MJF COLLEGE OF VETERINARY AND ANIMAL SCIENCE, CHOMU, JAIPUR

DEPARTMENT OF VETERINARY PATHOLOGY

Cellular Adaptations of Growth and Differentiation

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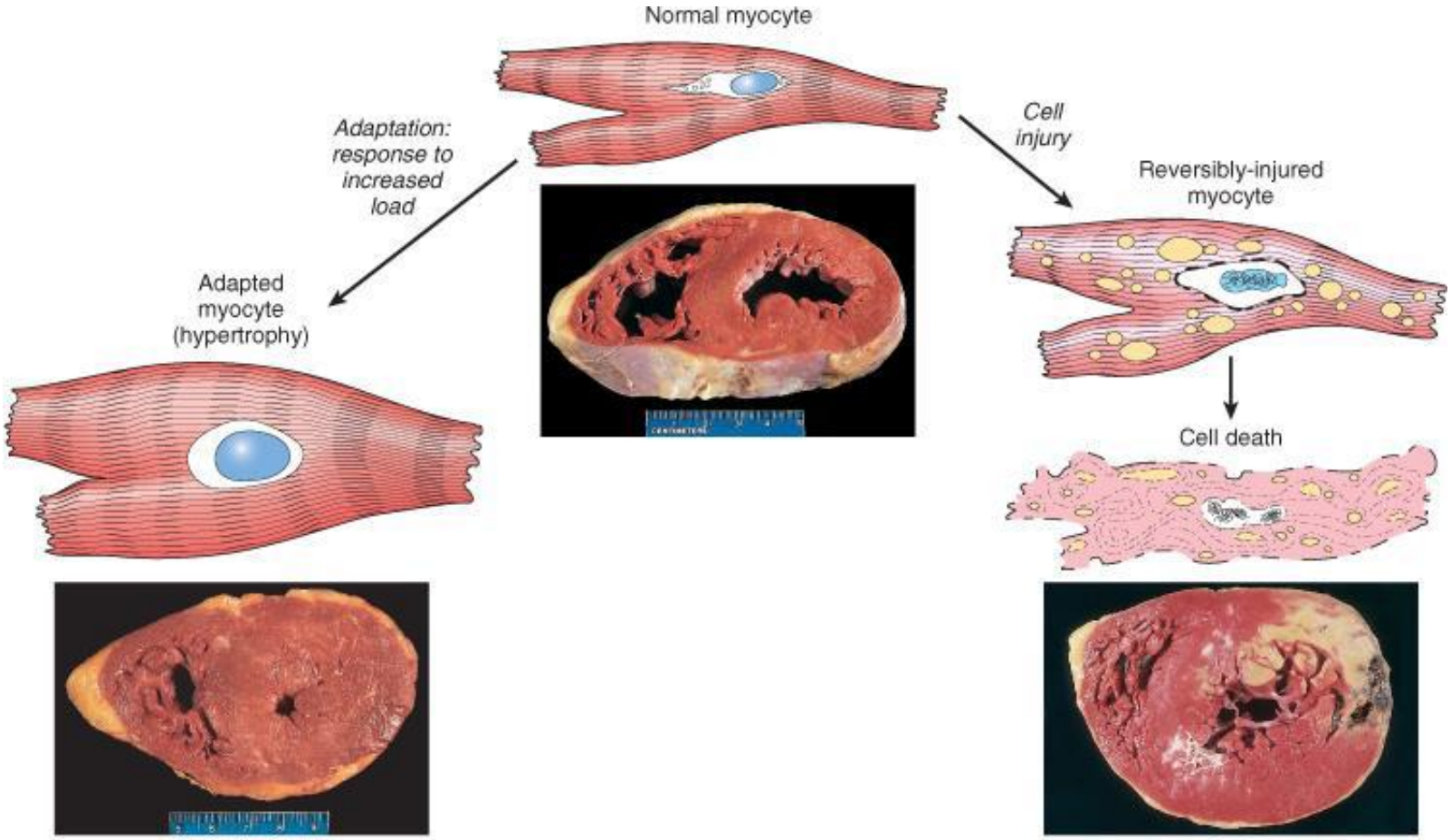
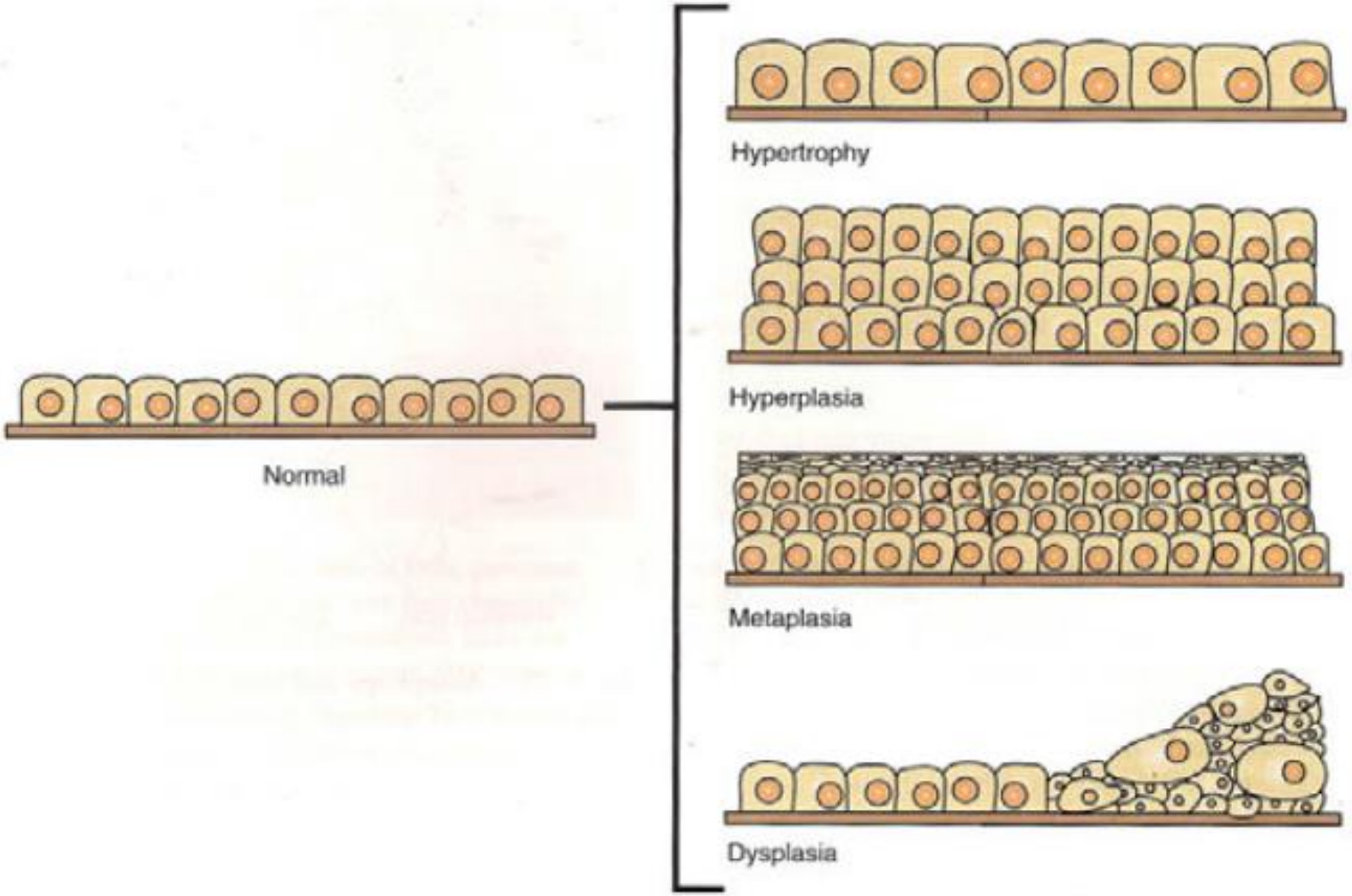


Cellular Adaptations

- **Physiological adaptations**
- Responses of cells to normal stimulation by hormones or endogenous chemical substances
- Enlargement of the mammary gland (breast in humans) and induction of lactation by pregnancy
- **Pathological adaptations**
- share the same underlying mechanisms
- Allow the cells to change their internal environment, and thus escape injury.


Normal
Hypertrophy
Hyperplasia
Metaplasia
Dysplasia

CELLULAR ADAPTATIONS

- Suffix _trophy – related to cell size
  - Atrophy- deceased in size
  - Hypertrophy- increased in size
- Suffix _plasia (more) - related to cell number
  - Hyperplasia- increased no. of cells
  - Metaplasia – Change in cells

ATROPHY

- Definition: *Shrinkage in the size of the cell by the loss of cell substance is known as atrophy.*
- Sufficient number of cells involved - the entire tissue or organ diminishes in size
- Atrophic cells may have diminished function, they are not dead.

