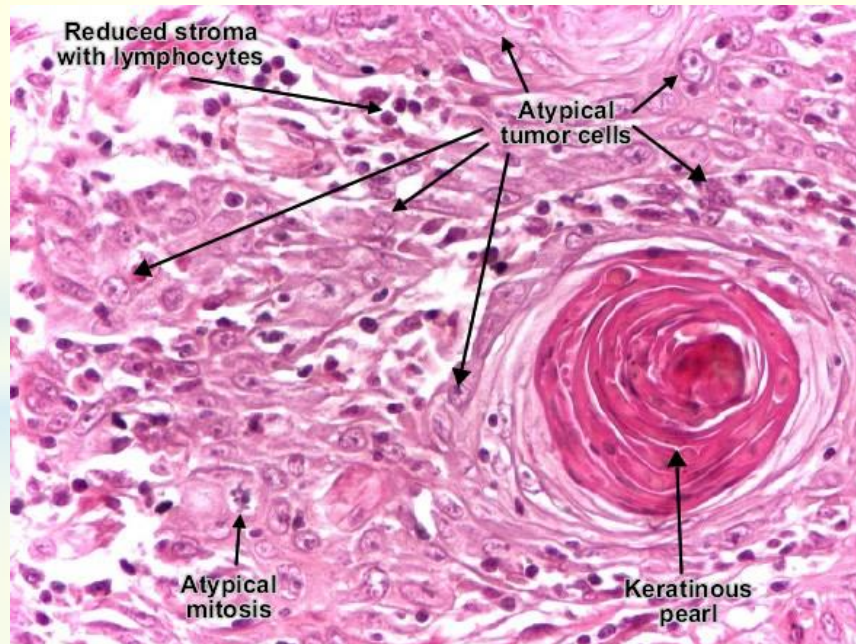


NATIONAL UNIVERSITY OF PHARMACY
DEPARTMENT OF PATHOLOGICAL PHYSIOLOGY

***DISTURBANCES OF
TISSUE GROWTH. TUMOR***



1. Hyperbiotic processes: hypertrophy, hyperplasia, regeneration, tumors.
2. Hypobiological processes: atrophy, dystrophy, degeneration.
3. Tumors: definition, etiology.
4. Pathogenesis of tumor growth.
5. Benign and malignant tumors.
6. Metastasis: definition, types.
7. Clinical stages of cancer.

***PLAN OF
LECTURE**

*** Questions of Independent work**

Tumors. General characteristics, biological features, etiology, mechanisms of tumor transformation.

*Suggested Reading

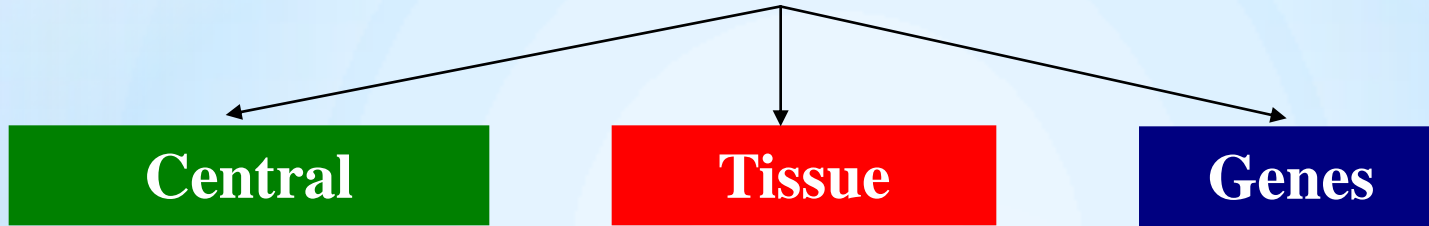
Basic

1. General and clinical pathophysiology/ Editor by Anatoliy V. Kubyshkin. - Vinnytsa : Nova Knyha Publishers, 2016. - 656 p.
2. Lecture notebook pathological physiology. Manual for working in lectures / N.M. Kononenko, S.I. Kryzhna, V.A. Volkovoy et al.; Kh.: NPhaU, 2013. - 99 p.
3. Pathological Physiology: The textbook for the students of higher pharmaceutical educational institutions and pharmaceutical faculties of higher medical educational institutions III-IV levels of accreditation / S/I/ Kryzhna, N.M. Kononenko, I.Yu. Tishenko et al.: under edition of the professor A.I. Bereznyakova. - Kharkiv: NphaU, 2006. - 416 p.

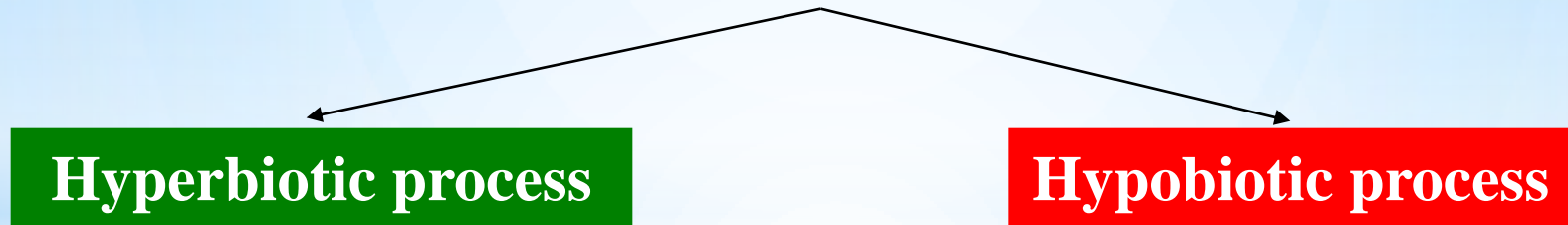
Auxiliary

1. Professional guide to Pathophysiology / M.H. Birney, C. L. Brady, K.T. Bruchak et al. - Lippincott Williams and Wilkins. - 2002. - 696 p.
2. Crowley L.V. An introduction to human disease: pathology and pathophysiology correlations / L.V. Crowley . - London : Lones and Bartlett Publishers International Bard House. 2001. - 790 p.

