LECTURE.

ADAPTATION AND TISSUE REPAIR.

ADAPTATION

ADAPTATION characterizes abilities of biological types.

This is a complex of self-regulating process, which permit to adapt for new environment and conditions.

ADAPTATION *is wide biological term, including phylogenies, ontogenesis, evolution, heredity and all types of regulations in normal and pathological conditions.*

compensation

This is a complex of biological reactions *after injury and diseases, directed to restoration of damaged functions*.

- Compensatory reactions are more narrow, than adaptive reactions
- Compensatory reactions are the part of adaptive reactions

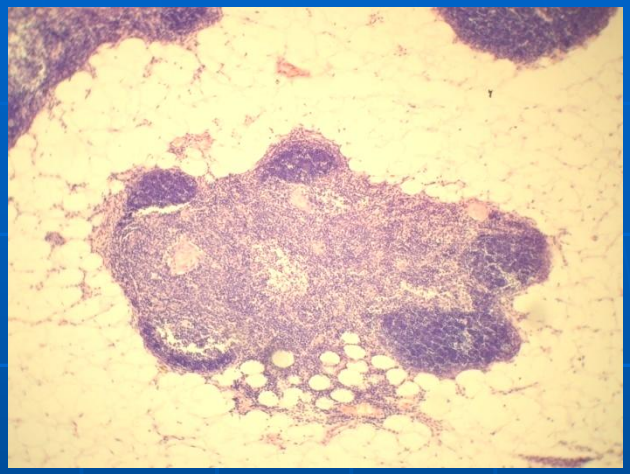
- **ATROPHY**
- Shrinkage in the size of the cell by loss of cell substance is known as atrophy.
- The causes of atrophy are the following:

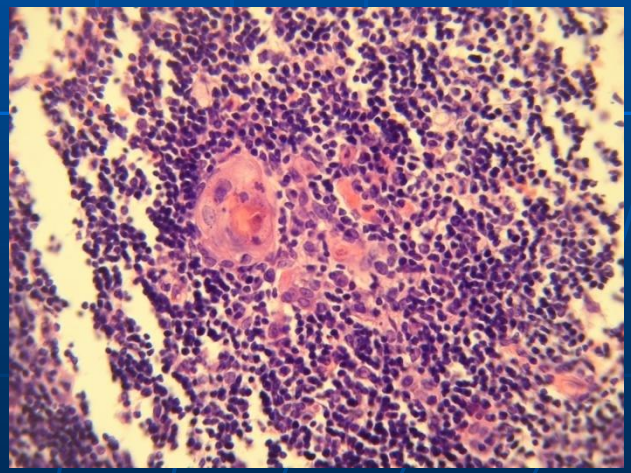
1. Decreased workload.
2. Loss of innervations.
3. Diminished blood supply.
4. Inadequate nutrition.
5. Loss of endocrine stimulation.
6. Aging.

Types of atrophy

- *Physiological;*
- *Pathological*.

- *Systemic*;
- *Local.*

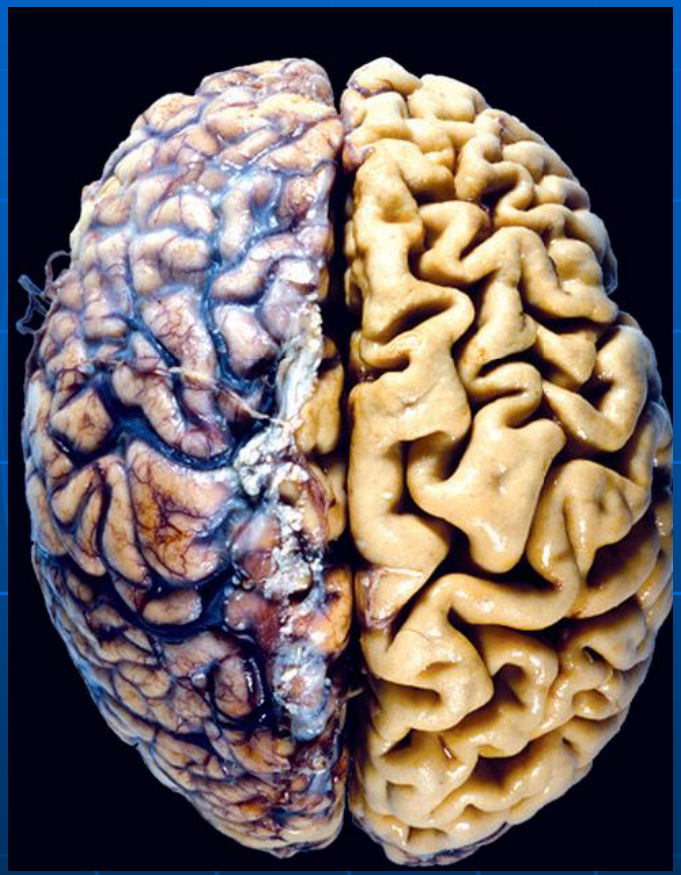




Types of pathological atrophy

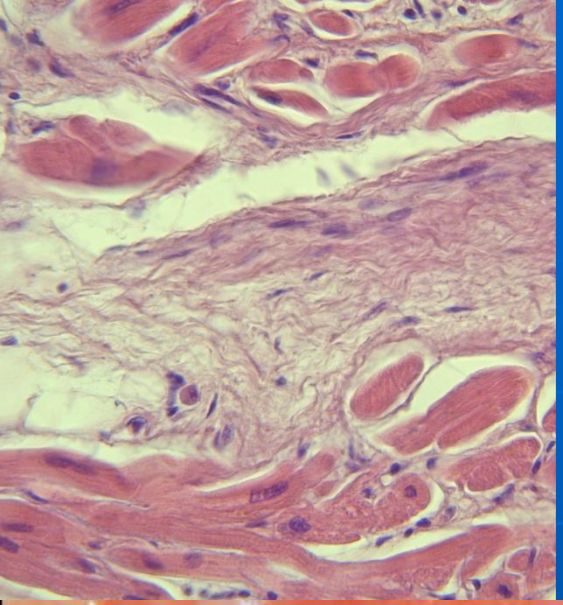
- ***dysfunctional atrophy*** *(atrophy skeletal muscle after bone* fracture);
- **atrophy *under the pressure*** (atrophy of the brain *under the pressure* of CSF);
- **atrophy due to ischemia** (atrophy of kidney during atherosclerosis of renal artery);
- ***neurotrophic* atrophy**, (*atrophy skeletal muscle* after loss of innervations due to polyomyelitis);
- **atrophy due to *chemical & physical factors*** (atrophy of red bone marrow after gamma rays).

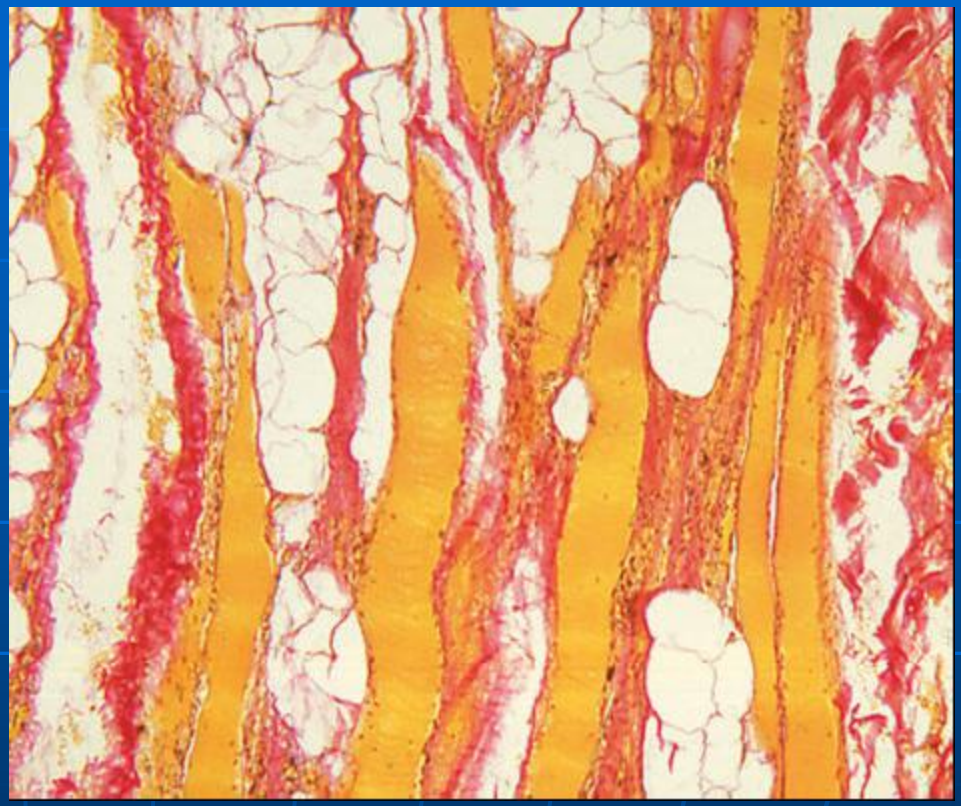
Atrophy

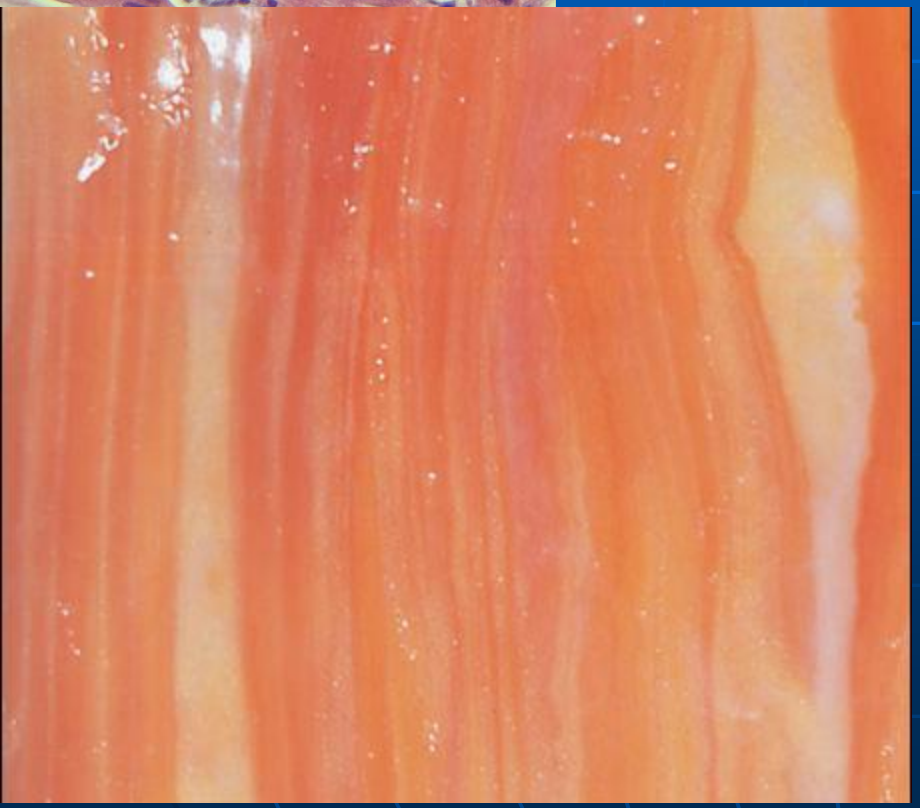


Atrophy of the brain. Note the narrow gyri and widened sulci. The meninges have been stripped from the right half of the brain.

