Cellular Adaptations

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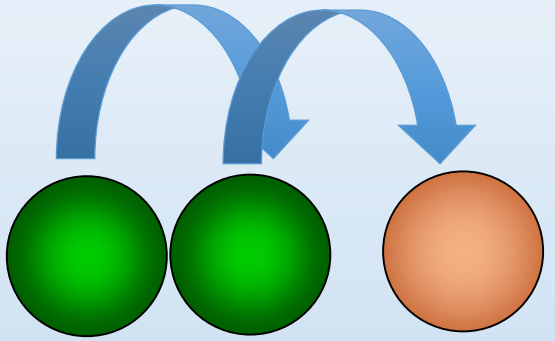
Cellular Adaptations

- Hyperplasia
- Hypertrophy
- Atrophy
- Metaplasia

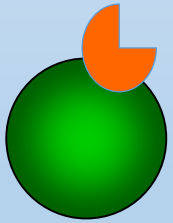
How are these changes brought about?

- Numerous molecular mechanisms



- Direct stimulation of cells by factors produced by responding cells or by other cells in the environment

- Activation of various cell surface receptors and downstream signaling pathways.



How are these changes brought about?

- Induction of new protein synthesis by target cells, in response of muscle cells to increased physical demand
- Induction of cell proliferation
- Changing of type of proteins the cell produces as in chronic inflammation

Hyperplasia

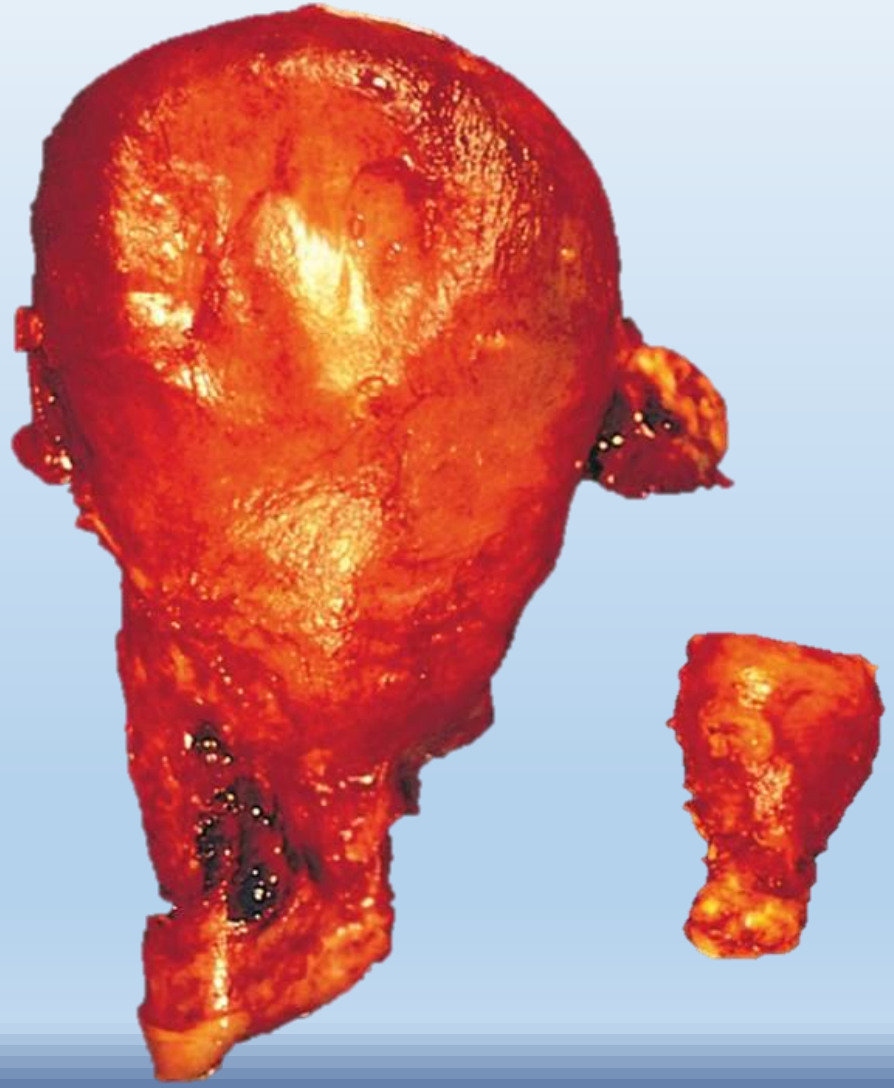
- Increase in the number of cells in an organ or tissue
- X → 4X
- Resulting in increased volume of the organ or tissue
- XL → 4XL
- Hyperplasia takes place if the cellular population is capable of synthesizing DNA