There are three levels of regulation



Disturbance of tissue growth



**The processes excessive
growth and reproduction
cells and tissues**

**The processes insufficient
growth and reproduction
cells and tissues**

Central regulatory influences

- **nervous (central and peripheral links, neurotropic effects are of particular importance);**
- **endocrine (endocrine glands and APUD-system cells);**
- **immune (central and peripheral immunocompetent organs; especially the cooperation of macrophages, T- and B-lymphocytes).**

Tissue regulatory influences

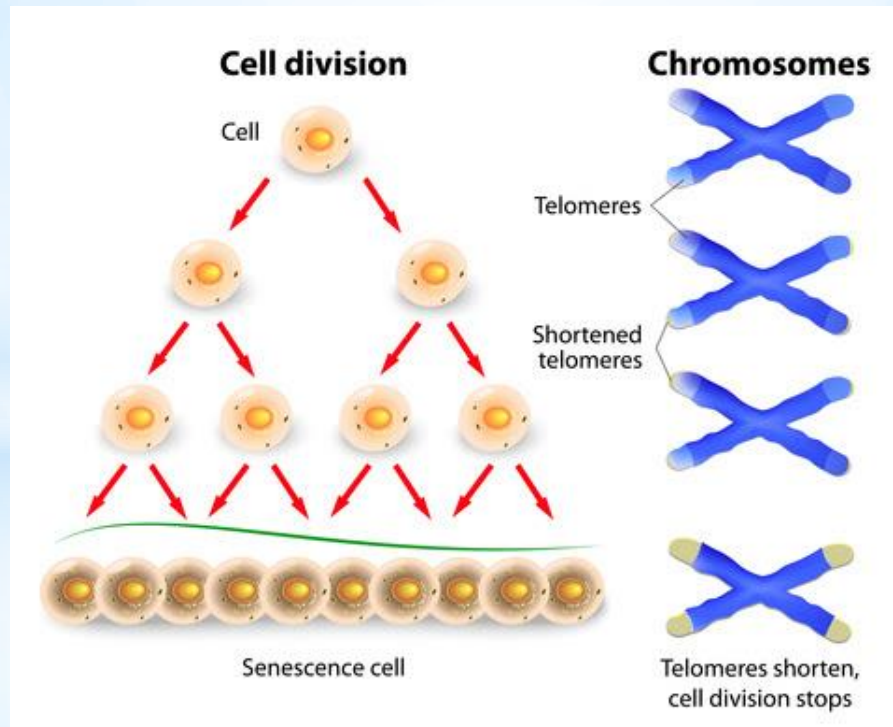
Intercellular and intracellular transmitters implementer it. Growth factors typically act as signaling molecules between cells.

- specialized growth factors: interleukins, epidermal growth factor enhances osteogenic differentiation, fibroblast growth factors and vascular endothelial growth factors stimulate blood vessel differentiation (angiogenesis), epidermal growth factor, ect.
- biologically active substances: biogenic amines, prostaglandins, nitric oxide, decay products of leukocytes - trefons; substances formed in the regenerating tissue - desmons; substances released from dividing cells and inhibiting the processes of division of neighboring cells - keilons, etc.

Genes regulatory influences

They are implemented with the participation of genes for cell division regulators

The **Hayflick limit**, or **Hayflick phenomenon**, is the number of times a normal human cell population will divide before cell division stops



Disturbances of tissue growth

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graph TD; A[Disturbances of tissue growth] --> B[Hyperbiotic process]; A --> C[Hypobiotic process];
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Hyperbiotic process

acceleration of the
tissue growth

- ☐ hypertrophy
- ☐ hyperplasia
- ☐ regeneration
- ☐ tumor

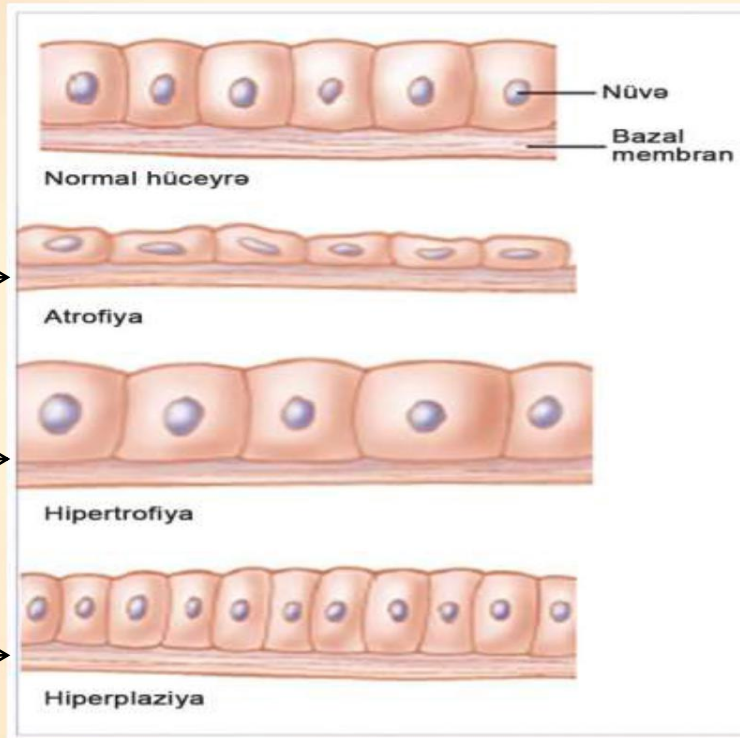
Hypobiotic process

inhibition of the
tissue growth

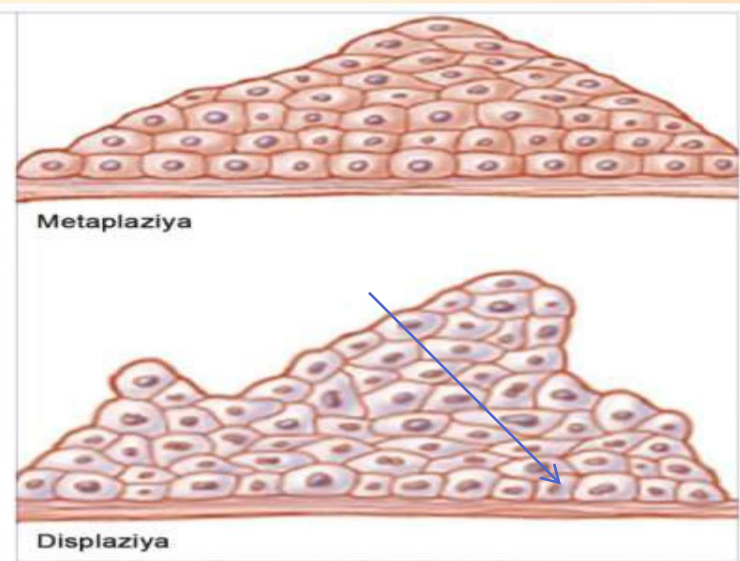
- ☐ dystrophy
- ☐ atrophy
- ☐ degeneration