Etiology of Atrophy

- due to:
  - Physiological – Thymus
  - Decrease in work load (disuse atrophy)
  - Loss of innervation
  - Loss of hormonal stimulation
  - Reduced blood supply / hypoxia
  - Inadequate nutrition
  - Compression
  - Persistent cell injury
  - Aging- testis and ovary

- atrophic cells have a reduced functional capacity
- in many cases return to 'normal' when causative stimulus is removed

Mechanisms & Biochemistry of Atrophy

- catabolic > anabolic processes;

  eg, muscle atrophy: ↓ myofilaments, ↓ mitoch., ↓ ER, ↓ metabolic activity

- cell shrinks in volume & decreases functions → ↓ energy requirements

- autophagic vacuoles increase and some cells may die

Brown atrophy

Gross Appearance of Atrophy

- tissue/organ is decreased in size

Microscopic Appearance of Atrophy

- cells are smaller &/or fewer than normal

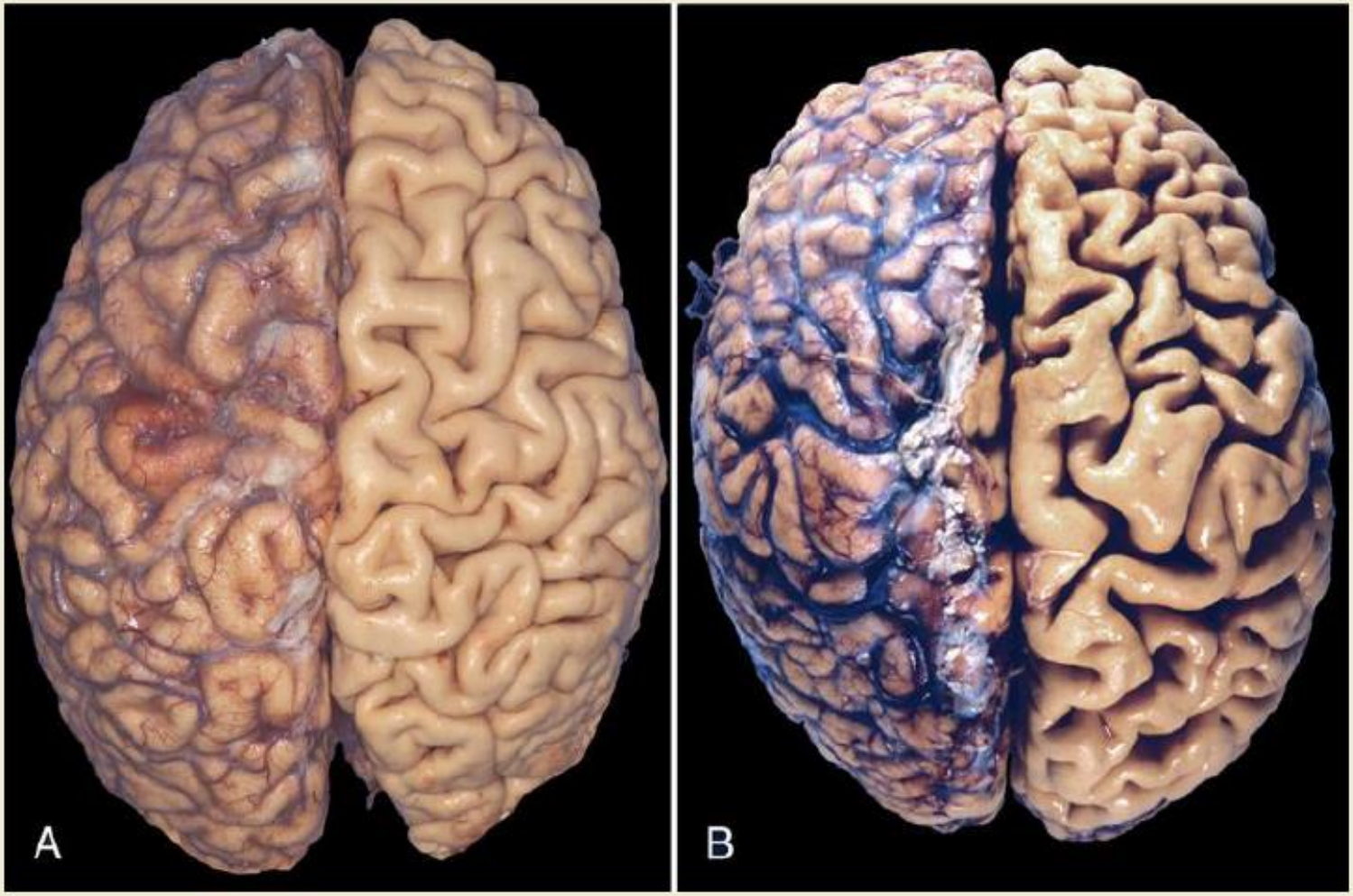
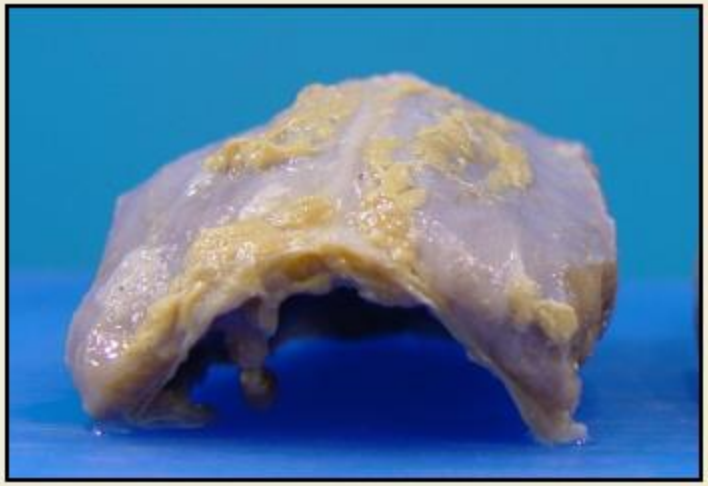
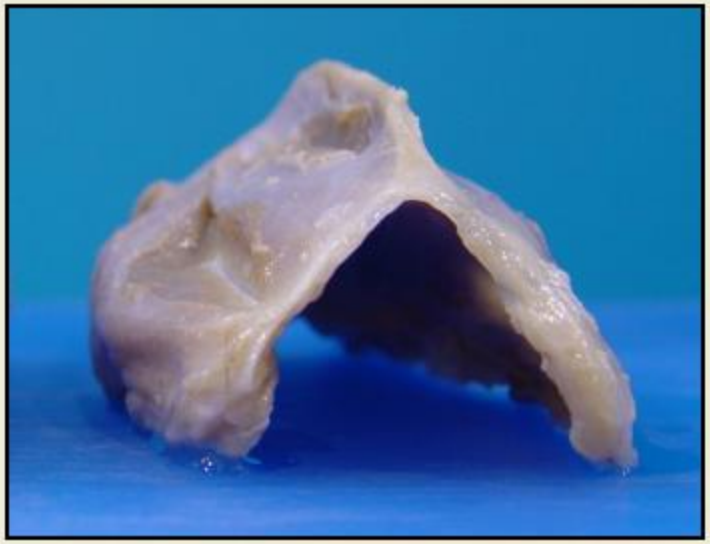
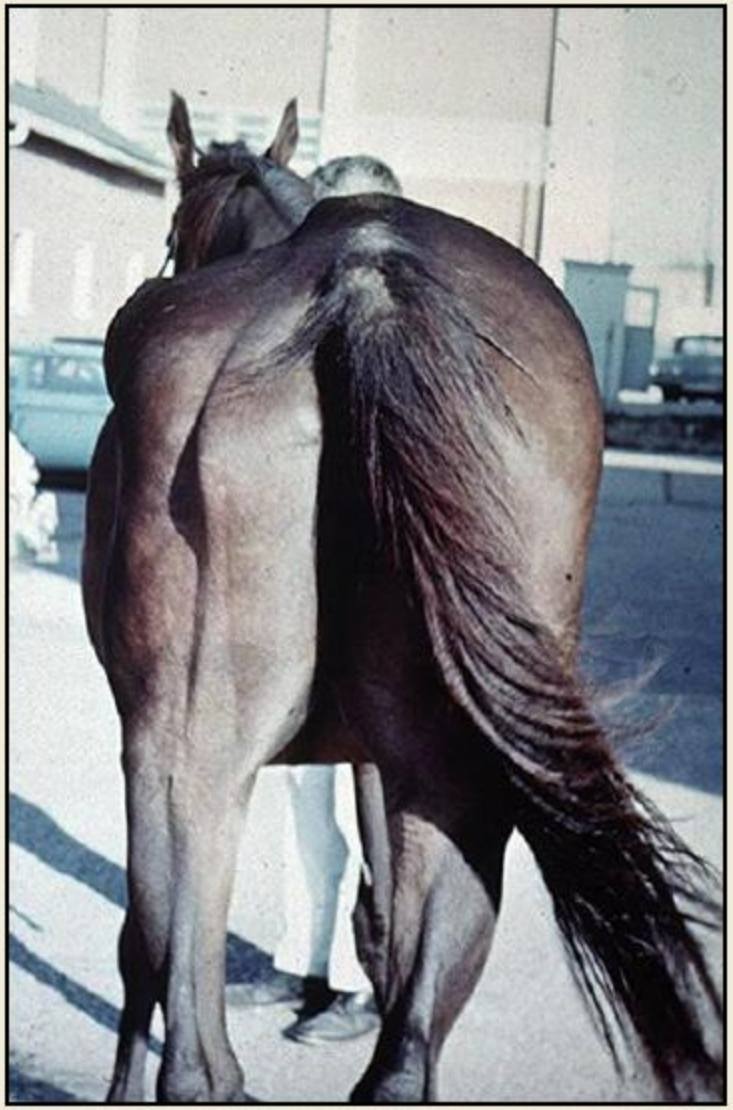


Figure 1-5 (Robbins) Atrophy. A, Normal brain of a young adult. B, Atrophy of the brain in an 82-year-old male with atherosclerotic cerebrovascular disease, resulting in reduced blood supply. Note that loss of brain substance narrows the gyri and widens the sulci. The meninges have been stripped from the right half of each specimen to reveal the surface of the brain.

