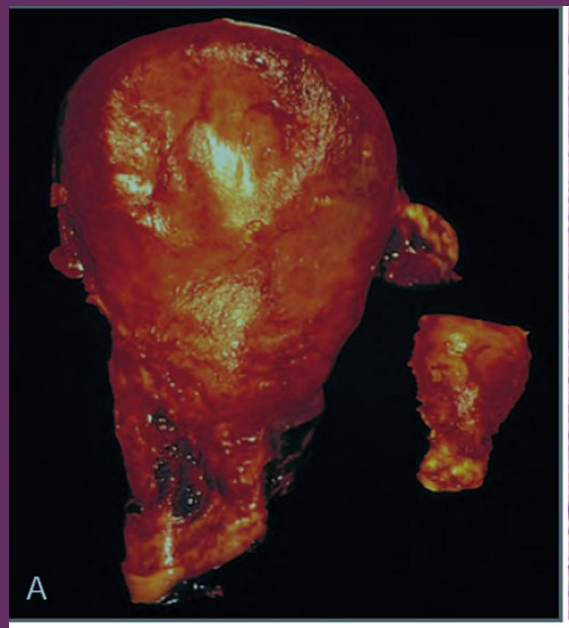
  Enlarged cells as well as nuclei.

  No increase in the number of cells

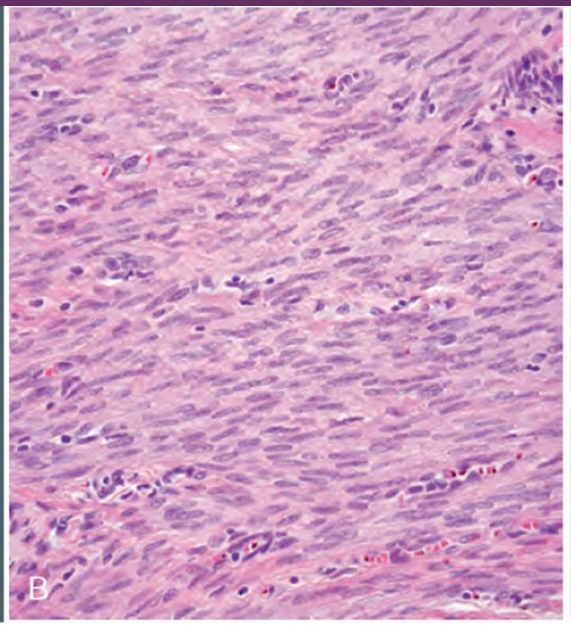
Left ventricular Hypertrophy



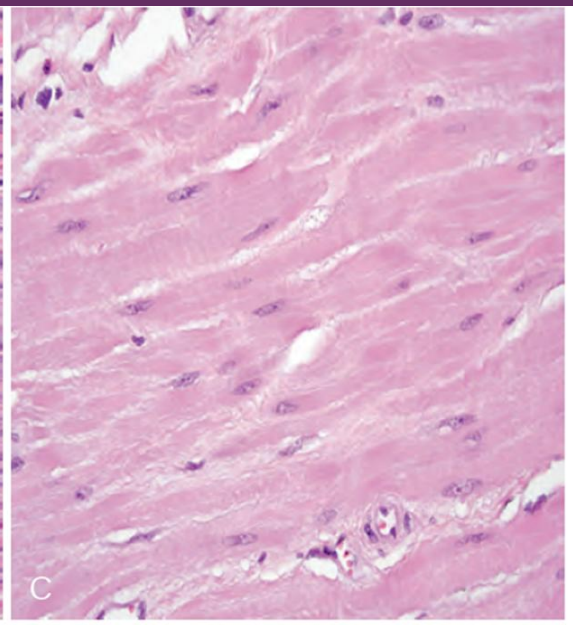




Physiologic hypertrophy of the uterus during pregnancy

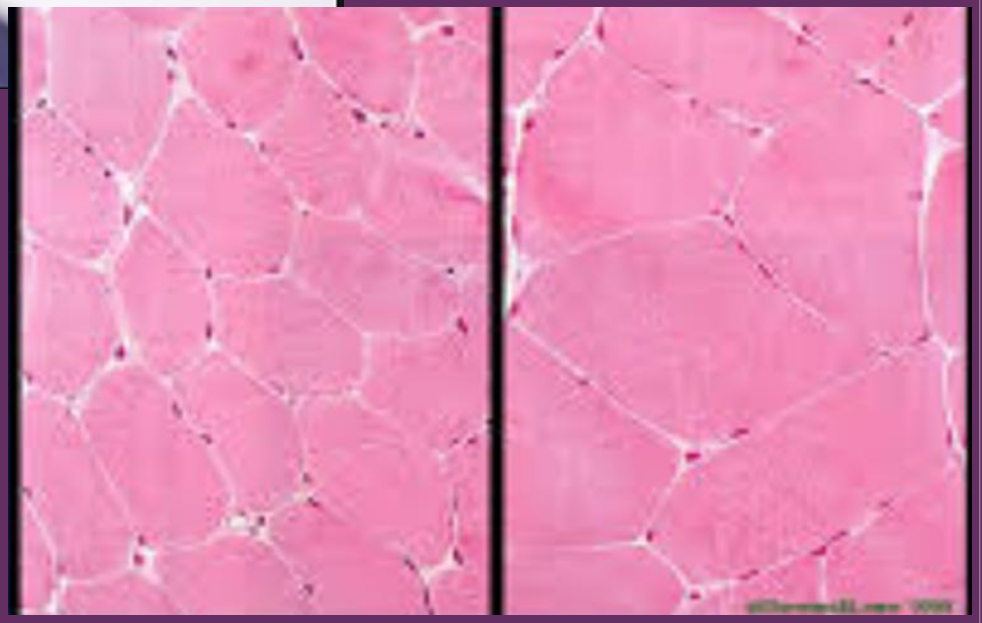


Small spindle-shaped uterine smooth muscle cells



Large plump cells from the gravid uterus


× 466



Hyperplasia

- Increase in number of parenchymal cells
- Both hyperplasia & hypertrophy occur together
- Hyperplasia occurs due to cells from G_0 Phase entering into cell cycle when they receive stimulus.
- Hyperplasia persists till the stimulus lasts.