The types of cellular response

Change in cell size or number

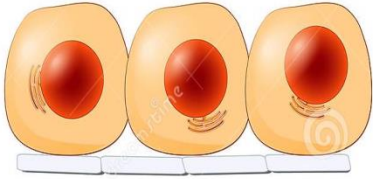


Change in cell type

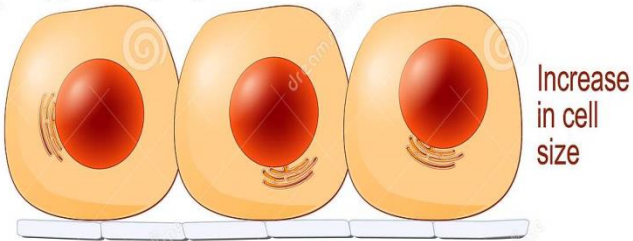


Hyperbiotic processes

Healthy cell



Hypertrophy



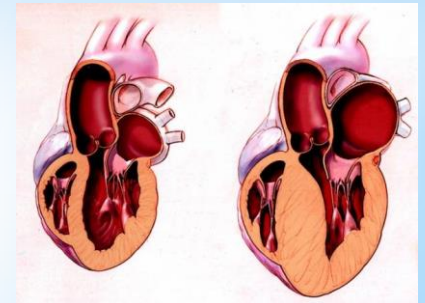
Hypertrophy



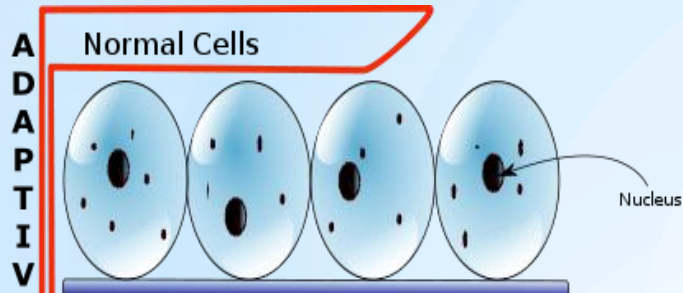
Hypertrophy is an increase in the size of a cell or organ due to an increase in workload.

Physiological hypertrophy reflects an increase in workload that is not caused by diseases – for **example**, the increase in muscle size caused by hard physical labor or weight training.

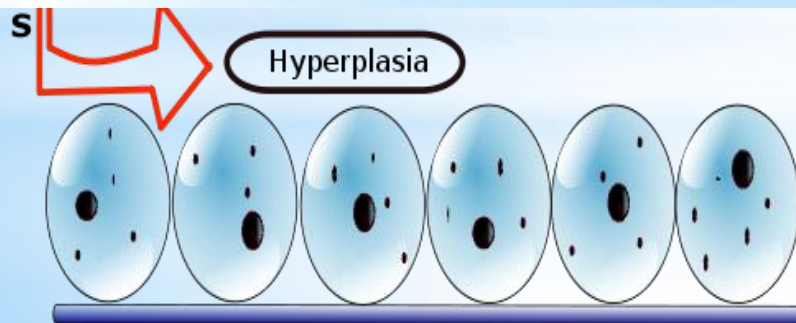
Pathological hypertrophy is a response to disease. **An example** is thickening of the heart muscle as the pumps against increasing resistance in patients with hypertension.



Hyperbiotic processes



Hyperplasia is an increase in the number of cells caused by increased workload, hormonal stimulation, or decreased tissue density.



Physiological hyperplasia is an adaptive response to normal changes. **An example** is the monthly increase in number of uterine cells that occurs in response to estrogen stimulation of the endometrium after ovulation.

Pathological hyperplasia is a response to either excessive hormonal stimulation or abnormal production of hormonal growth factors.

Examples include acromegaly, in which excessive growth hormone production causes bones to enlarge, and endometrial hyperplasia, in which excessive secretion of estrogen causes heavy menstrual bleeding and possibly malignant changes.

HYPERTROPHY HYPERPLASIA

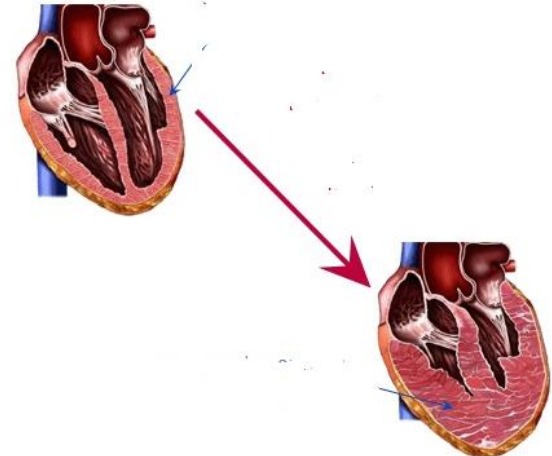
- Increase in size of cells.
- Occurs only in Cells WITHOUT the ability to REPLICATE!
- Can be Physiologic or Pathologic.
- Can Coexist with Hyperplasia.

- Increase in no.of cells.
- Occurs only in Cells WITH the ability to REPLICATE!
- Can be Physiologic or Pathologic.
- Can Coexist with Hypertrophy.