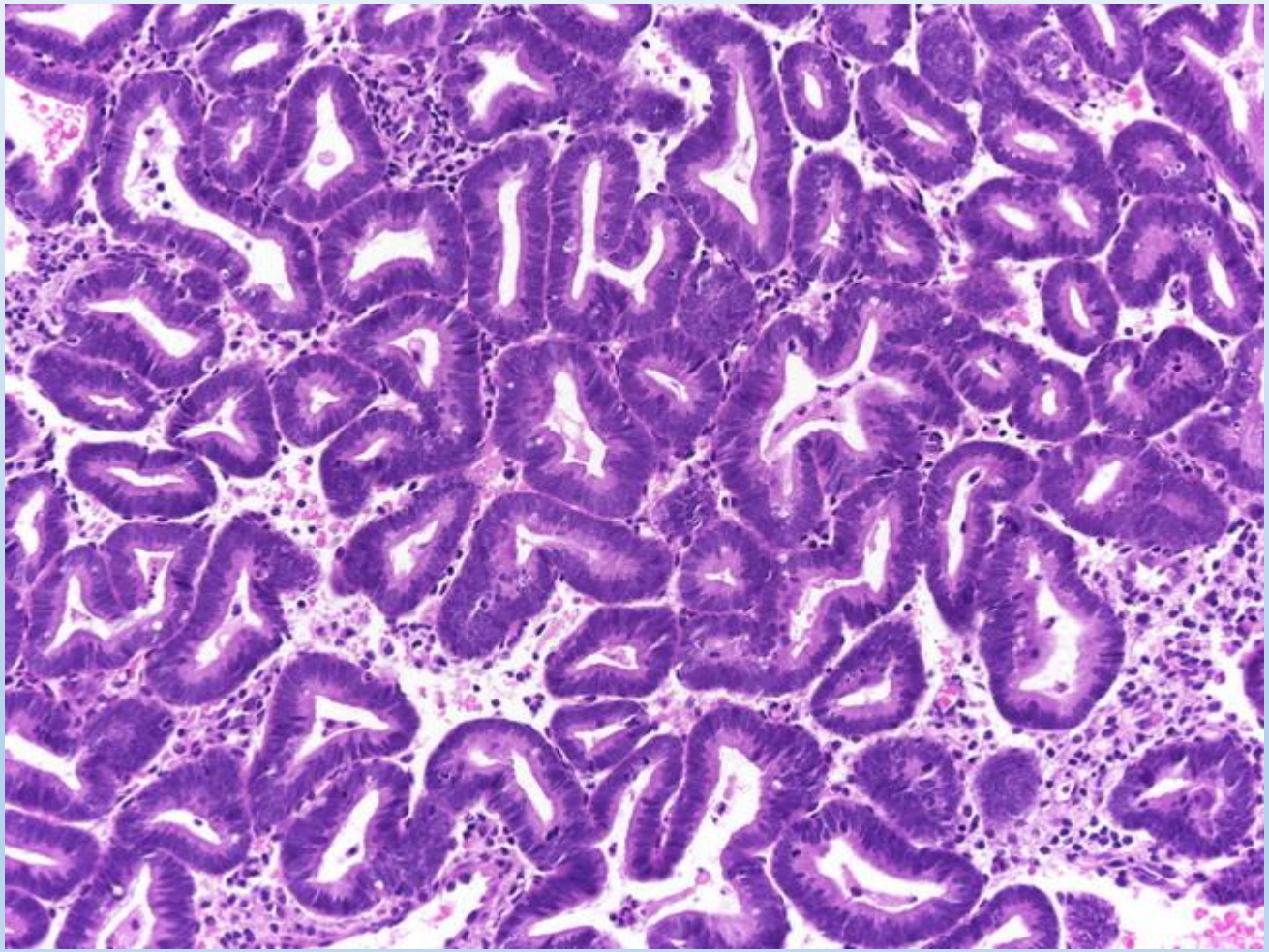
- Hyperplasia → physiological
  → pathological

Mechanisms of Hyperplasia.

- Caused by increased local production of growth factors
- Hormonal hyperplasia → hormones → growth factors
- increased levels of growth factor receptors on the responding cells,
- Increase in tissue mass by proliferation of remaining cells but also by the development of new cells from *stem cells*.

Hyperplasia of the uterus larger than normal due to increase number of cells





Hyperplasia

- Hyperplasia and hypertrophy are 2 distinct processes,
- Frequently occur together
- May be triggered by the same stimulus
- Eg. Hormone-induced growth in the uterus involves
- increased numbers of smooth muscle and epithelial cells and the enlargement of these cells.