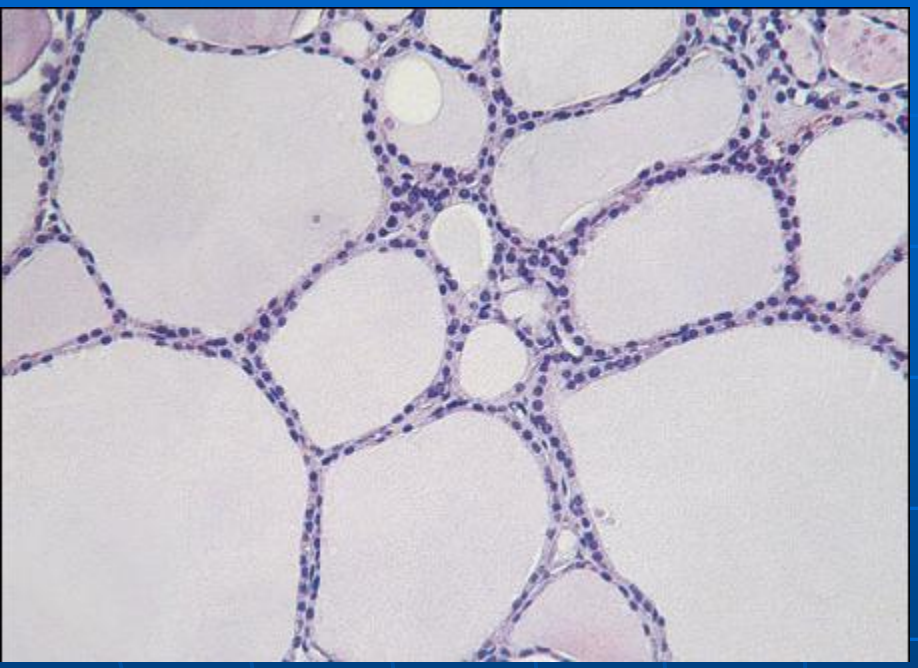
Atrophy



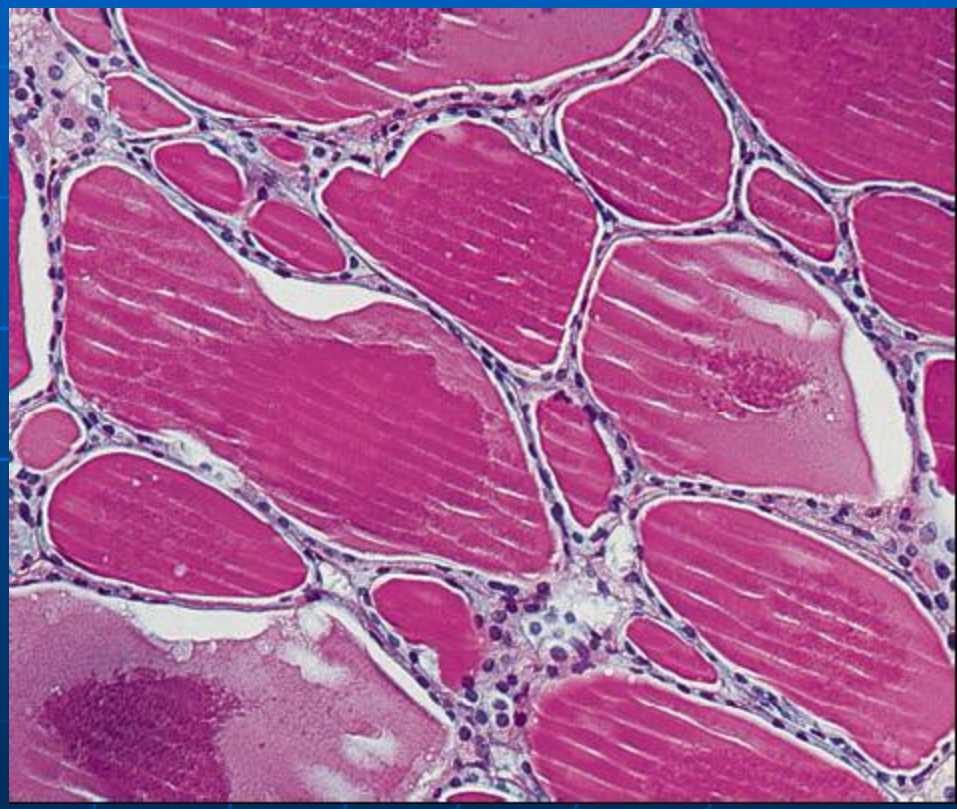




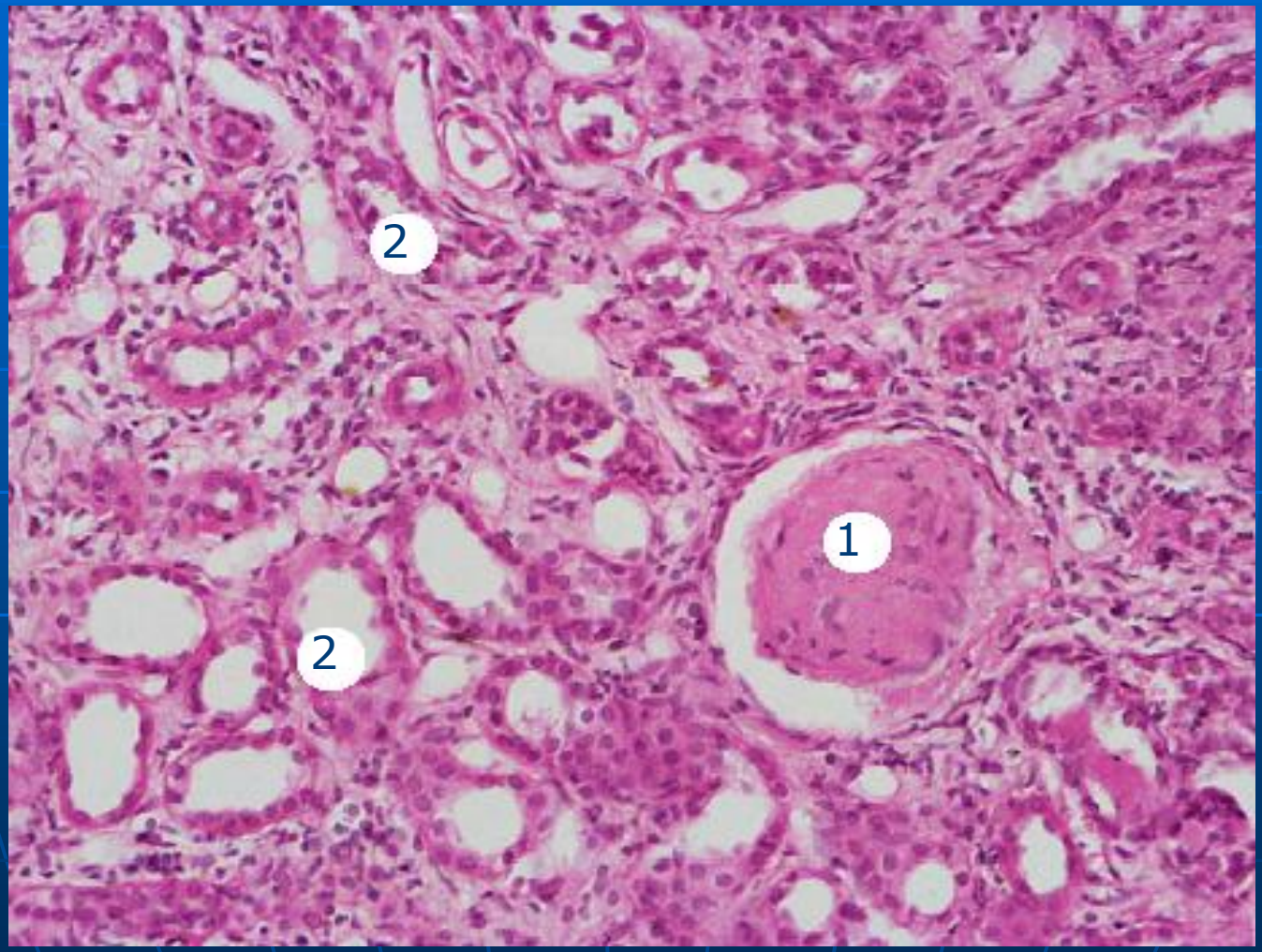
Euthyroid goiter



Hypothyroid goiter

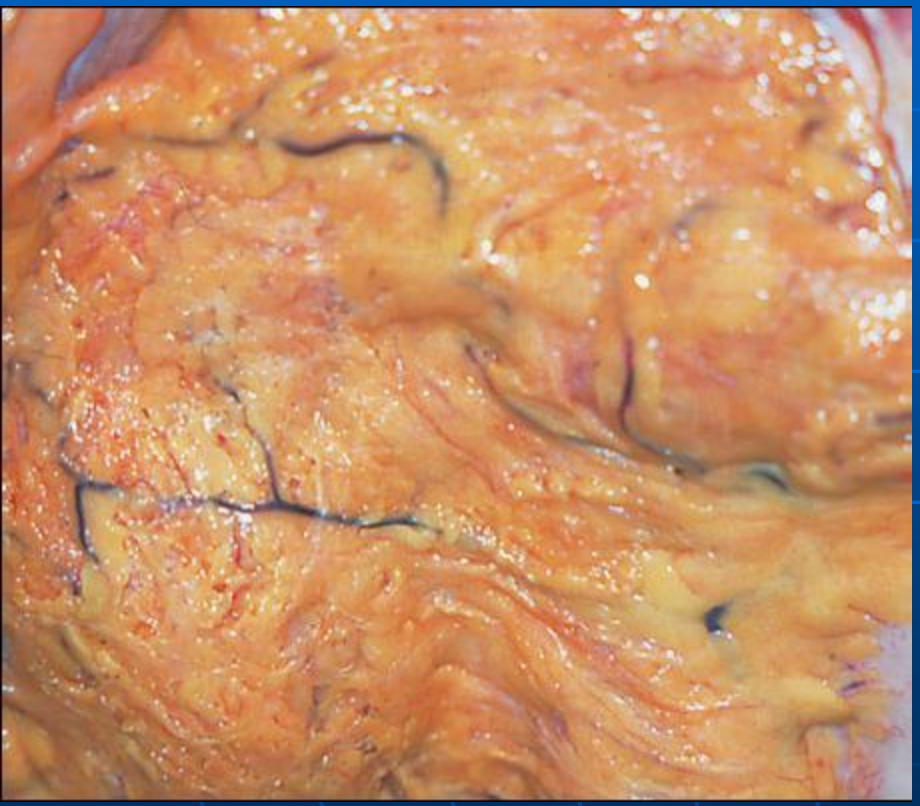


Atrophy

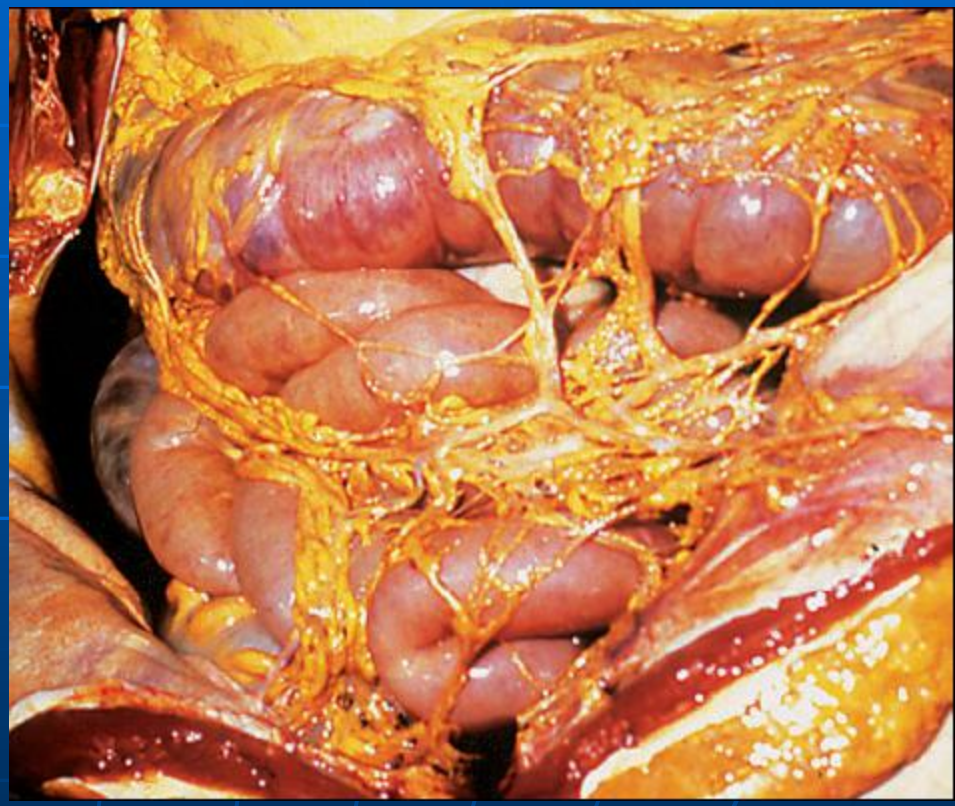


Atrophy of glomeruli (1) & convoluted tubules (2) due to hydronephrosis.

Normal greater omentum.



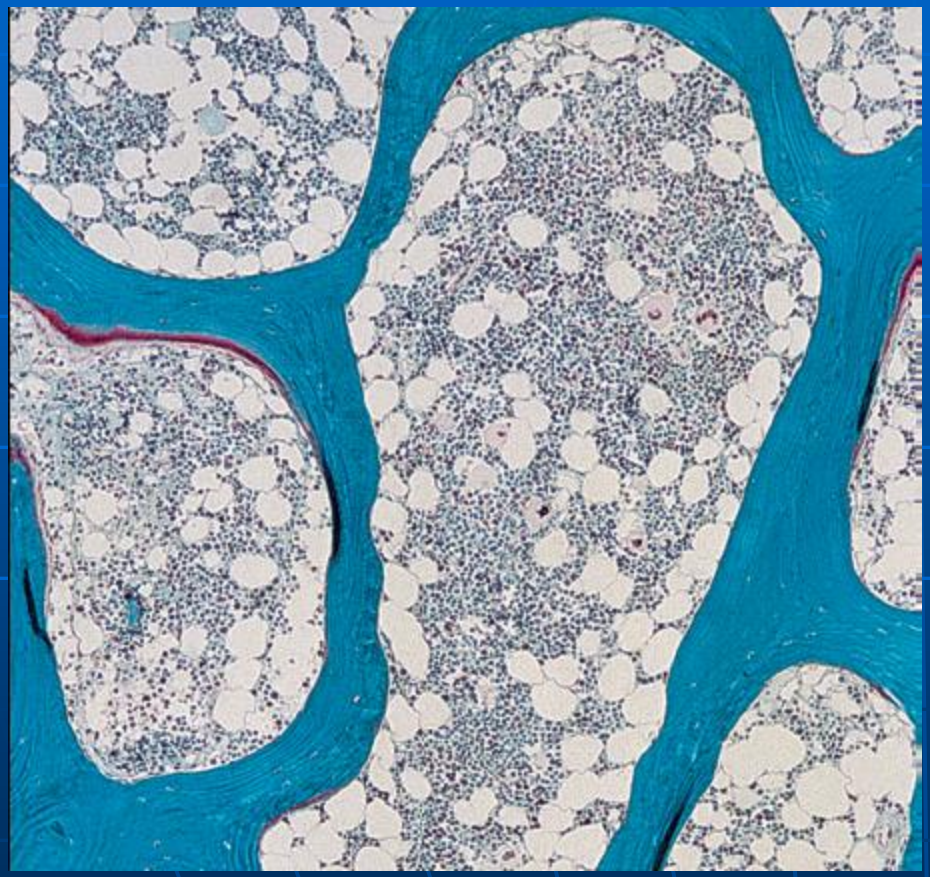
Greater omentum in cachexia



Normal femur

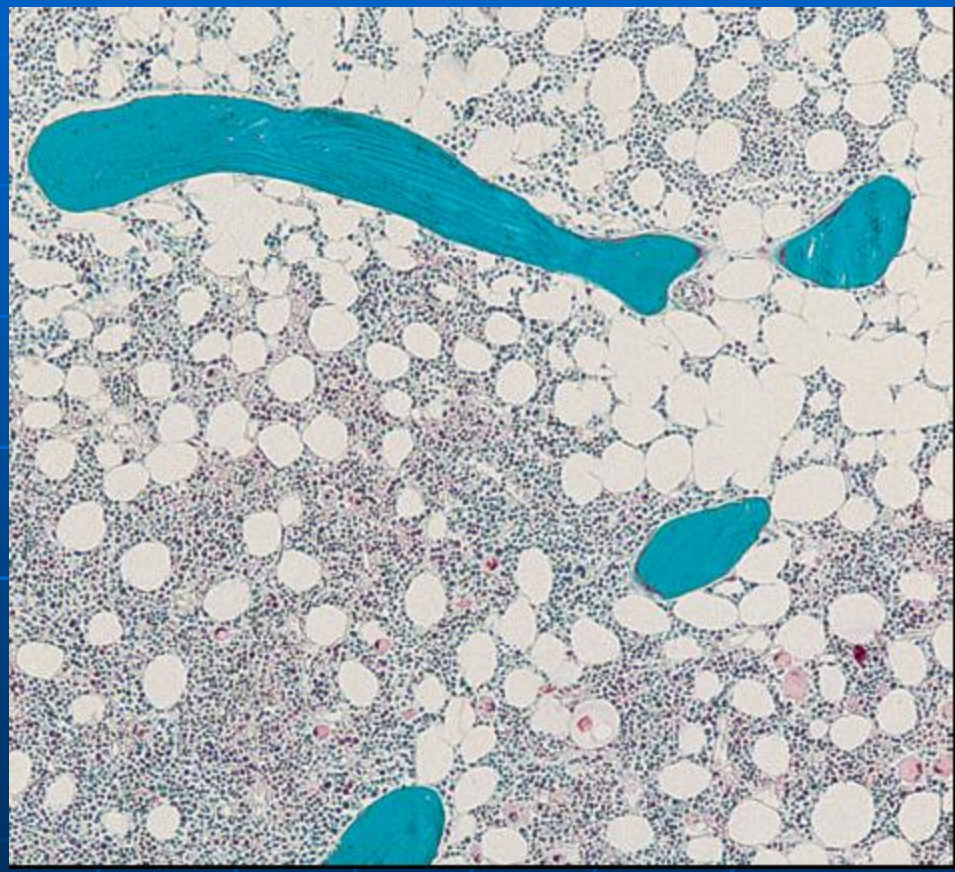
Femur in osteoporosis

Normal femur



Trihrom. X75

Femur in osteoporosis



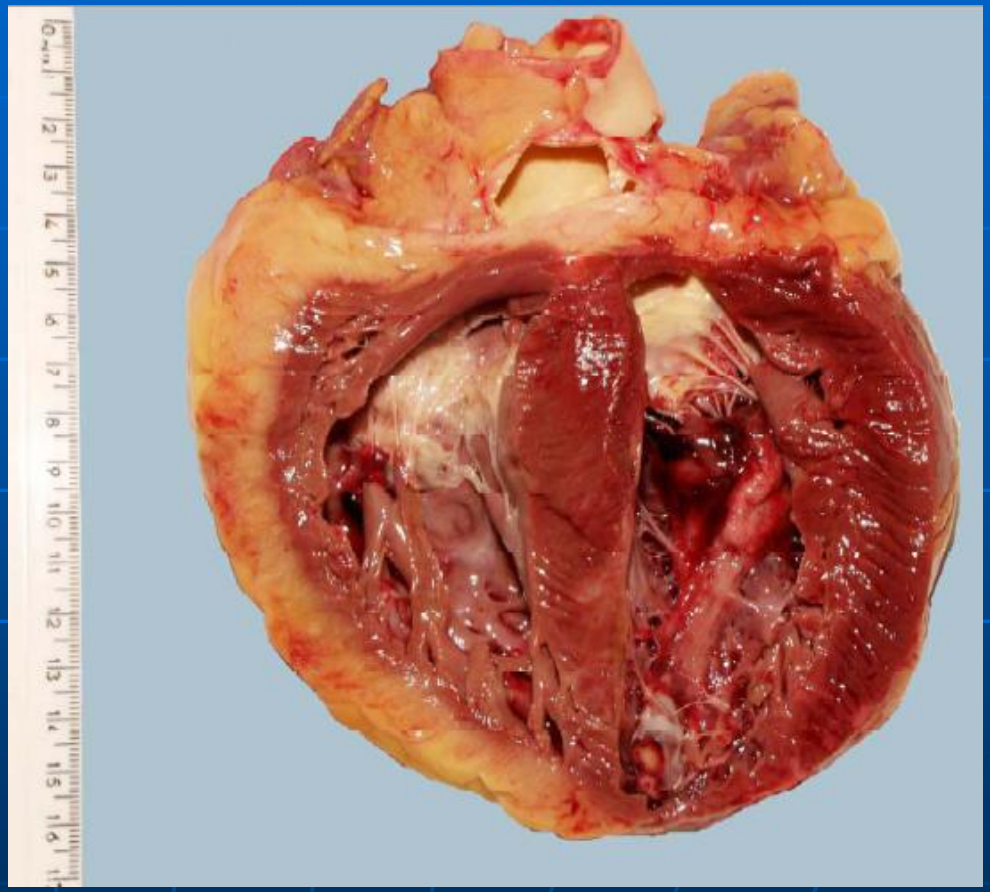
Trihrom. X75

HYPERTROPHY

Hypertrophy refers to an increase in the size of cells and, with such change, an increase in the size of the organ

HYPERTROPHY

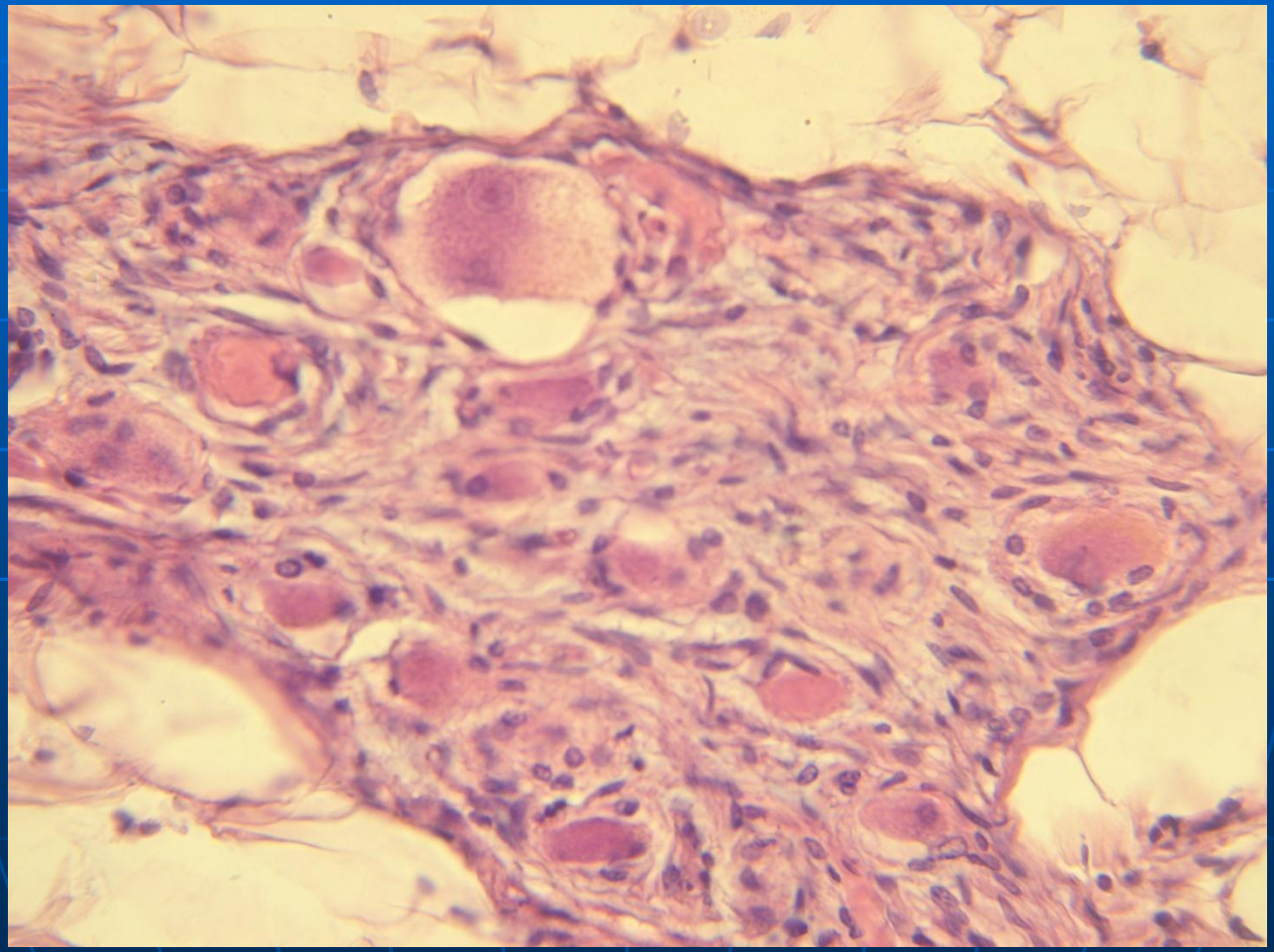
Hypertrophy can be physiologic and pathologic and is caused by increased functional demand or by specific hormonal stimulation



Hypertrophy

- Hypertrophy can be **physiological** and **pathological** and is caused by increased functional demand or by specific hormonal stimulation.
- The **physiologic** growth of the uterus during pregnancy involves both hypertrophy and hyperplasia. The cellular hypertrophy is stimulated by estrogenic hormones through smooth muscle estrogen receptors, which allow for interactions of the hormones with nuclear DNA, eventually resulting in increased synthesis of smooth muscle proteins and an increase in cell size. This is then physiologic hypertrophy effected by hormonal stimulation.
- **Hypertrophy** as an adaptive response is exemplified by muscular enlargement. The striated muscle cells in both the heart and skeletal muscles are most capable of hypertrophy, perhaps because they cannot adapt to increased metabolic demands by mitotic division and formation of more cells to share the work.