Types of hypertrophy (depending on the causes)

Working hypertrophy

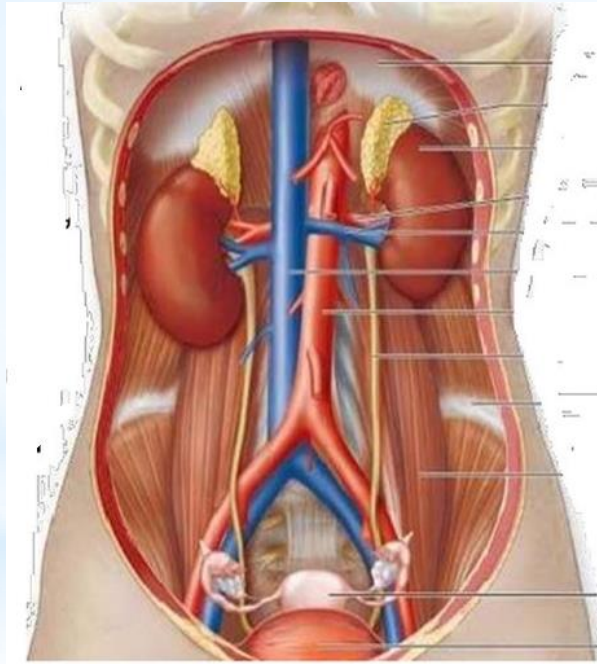
It is due to an increase in functional load on the organ or tissue. For example, hypertrophy of skeletal muscles develops under exercise conditions or myocardial hypertrophy develops in arterial hypertension



Types of hypertrophy (depending on the causes)

Compensatory (substitution) hypertrophy

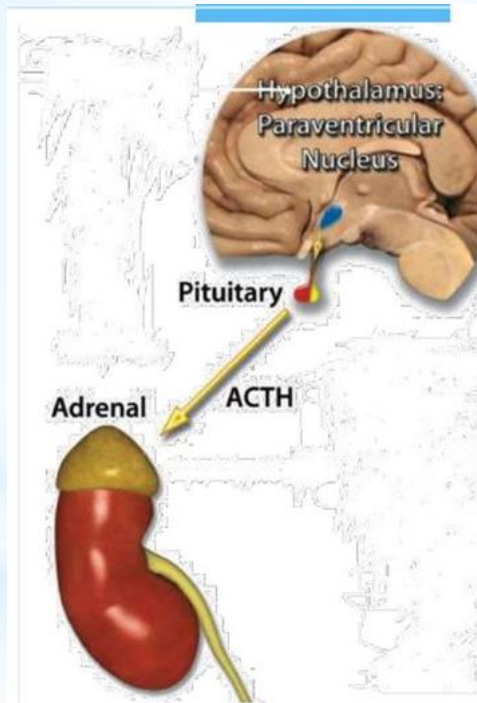
It takes place when cell size increases to take over for non-functioning cells. For instance, one kidney will enlarge when the other is not functioning or is removed.



Types of hypertrophya (depending on the causes)

Correlation hypertrophy

It occurs in one of the organs included in a single physiological system. For example, breast hypertrophy develops when the ovary or testis is removed, pituitary hypertrophy develops when the adrenal gland is removed.



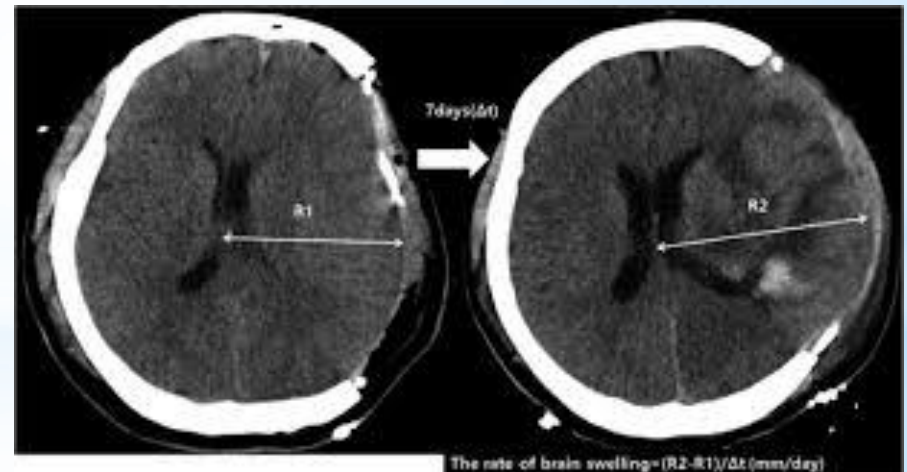
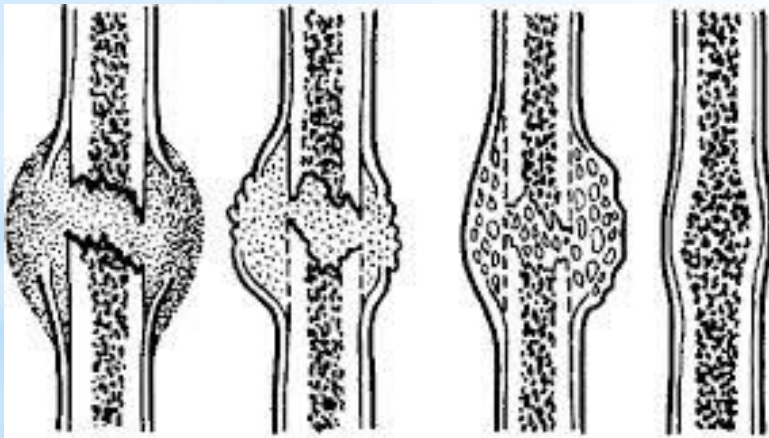
Types of hypertrophy (depending on the causes)

Regeneration hypertrophy

It occurs in the rest of the organ when the other part is partially damaged. For example, liver cells regenerate when part of the liver is surgically removed

Vakalnaya hypertrophy

It is characterized by proliferation of connective, adipose or other tissue during atrophy of any organ. For example, with muscle atrophy, adipose tissue grows between muscle fibers, and with a brain atrophy, thickening of the cranial bones is observed.



Bovine heart



Cardiac hypertrophy



Hyperbiotic processes

Regeneration

It is the process of renewal and growth to repair or replace tissue that is damaged or suffers from a disease

Physiological regeneration

represents the process in which regeneration takes place under normal conditions, not in response to injury.

Physiological regeneration is associated with the constant renewal of aging and dying cells from apoptosis or their intracellular structures and occurs in organs and tissues with renewing cell population (blood cells, epidermis, epithelium of gastrointestinal tract).

Pathological regeneration is the restoration of organs and tissues after their damage. –

Types:

-*hyperregeneration* (excess regeneration)

-*hyporegeneration* (insufficient regeneration)

-*Metaplasia* means replacement of one type of the cells by other one derived from the same tissue.