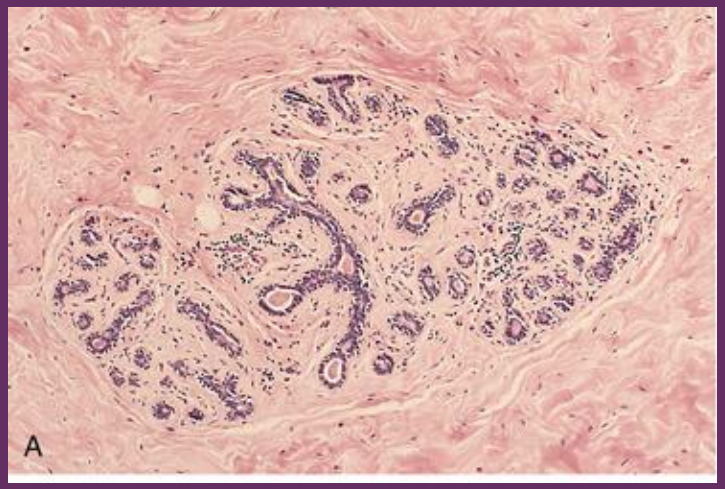
- Physiologic
- Pathologic

Hyperplasia

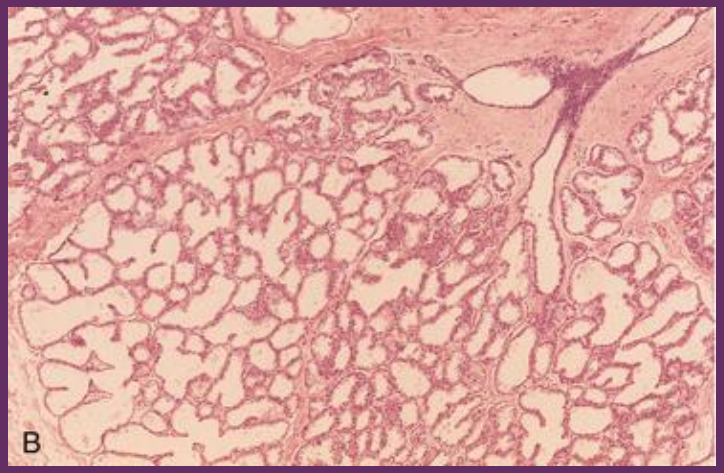
- **Physiologic:**
- **1.Hormonal –**
- Hyperplasia of breast during puberty, pregnancy, lactation.
- Hyperplasia of pregnant uterus
- Proliferative endometrium in normal menstrual cycle
- Prostatic Hyperplasia in old age

2. Compensatory Hyperplasia

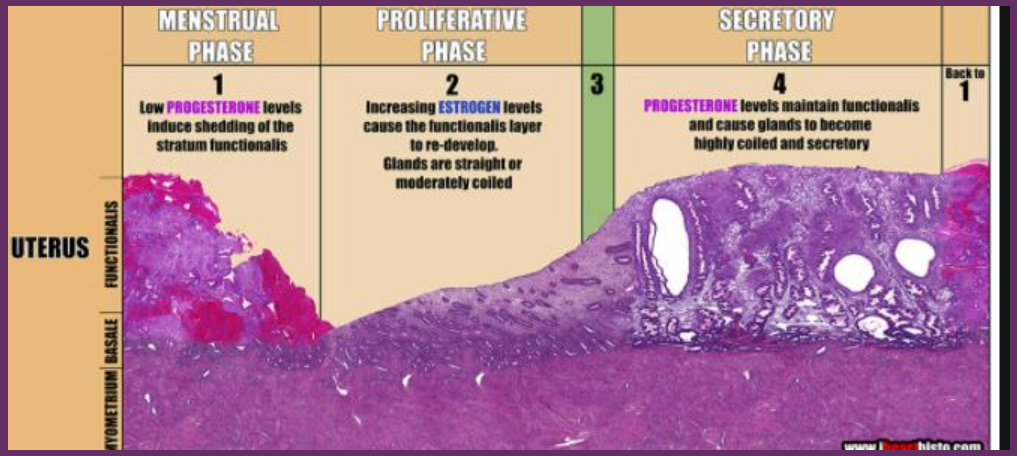
- Liver or one kidney if other is removed
- Regeneration of epidermis after skin abrasion



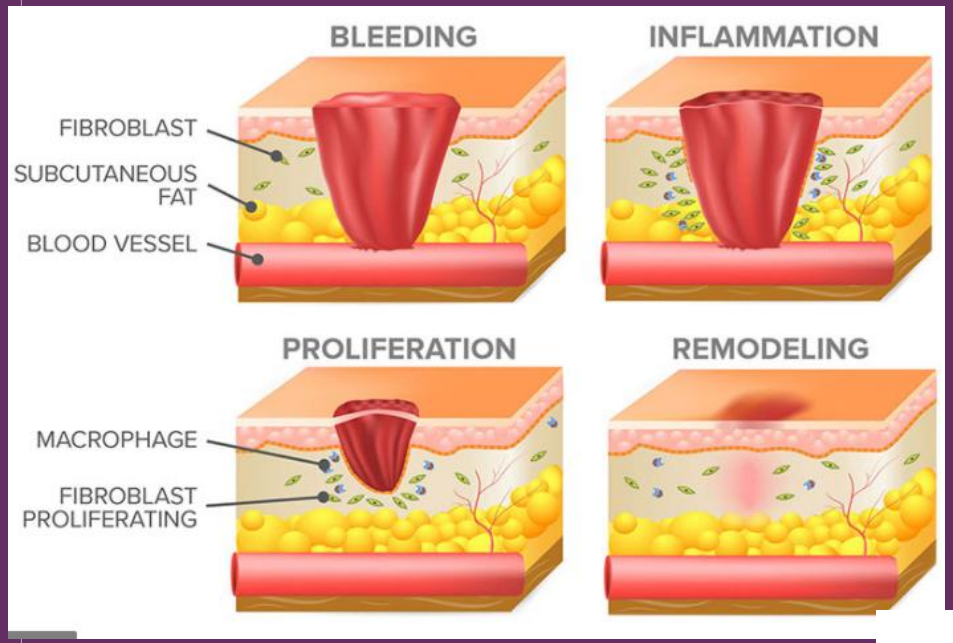
Normal breast



Hyperplasia of breast

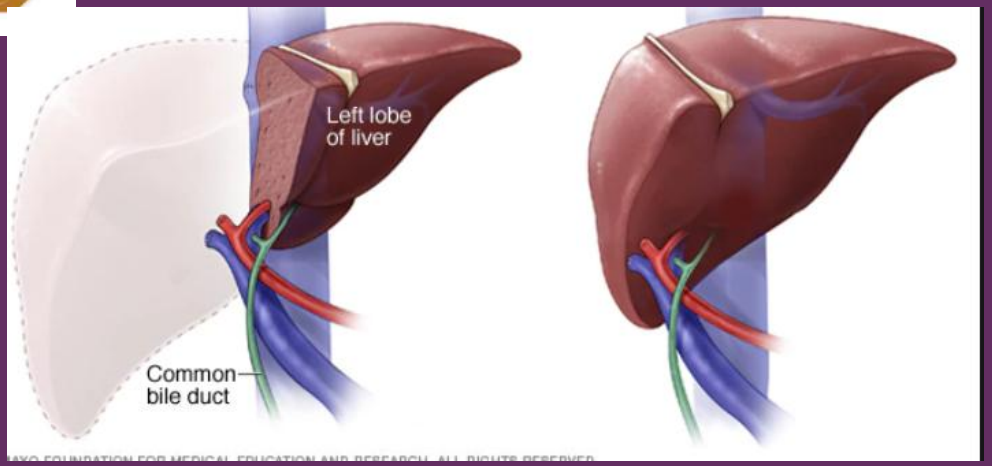


Endometrial proliferation after menstrual cycle



Regeneration of epidermis in wound healing

Compensatory liver hyperplasia



Hyperplasia

- **Pathologic:**
  - Erythroid tissue hyperplasia in hypoxia or anaemia.
  - Hyperplasia of the epithelium covering skin & mucosae e.g. HPV infection → Wart
  - Endometrium hyperplasia following oestrogen excess.