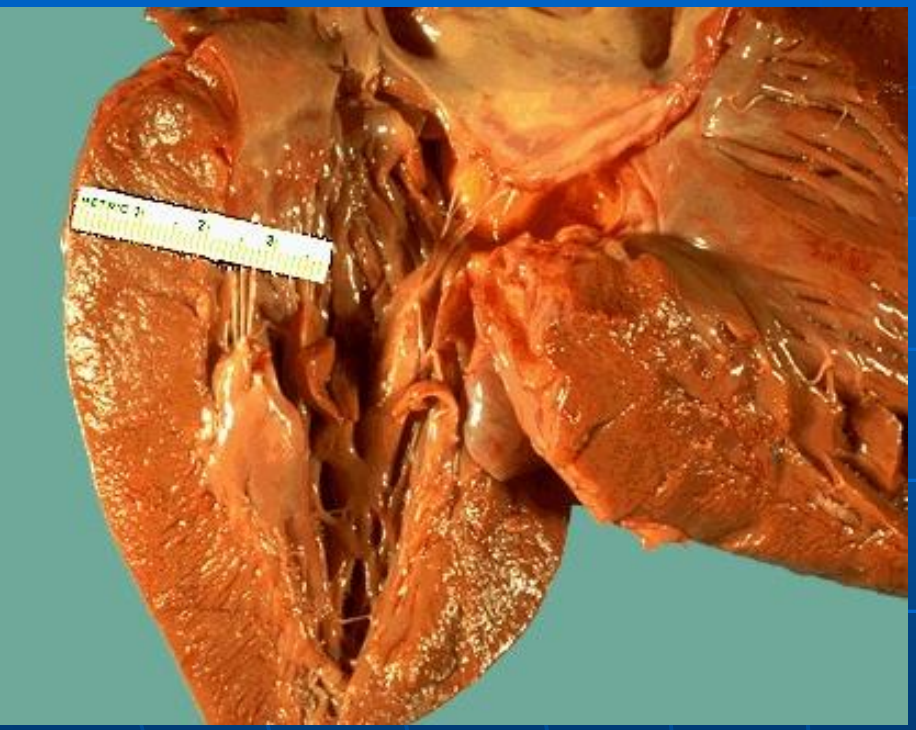
Physiological hypertrophy

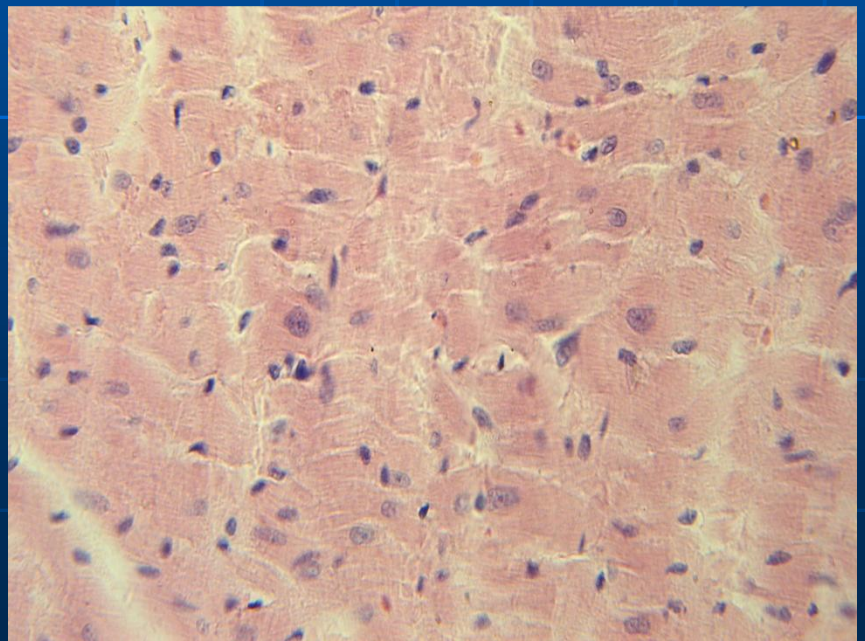


There are following types of hypertrophy:

- **working hypertrophy** develops in increased workload of the organ; increasing of volume (number) of the cells determining the specialized function of the organ takes place in this type of hypertrophy. Hypertrophy of the heart described before is the example of such hypertrophy;
- **neurohumoral hypertrophy** appears because of the disturbance of functions of endocrine glands. The changes in uterus and mammalian glands during pregnancy is the example of this hypertrophy;
- **replacement hypertrophy** takes place after the loss of one of twin organs because of the disease or surgical operations when the remained organ takes on itself the function of the lost one;
- **regenerative hypertrophy** takes place after the loss of part of the parenchyma due to the disease or surgical operations when the remained tissue takes on itself the function of the lost one (e.g. hypertrophy of myocardium after infarction).

Compensatory hypertrophy of myocardium

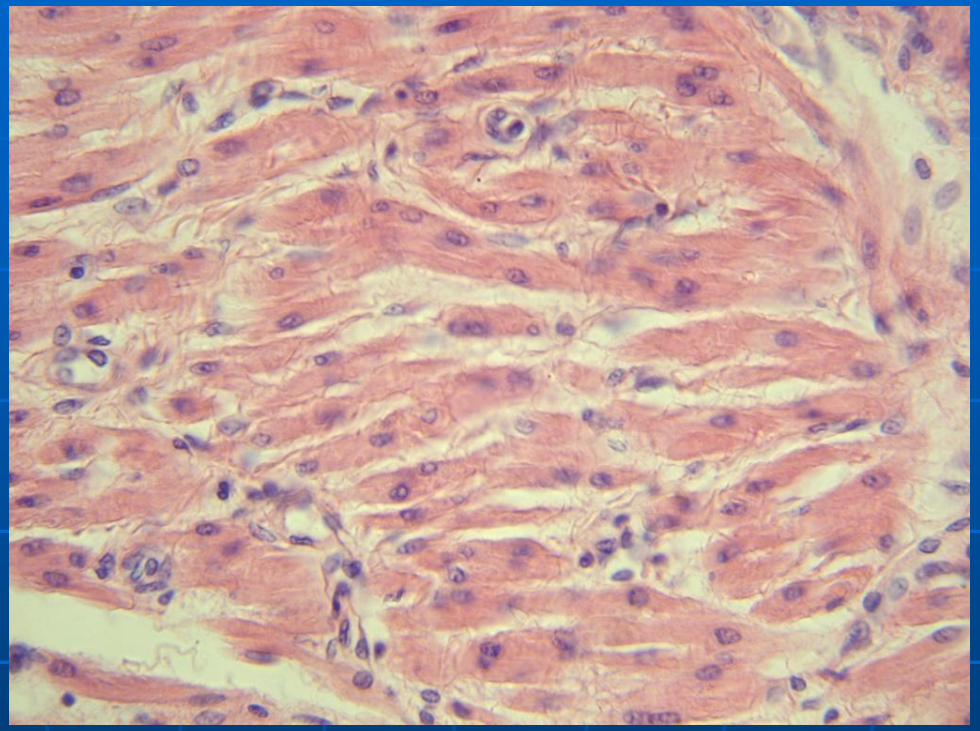




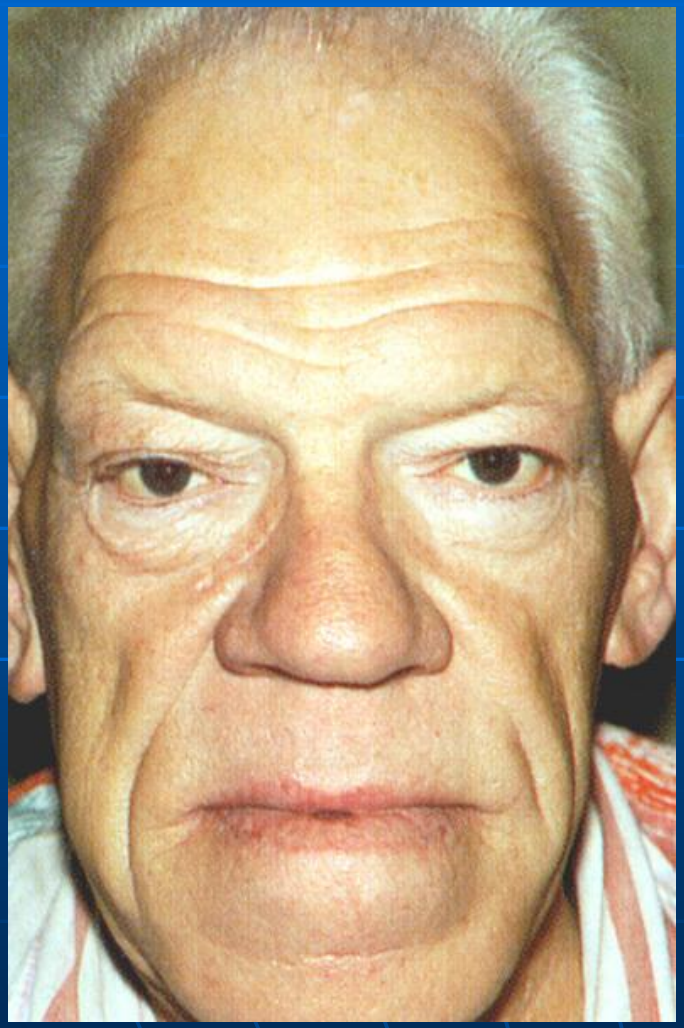
Compensatory hypertrophy of myocardium

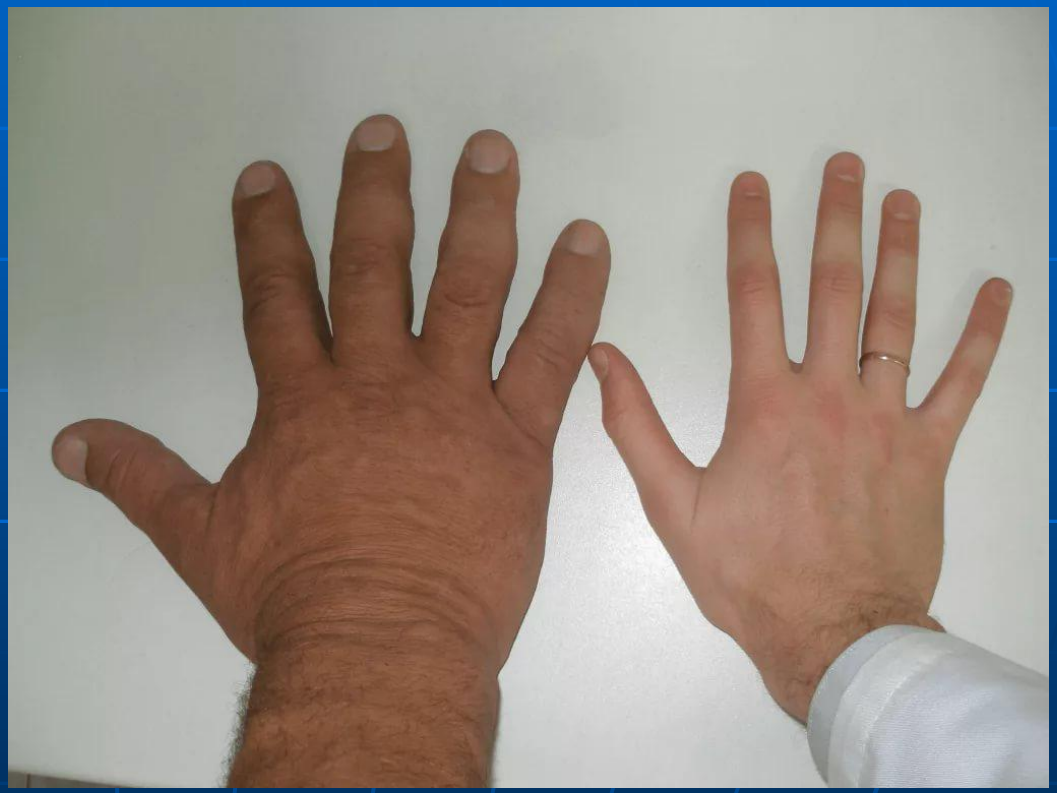
Neurohumoral hypertrophy

neurohumoral hypertrophy appears because of the disturbance of functions of endocrine glands.



Acromegaly





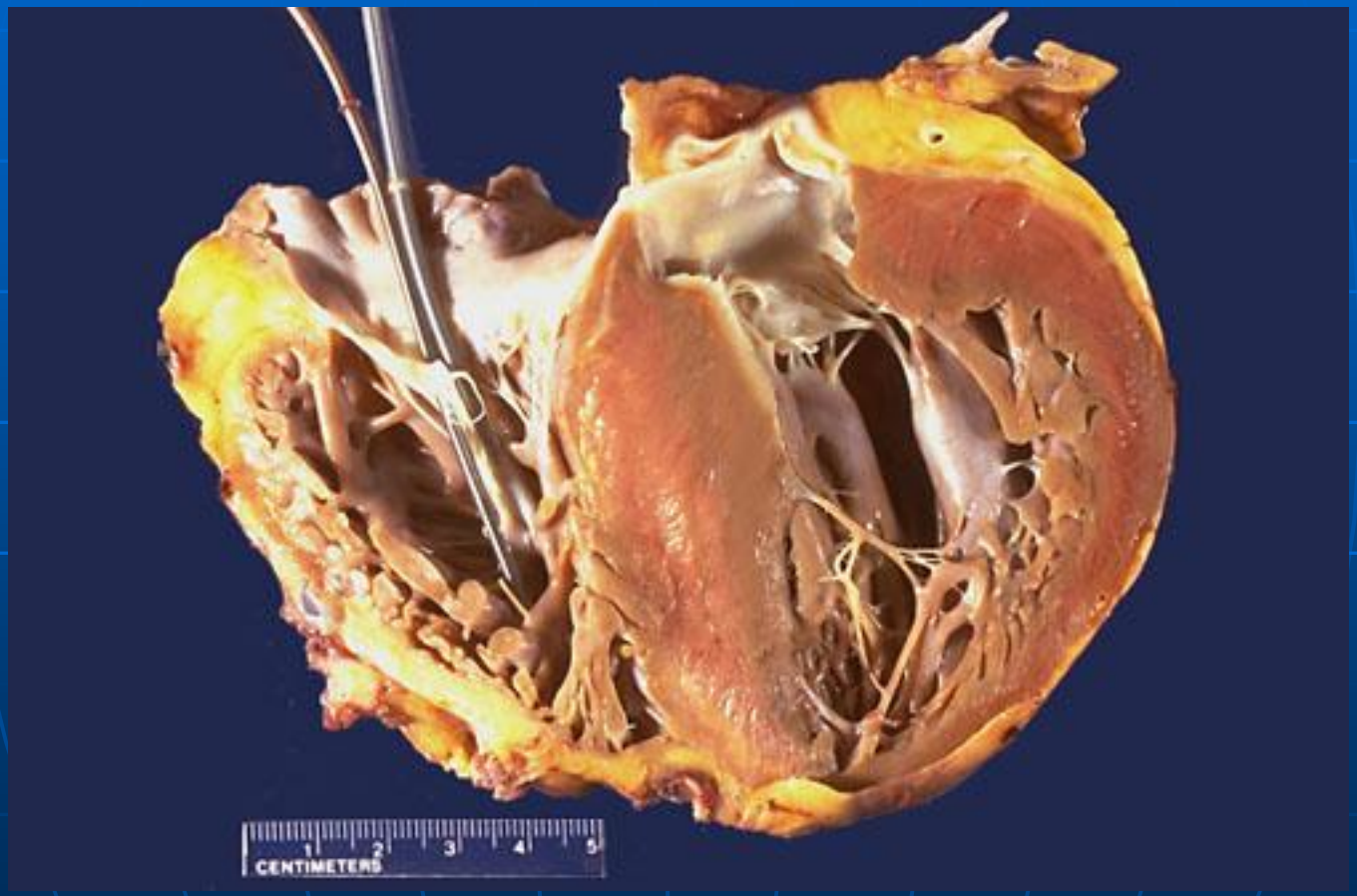
Mechanism of hypertrophy

Whatever the exact mechanism of hypertrophy is, it eventually reaches a limit beyond which enlargement of muscle mass is no longer able to compensate for the increased burden, and cardiac failure ensues. At this stage, a number of "degenerative" changes occur in the myocardial fibers, of which the most important are lysis and loss of myofibrillar contractile elements. The limiting factors for continued hypertrophy and the causes of the cardiac dysfunction are poorly understood; they may be due to limitation of the vascular supply to the enlarged fibers, diminished oxidative capabilities of mitochondria, alterations in protein synthesis and degradation, or cytoskeletal alterations.