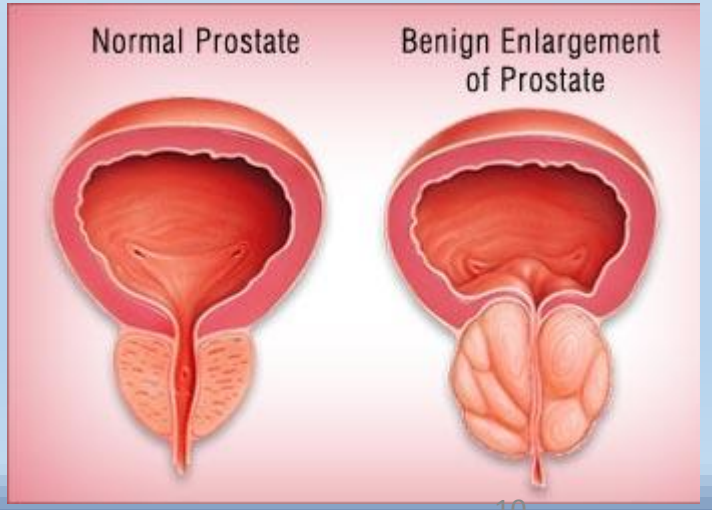
Physiologic Hyperplasia

- **Hormonal hyperplasia,**
- Increases functional capacity of a tissue when needed
- E.g. proliferation of glandular epithelium of female breast at puberty and during pregnancy
- physiologic hyperplasia that occurs in the pregnant uterus.

- **Compensatory hyperplasia**
- Increases tissue mass after damage or partial resection

Pathologic Hyperplasia

- Caused by excessive hormonal stimulation or
- Growth factors acting on target cells.
- Eg. Benign prostatic hyperplasia with androgens.
- Endometrial hyperplasia with estrogens
- Though these forms of hyperplasia are abnormal, it regresses if the hormonal stimulation is eliminated.



Pathological Hyperplasia

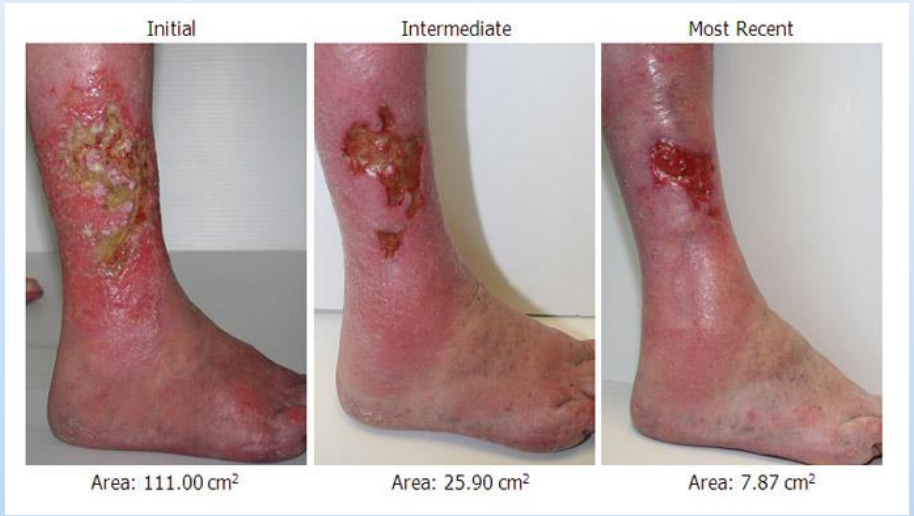
- Response to normal regulatory control distinguishes benign pathologic hyperplasias from cancer.

- *Pathologic hyperplasia, is a fertile soil in which a cancerous proliferation may eventually arise.*

- Patients with hyperplasia of the endometrium are at higher risk for developing endometrial cancer

Pathologic Hyperplasia

- Hyperplasia is also important in connective tissue cells in wound healing
- Proliferating fibroblasts
- Blood vessels aid in repair



- Hyperplasia associated with certain *viral infections*
- Papilloma viruses -

Hypertrophy

- Hypertrophy involves cell enlargement **without** cell division.
- Increase in the size of cells, resulting in an increase in the size of the organ.
- The hypertrophied organ has **no new cells, just larger cells.**