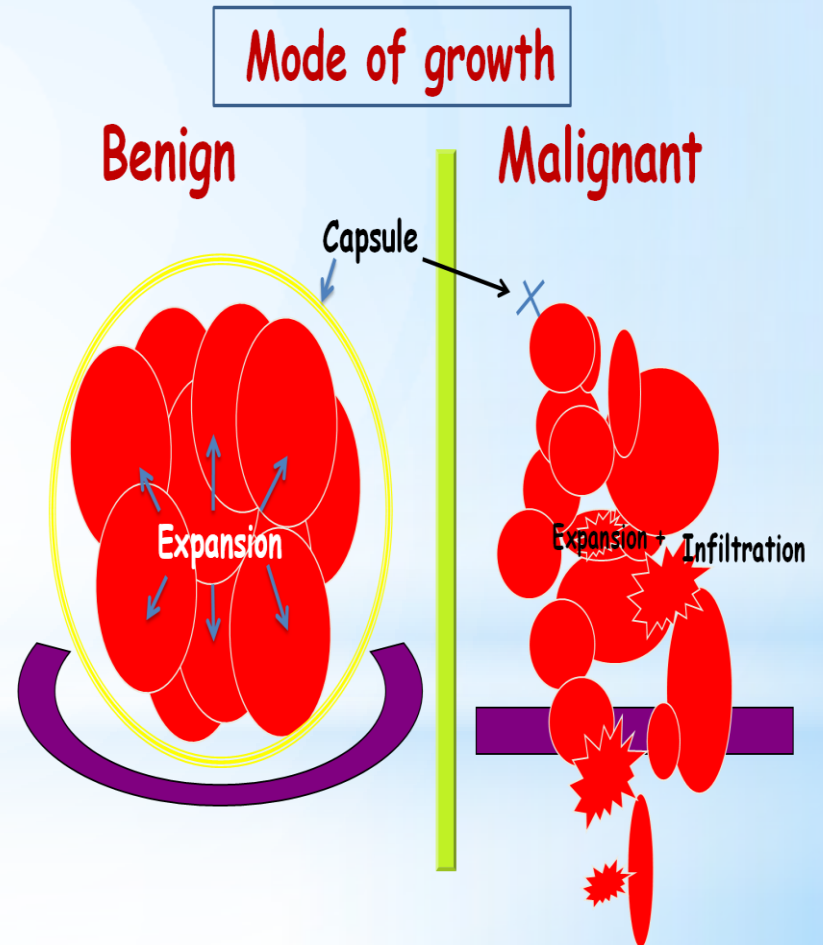
-*Dysplasia* is the proliferation and formation of different sized, shaped and structured cells in the tissue due to genetic reprogramming

Hyperbiotic processes

Tumor (Neoplasia)

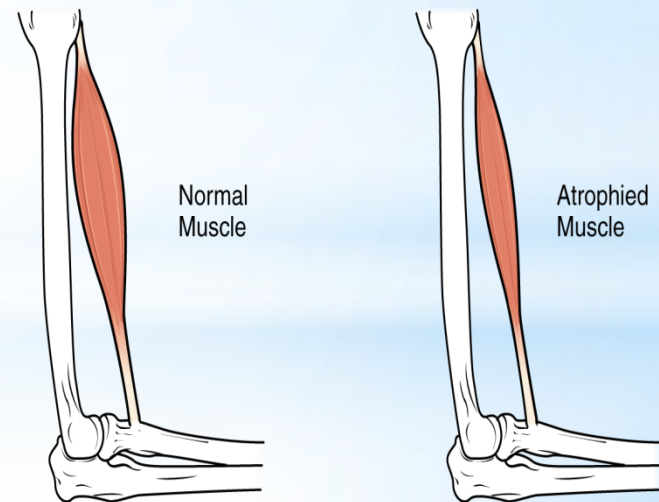
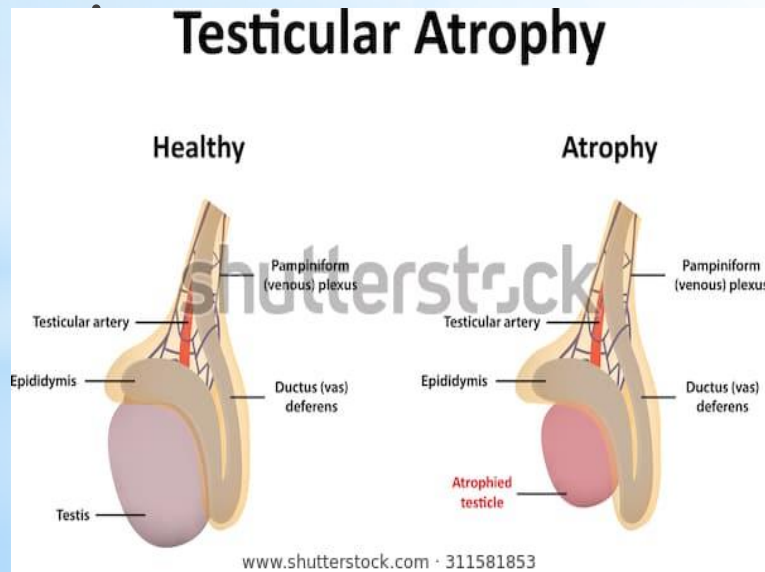
- noncontrollable, uncoordinated, unlimited excessive, rapid, abnormal proliferation of cells.

This typical pathological process arise under influence of cancerogenous factors.



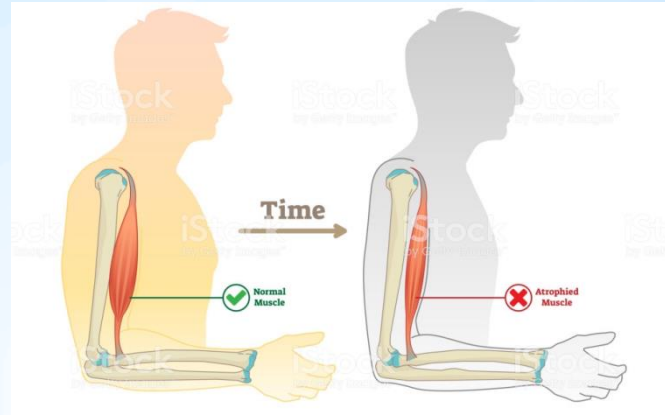
Hypobiotic processes

Atrophy is a reduction in the size of a cell or organ that may occur when cells face reduced workload or disuse, insufficient blood flow, malnutrition, or reduced hormonal and nerve stimulation.