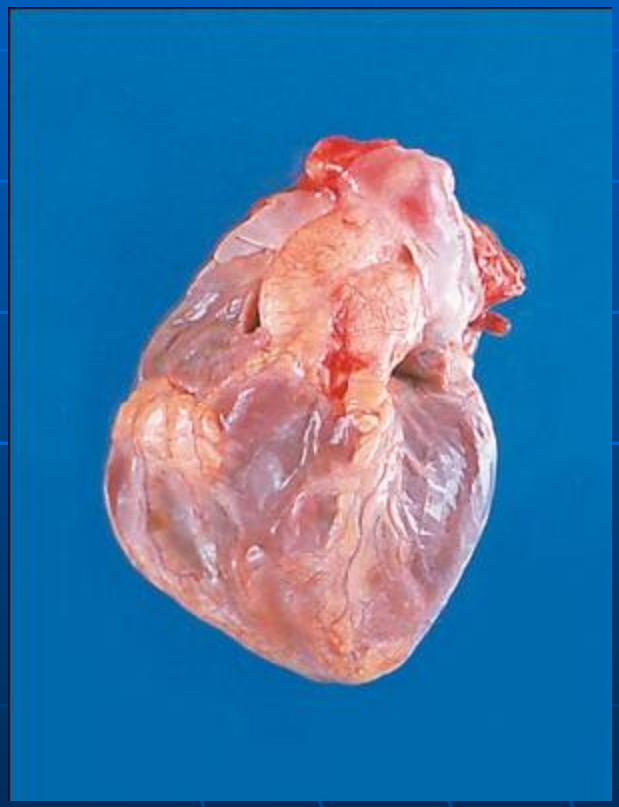
- **Pathological hypertrophy.** There is enlargement of mass and volume of organ, but it isn't compensatory reaction. It is feature of disease. Such types of growths leading to the increasing of size of tissues and organs appears in chronic inflammation, disturbances of lymph circulation or lymphostasis.

- **False hypertrophy** is enlargement of fat tissue and fibrous tissue instead atrophic functioning tissue. It is **not hypertrophy.**

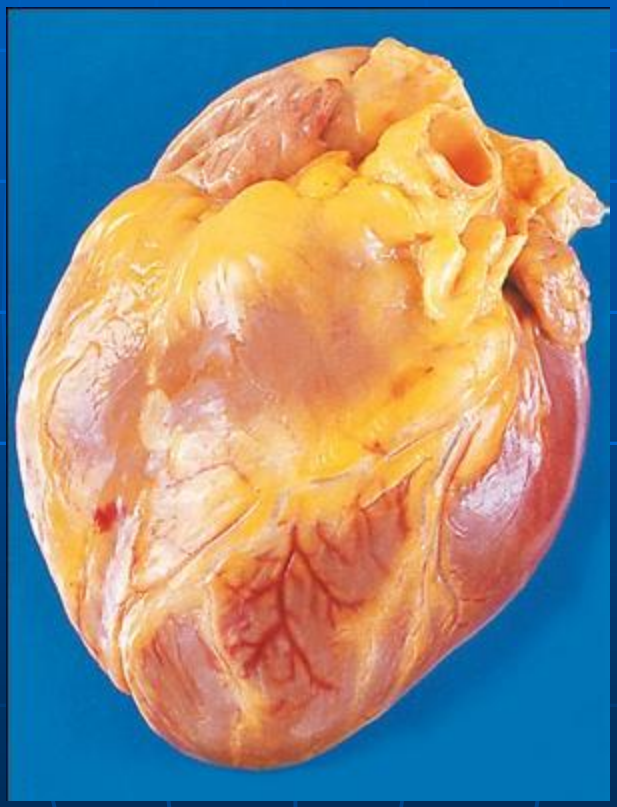
Hypertrophic cardiomyopathy



Norm

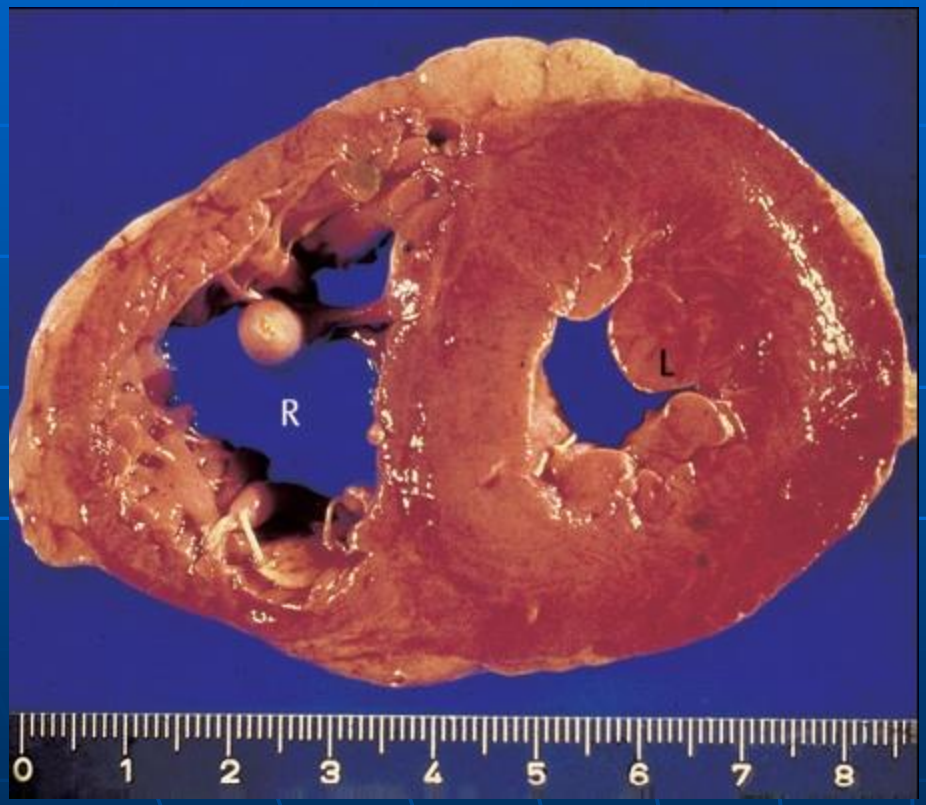


Hypertrophy



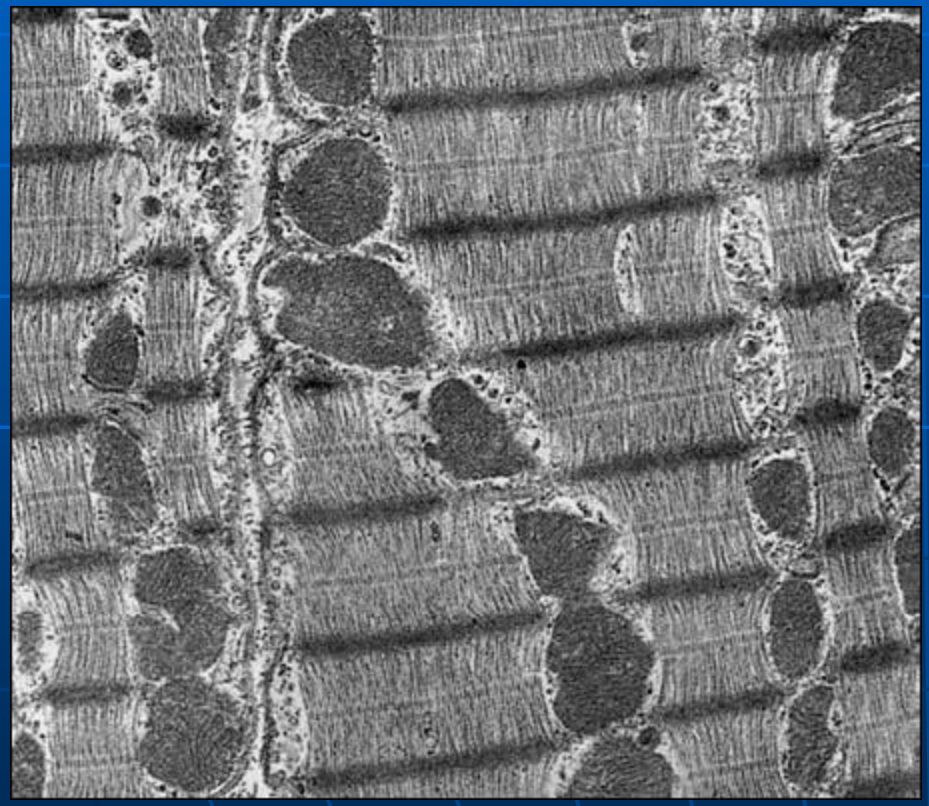
Norm

Hypertrophic cardiomyopathy



Toludin Blue. X 75.

Norm



Hypertrophy

HYPERPLASIA

Hyperplasia constitutes an increase in the number of cells in an organ or tissue, which may then have increased volume. Hypertrophy (increase in cell size) and hyperplasia are closely related and often develop concurrently

Hyperplasia can be physiologic and pathologic.

Physiologic hyperplasia can be hormonal hyperplasia (proliferation of the glandular epithelium of the female breast at puberty and during pregnancy).

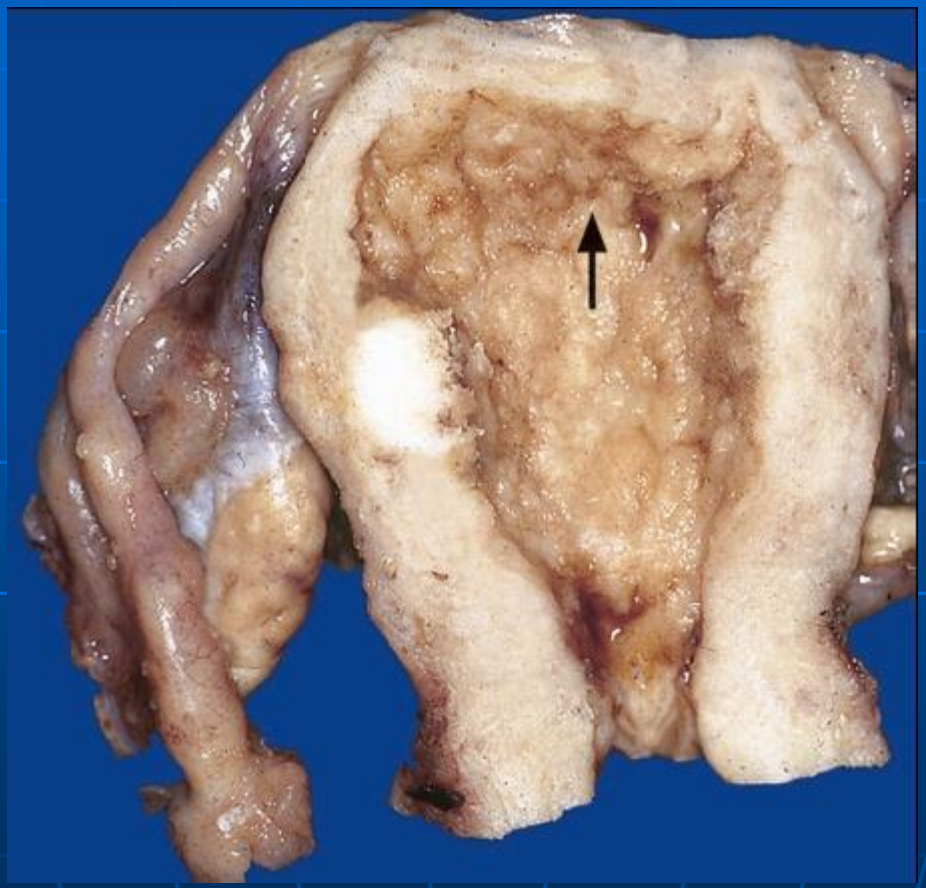
Pathologic hyperplasia can be divided into:

- 1) **hormonal hyperplasia** (hyperplasia of endometrium)
- 2) **reactive hyperplasia** (lymph node)
- 3) **compensatory hyperplasia**

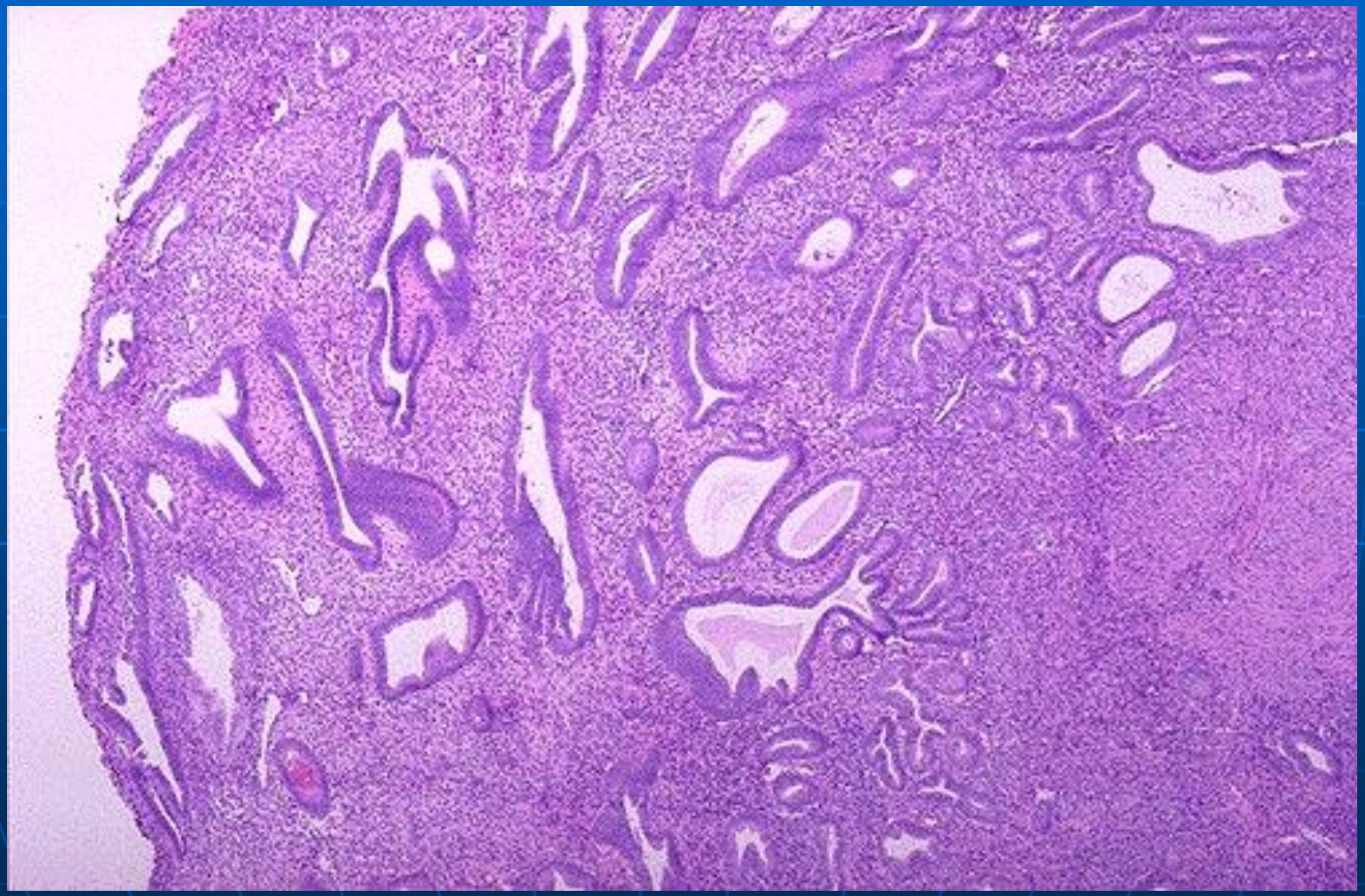
Hormonal hyperplasia

After a normal menstrual period, there is a rapid burst of proliferative activity, which might be viewed as reparative proliferation or physiologic hyperplasia in the endometrium. As is well known, this proliferation is potentiated by pituitary hormones and ovarian estrogen. It is brought to a halt by the rising levels of progesterone, usually about 10 to 14 days before the anticipated menstrual period. In some instances, however, the balance between estrogen and progesterone is disturbed. This results in absolute or relative increases in the amount of estrogen, or both, with consequent hyperplasia of the endometrial glands.