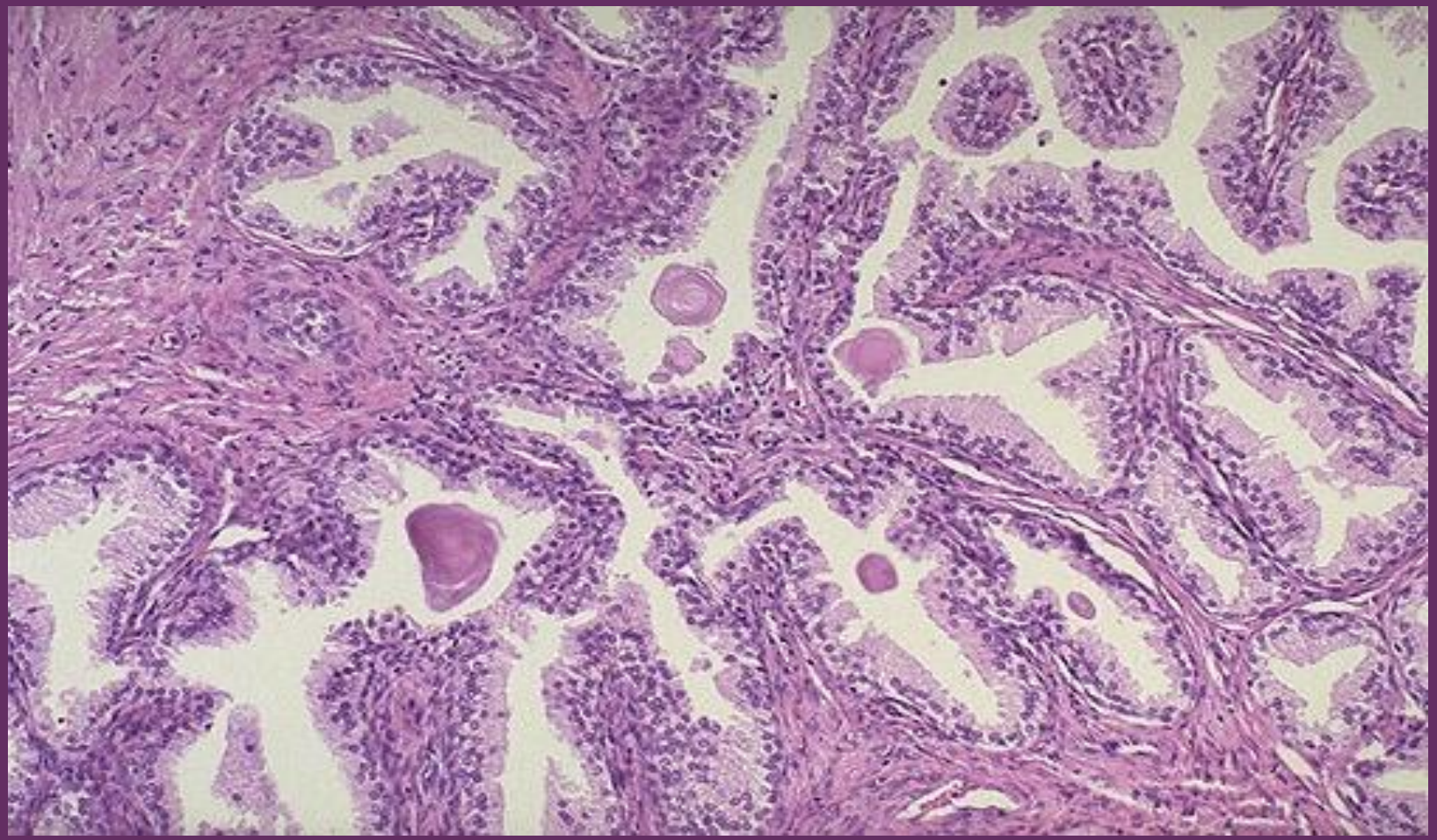
Gross:

Organ is enlarged

Microscopy:

Increase in the number of cells due to increased DNA synthesis and proliferation of cells

Prostatic Hyperplasia



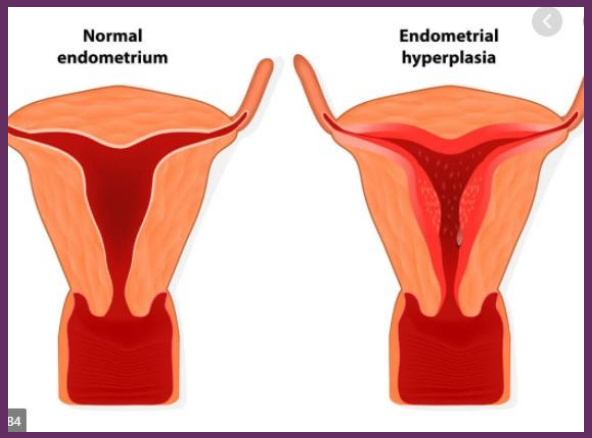
Pathologic changes:

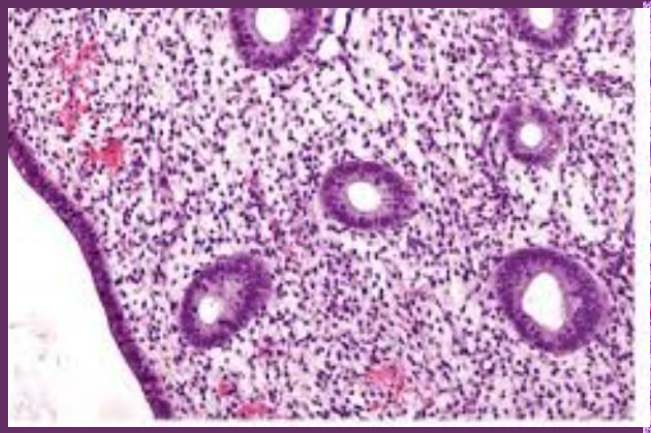
Grossly in both Hyperplasia & Hypertrophy organ is Enlarged & heavy