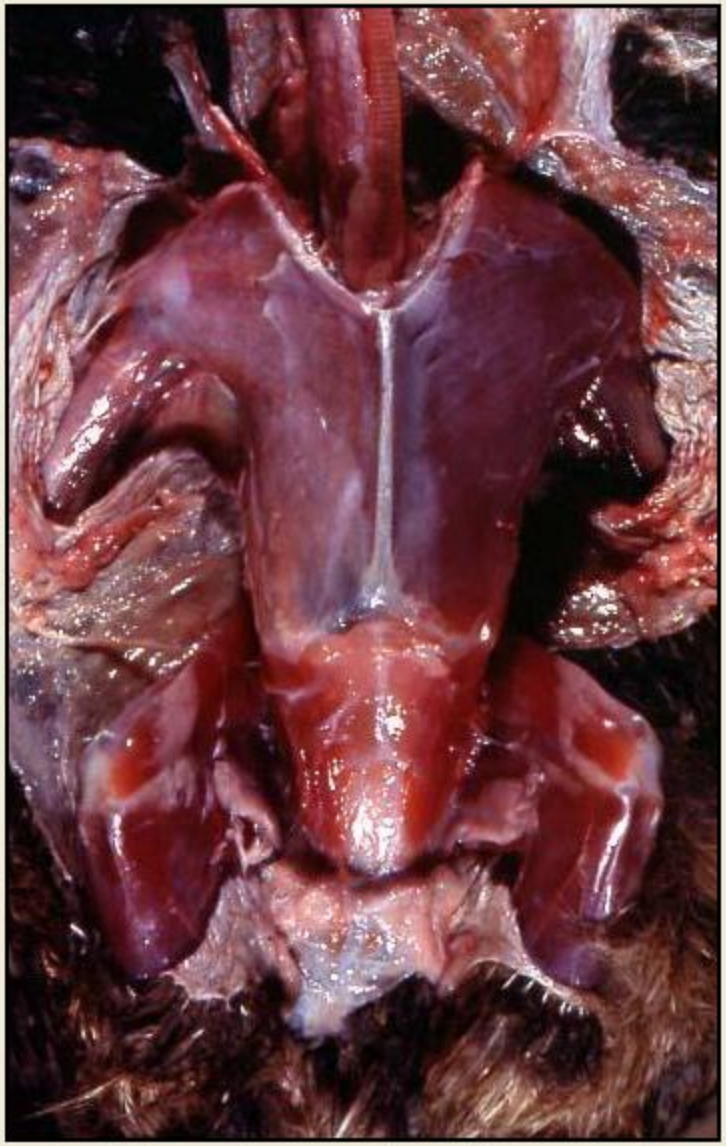




Normal pectoral muscle bird (top) compared to marked bilateral pectoral muscle atrophy (bottom) due to malnutrition / starvation, ie muscle proteins broken down and used for basic energy requirements



Horse with atrophy of the muscles of the left upper hindlimb; could be due to nerve damage or disuse secondary to a local injury



Great horned owl, unilateral atrophy of pectoral muscles.

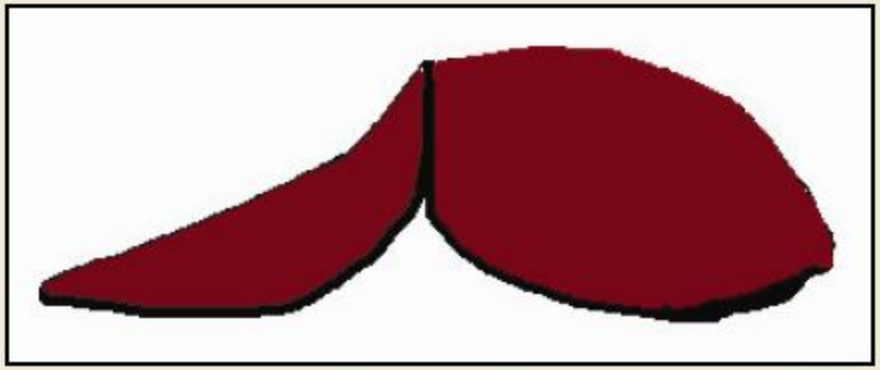
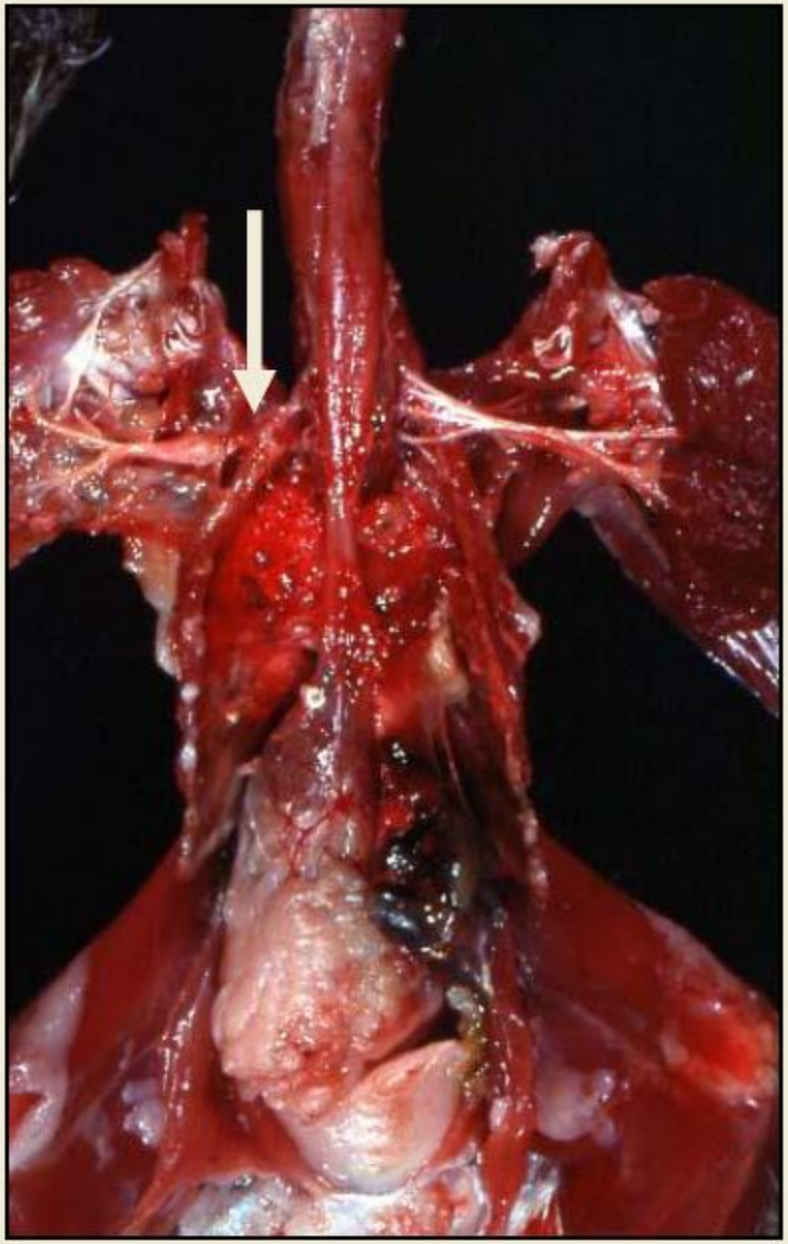
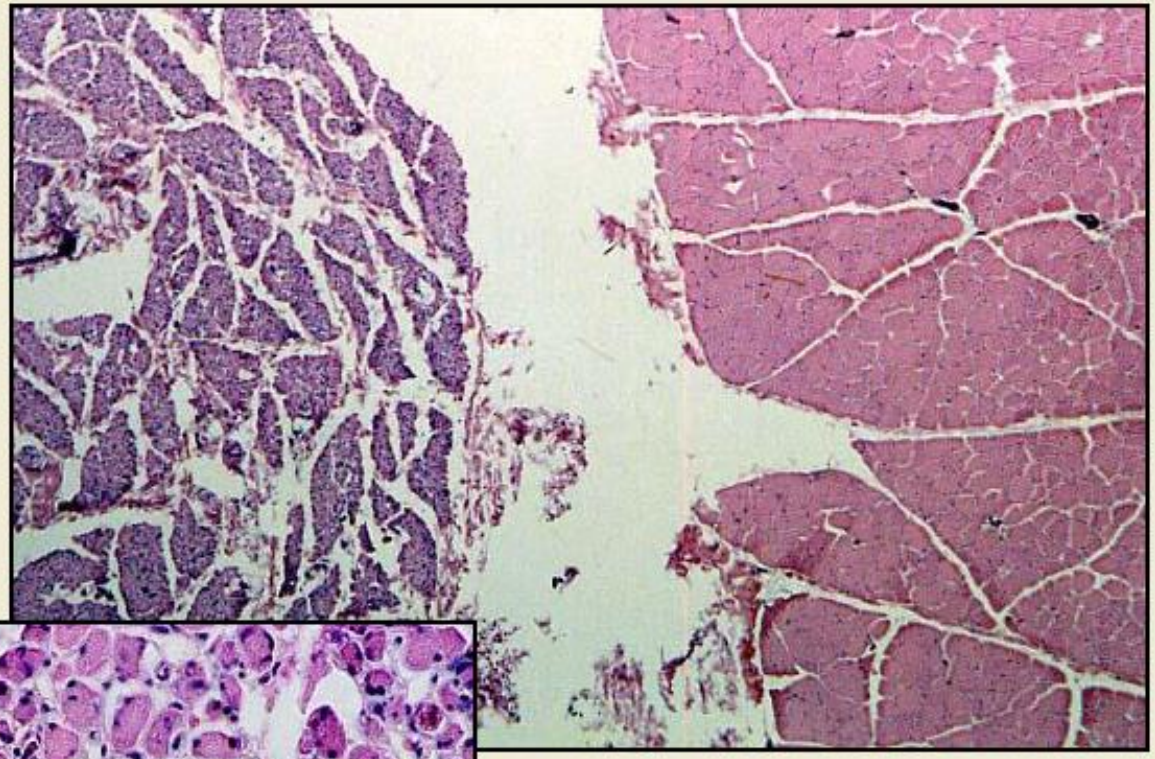