X cells → X cells

1 mg → X Kg

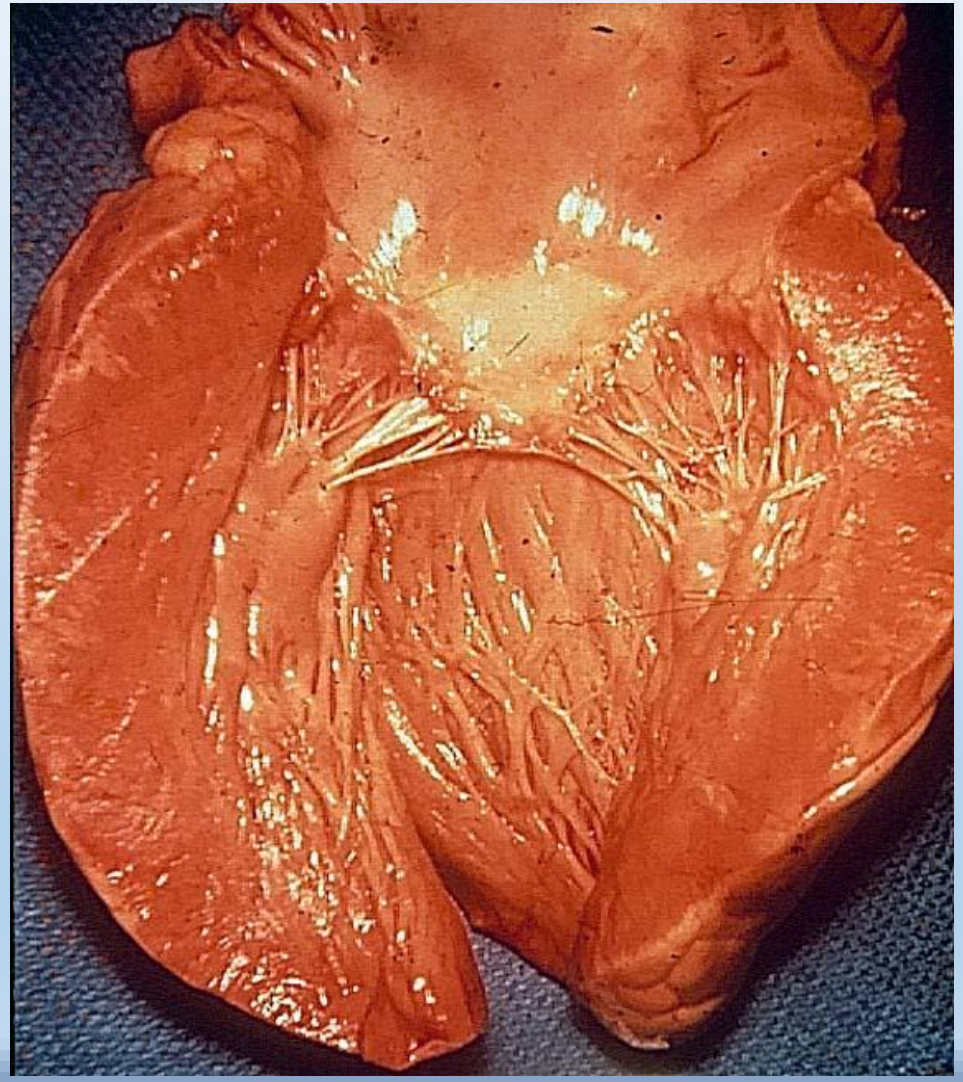
Hypertrophy

- The increased **size** of the cells is due **not to cellular swelling** but to the synthesis of more structural components.

- Cells able to divide respond to stress by undergoing both hyperplasia and hypertrophy

- Cells that cannot divide undergo hypertrophy (e.g., myocardial fibers)

Hypertrophic cardiac muscle



Hypertrophic skeletal muscle

Hypertrophy

- Physiological
- Increased functional demand or hormonal stimulation.
- Striated muscle cells
- Heart
- skeletal muscles
- Commonest stimulus is increased workload.

- Pathological
- Chronic hemodynamic overload
- Systemic hypertension
- Faulty heart valves

Mechanisms of Hypertrophy

- Cardiac muscle hypertrophy involves many signal transduction pathways
- Induction of a number of genes
- Induction of transcription factors
- growth factors (TGF-β, insulin-like growth factor-1 [IGF-1], fibroblast growth factor); and
- vasoactive agents (α-adrenergic agonists, endothelin-1, and angiotensin II).

Atrophy

- Shrinkage in the size of the cell by loss of cell substance ➔ atrophy.
- An adaptive response ➔ culminate in cell death.
- When a sufficient number of cells are involved, the entire tissue or organ diminishes in size, or becomes atrophic.

Atrophy

- Atrophy → physiologic
  pathologic
- Physiologic atrophy - during early development.
- Embryonic structures, such as the notochord and thyroglossal duct, undergo atrophy during fetal development.
- Uterus shortly after parturition ➔ physiologic atrophy.