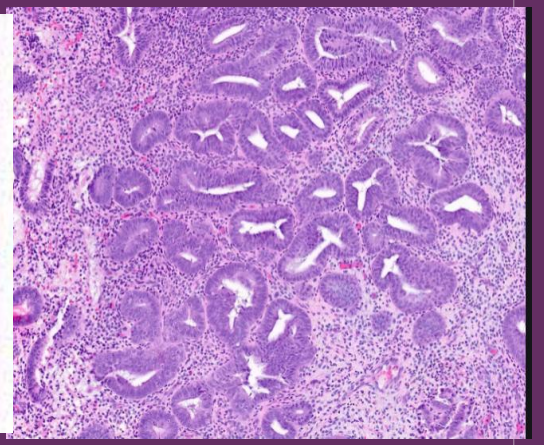
Microscopically,

Hypertrophy –no. of cells constant, size increased

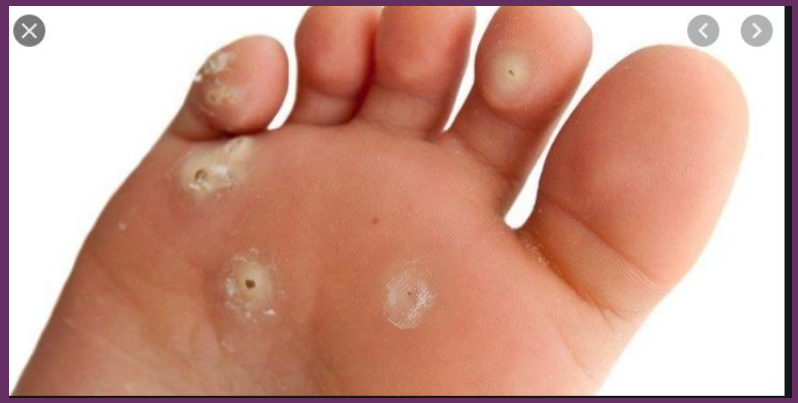
Hyperplasia – no of cells increased & size of the cell is normal

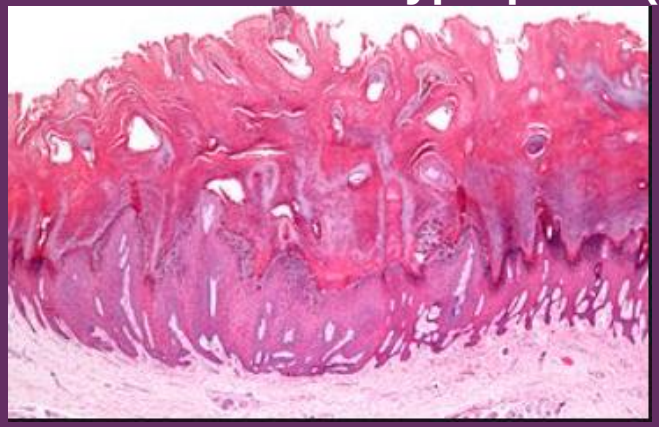






Normal endometrium(L) and endometrial hyperplasia(R)





Skin warts-pathological hyperplasia

Metaplasia

Def: Reversible change of one type of adult tissue to another type of adult tissue in response to abnormal stimulus and reverts back to normal on removal of stimulus.

A] Epithelial metaplasia:

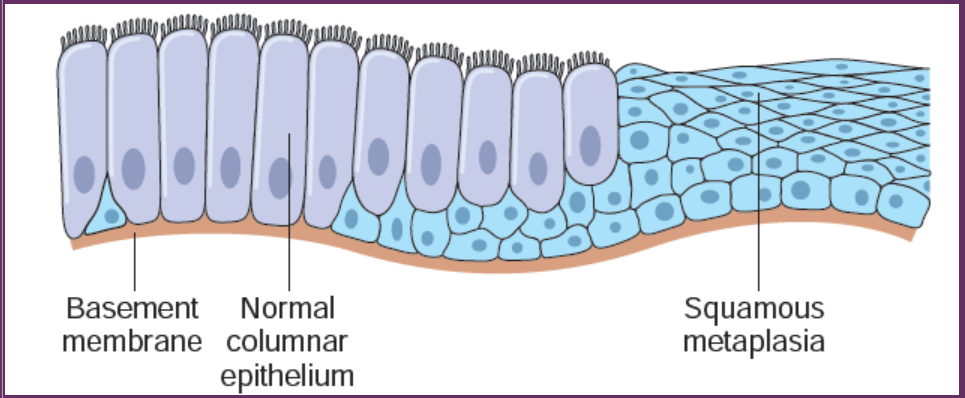
- Squamous metaplasia – e.g. in respiratory tract, lining of ducts, lining of cervix
- Columnar metaplasia – e.g. Barret's oesophagus.

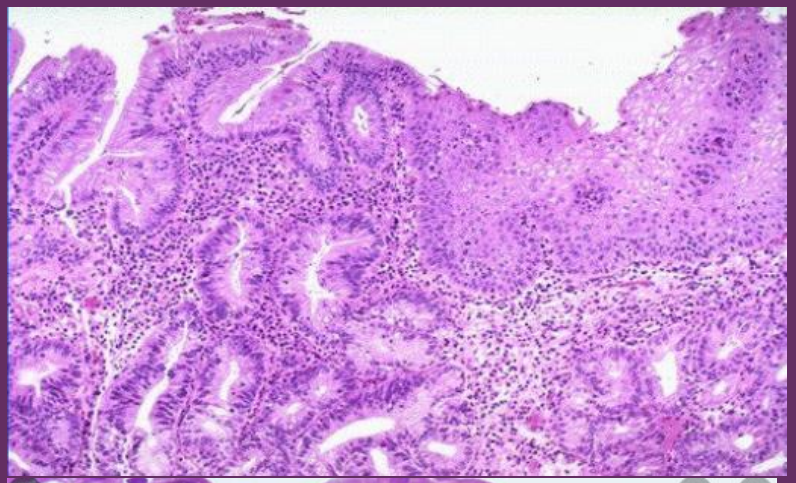
B] Mesenchymal metaplasia:

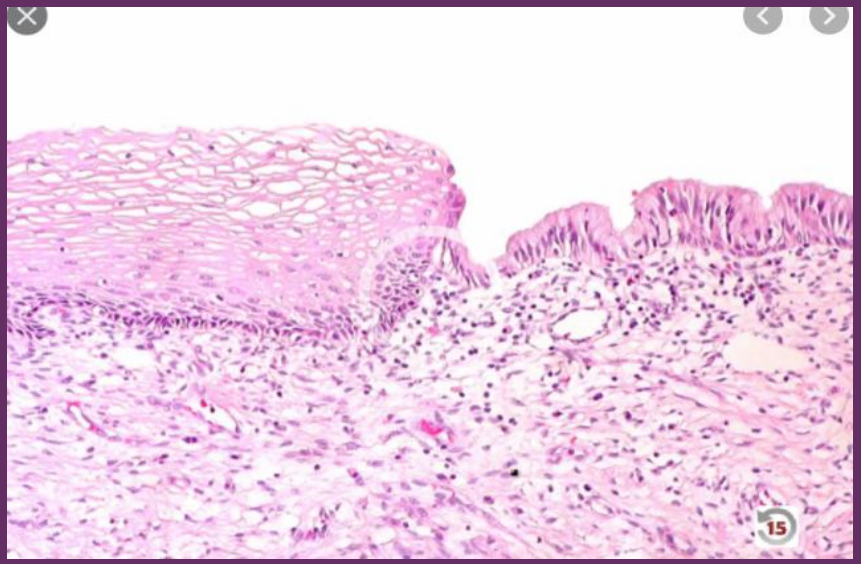
Osseous Metaplasia - Fibrous, myxomatous or cartilaginous bone