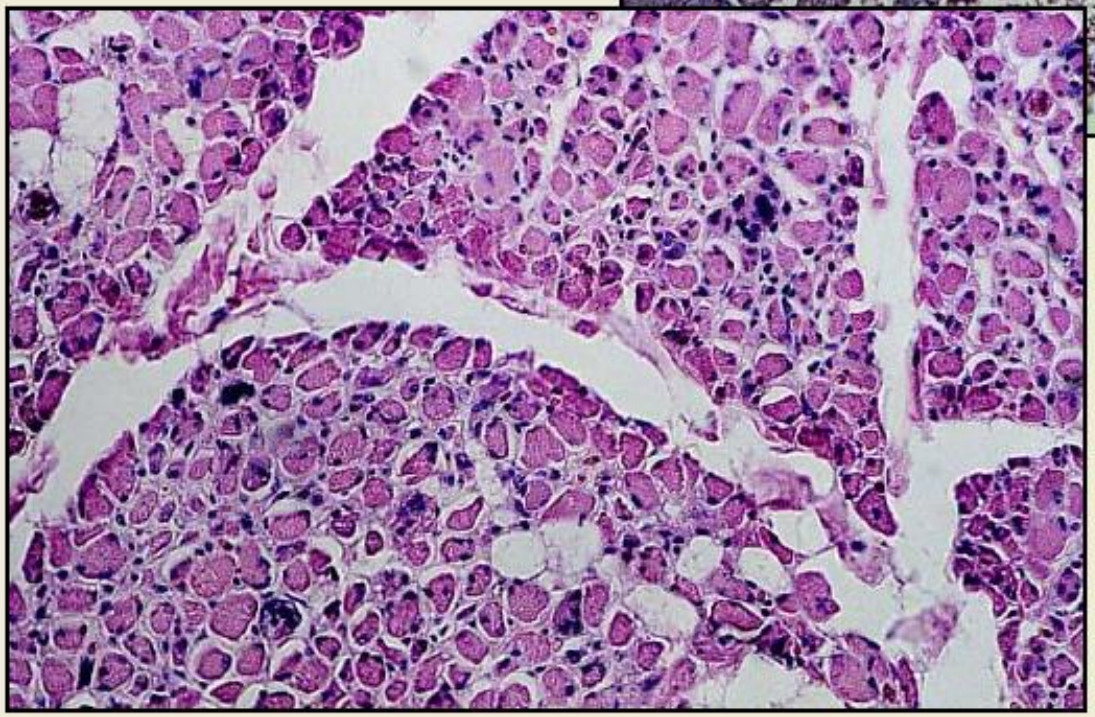
Illustration showing what the pectoral muscles in this bird would look like in cross-section; note "shrinkage" of right pectoral muscle indicating atrophy



Great horned owl, further dissection shows cause of the unilateral pectoral muscle atrophy; ie tearing / damage (avulsion) of right brachial plexus (see arrow) resulting in denervation atrophy.

Great horned owl, normal muscle on right of screen, atrophic muscle on left.





Close-up of atrophic muscle (cross-section), showing reduced diameter of most myocytes.

HYPERTROPHY

Hypertrophy is an increase in the size of cells resulting in increase in the size of the organ.

- In pure hypertrophy
  - No new cells
  - Just bigger cells
  - Containing increased amounts of structural proteins and organelles
- hypertrophy occurs when cells have a limited capacity to divide
- Hypertrophy and hyperplasia can occur together
- Hypertrophy can be physiologic or pathologic

Etiology of Hypertrophy

- a response to increased work load:

  physiological - eg, with exercise see increase in muscle cell size

  pathological - eg, heart failure see enlargement of cardiac myocytes

- a response to trophic signals:

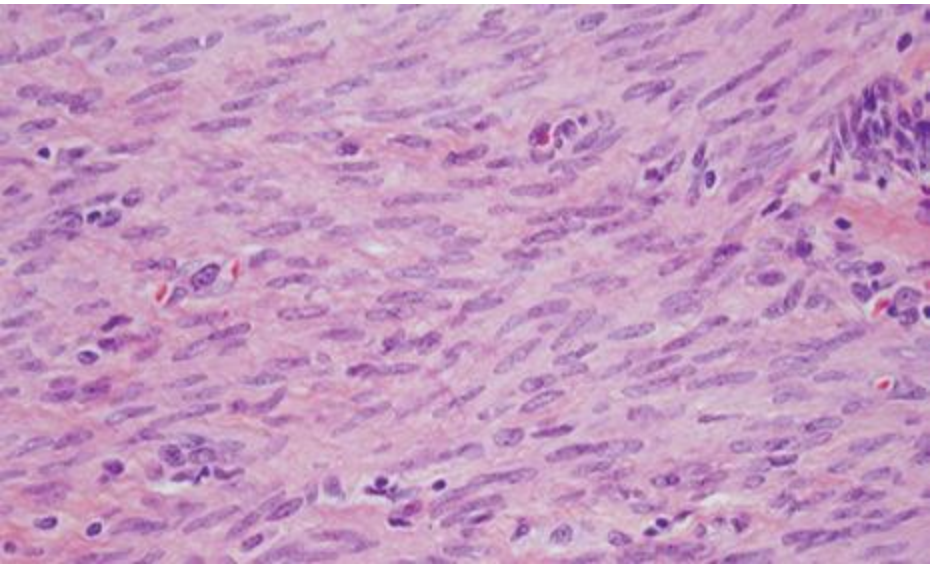
  physiologic hypertrophy (& hyperplasia)
  eg: uterus and mammary gland in pregnancy, lactation

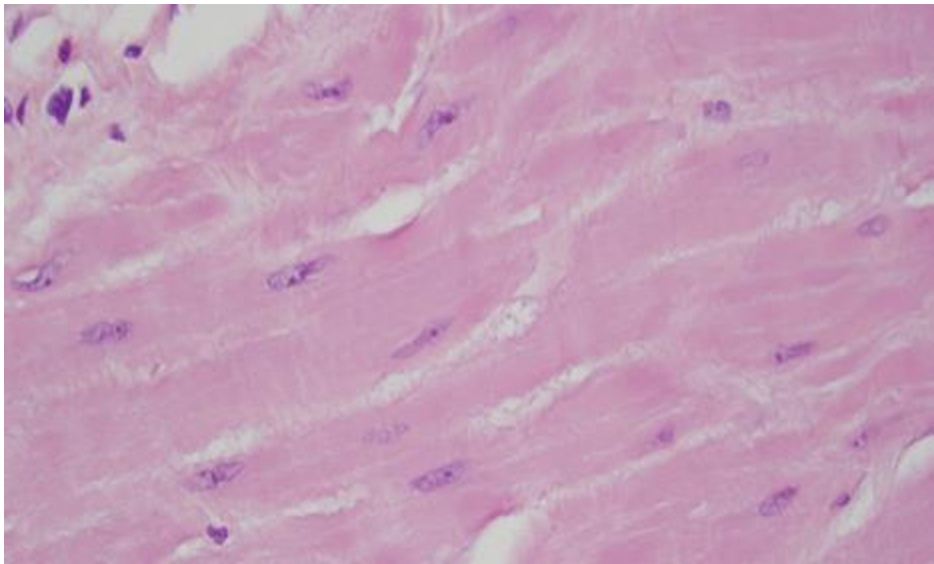
  pathological hypertrophy
  eg: myocardial hypertrophy in hyperthyroid cats

- **Compensatory hypertrophy**

•Physiologic enlargement of the uterus during pregnancy occurs as a consequence of estrogen stimulated smooth muscle hypertrophy and hyperplasia

• Striated muscle cells in both the skeletal muscle and the heart can undergo only hypertrophy because adult muscle cells have a limited capacity to divide.