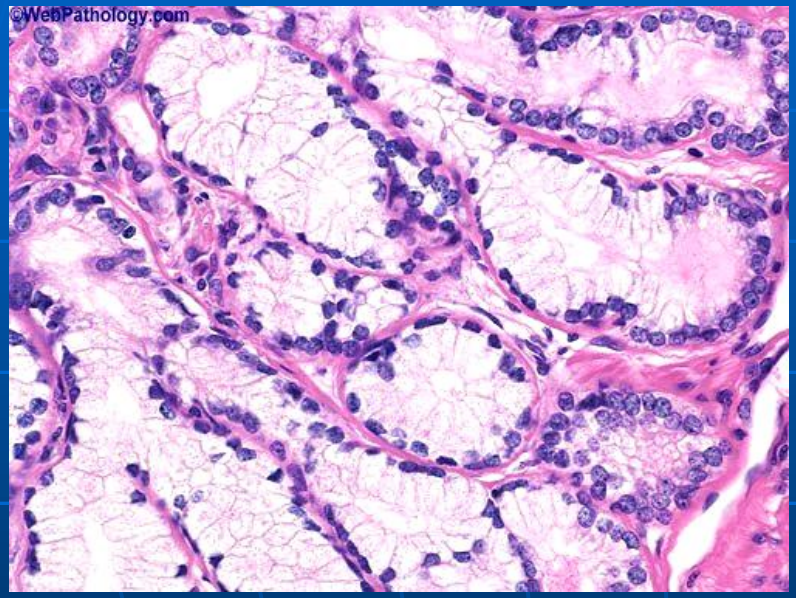
Hyperplasia of endometrium

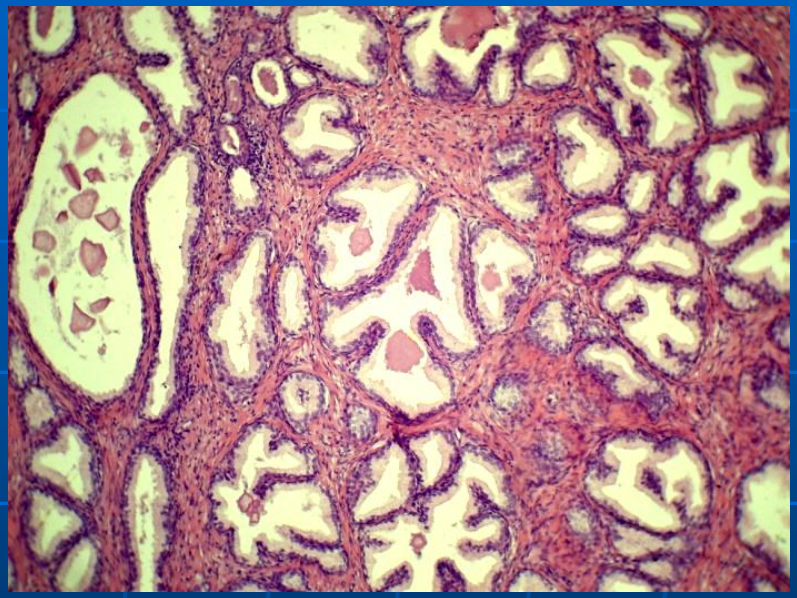


Hormonal hyperplasia

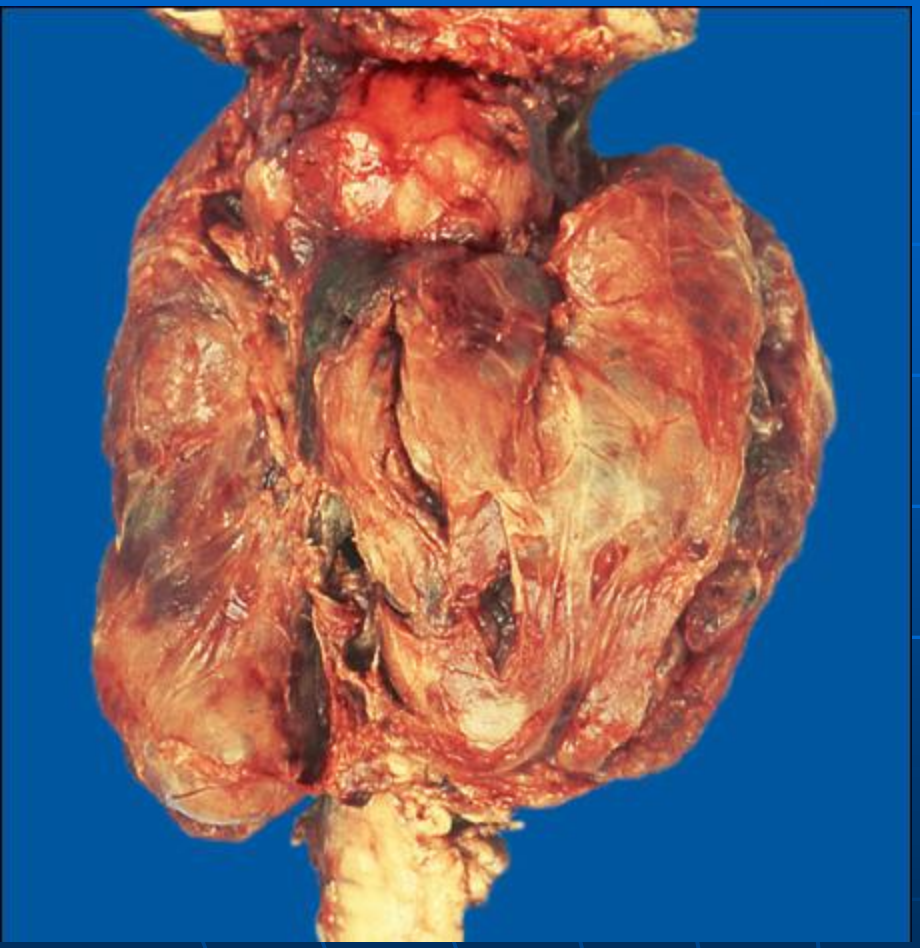


Hormonal hyperplasia

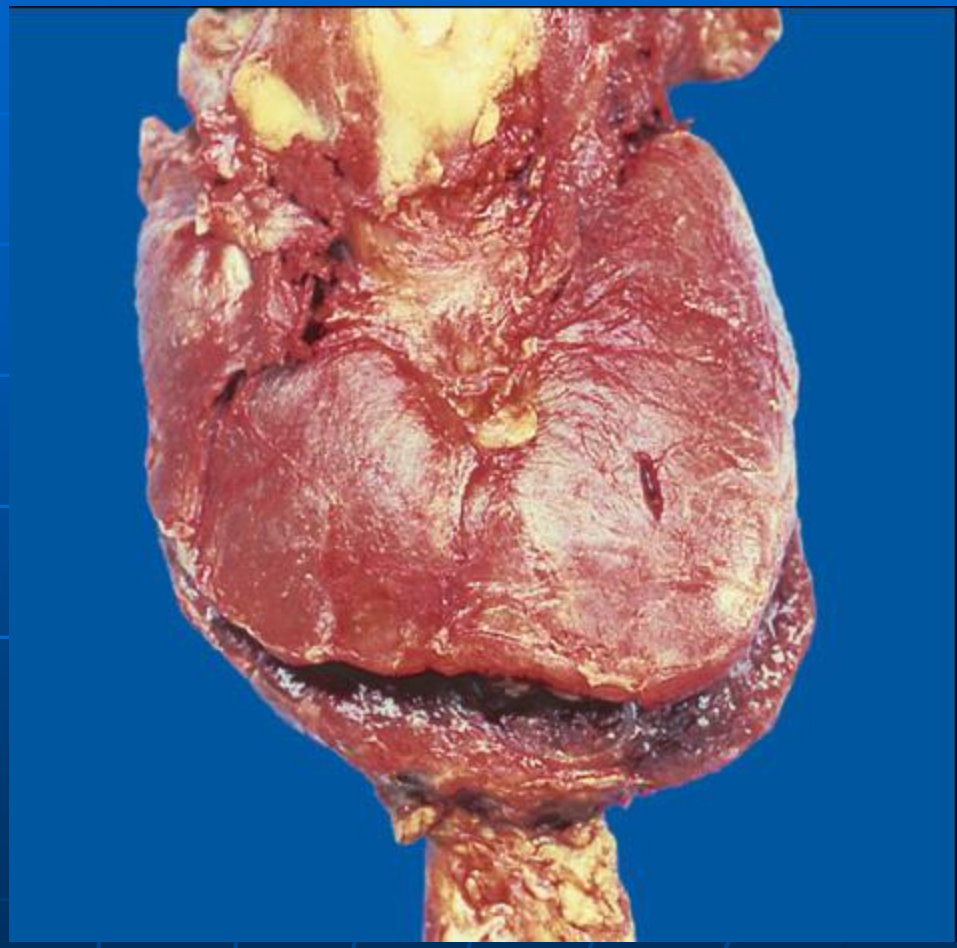




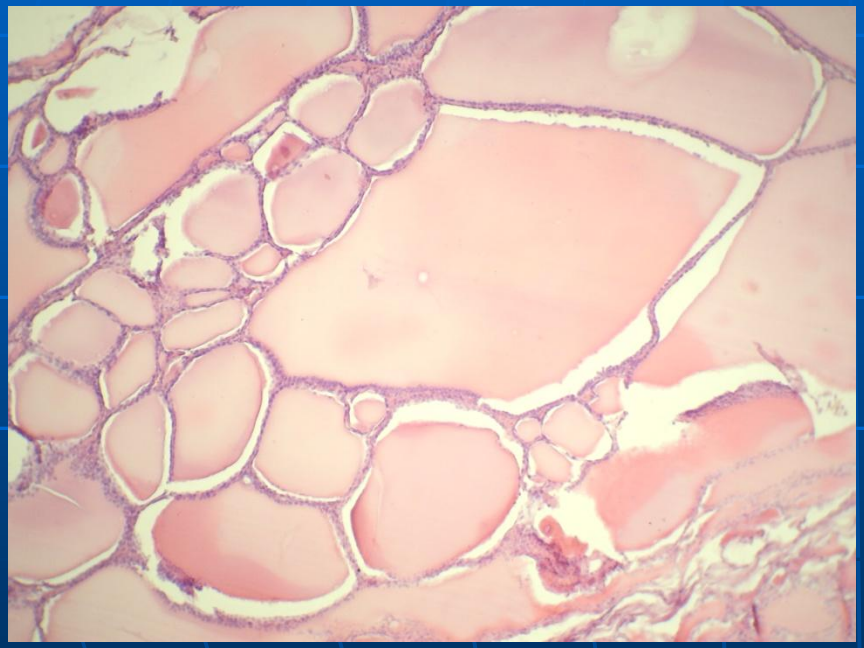
Nodular goiter

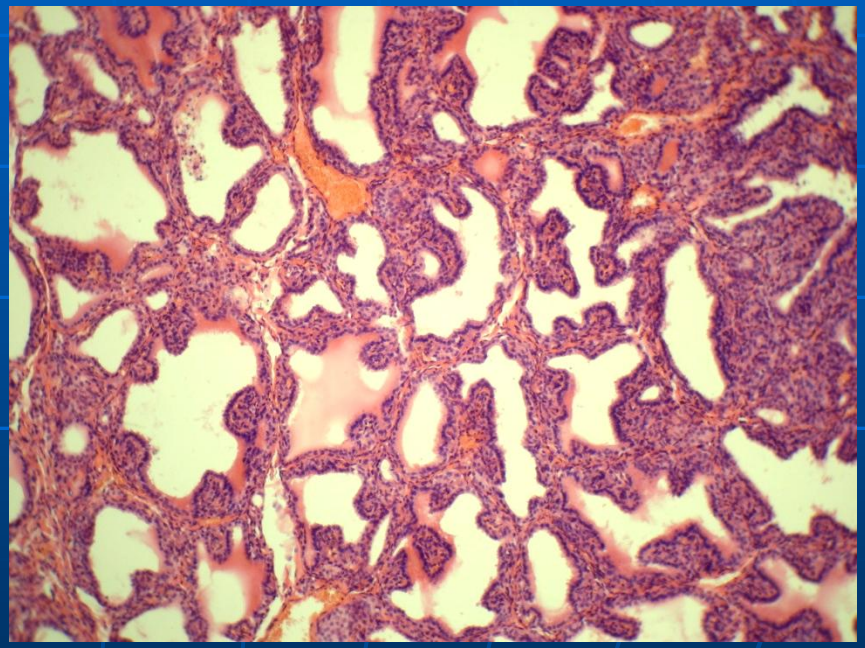


Diffuse goiter

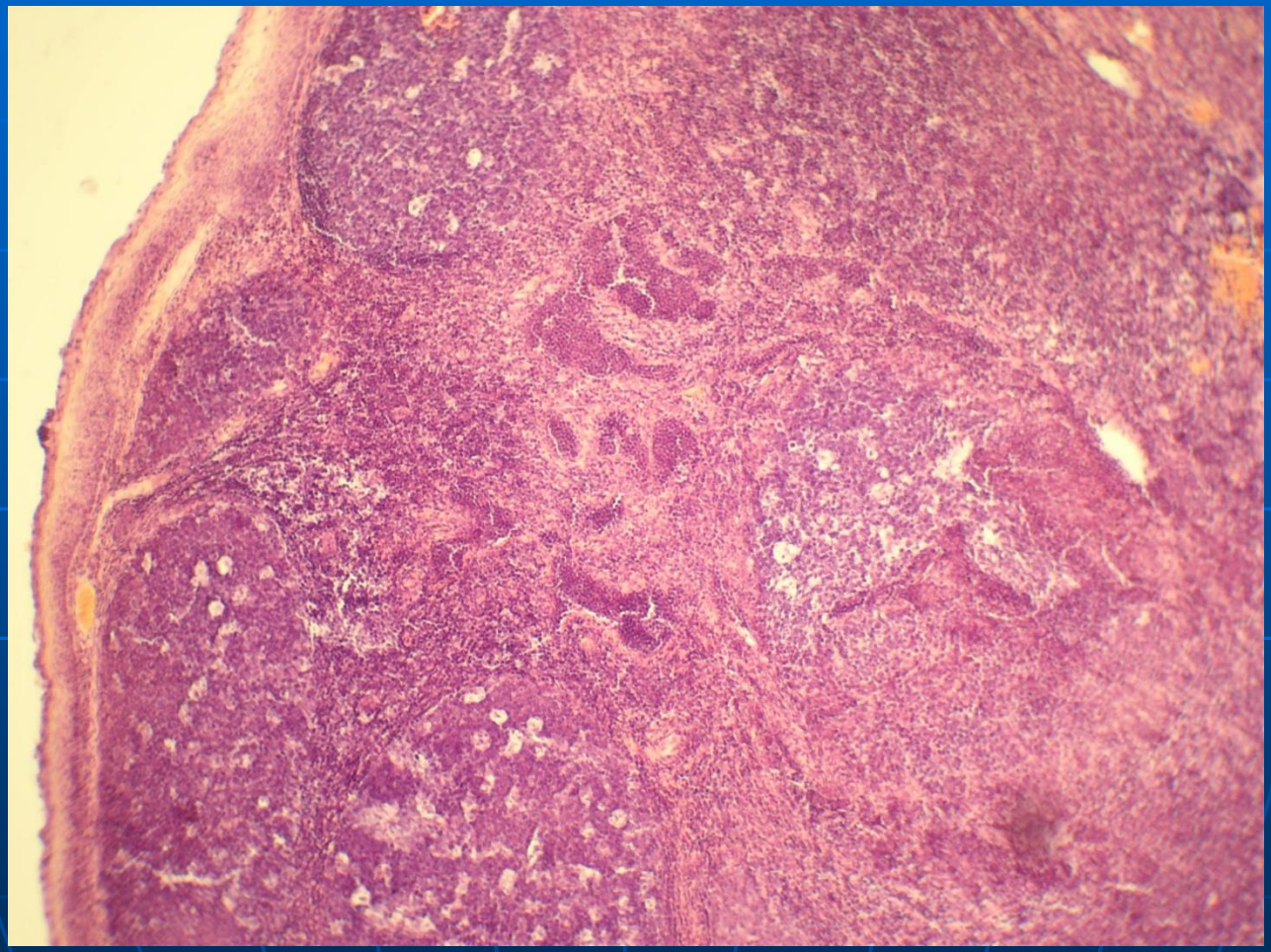


Hormonal hyperplasia





Reactive hyperplasia



Reactive hyperplasia of lymphoid tissue of tonsil

Compensatory hyperplasia

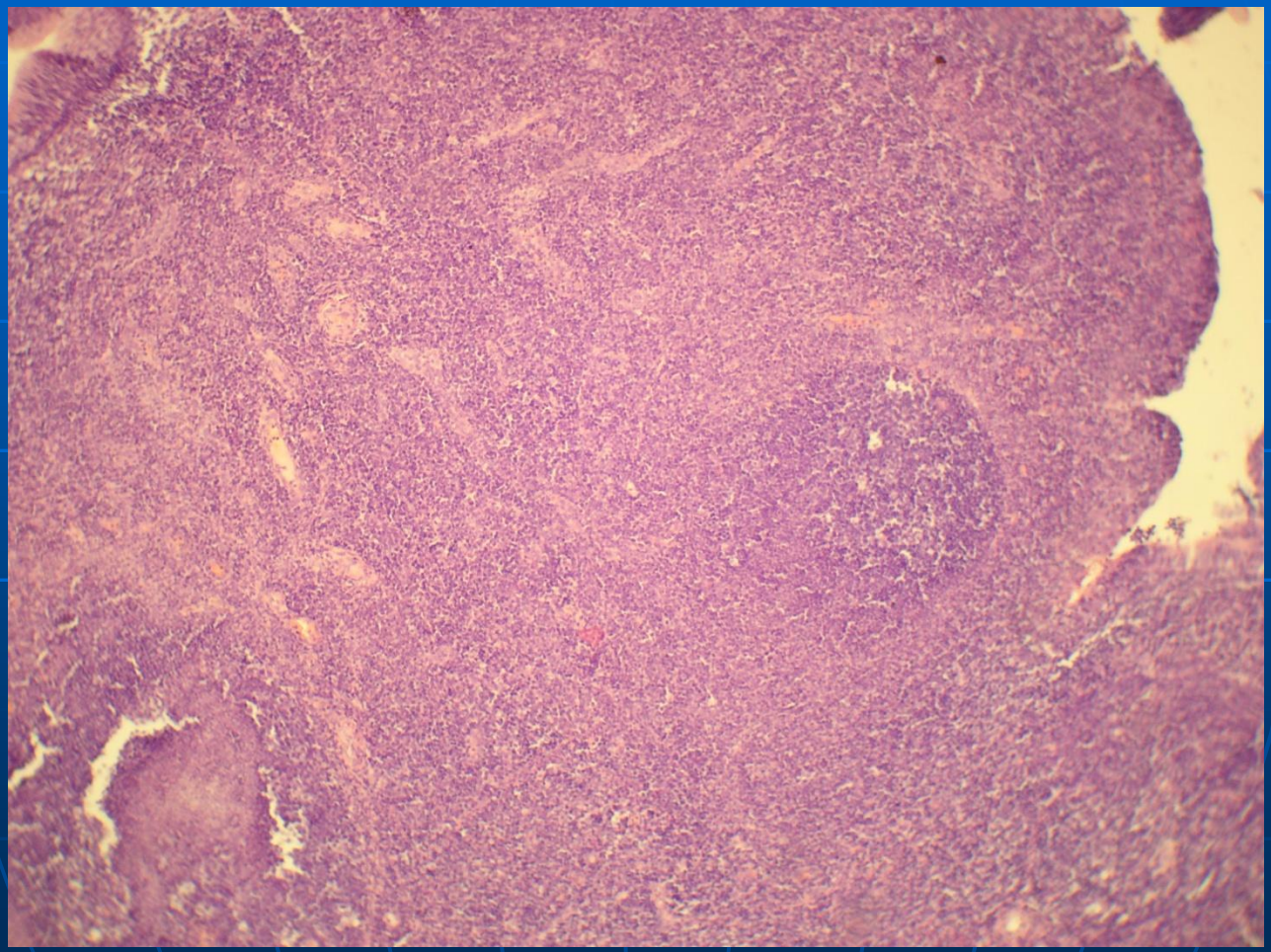
- It is found during long term regeneration, e.g. in the red bone marrow during anemia.
- Compensatory hyperplasia may be found together compensatory hypertrophy, e.g. pyloric stenosis, hypertrophy of muscular layer of urinary bladder due to enlargement of prostate.

REGENERATION.

- The cells of the body can be divided into three groups according to their capacity to regenerate.
- 1. Labile cells continue to multiply throughout the life, even under normal physiological conditions. They include the epithelial cells of the skin and mucous membranes and the cells of the bone marrow and lymph nodes.
- 2. Stable cells have a decrease or loss of ability for physiologic regeneration in adolescence but retain the ability to proliferate throughout adult life. They include parenchymatous cells of the liver, pancreas, kidney, adrenal, and thyroid.
- 3. Permanent cells lose their ability to proliferate around the time of birth. The most important example is the neuron in the central nervous system.

- There are three types of regeneration:
- **physiological**,
- **reparative**,
- **pathological**.