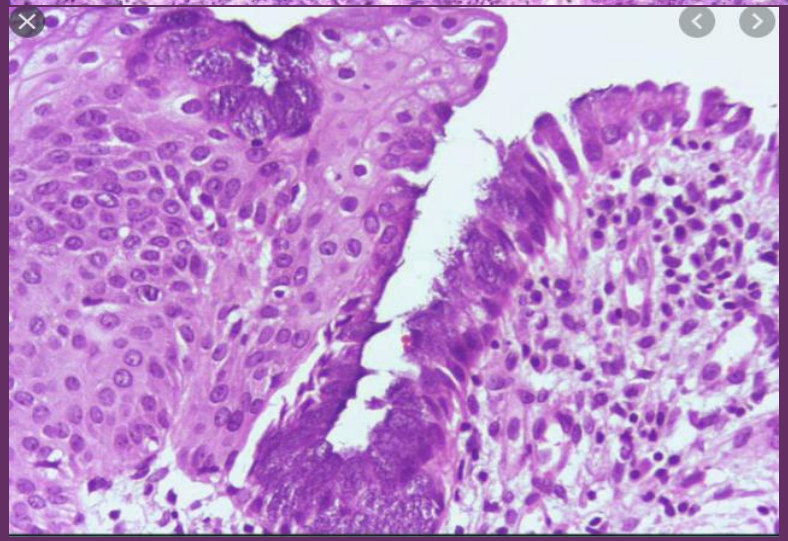
e.g. in old scars, necrotic areas, injured soft tissue, in stroma of connective tissue tumors

Squamous metaplasia in cervix









Normal squamocolumnar junction

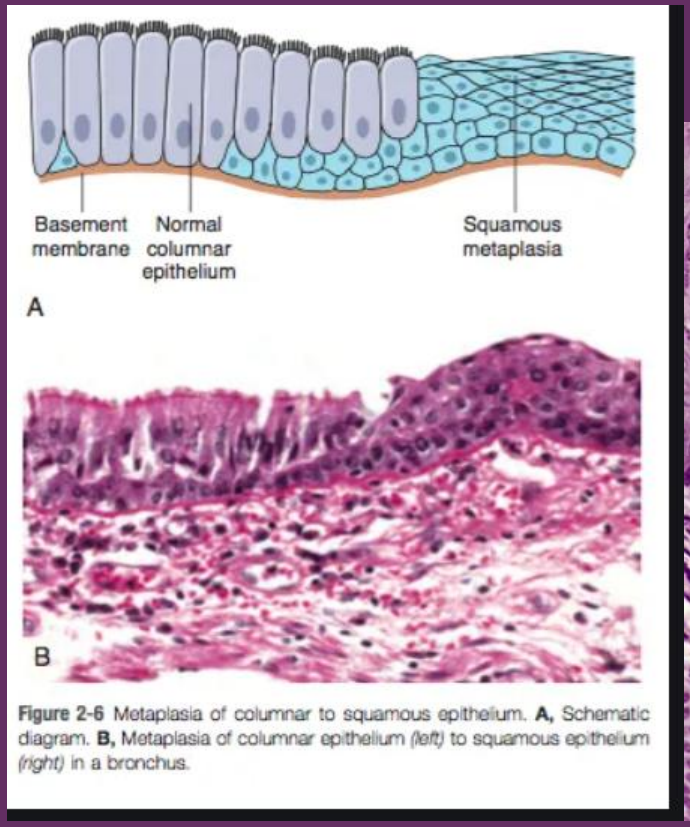
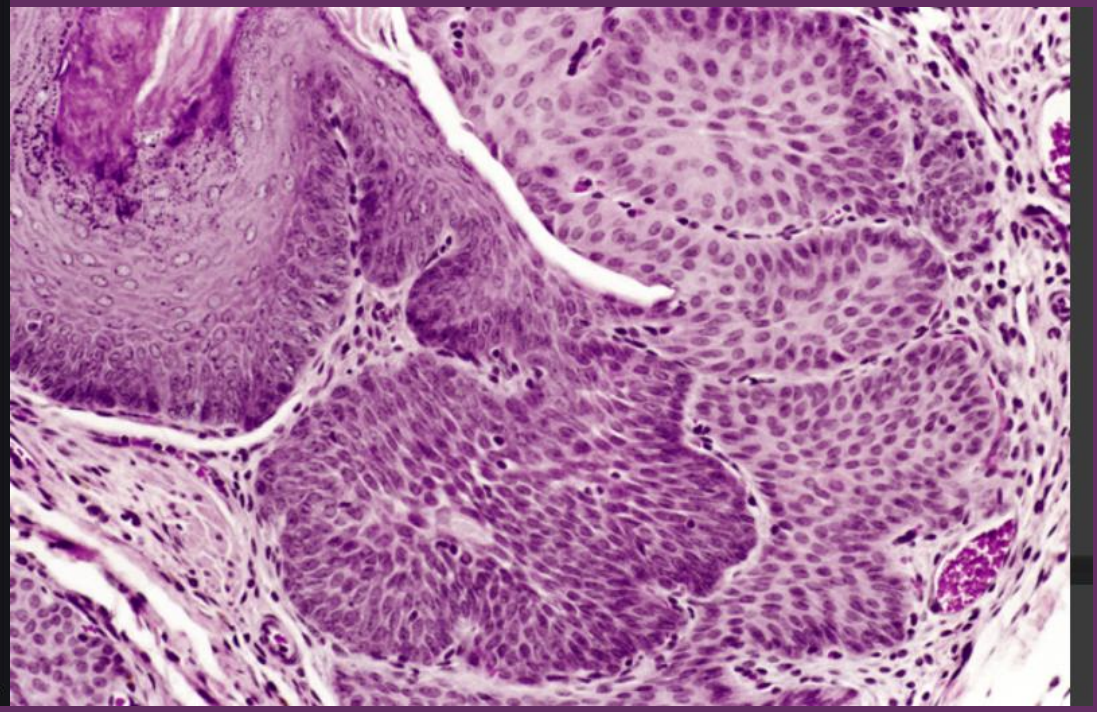


Figure 2-6 Metaplasia of columnar to squamous epithelium. **A,** Schematic diagram. **B,** Metaplasia of columnar epithelium *(left)* to squamous epithelium *(right)* in a bronchus.

Squamous metaplasia- bronchus



Squamous metaplasia in bladder

COLUMNAR METAPLASIA

- *Intestinal metaplasia* in healed chronic gastric ulcer
- Columnar metaplasia in ***Barrett's oesophagus***, in which there is change of normal squamous epithelium to columnar epithelium.
- Conversion of pseudostratified ciliated columnar epithelium in *chronic bronchitis and bronchiectasis* to columnar type.

MESENCYMAL METAPLASIA

- **Osseous metaplasia-**
- Formation of bone in fibrous tissue, cartilage and myxoid tissue.

i) In arterial wall in old age -Mönckeberg's medial calcific sclerosis

ii) In soft tissues - myositis ossificans

iii) In cartilage of larynx and bronchi in elderly people

iv) In scar of chronic inflammation of prolonged duration

- **2. Cartilaginous metaplasia-**

In healing of fractures, cartilaginous metaplasia →where there is undue mobility

PATHOGENESIS

- Metaplasia does not result from a change in the phenotype of an already differentiated cell type.

- Result of a **reprogramming of stem cells** that are known to exist in normal tissues, or of undifferentiated mesenchymal cells present in connective tissue.

Dysplasia: Disordered cell growth.