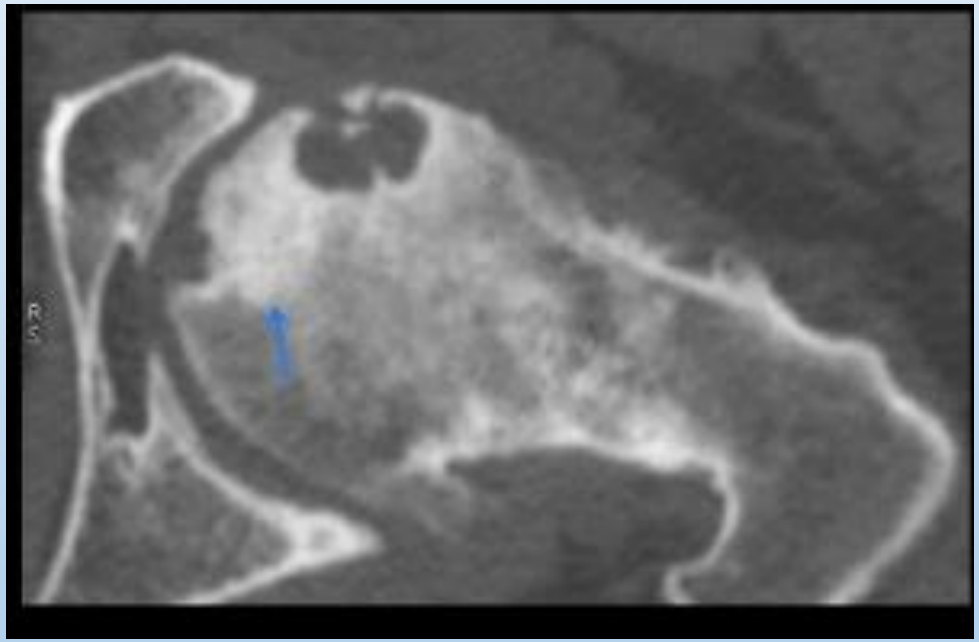
Common causes of atrophy - Pathological

- Inadequate nutrition
- Loss of endocrine stimulation
- Aging (senile atrophy)
- Pressure atrophy

Disuse atrophy

Denervation atrophy

Loss of blood supply to femoral head



malnutrition

Atrophy

- Although atrophic cells may have diminished function, they are not dead.
- However, atrophy may progress to the point at which cells are injured and die.
- In ischemic tissues, if blood supply is inadequate to maintain the life of shrunken cells, injury and cell death may occur.
- For eg. apoptosis contributes to the regression of endocrine organs after hormone withdrawal.

Mechanisms of Atrophy.

- Increased protein degradation

- Increases in the number of *autophagic vacuoles*.

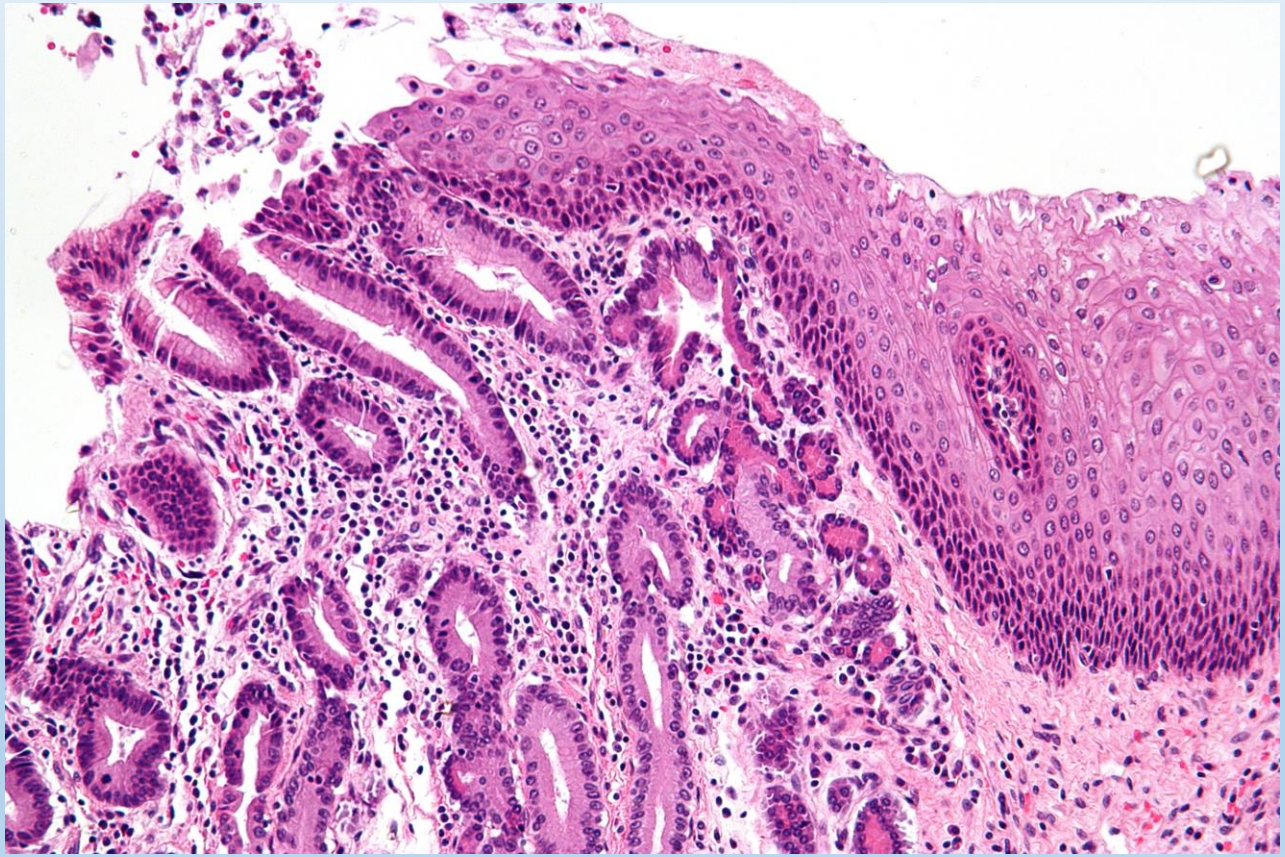
- *lipofuscin granules*, when present in sufficient amounts, they impart a brown discoloration to the tissue *(brown atrophy)*.