Types of atrophy

❑ atrophy from inactivity is due to the decreased workload upon the skeletal muscles



Atrophy of the tibia after the fracture and removal of gypsum

❑ neurogenic atrophy (Denervation atrophy occurs in the muscles of paralyzed limbs)



Atrophy of the tibia in paralysis

❑ atrophy due to prolonged compression



A 3-year-old child with hydrocephalus (it is the buildup of fluid in the cavities within the brain)

Hypobiotic processes

Dystrophy

It is a disorder in the composition of cell and tissue structures caused by a disturbance of metabolic processes (the nature and intensity of metabolism) and accompanied by either the accumulation or decrease of certain substances (compounds) or the appearance of substances that are not normally found.

Types: parenchymal, mesenchymal and mixed.

Degeneration

It is a deterioration of a tissue or an organ in which its function is diminished or its structure is impaired

It is the change of tissue to a lower or less functionally active form

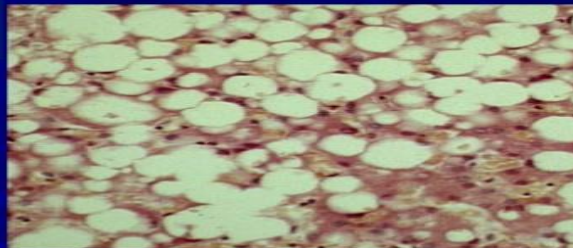
Degeneration refers to the process by which tissue deteriorates and loses its functional ability due to traumatic injury, aging and wear and tear.

Parenchymatous fatty degenerations



This liver is enlarged and has a pale yellow appearance. It is greasy to touch. It is called "Goose liver".

Microscopically: there are numerous lipid vacuoles in the cytoplasm of hepatocytes.



Classification of dystrophy

1. Classification in depending on localization of metabolism:

- parenchymal
- stromally - vascular
- mixed

2. Classification in depending on deposition of protein, lipids, carbohydrate, mineral (on predominance of the broken exchange):

- Proteinous (Dysproteinoses)
- Fatty (lipidoses)
- Carbohydrate
- Mineral
- Pigmental

3. Classification in depending on prevalence of process:

- Local
- System

4. Classification in depending on an origin:

- Acquired
- Hereditary

TUMOR or NEOPLASMA (greek)

**Tumor is a pathological
process characterized
uncontrolled multiplication
cellular elements
without the phenomena of maturation**

ONCOLOGICAL SITUATION IN UKRAINE



**Each of the 50 th citizen
of Ukraine has cancer!**

**Each year, registered 165,000
new cases of cancer**

**Mortality from cancer pathology - 190 people per
100,000 population**

**Chief Oncologist
Igor Schepotin**

ETIOLOGY

Carcinogens are factors that cause the transformation of normal cells into tumor

Cocarcinogens are factors that increase the action of carcinogens

Carcinogen

chemical

- ☐ Professional (asbestos, vinylchloride, arsenic, nitrosamines)
- ☐ medicinal (cyclophosphamide, phenacetin, chloroquine)
- ☐ Natural (aflatoxin)

physical

- ☐ radiation
- ☐ UV radiation
- ☐ ozone

biological

- ☐ DNA or RNA tumor viruses



PATHOGENESIS

Stage 1. Initiation (transformation) – normal cell under the action of etiological (carcinogenic) factors attains capability to boundless growth and becomes tumor cell.

Stage 2. Promotional (activation) - the division of transformed cells and the formation of tumor nodule under the influence of co-carcinogenic factor

Stage 3. Progression. Regulatory systems of the organism affect the multiplying tumor cells. Tumor cells, in their turn, begin to adapt to the influence of regulatory systems.

Thus, tumor cells getting from under the control of immune, endocrine and other regulatory systems of the organism, create new clones of cells.

Tumor tissue obtains polymorphism (consists of different cellular clones that differ from each other), increases the speed of its growth, and obtains malignant character.

FEATURES OF TUMOR GROWTH

Atypia - a set of characteristics that distinguish tumor tissue from normal

Types of atypia:

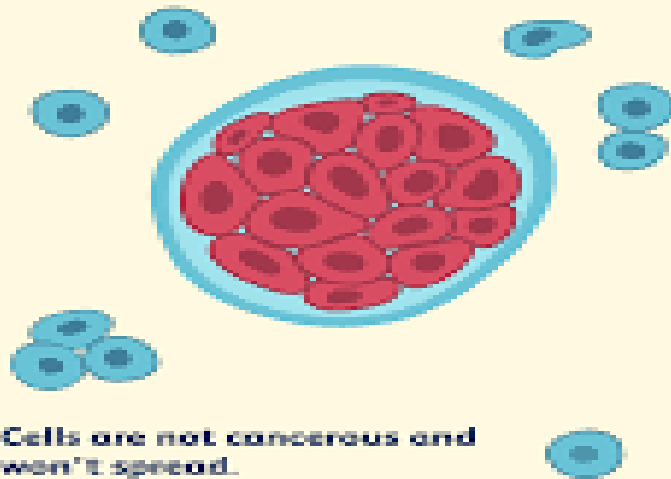
- ❑ Morphological - changes of size, shape, color of the cells, increase numbers of nucleus, mitochondria, ribosome, etc.
- ❑ Metabolic - transfer to the oxygenless glycolysis, the appearance of abnormal proteins – fetoproteins, a negative nitrogen balance
- ❑ Physical and chemical (rise concentration of potassium and water, fall concentration calcium and magnesium, acidosis, etc.)
- ❑ Immunological - disappear the organ specific antigens of cells, synthesis antigens of another's organ, synthesis embryonic antigens
- ❑ Functional - rise or fall functional activity of tissue, formation new functions (examples, tumor of lung synthesizes pituitary hormones)

Tumor

(depends on the degree of atypia)