- Most common cause is Chronic irritation & inflammation
- cervix, oesophagus are best examples.
- May progress to Carcinoma in situ and then to invasive carcinoma.

DYSPLASIA

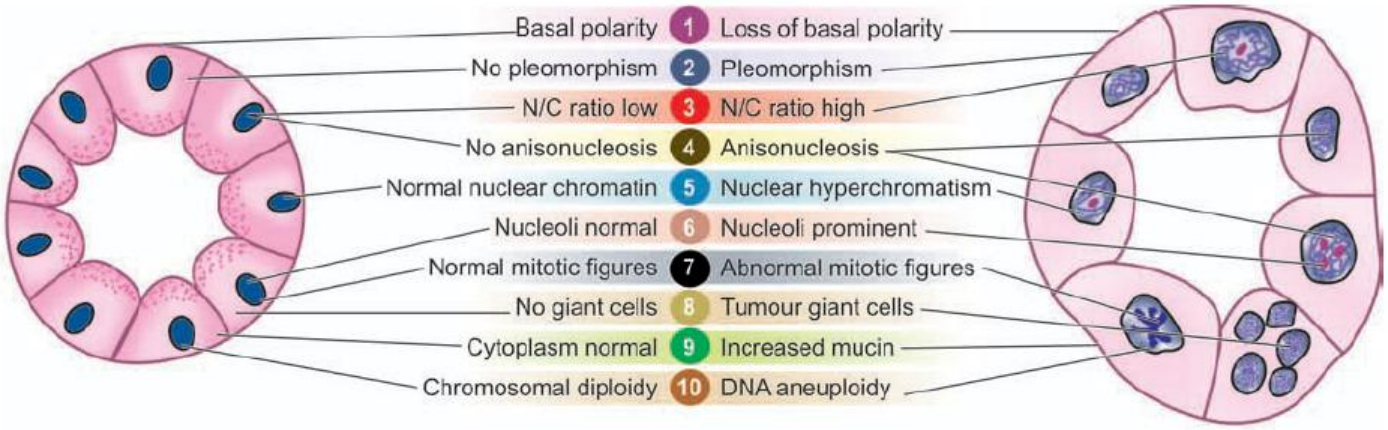
- ‘Disordered cellular development’,
- Seen in epithelial cells & is characterized by cellular proliferation and cytologic changes.

1. Increased ***number of layers*** of epithelial cells
2. Disorderly arrangement of cells from basal layer to the surface layer.
3. ***Loss of basal polarity***
4. ***Cellular and nuclear pleomorphism***
5. Increased ***nucleocytoplasmic ratio***
6. Nuclear ***hyperchromatism***
7. Increased mitotic activity.

- **Dysplasia**
- **Dysplasia occur most often in epithelial cells**

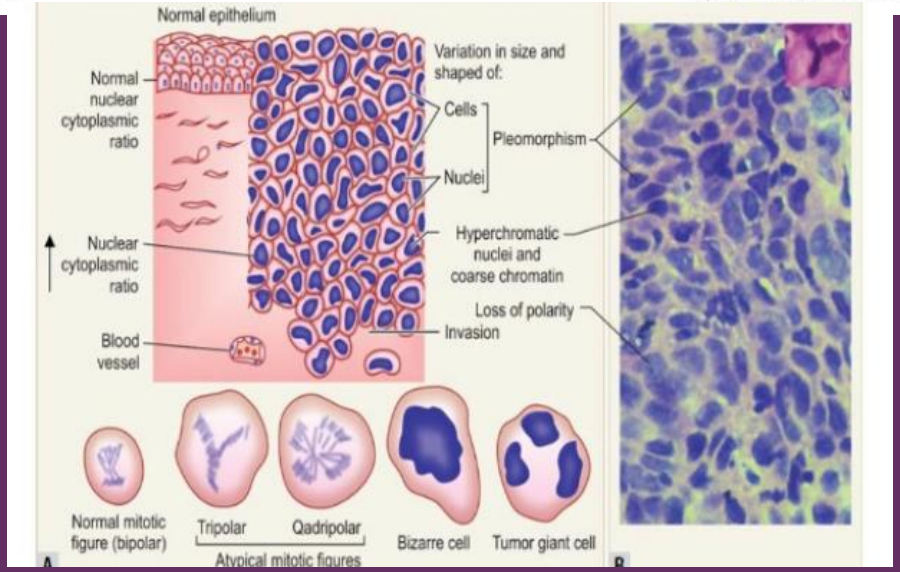
Features of Dysplasia

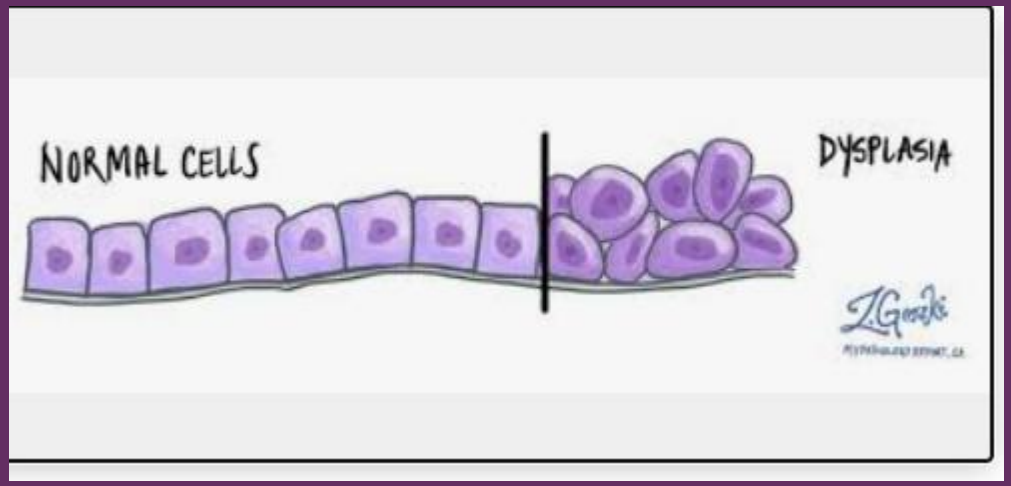
- Increase number of layers of epithelial cells
- Disorderly arrangement of cells from basal layer to the surface layer
- Loss of basal polarity i.e. nuclei lying away from basement membrane
- Cellular & nuclear peomorphism
- Increased necleocytoplasmic ratio
- Increase mitotic activity but no atypical mitotic figures