METAPLASIA

- Reversible change in which one adult cell type (epithelial or mesenchymal) is replaced by another adult cell type.

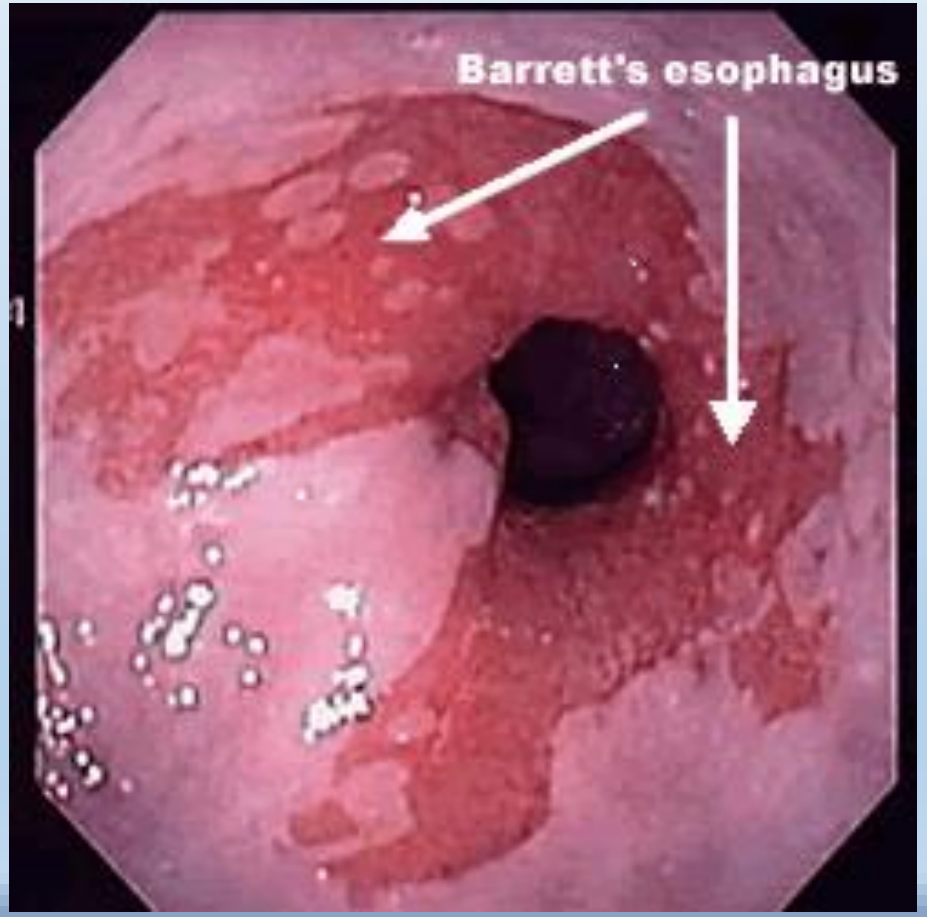
- An adaptive substitution of cells that are sensitive to stress by cell types better able to withstand the adverse environment.