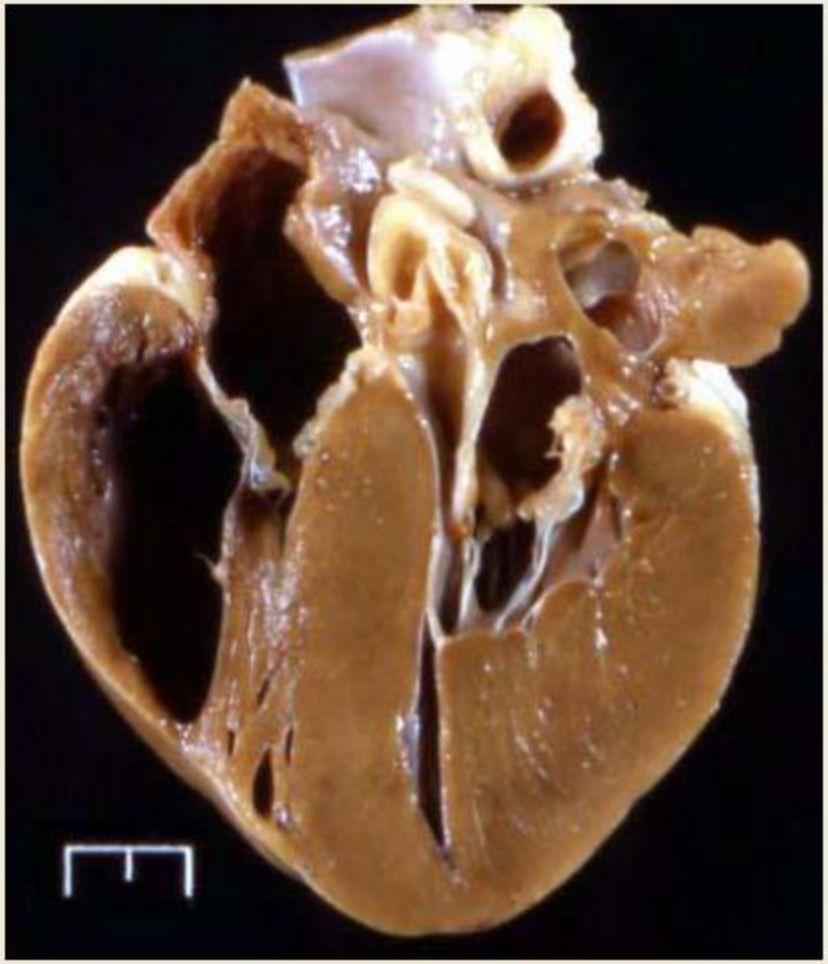
Mechanisms & Biochemistry of Hypertrophy

- anabolic processes > catabolic ones
- Increase in organelles / cellular proteins: eg, mitochondria, ER, myofibrils
- Chronic exposure to drugs such as phenobarbital, dilantin, and alcohol lead to enlargement of the SER in hepatocytes, to increase cytochrome P-450 for detoxification
- When adaptation beyond limit cell go towards necrosis or apoptosis

Gross changes

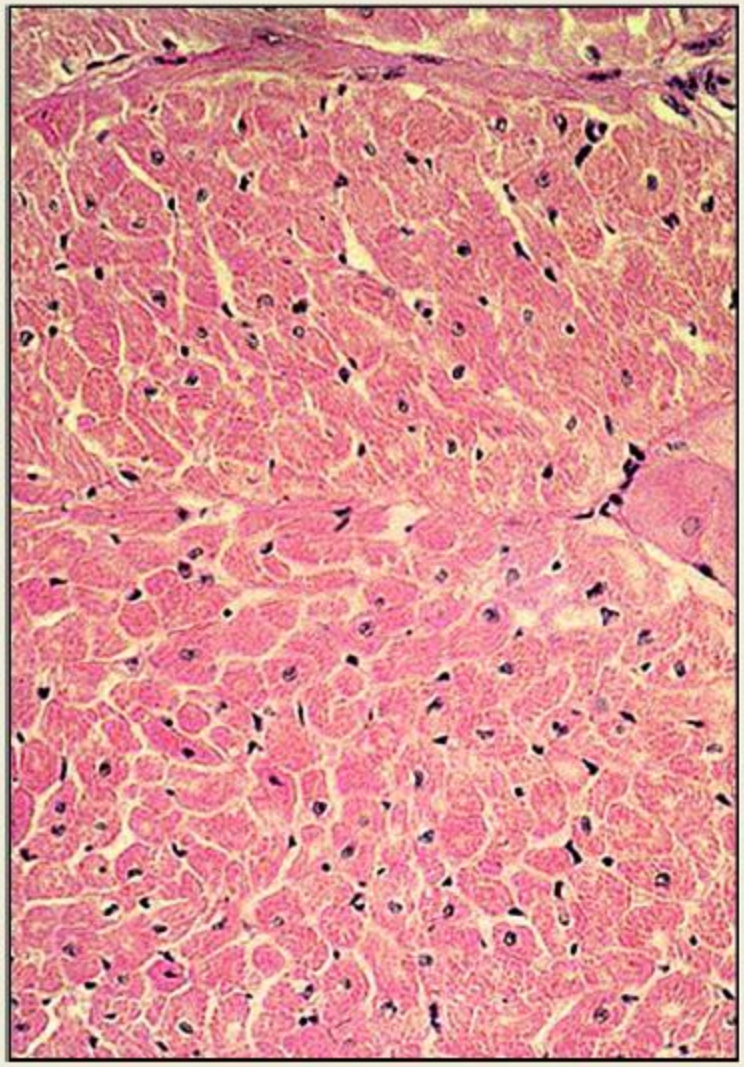
HYPERTROPHY

Canine, normal heart

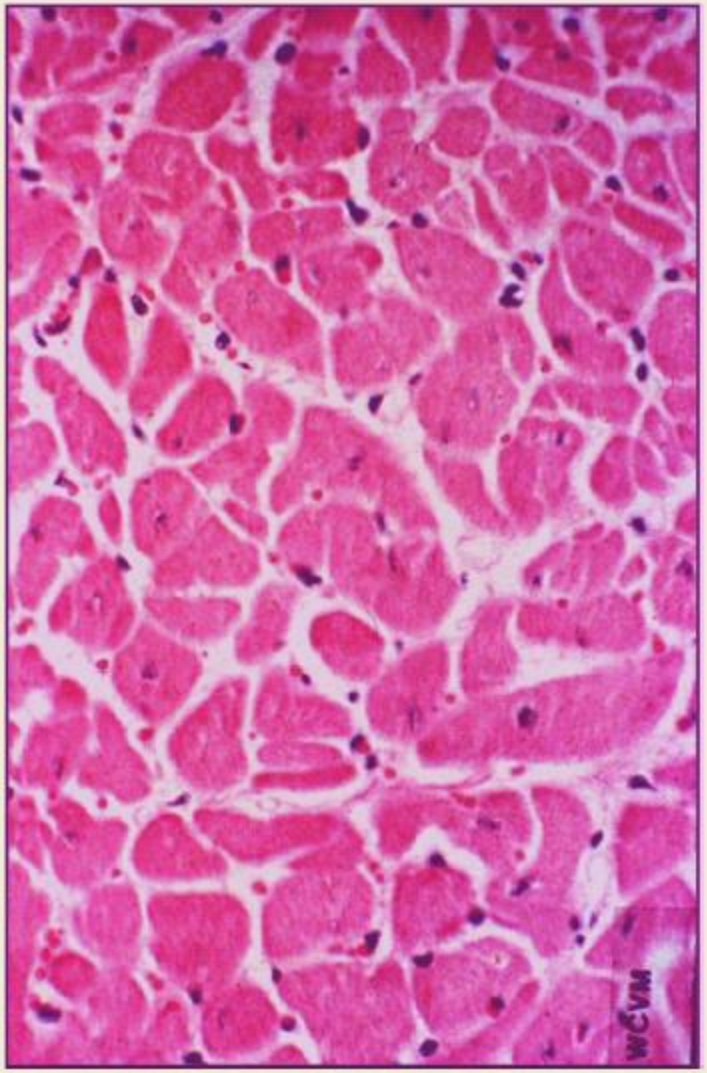


Canine, left ventricular hypertrophy
(in this case due to hypertension).

Microscopic changes



Canine, normal myocardium



Canine, left ventricle, cardiac myocyte hypertrophy; (same magnification as normal slide to left) note enlargement of individual myocytes

HYPERPLASIA

- **Hyperplasia is an increase in the number of cells in an organ or tissue**
- Cells replicate/go for mitotic division
- Depends on adult cell types to undergo hyperplasia
  - **Labile cells** - epidermis, intestinal epithelium, and bone marrow cells-readily become hyperplastic
  - **Permanent cells** - neurons and cardiac and skeletal muscle myocytes – little capacity to replicate – normally hypertrophy occur
  - **Stable cells -** bone, cartilage, and smooth muscle – intermediate ability to become hyperplastic.