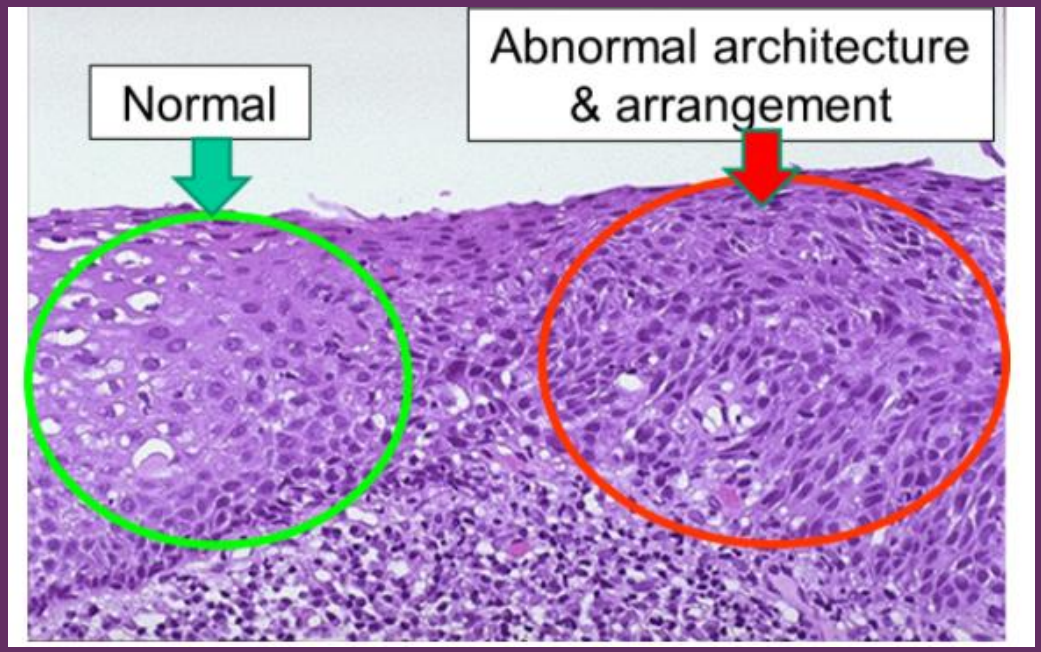


A. NORMAL MORPHOLOGY

B. CYTOMORPHOLOGY IN CANCER



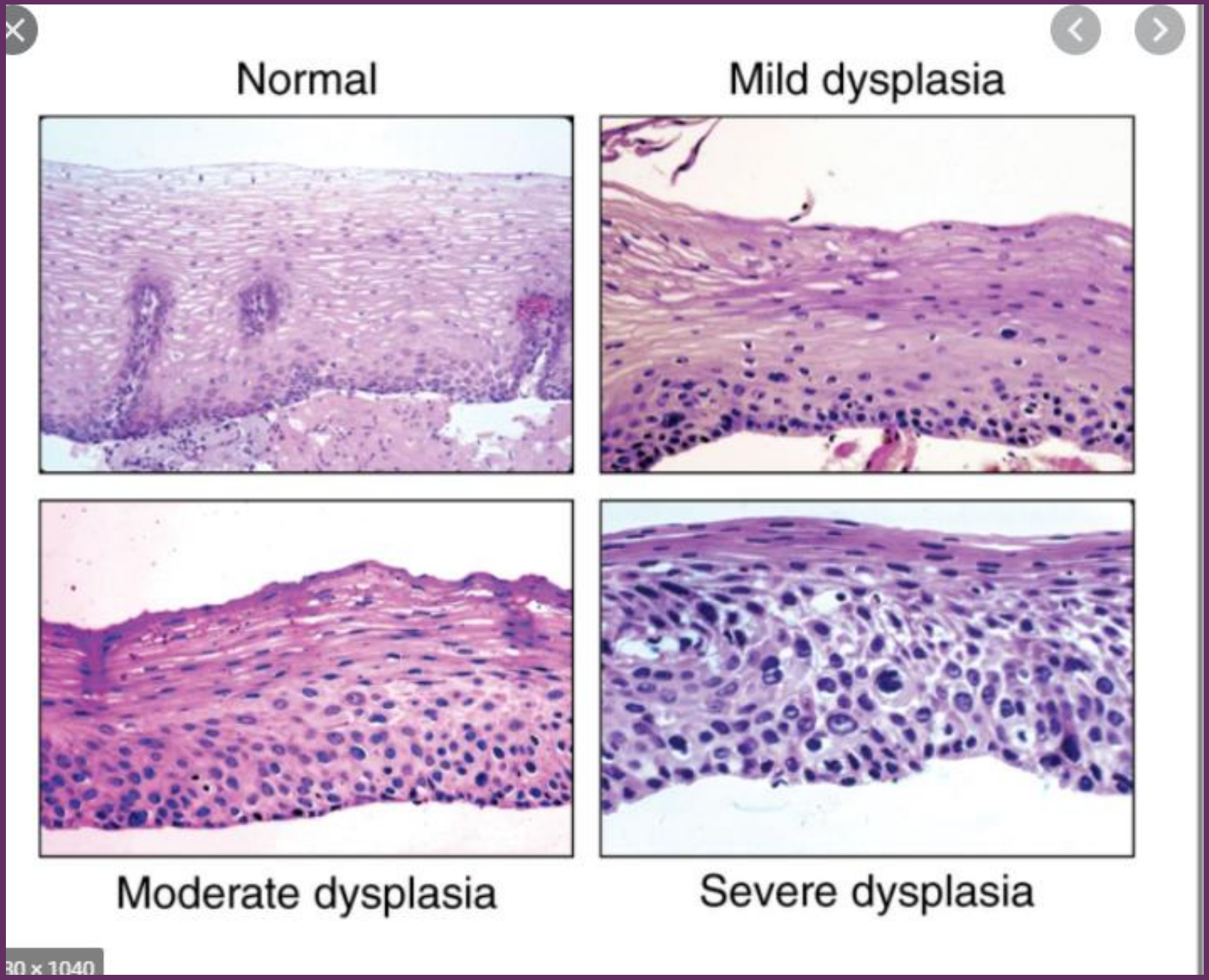


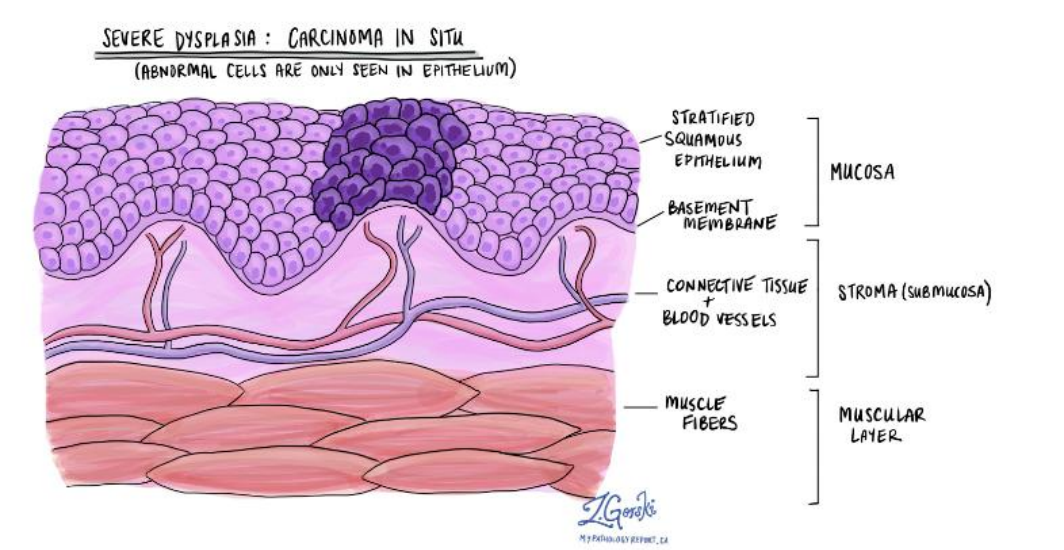


NORMAL VS DYSPLASIA

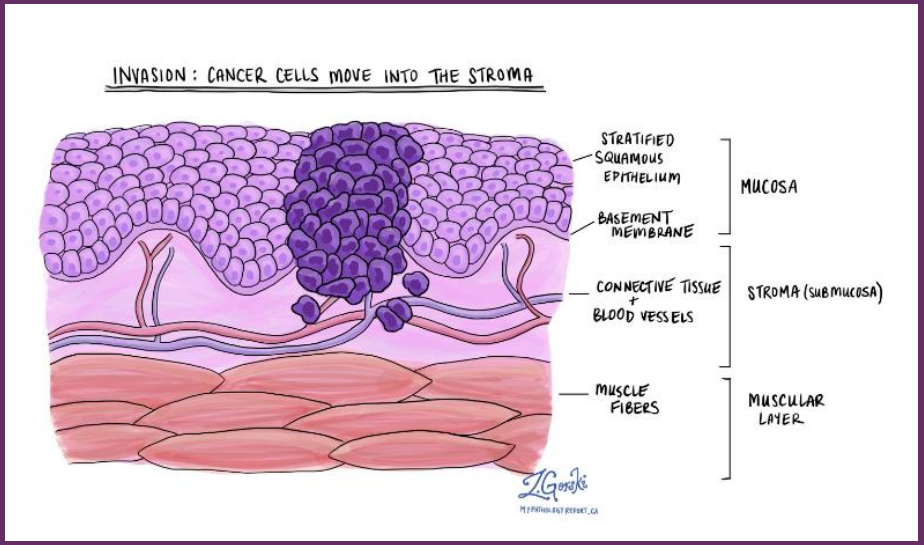
TABLE 3.7: Differences between Metaplasia and Dysplasia.

Feature	Metaplasia	Dysplasia
i) Definition	Change of one type of epithelial or mesenchymal cell to another type of adult epithelial or mesenchymal cell	Disordered cellular development, may be accompanied with hyperplasia or metaplasia
ii) Types	Epithelial (squamous, columnar) and mesenchymal (osseous, cartilaginous)	Epithelial only
iii) Tissues affected	Most commonly affects bronchial mucosa, uterine endocervix; others mesenchymal tissues (cartilage, arteries)	Uterine cervix, bronchial mucosa
