INFLAMMATION AND REGENERATION

LECTURE
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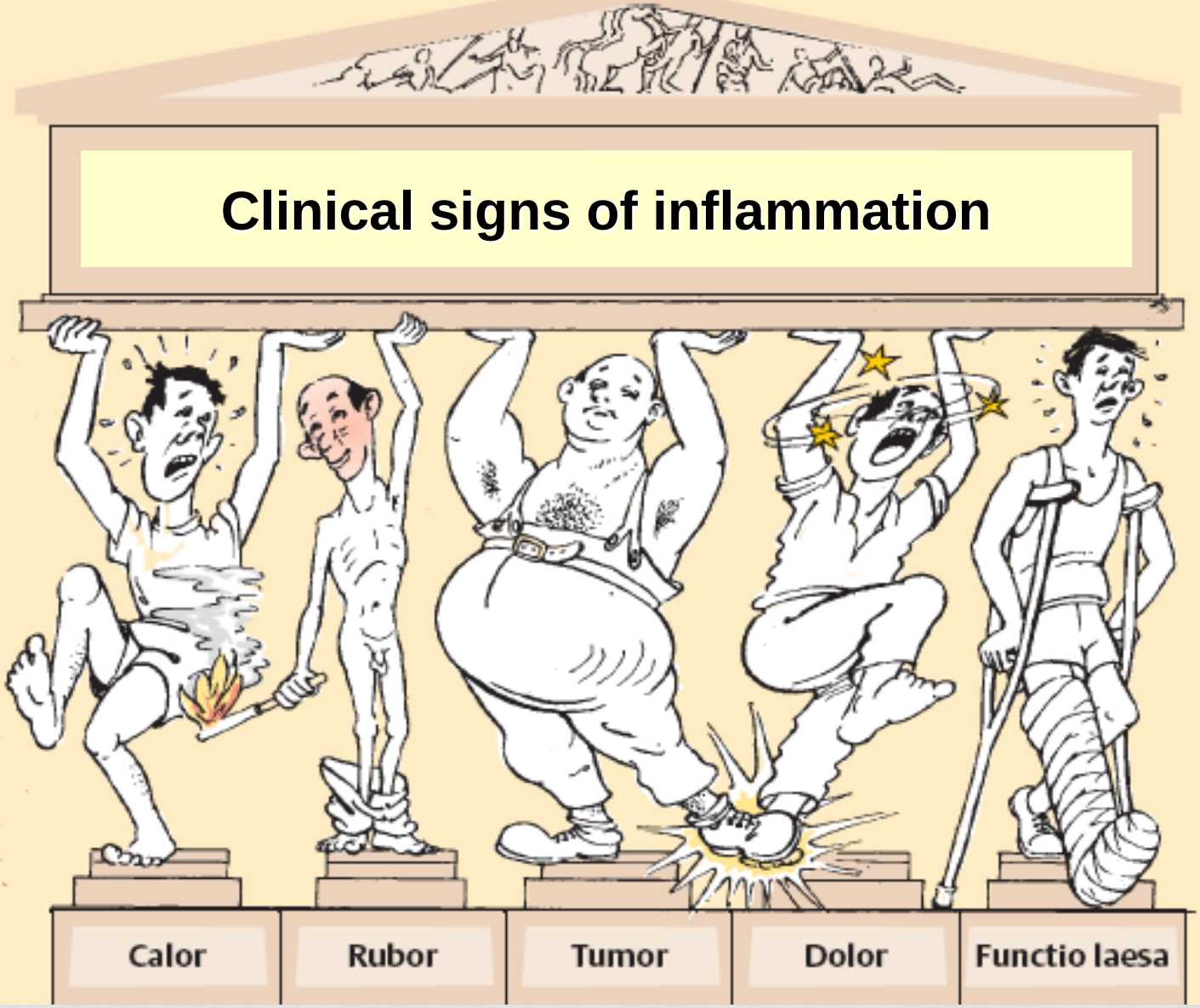
INFLAMMATION

- **Inflammation is a complex vascular-mesenchymal reaction to damage caused by the action of various agents.**
- **Inflammation is a protective-adaptive reaction directed to:**
  - **Delimitation of the damage site,**
  - **The destruction (neutralization) of agents that caused inflammation,**
  - **Restoration of damaged tissues (repair).**

ETIOLOGY OF INFLAMMATION

- **Biological (exogenous and endogenous) factors:**
  - **Microorganisms and products of their vital activity,**
  - **Immune factors (antibodies, immune complexes),**
  - **Necrosis (demarcation inflammation).**
- **Physical factors:**
  - **Injury,**
  - **High and low temperatures,**
  - **Electricity,**
  - **Radiation.**
- **Chemical factors:**
  - **Medicines,**
  - **Toxins,**
  - **Poisons.**