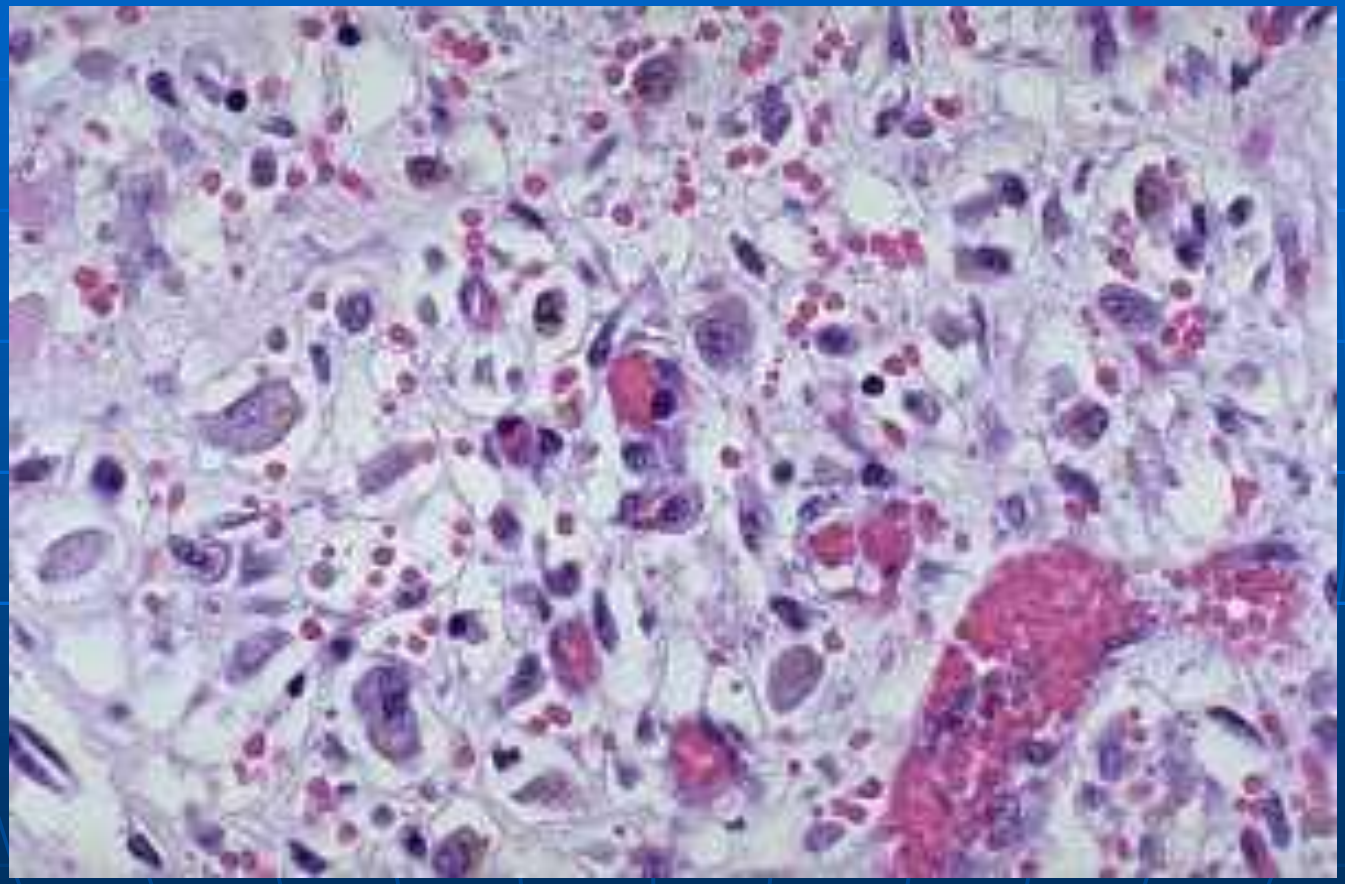
Physiological regeneration

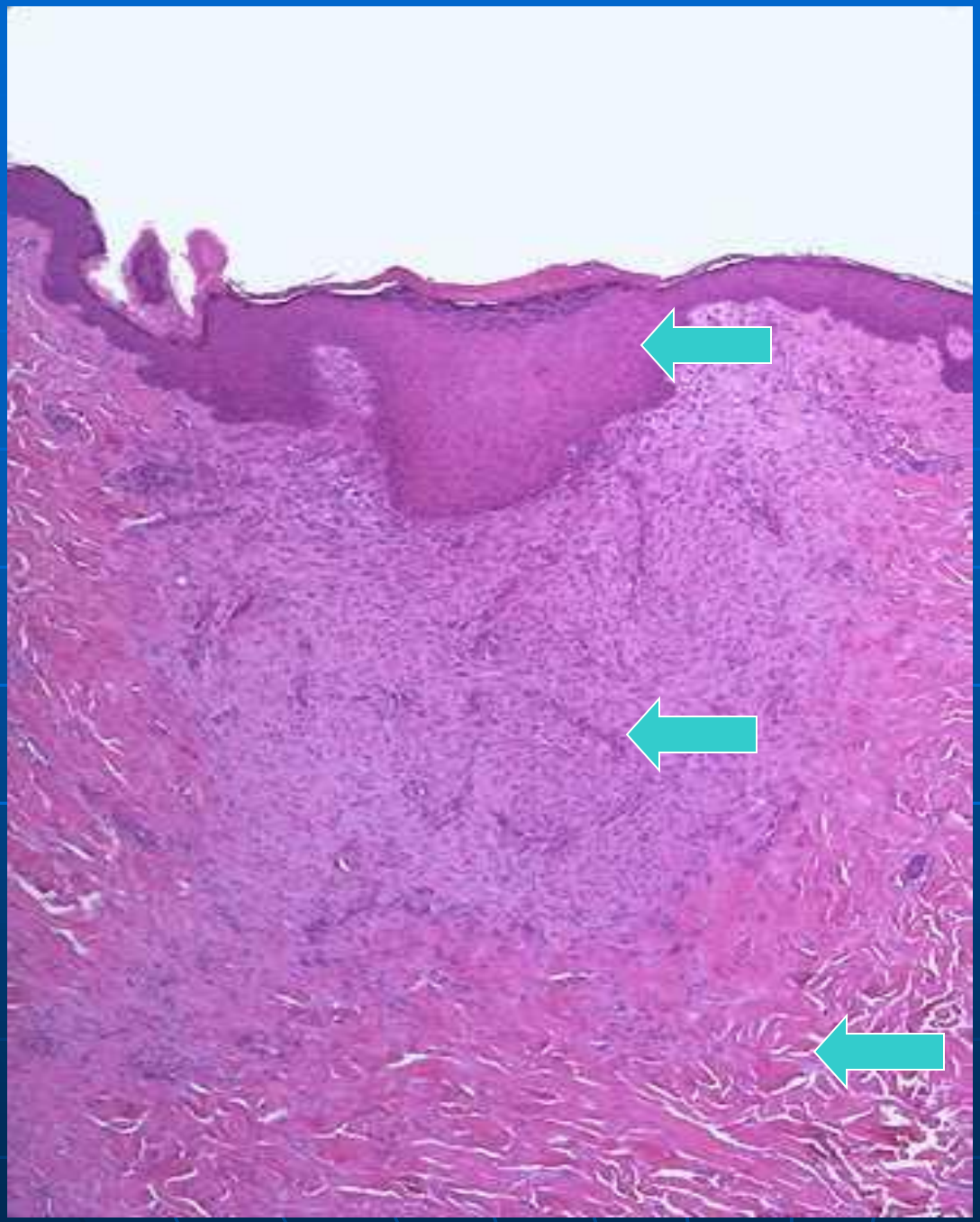


- **Physiologic regeneration** takes place during the whole life and is characterized by permanent renewal of the cells, fibrotic structures and matrix of connective tissue.
- **Reparative (restoration) regeneration** takes place in different pathological processes leading to damage of the cells and tissues. Complete regeneration or restitution is characterized by restoration of tissue defect with the tissue which is identical to the lost tissue. Uncompleted regeneration or substitution is connected with replacement of the dead tissue by connective tissue or scar.
- **Pathologic regeneration** is connected with perversion of regeneratory process and breach of phases of proliferation and differentiation.

- Morphogenesis of the regeneratory process consists of two phases: proliferation and differentiation. In proliferative phase young, undifferentiated cells (cambial cells, stem sells, cells-precusors) proliferate.

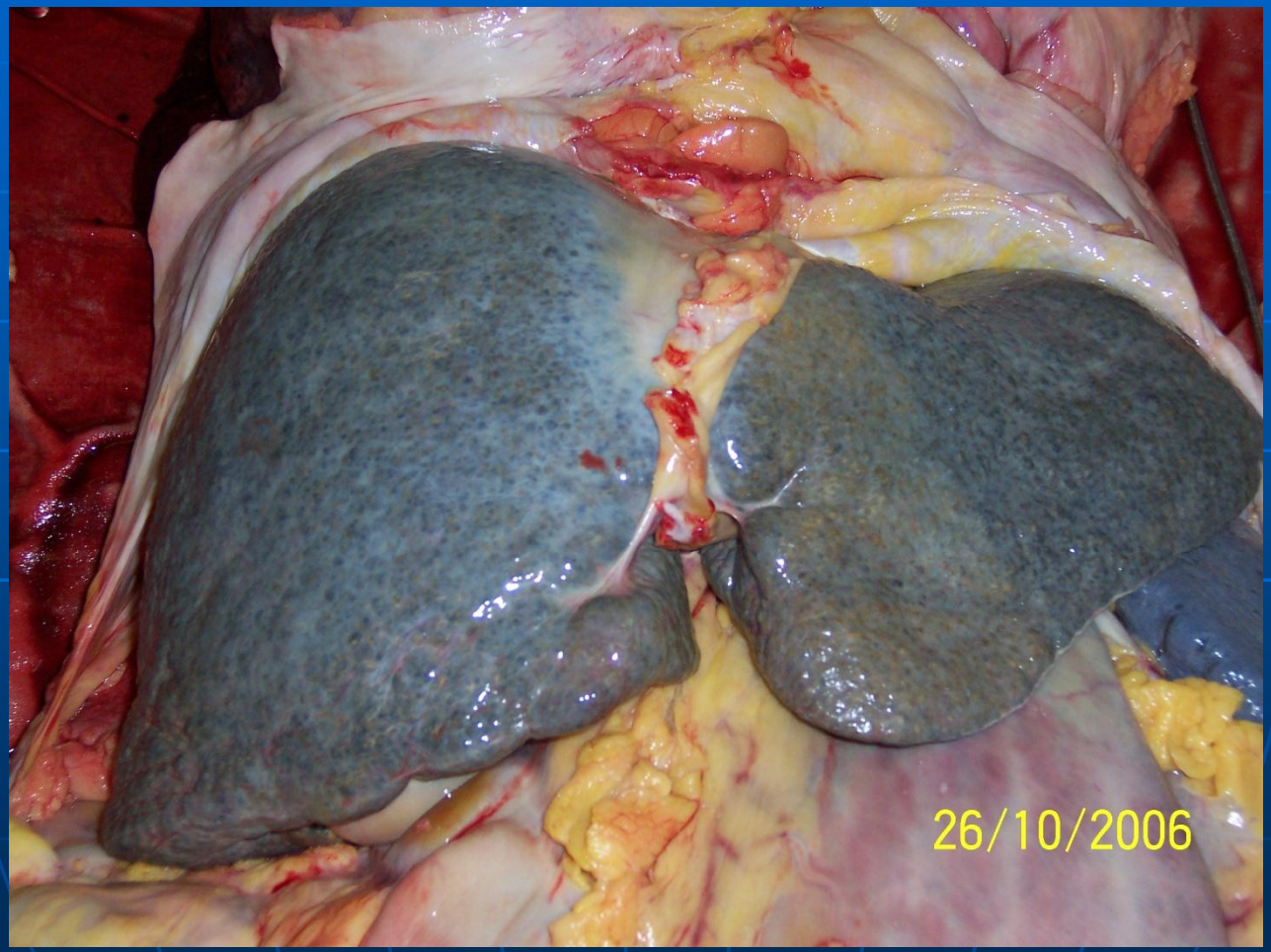
Granulation tissue

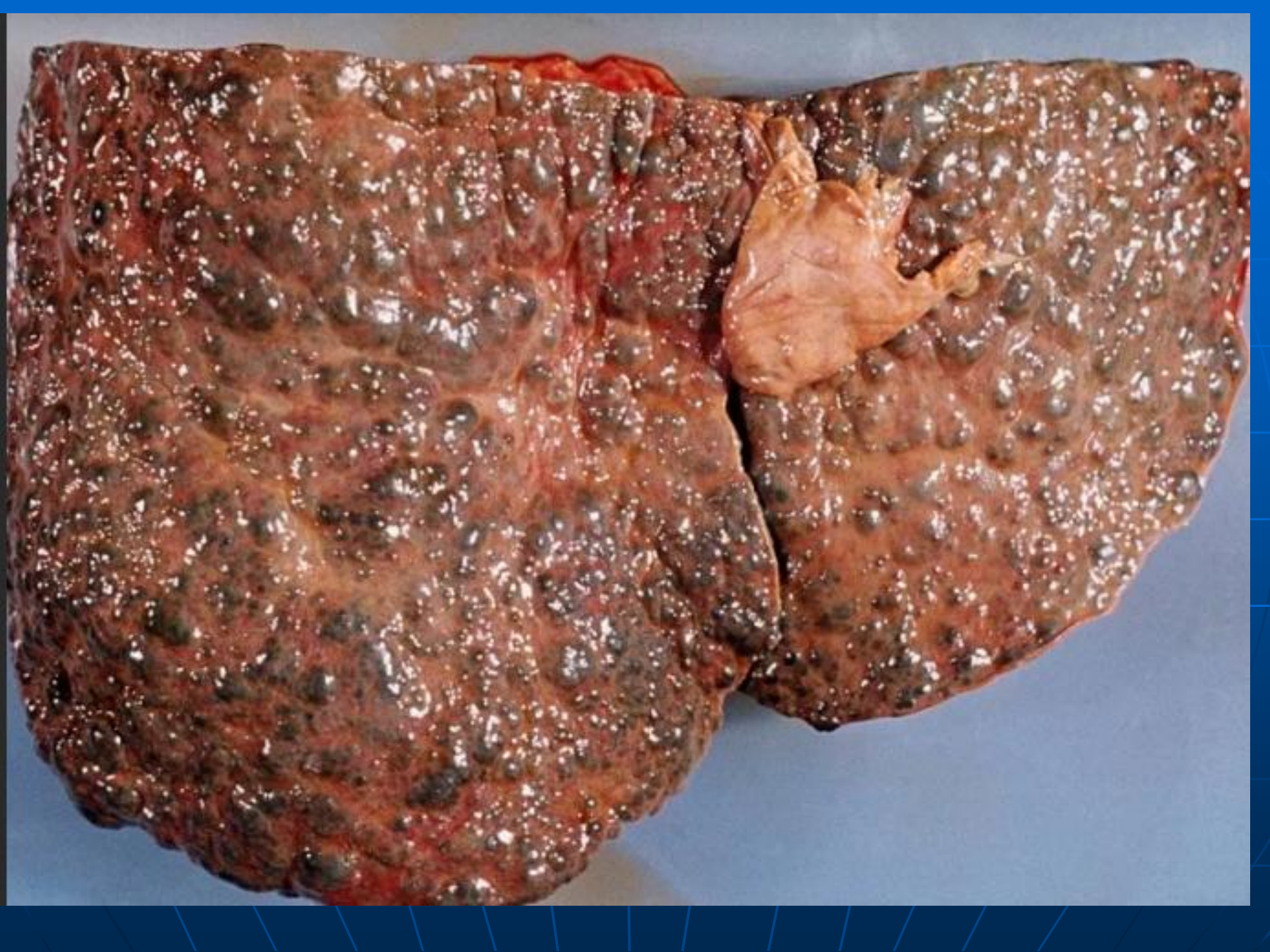




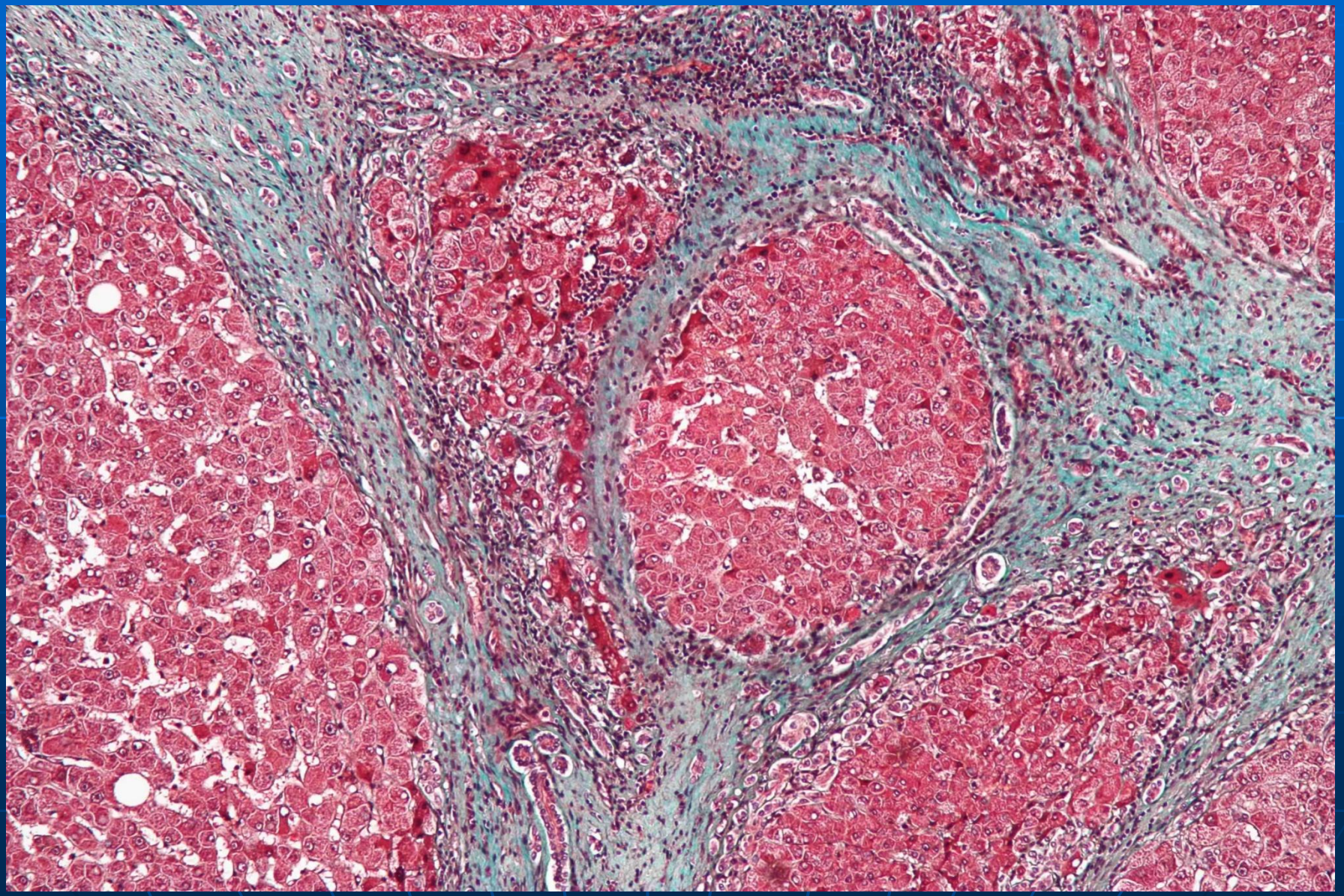
Wound healing in the skin

Liver cirrhosis





Liver cirrhosis



METAPLASIA

- Metaplasia is a reversible change in which one adult cell type (epithelial or mesenchymal) is replaced by another adult cell type.
- The most common adaptive change is columnar to squamous, as occurs in the respiratory tract in response to chronic irritation. In the habitual cigarette smoker, the normal columnar ciliated epithelium of the trachea and bronchi is often replaced focally or widely by stratified squamous epithelial cells. A deficiency of vitamin A (retinoid acid) induces squamous metaplasia in the respiratory epithelium, and vitamin A excess suppresses keratinization