Two type 1. Physiological and 2. Pathological

1. Physiological hyperplasia

(A) Hormonal hyperplasia

- Proliferation of the glandular epithelium of the mammary gland (puberty and during pregnancy)

(B) Compensatory hyperplasia

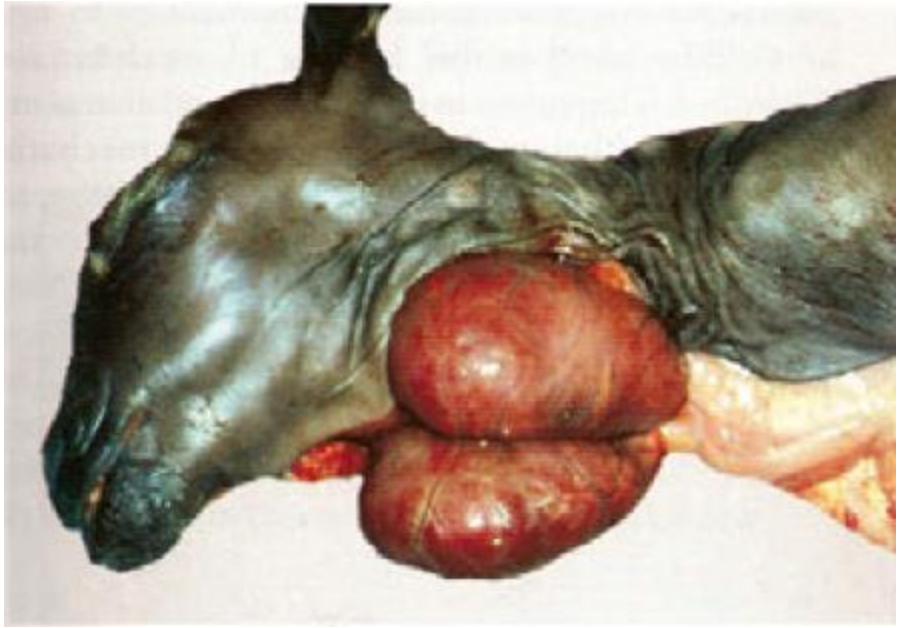
- Residual tissue grows after removal or loss of part of an organ.
- E.g. Skin injury and partial hepatectomy
- Mitotic signal given by health cells
- After restoration, cell proliferation

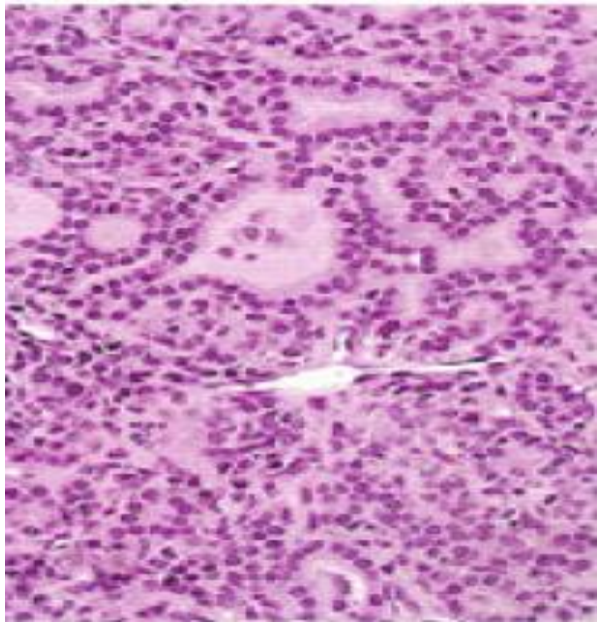
"turned off" by various growth inhibitors

2. Pathologic Hyperplasia

Caused by

- Excessive hormonal stimulation
  - Cystic endometrial hyperplasia due to prolonged progesterone.
  - Prostatic hyperplasia in dogs
  - Goiter (hyperplasia of the thyroid gland)
  - cause diffuse or nodular enlargement of an organ
- Chronic irritation
  - Calluses on the elbows and stifles of dogs, and the hands of workmen
- Infectious agent
  - Pox virus



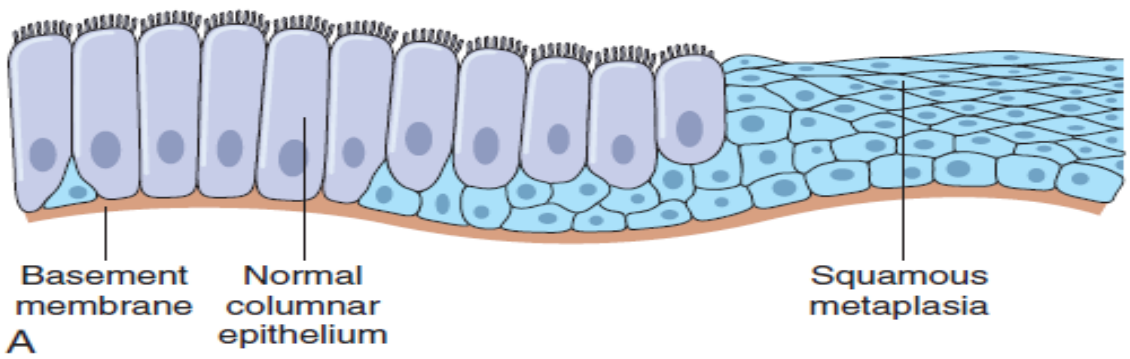


Hyperplasia, thyroid gland (goiter) goat, Deficiency of Iodine

Thyroid follicular epithelial cells from a normal thyroid gland.

Metaplasia

- *Metaplasia is a reversible change in which one adult cell type (epithelial or mesenchymal) is replaced by another adult cell type.*
- Cell type sensitive to a particular stress is replaced by another cell type better able to withstand the adverse environment.
- Can be preneoplastic



❖ **Chronic irritation**

- Lungs of smokers – cuboidal and columnar epithelium of airways to become stratified squamous.

❖ **Vitamin A deficiency**

Squamous metaplasia of

- The transitional epithelium of the urinary tract
- Cells lining the ducts within the salivary glands
- Epithelium of the mucous glands of esophageal mucosa in birds

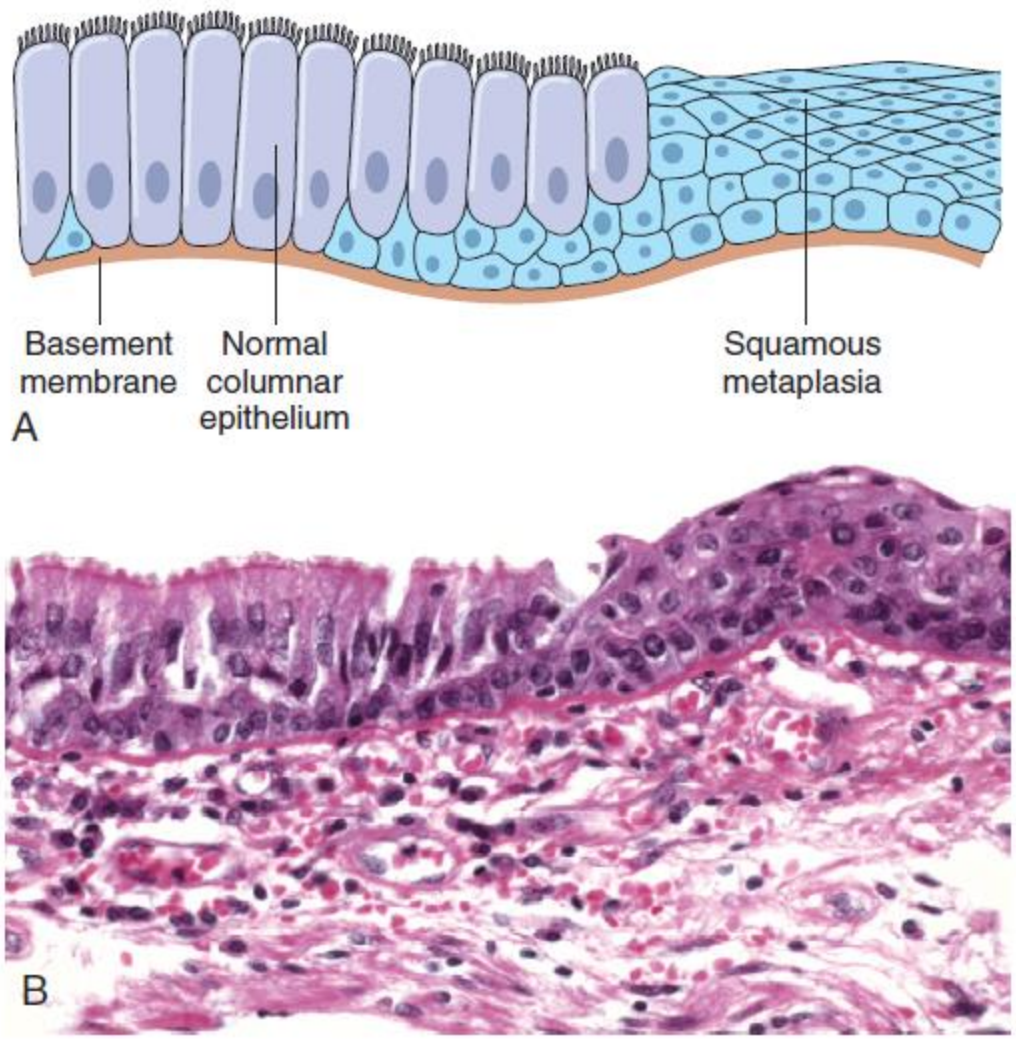
❖ **Estrogen toxicity**

- Squamous metaplasia of the urinary tract and prostate.