iv) Cellular changes	Mature cellular development	Disordered cellular development (pleomorphism, nuclear hyperchromasia, mitosis, loss of polarity)
v) Natural history	Reversible on withdrawal of stimulus	May regress on removal of inciting stimulus, or may progress to higher grades of dysplasia or carcinoma *in situ*


Normal
Mild dysplasia
Moderate dysplasia
Severe dysplasia

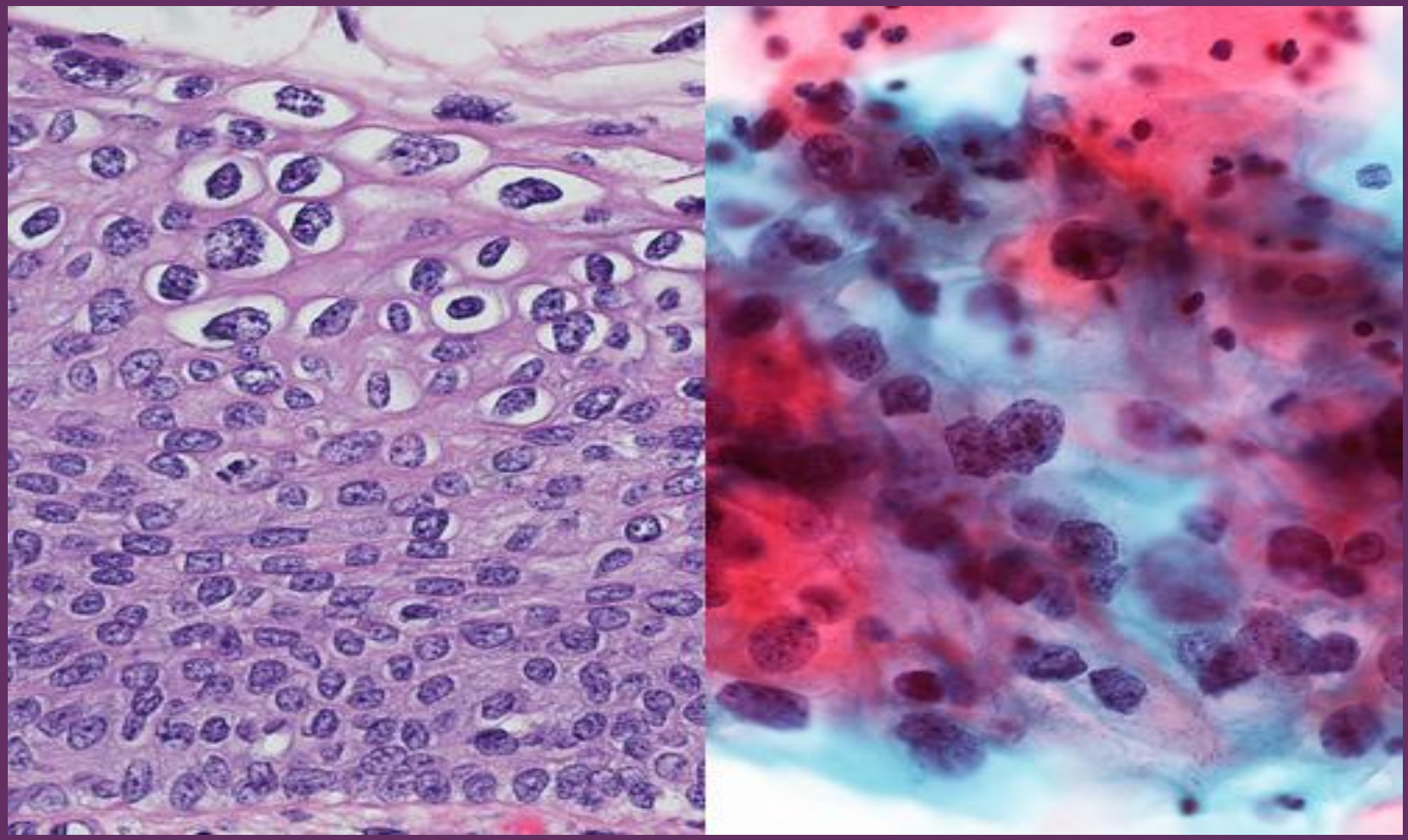


Severe dysplasia/ carcinoma in situ- **basement membrane intact**



Carcinoma- **basement membrane disrupted**

Dysplasia



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CELLULAR ADAPTION

NORMAL

ATROPHY
(decrease in cell size)

HYPERPLASIA
(increased cell number)

HYPERTROPHY
(increase in cell size)

METAPLASIA
(conversion of one type of cell to another)

DYSPLASIA
(disorderly growth)


Thank
you!