Benign

Benign Tumor

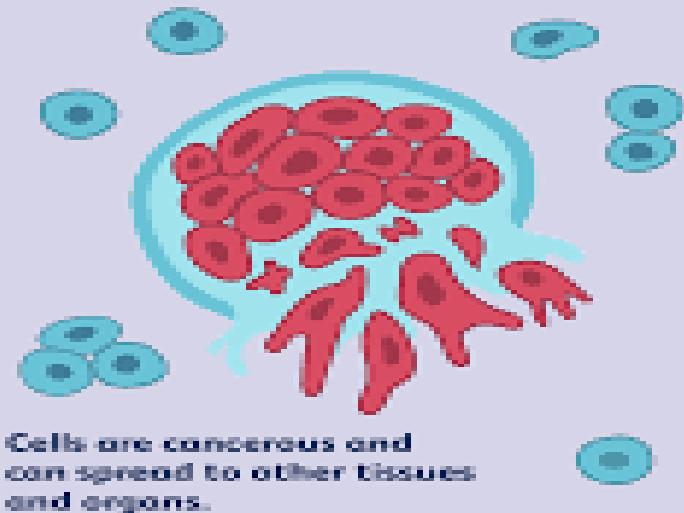


verywell

If the tumor is confined to a local area and does not infiltrate surrounding tissue, it is called a **benign tumor**

Malignant

Malignant Tumor

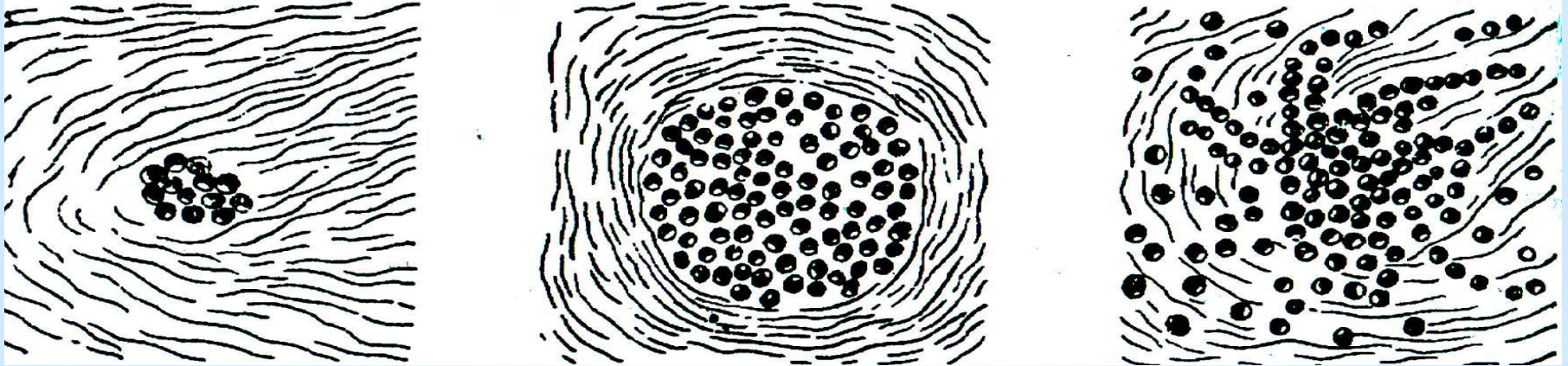


If the tumor infiltrates surrounding tissue or distant parts of the body, it is called a **malignant tumor**.

Differences of benign and malignant tumors

Sign	Malignant	Benign
Morphological atypia	cell and tissue	tissue
Metabolic atypia	perversion of metabolism	normal metabolism
The presence of capsules	no	yes
The types of growth	infiltrative	expansive
Metastasis	yes	no
Recurrence	yes	no(rarely)
Cachexia	yes	no

Character of tumor growth



a

b

c

The growth of tumors:

a) - tumor germ;

b)- a benign tumor (expansive growth);

c) - a malignant tumor (infiltrative growth)

Malignant tumors



Asymmetry



Border
irregularity



Color



Diameter:
 $\frac{1}{4}$ inch or
6mm

Metastasis is the process of detachment from the tumor of atypical cells and transfer them into another organs with the development on the site of attachment of a similar tumor

Common sites of metastasis

The most common sites for cancers to metastasize include the brain, bones, lungs and liver. Other places can include the adrenal gland, lymph nodes, skin and other organs



**metastases of breast cancer
in the liver**



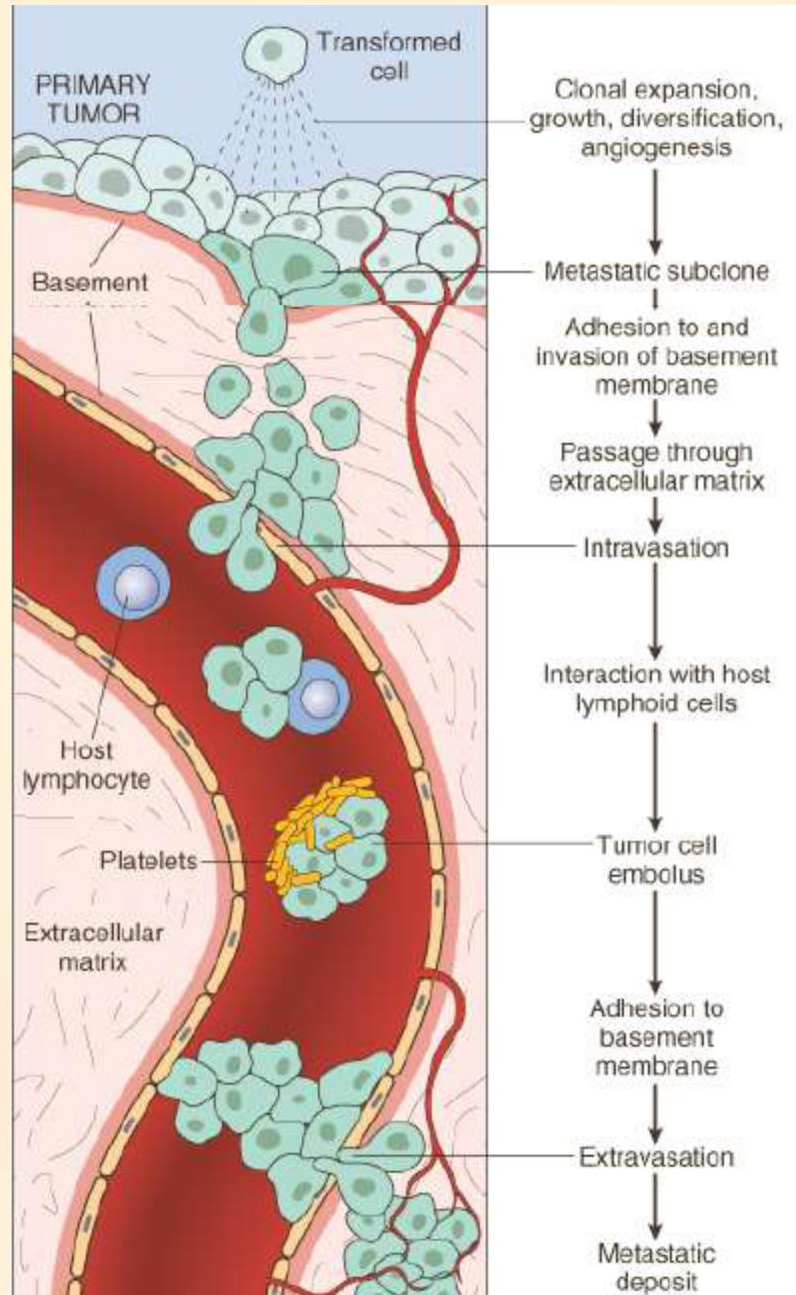
**metastases of lung cancer
in the adrenal gland**