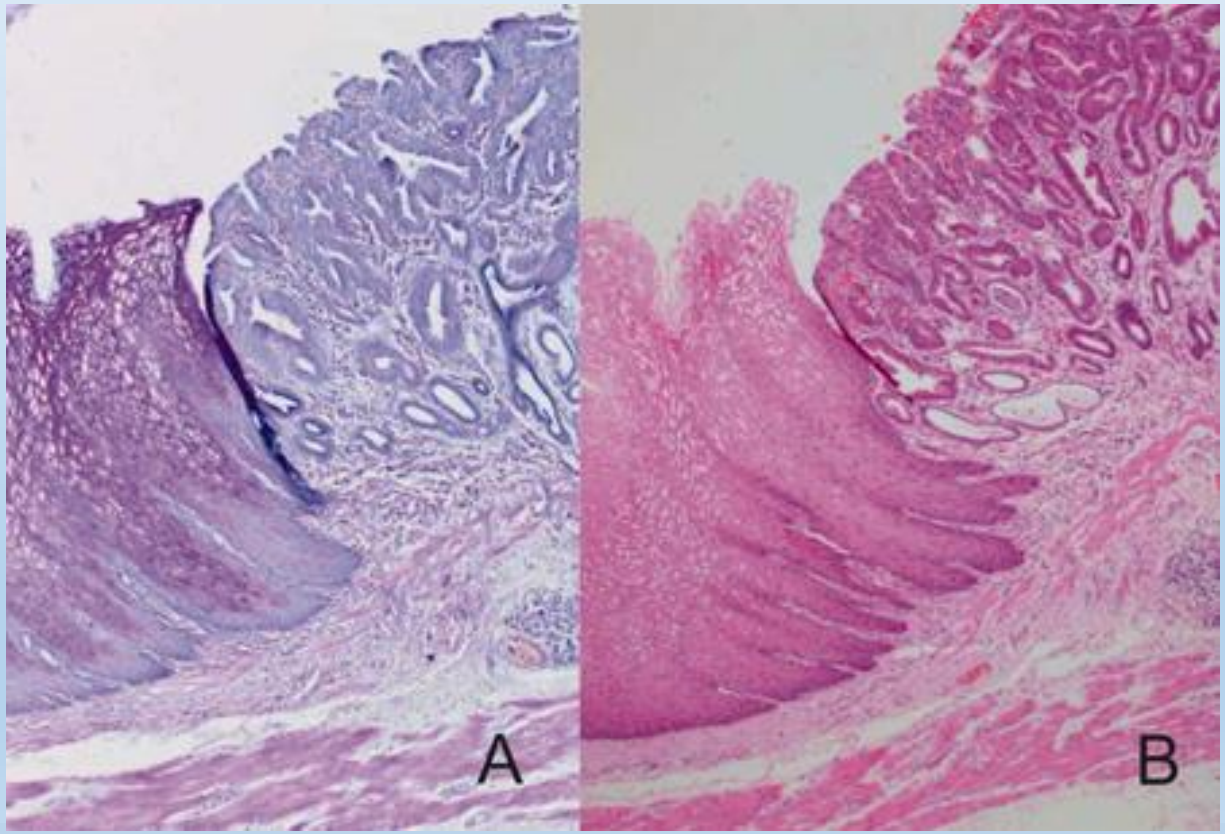
Eg. *columnar* ➔ *squamous* as occurs in the respiratory tract in chronic irritation in habitual cigarette smokers



Metaplasia

- *From squamous to columnar type* in *Barrett esophagus*



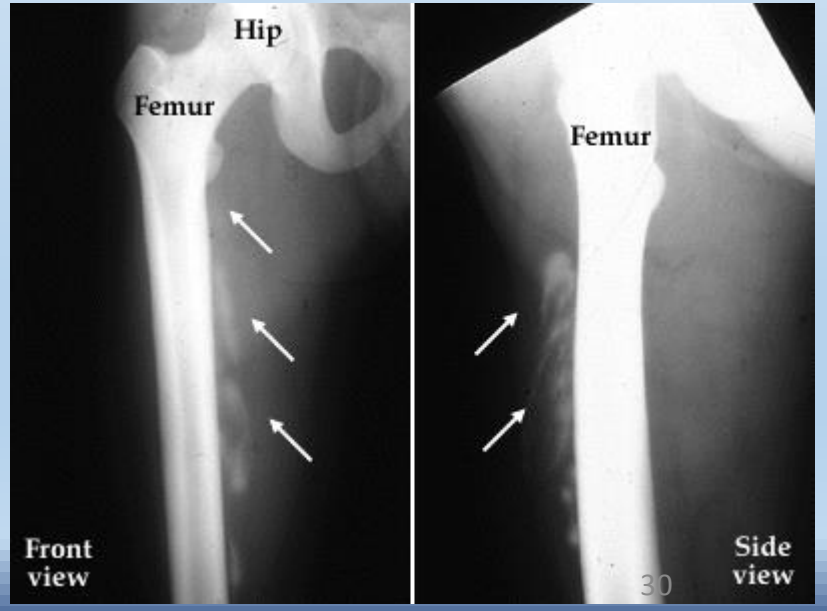


Connective tissue metaplasia

- Formation of cartilage, bone, or adipose tissue (mesenchymal tissues) in tissues that normally do not contain these elements.
- For example, bone formation in muscle, designated

myositis ossificans, occasionally occurs after bone fracture.

This type of metaplasia is less clearly seen as an adaptive response.