Clinical signs of inflammation



PHASES OF INFLAMMATORY REACTION

- **Inflammation consists of 3 phases:**
  - **Alteration (or damage)**
  - **Exudation**
  - **Proliferation**

ALTERATION

- **Alteration is the initial phase of inflammation, leading to the release of mediators, which determine all subsequent development of the inflammatory reaction.**
- **Alteration is represented by dystrophy and necrosis.**

MEDIATORS OF INFLAMMATION

- Mediators can be:
  - Plasmatic
  - Cellular

PLASMA MEDIATORS

- Provide increased vascular permeability.
- Activate the chemotaxis of leukocytes for phagocytosis.
- Activate intravascular coagulation in the vessels draining the focus of inflammation to separate the pathogen and the focus itself.
- Appear when the circulating factors in the blood are activated.
- Presented by the following systems:
  - Kallikrein-kinin system,
  - The complement system,
  - Hemocoagulation system and fibrinolytic system.

CELL MEDIATORS

- Produced by different cells.
- Contained in the cells in the prepared form (histamine, serotonin, lysosomal enzymes).
- Are formed in the course of an inflammatory reaction.
- Provide:
  - Increase of vascular permeability, chemotaxis and phagocytosis,
  - The inclusion of an immune response to remove the damaging agent,
  - Restoration of damaged tissue by proliferation and differentiation of cells in the focus of inflammation.

EXUDATION

- **Exudation is the exit of the liquid part of the blood and the blood cells out of the vascular bed.**
- Exudation stages:
  - The reaction of the microcirculatory bed with a violation of the rheological properties of the blood,
  - Increase of microcirculation bed permeability,
  - The exit of liquid and plasma proteins,
  - Emigration of cells (cell exit from vessels),
  - Phagocytosis,
  - Formation of exudate and inflammatory cell infiltrate.

MICROCIRCULATION BED REACTION

- Short-term vasoconstriction.
- Vasodilation (arterioles, capillaries and post-capillaries) with the development of inflammatory hyperemia.
- Slowing blood flow, increasing hydrostatic pressure, plasmorrhagia, increasing viscosity, stasis.

INCREASE IN PERMEABILITY

- The appearance of pores between endothelial cells due to:
  - Their contraction and expansion of the lumen of blood vessels,
  - Endothelial damage.

EMIGRATION OF CELLS

- Occurs mainly in postcapillaries and venules.
- The first to enter the focus of inflammation are polymorhonuclear leukocytes (PNL).

EMIGRATION OF CELLS

- Stages of leukodiapedesis:
  - Marginal standing (marginalization).
  - Adhesion to the endothelium (adhesion).
  - Emigration.

EMIGRATION OF CELLS

- Emigration:
  - Occurs interendothelially: leukocytes with pseudopodia push apart the interendothelial contacts and migrate between the endothelium and the basal membrane.
  - The penetration of PNL through the basal membrane of the endothelium is associated with the phenomenon of thixotropy, which is based on the transition of the basal membrane from the state of the gel to the sol and vice versa (hypothesis).
  - Movement of PNL towards the lesion focus is carried out with the help of chemotactic factors.

PHAGOCYTOSIS

- Absorption and digestion by cells (phagocytes) of various particles (microbial bodies, necrotic detritus, foreign bodies, etc.).
- The most important phagocytic cells are PNLs and macrophages (monocytes released into tissues).
- Phagocytosis can be:
  - Completed,
  - Unfinished (microorganisms are not digested by phagocytes and proliferate in their cytoplasm leading to chronic inflammation).

FORMATION OF EXUDATE AND INFILTRATE

- Exudate is an inflammatory fluid containing protein (more than 2%) and cellular elements.
- Accumulation of cells in the tissues is called an inflammatory cell infiltrate.

PROLIFERATION

- Proliferation is the final phase of inflammation, which is characterized by:
  - Reproduction of cells able to proliferate in the inflammatory focus : macrophages, cambial mesenchymal cells, smooth muscle cells, epithelium.
  - Differentiation and transformation of cells:
    - The macrophage can be transformed into an epithelioid and a giant cell;
    - B-lymphocyte - into the plasma cell;
    - The cambial mesenchymal cell turns into fibroblast.

PROLIFERATION

- Proliferation of cells in the focus of inflammation with the appearance of a large number of fibroblasts serves to repair damaged tissues.