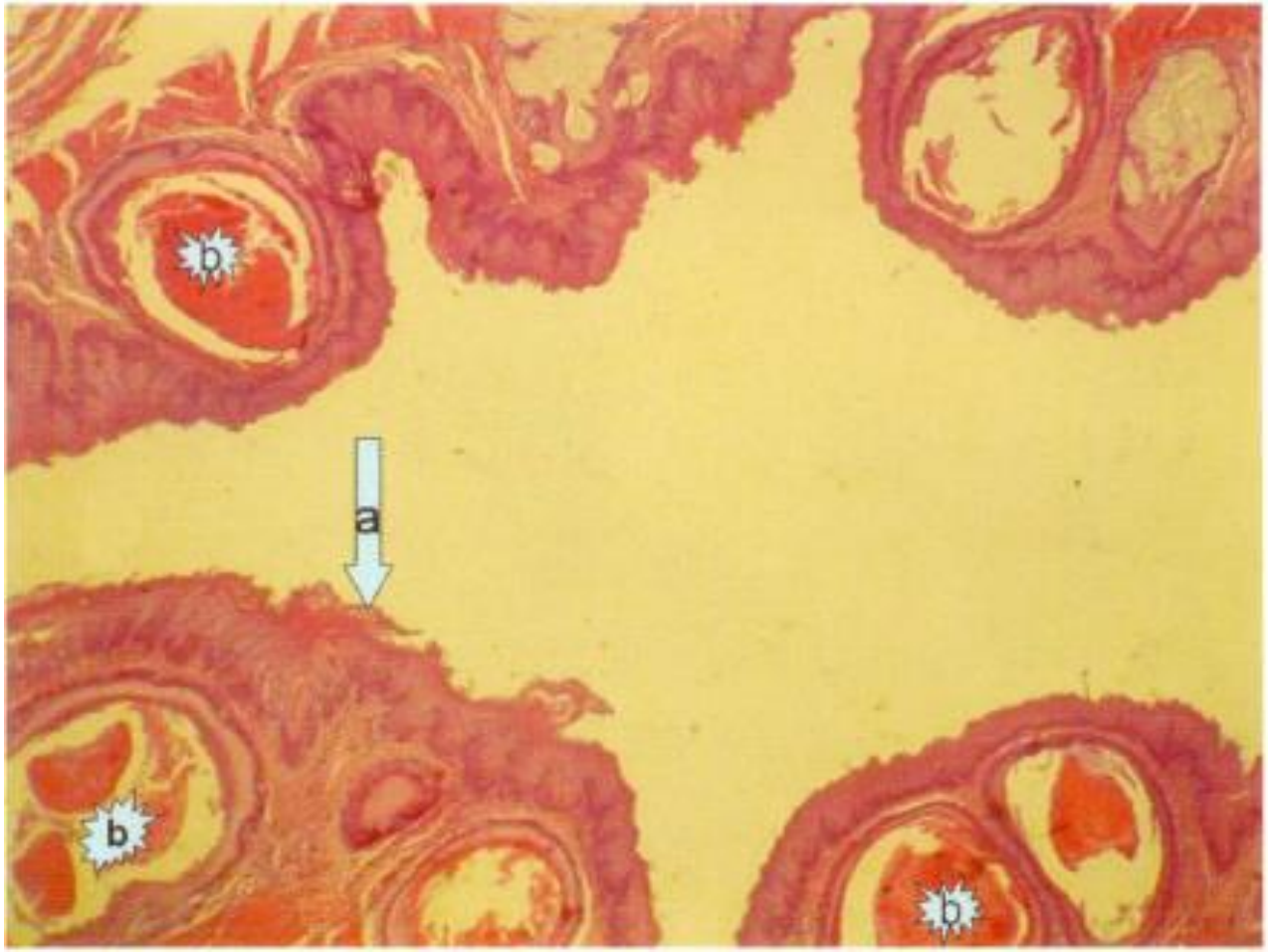
❖ Metaplastic bone (**osseous metaplasia**) occasionally occurs in injured soft tissue.

❖ **Myeloid metaplasia** (extramedullary hematopoiesis) in adult spleens and livers

Metaplasia occur for survival but specific function lost



Chronic irritation from particles and chemicals in the lungs of smokers may cause the normal cuboidal and columnar epithelium of airways to become stratified squamous.

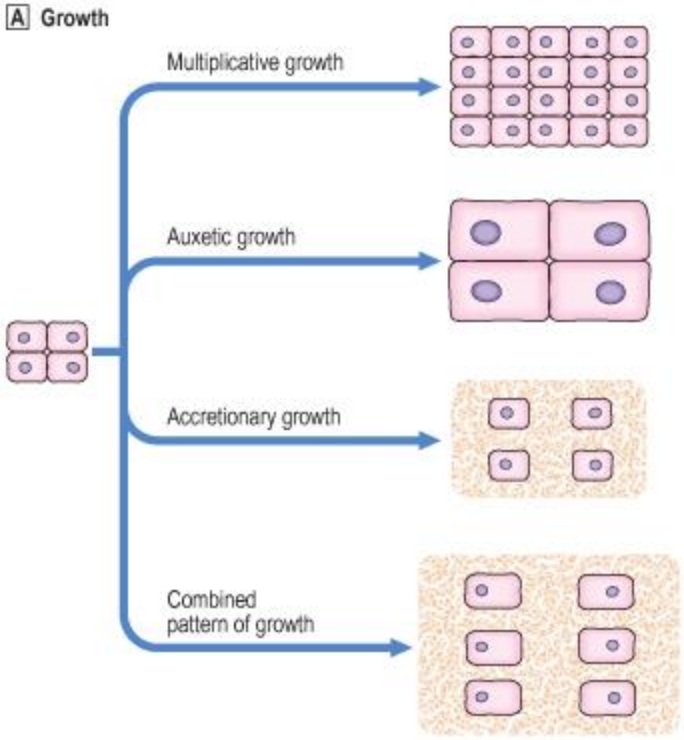


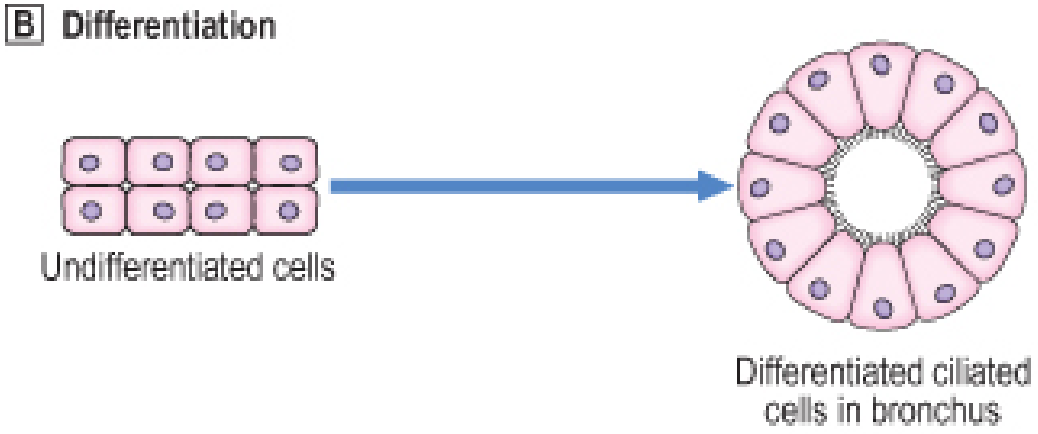
Esophagus, Hen , Vitamin A deficiency
Hyperkeratinization (arrow a) and metaplasia (b) of glandular epithelium.

Growth and Differentiation

- **Growth** is the process of increase in size resulting from the synthesis of specific tissue components.
- **Differentiation** is the process whereby a cell develops an overt specialized function or morphology which distinguishes it from its parent cell

Morphogenesis : Development of structural shape and form of organs, limbs, facial features, etc. from primitive cell masses during embryogenesis