Metaplasia

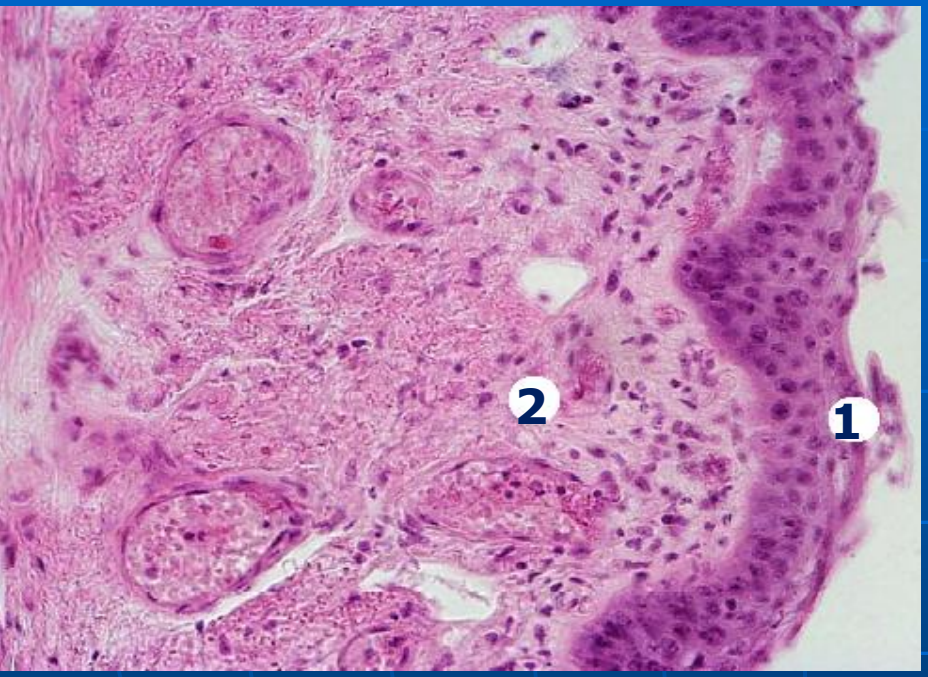
Metaplasia from glandular to squamous epithelium

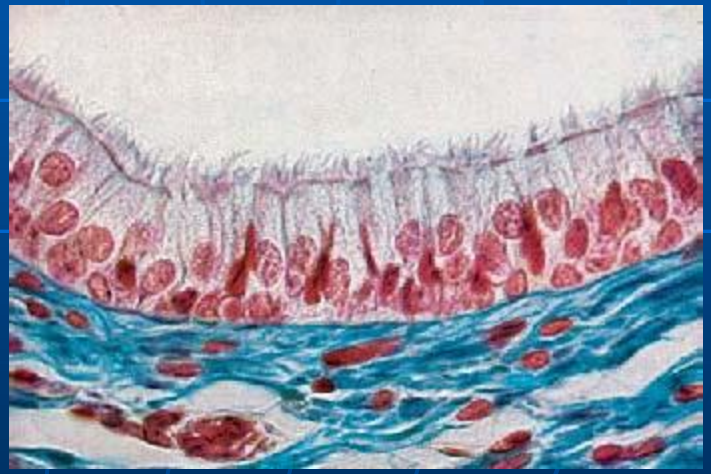
1) This occurs in the mainstem bronchus epithelium when pseudostratified columnar epithelium of the mainstem bronchus epithelium develops squamous metaplasia in response to irritants in cigarette smoke.

- There is an increased risk for developing squamous cancer of the mainstem bronchus.

2) Mucus-secreting endocervical cells encountering the acid pH of the vagina undergo squamous metaplasia.

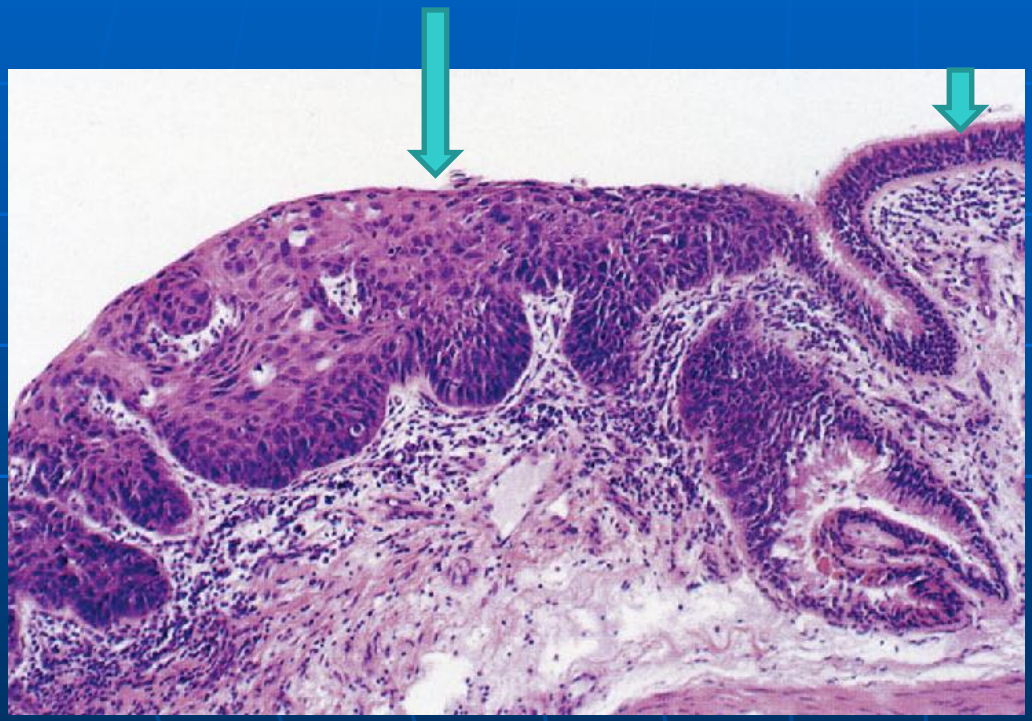
METAPLASIA





Replacement of respiratory epithelium of bronchus - 1. Productive inflammation -2

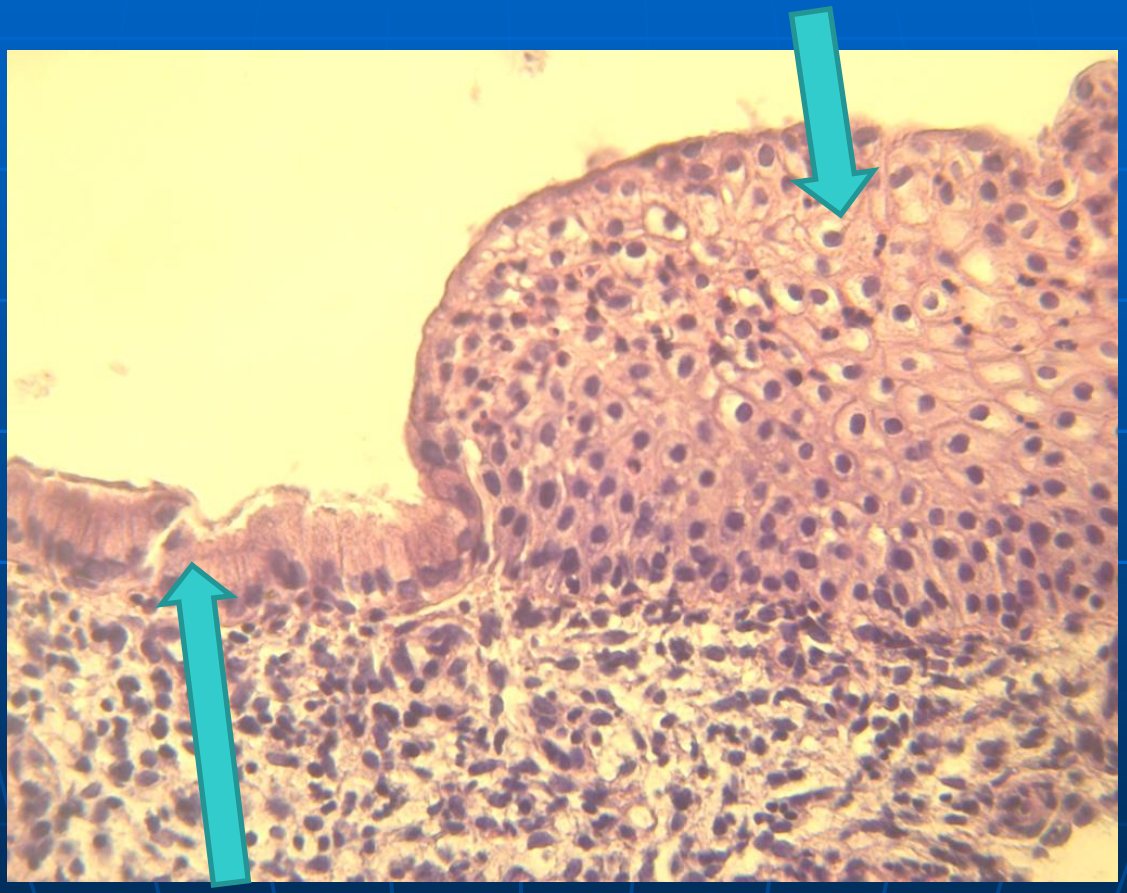
METAPLASIA



Section of bronchus from a smoker showing focal squamous metaplasia (*long arrow). Normal ciliated,* pseudostratified columnar epithelium is present on the right (*short arrow).*

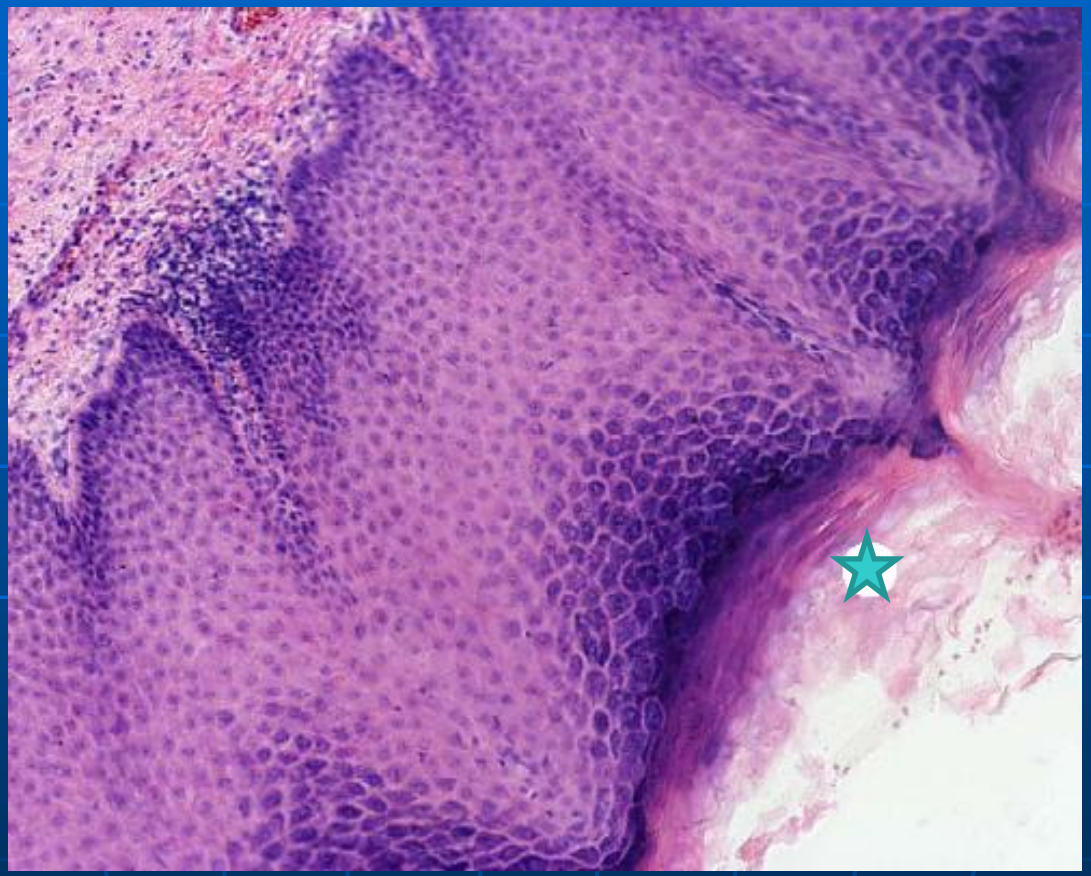
METAPLASIA

Normal stratified squamous non-keratinized epithelium



Ectropion - endocervicosis

METAPLASIA



Replacement of stratified squamous nonkeratinized epithelium of uterine cervix to stratified squamous keratinized epithelium (leucoplakia). - **keratin.**

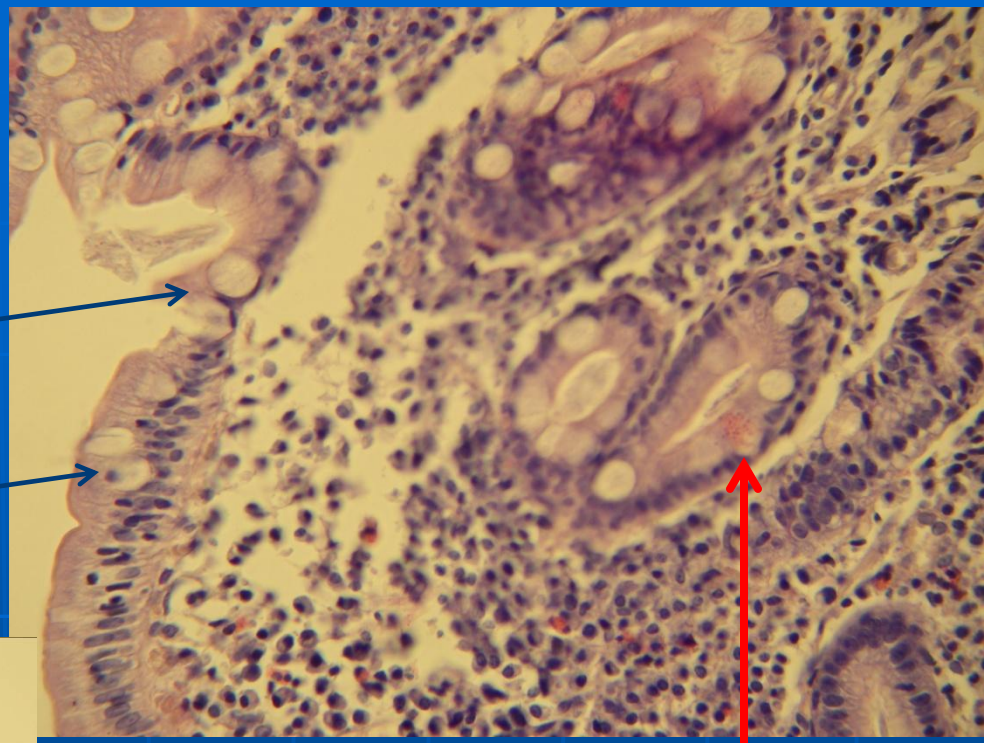
Metaplasia from glandular to other types of glandular epithelium

1) This occurs in the pylorus and antrum epithelium in the stomach when there is an infection caused by *Helicobacter pylori.*

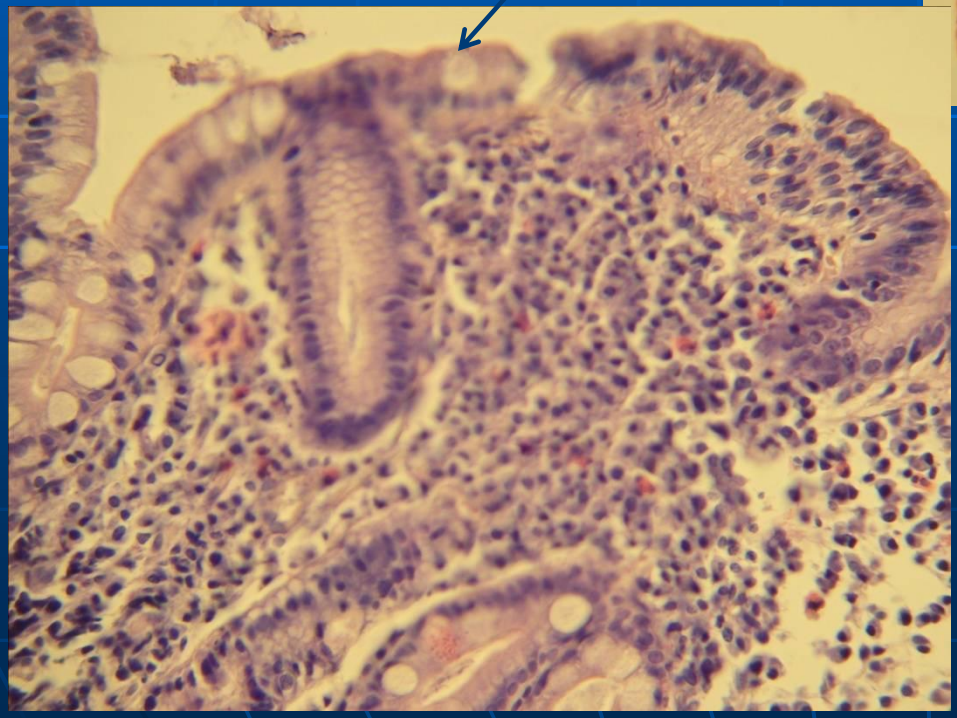
2) Inflammatory cytokines, which are released by the pathogen, produce a chronic gastritis that is characterized by an increase in the synthesis of goblet cells and Paneth cells; these cell types are normally present in intestinal epithelium (intestinal metaplasia).