Ways of metastasis:

Metastases can occur in three ways:

1. Cells can travel through the bloodstream to distant locations (**hematogenous**);
2. Cells can travel through the lymph system to nearby or distant lymph nodes (**lymphogenous**).
3. They can grow directly into the tissue surrounding the tumor (**tissue**);

Metastasis by hematogenous pathway



Benign tumors



Papilloma (soft fibroma) is a common benign polyps arising in the skin folds



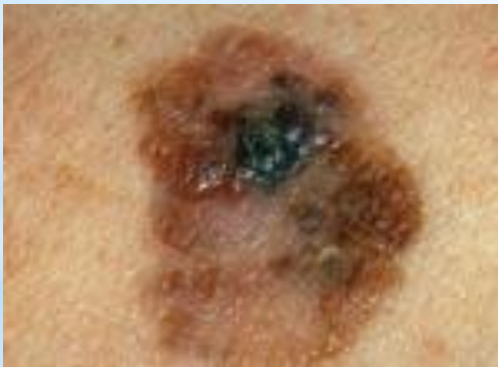
Polyp of the stomach

Nomenclature of tumors

- * The name of tumors are formed by adding the ending “-oma” to the names of tissue from which they develop.
- * Examples,
 - * tumors of bones – *osteoma*,
 - * tumors of fat tissue – *lipoma*,
 - * vascular tumors -*angioma*,
 - * tumors of glands – *adenoma*
- * Malignant tumors of the epithelial tissue are called *cancer* or *carcinoma*, and malignant tumors of connective tissue-*sarcoma*.
- * Names of mesenchymal tumors requires the type of these tissue – *osteosarcoma*, *myosarcoma*, *angiosarcoma*, *fibrosarcoma* and etc

Types of malignant tumors

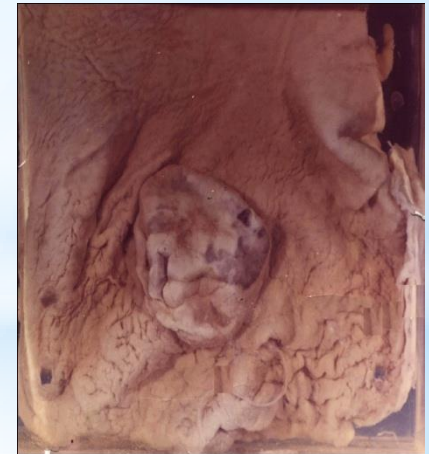
Melanoblastoma
(pigment tumor)



Sarcoma
(from connective tissue)

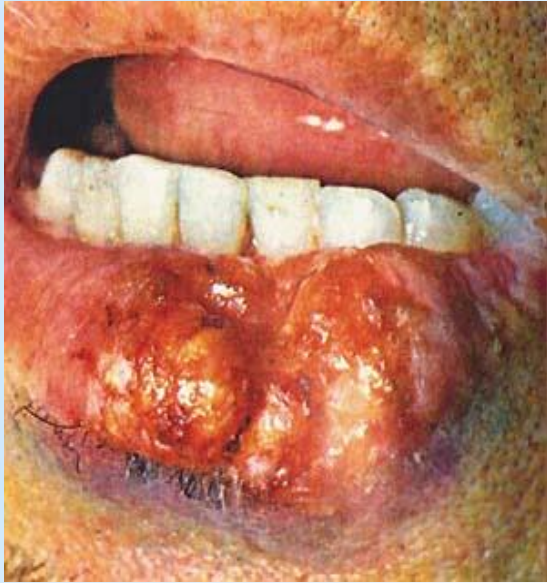


Carcinoma
(from glandular tissue)



THE CLINICAL STAGE OF CANCER

The first stage - the appearance of tumor



**cancer of the lower
lip**



cancer of the tongue



Cancer of breast

The second stage – increased of lymphatic nodes (node enlargement)



The third stage – metastases



**Metastases of lung cancer in the heart
(very rare)**



Metastases of lung cancer in the liver (in the form of white spots)

The fourth stage – cancer cachexia



Cachexia, a generalized wasting of fat and protein, is common in individual with cancer.

A person with cachexia typically appears emaciated and wasted, and experiences an overall deterioration in physical status.

Cachexia is characterized by anorexia (loss of appetite), alterations in taste perception, early satiety, weight loss, anemia, marked weakness, and altered metabolism of proteins, carbohydrates, and lipids



General principles of treatment of malignant tumors

- ☐ **Surgery** (surgical removal of the tumor within normal tissue)
- ☐ **Chemotherapy** (a wide range of antineoplastic drugs, which may induce regression of a tumor and its metastasis)
- ☐ **Radiation therapy** (ionizing radiation and particle beam radiation)
- ☐ **Biotherapy (immunotherapy):** interferons, interleukines, hematopoietic growth factors and monoclonal antibodies.

Thanks for attention

Be healthy!