APLASIA

Failure of an organ or tissue to develop

Occurs in the embryo or foetus during intrauterine development

Causes include

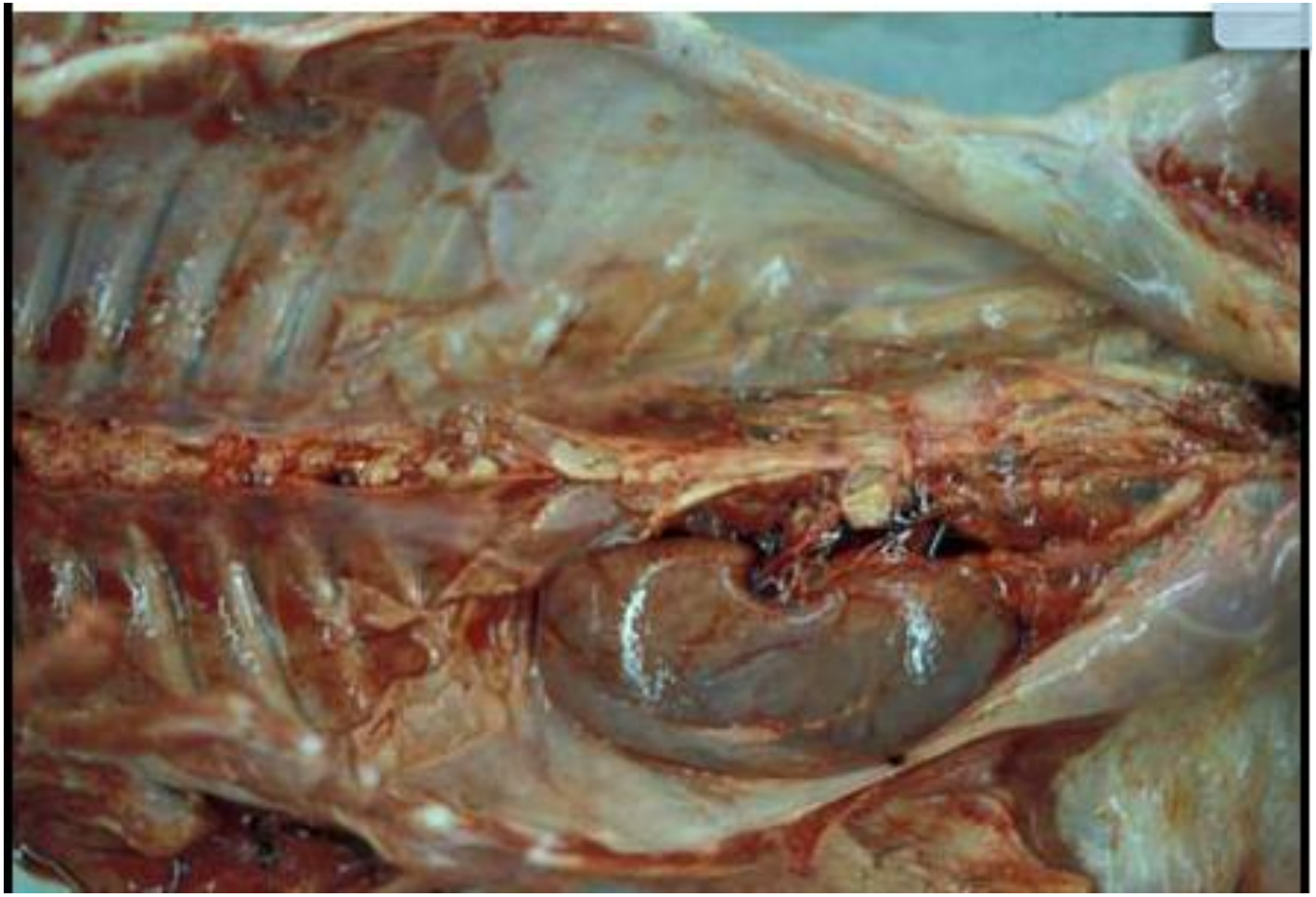
(1) Hereditary defects in germplasm,

(2) Death of a cell at some critical point in the development

(3) Diseases, particularly viral, of the dam during gestation, may invade the foetus and cause cellular damage

Macroscopically

- An absence of that organ or tissue.
- In place of the aplastic organ, a fatty or fibrous mass may be present



Unilateral Agenesis or Aplasia of kidney

HYPOPLASIA

- Failure of cells, tissues, or organs to attain their mature size
- Incomplete development or underdevelopment of an organ, with decreased number of cells
- Differs from atrophy
  - Atrophic cells already attain their adult size before reverting to small form.

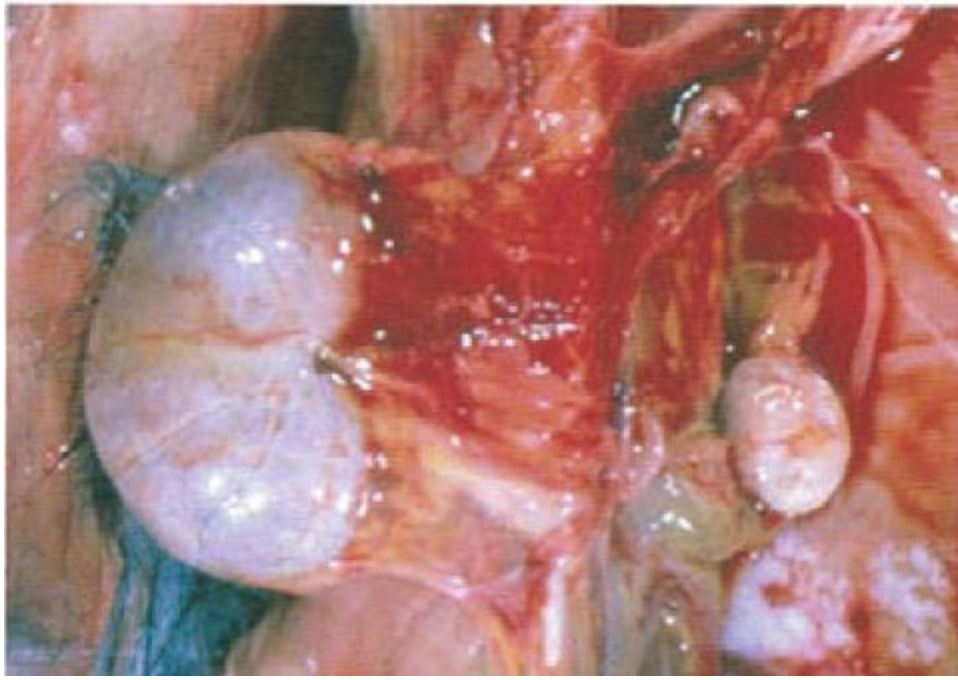
Causes include

(1) Congenital anomalies

(2) Inadequate blood supply

(3) Inadequate innervation.

(4) malnutrition.

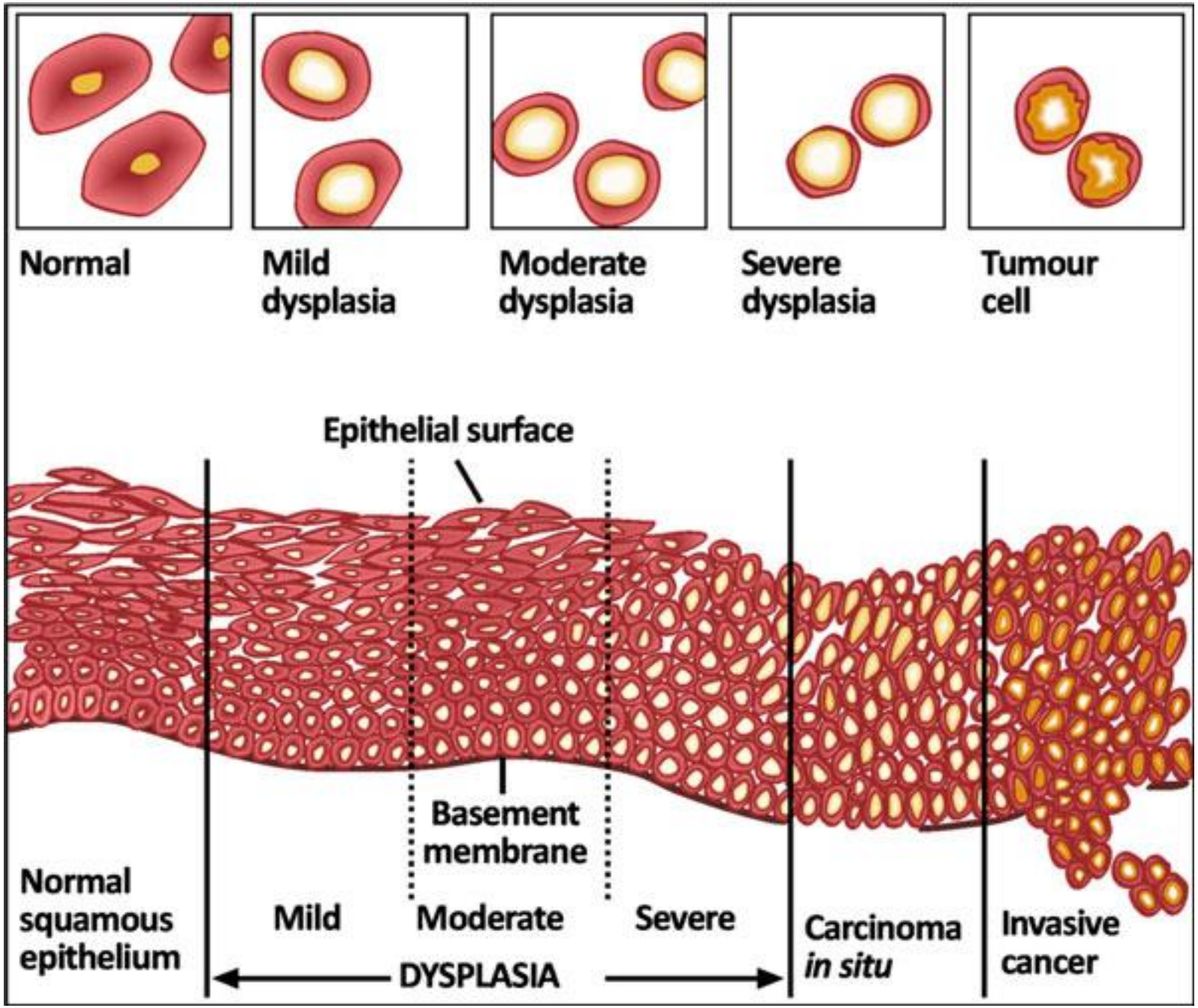


Unilateral hypoplastic kidney

DYSPLASIA

Not adaptive response

- Characterized by
  - Increased cell growth
  - More mitoses visible than normal
  - Presence of atypical morphology (e.g. abnormally large nuclei)
  - Decreased differentiation (e.g. cellular immaturity)
- May be caused by chronic physical or chemical injury
- May be reversible only in early stages
- Often pre-neoplastic
- Can be seen with metaplasia


Normal
Mild dysplasia
Moderate dysplasia
Severe dysplasia
Tumour cell
Epithelial surface
Basement membrane
Normal squamous epithelium
Mild
Moderate
Severe
DYSPLASIA
Carcinoma in situ
Invasive cancer