3) In this type of chronic gastritis, there is an increased risk for developing a gastric cancer in the pylorus or antrum.

Intestinal metaplasia



goblet cells



Paneth cells

stomach

Dysplasia

1. Definition—disordered cell growth
   - Potential precursor to cancer if the irritant is not removed
2. Risk factors for developing dysplasia
   a. Some types of hyperplasia (e.g., endometrial gland hyperplasia)
   b. Some types of metaplasia (e.g., Barrett esophagus)
   c. Infection
      - Example—HPV types 16 and 18 causing squamous dysplasia of the cervix

   d. Chemicals
      - Example—irritants in cigarette smoke, causing squamous metaplasia to progress to squamous dysplasia in the mainstem bronchus

   e. Ultraviolet (UV) light
      - Example—solar damage of the skin, causing squamous dysplasia

   f. Chronic irritation of skin
      - Example—skin in a third degree burn developing squamous dysplasia

Microscopic features of dysplasia

a. Nuclear features of dysplasia

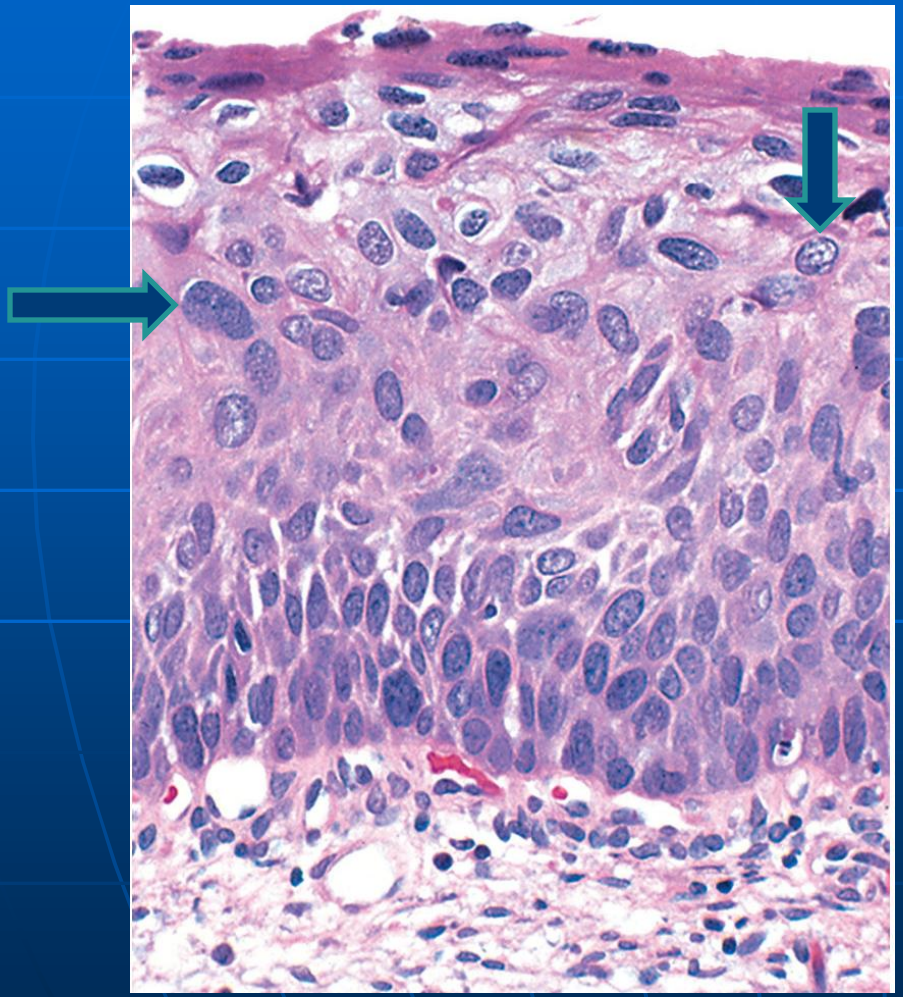
1) Increased mitotic activity, with *normal mitotic spindles*

2) Increased nuclear size and chromatin

b. Disorderly proliferation of cells with loss of cell maturation as cells progress to the surface

- Dysplasia may involve squamous, glandular, or transitional epithelium.
- Dysplasia is sometimes reversible if the irritant is removed.

Dysplasia

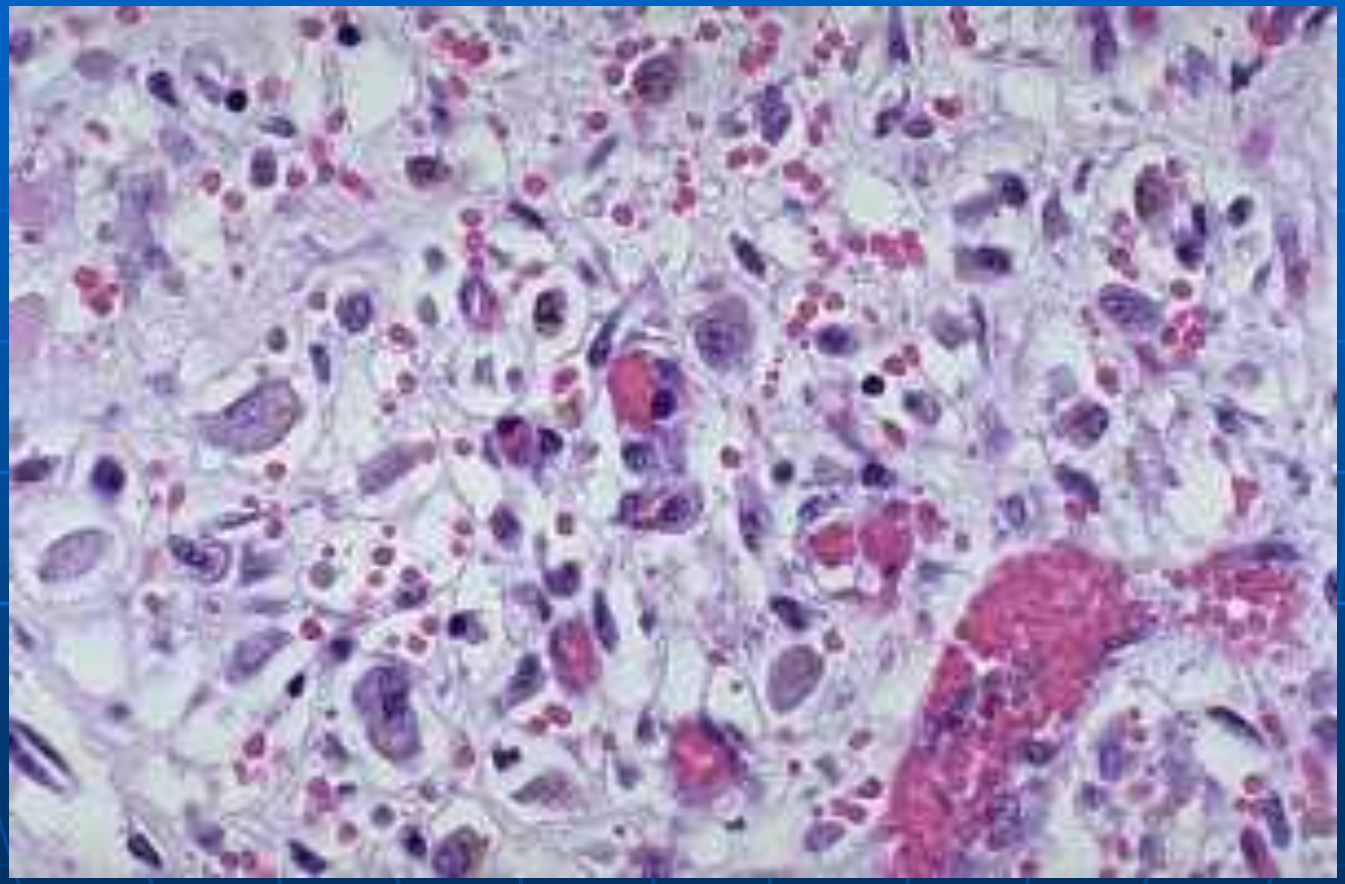


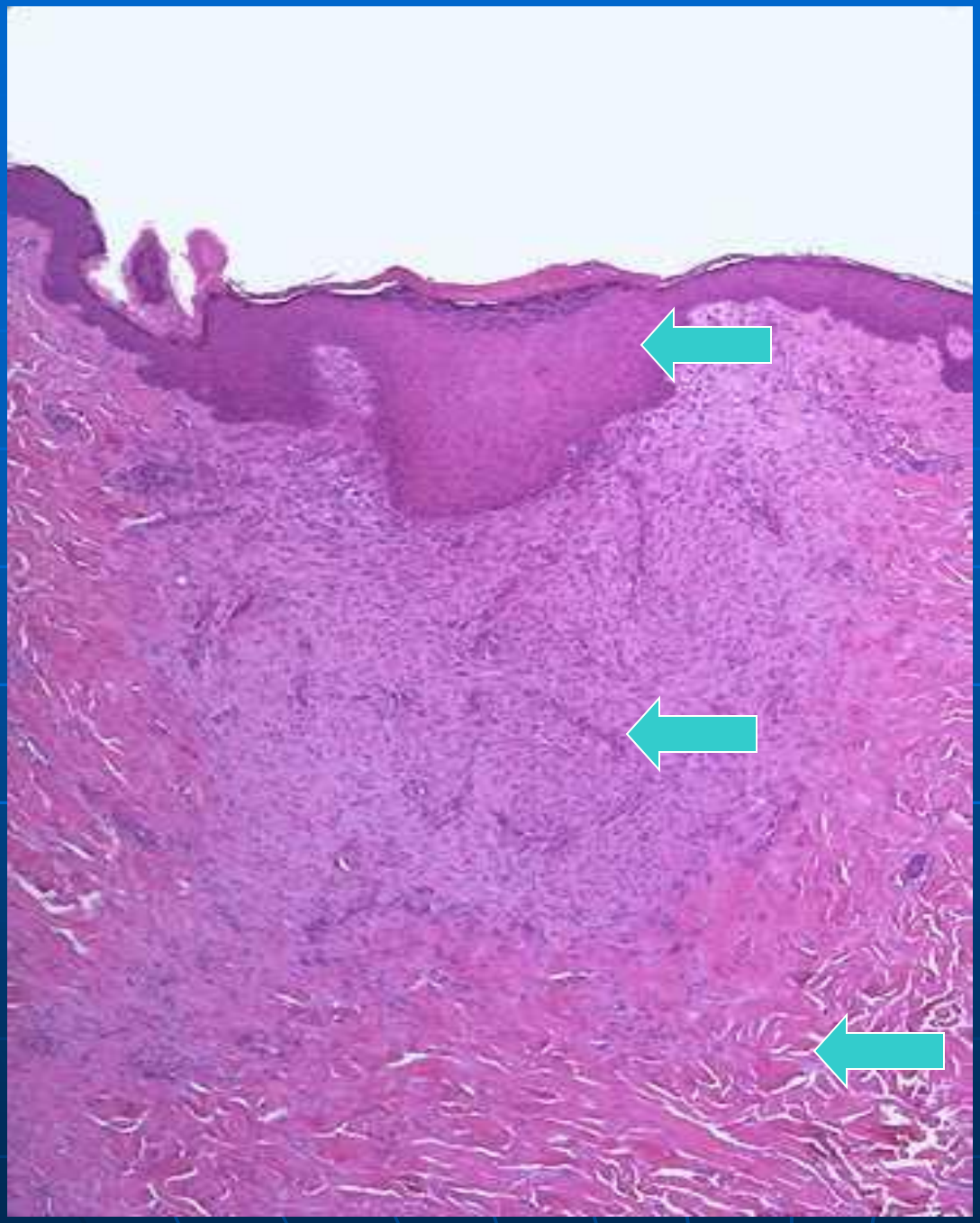
Dysplasia of the cervix, a precursor of squamous cell carcinoma. There is a lack of orientation of the squamous cells throughout the lower two thirds of the epithelium. Many of the nuclei are enlarged (*arrows), are hyperchromatic,* and have irregular nuclear margins.

Stages of Healing:

- Hemorrhage
- Inflammation
- Granulation tissue (soft callus)
- Scar – Fibrosis (hard callus)
- Remodeling & Wound strength

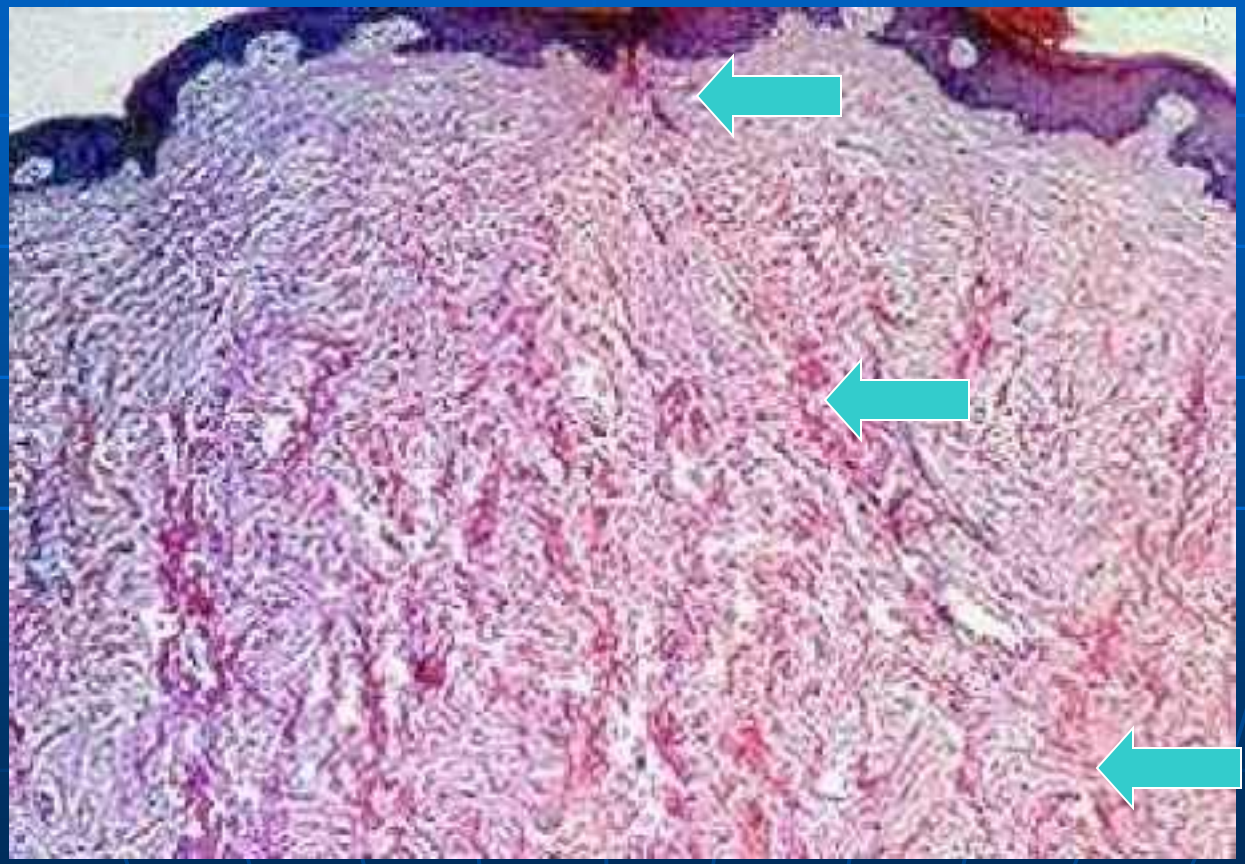
Granulation tissue





Healing Skin wound

Healing - Skin Scar



Factors affecting Healing:

Systemic

- Nutrition
- Vitamin def.
- Age
- Immune status
- Other diseases

Local

- necrosis
- Infection
- apposition
- Blood supply
- Mobility
- Foreign body

WOUND HEALING

- The least complicated example of wound repair is the healing of a clean, uninfected surgical incision approximated by surgical sutures. Such healing is referred to as primary union or healing but first intention. The incision causes death of a limited number of epithelial cells and connective tissue cells as well as disruption of epithelial basement membrane. The narrow incisional space is immediately filled with clotted blood containing fibrin and blood cells. Within 24 hours, neutrophils appear at the margins of the incision moving toward the fibrin clot Within 24 to 48 hours spurs of epithelial cells from the edges both migrate and grow along the cut margins of the dermis, depositing basement membrane components as they move.

WOUND HEALING

- By day 3 the neutrophils have been largely replaced by macrophages. Granulation tissue progressively invades the incision space. Epithelial cell proliferation continues, thickening the epidermal covering layer. By day 5 the incisional space is filled with granulation tissue. Neovascularization is maximal. Collagen fibrils become more abundant and begin to bridge the incision. During the second week, there is a continued accumulation of collagen and proliferation of fibroblasts. The leukocytic infiltrate, edema, and increased vascularity have largely disappeared. By the end of the first month, the scar comprises a cellular connective tissue devoid of inflammatory infiltrate, covered now by intact epidermis.

Secondary healing differs from primary healing in several respects:

- 1. Inflammatory reaction is more intensive.
- 2. Much larger amounts of granulation tissue are formed.
- 3. Perhaps the feature that most clearly differentiates primary from the secondary healing is the phenomenon of wound contraction, which occurs in large surface wounds. Contraction has been ascribed to the presence of myofibroblasts - altered fibroblasts that have the ultrastructural characteristics of smooth muscle cells.

Thank You!