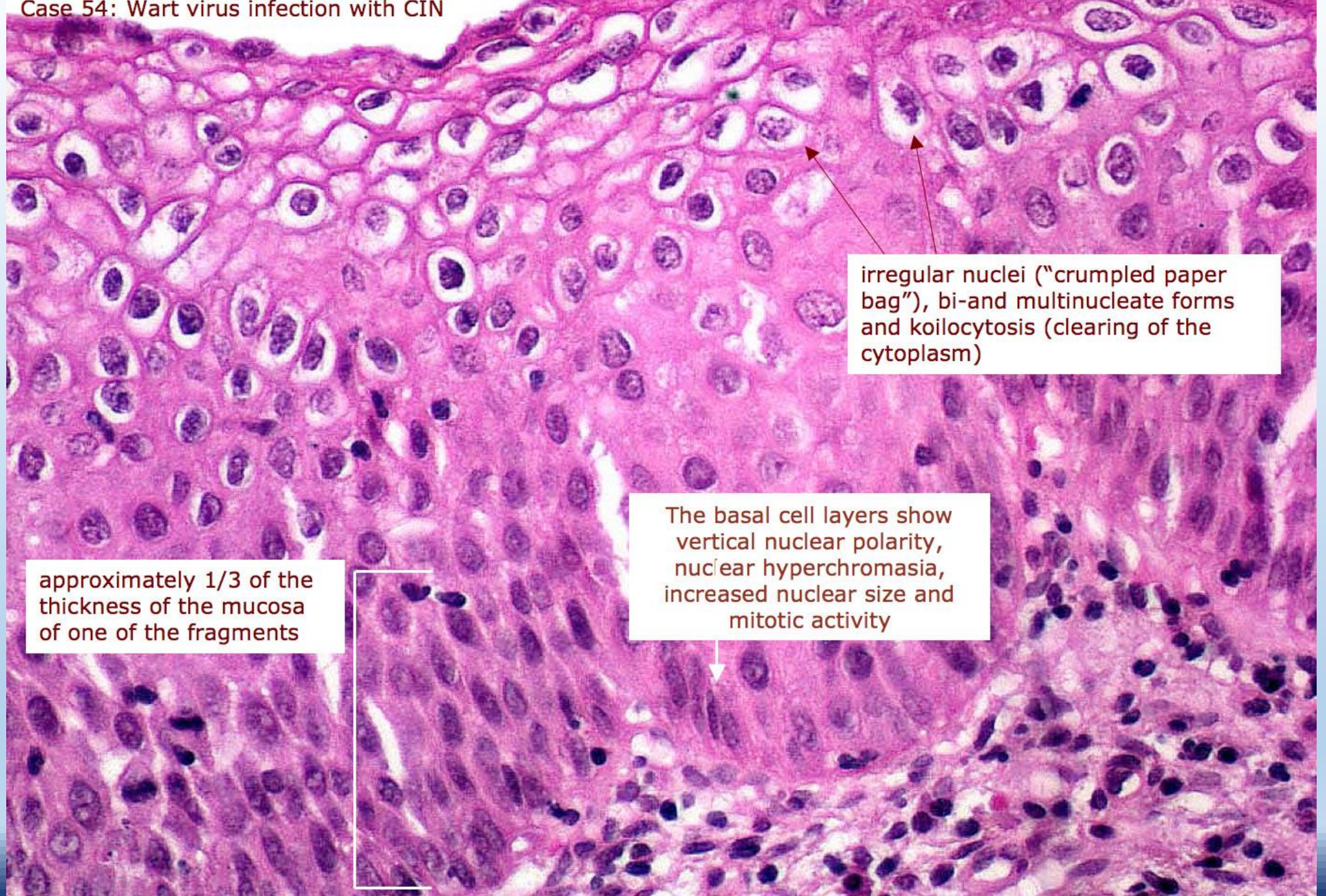


Mechanisms of Metaplasia.

- Result of a reprogramming of stem cells that known to exist in normal tissues
- Or of undifferentiated mesenchymal cells present in connective tissue.
- In metaplastic change, these precursor cells differentiate along a new pathway
- These changes are brought about by
- Cytokines
- Growth factors
- Extracellular matrix components in the cell's environment.

Dysplasia

- Disordered growth.
- Encountered principally in epithelia,
- Loss in the uniformity of the individual cells
- Loss in their architectural orientation.
- Dysplastic cells exhibit pleomorphism
- Contain hyperchromatic nuclei
- Nuclei are abnormally large for the size of the cell.
- Mitotic figures are more abundant than usual,


Case 54: Wart virus infection with CIN
irregular nuclei ("crumpled paper bag"), bi-and multinucleate forms and koilocytosis (clearing of the cytoplasm)
The basal cell layers show vertical nuclear polarity, nuclear hyperchromasia, increased nuclear size and mitotic activity
approximately 1/3 of the thickness of the mucosa of one of the fragments

Dysplasia

- Mitoses appear in abnormal locations within the epithelium.
- The architecture of the tissue is disorderly.
- Progressive maturation of cells in the basal layer to flattened squames to the surface is lost
- When dysplastic changes involve the entire thickness of the epithelium, but the lesion remains confined to the normal tissue, it is considered a preinvasive neoplasm and is referred to as **carcinoma in situ.**

Dysplasia

- Often found adjacent to foci of invasive carcinoma,
- In long-term cigarette smokers and Barrett esophagus, severe epithelial dysplasia frequently antedates the appearance of cancer.
- However, dysplasia **does not necessarily progress to cancer.**
- Mild to moderate changes that do not involve the entire thickness of epithelium **may be reversible, and with removal of the inciting causes, the epithelium may revert to normal**.