CLASSIFICATION OF INFLAMMATION

- Depending on the progress:
  - Acute,
  - Subacute,
  - Chronic.
- By the predominance of the phase:
  - Exudative inflammation (mainly acute),
  - Productive inflammation (mainly chronic).

EXUDATIVE INFLAMMATION

- It is characterized by the predominance of exudation and the formation of exudate in the tissues and cavities of the body.
- The nature of the exudate depends on the state of vascular permeability and the depth of damage, which is determined by the type and intensity of the damaging factor.

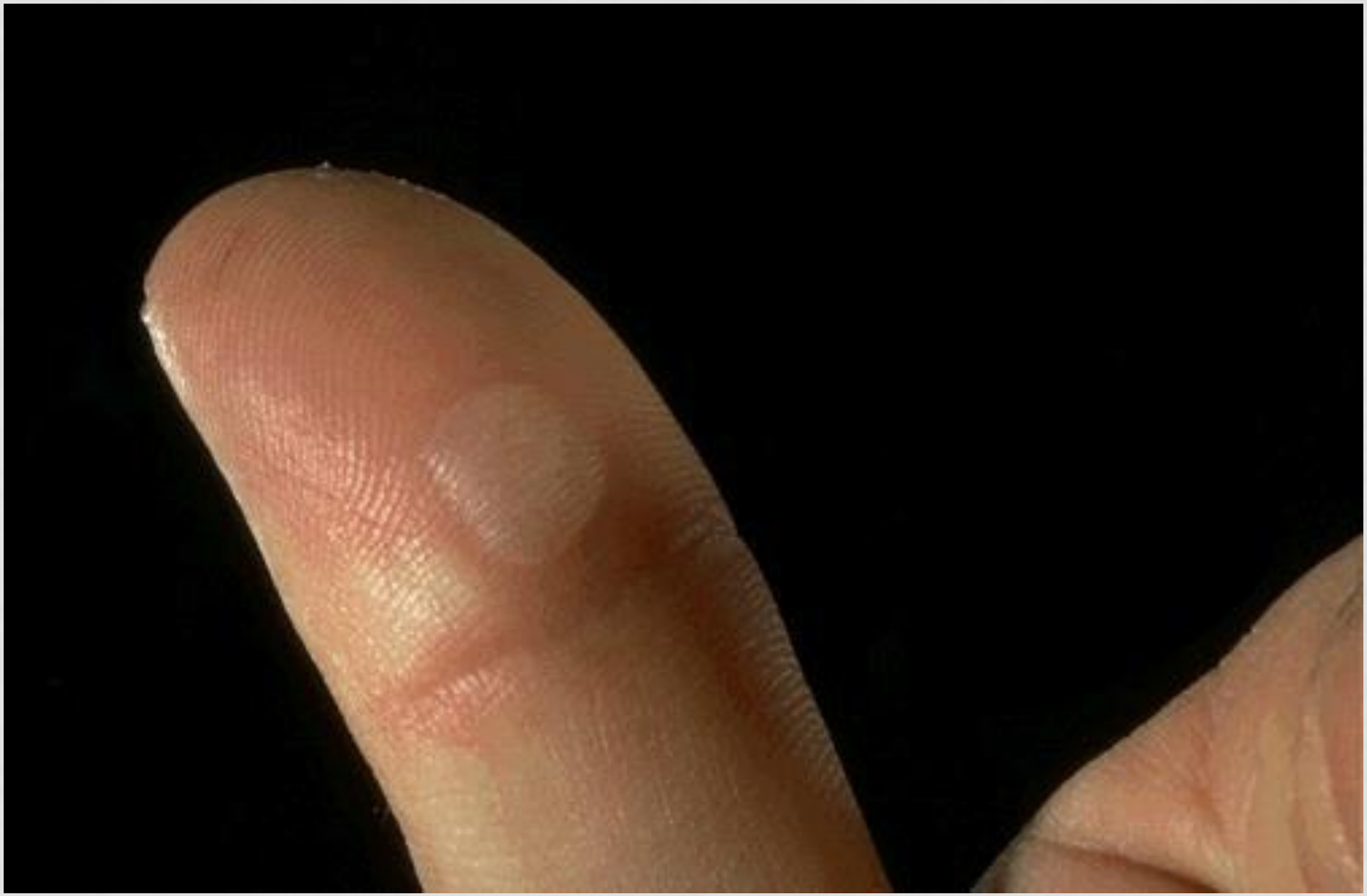
TYPES OF EXUDATIVE INFLAMMATION

- Depending on the nature of the exudate, the following types of inflammation are distinguished:
  - Serous,
  - Fibrinous,
  - Purulent,
  - Putrid,
  - Hemorrhagic,
  - Mixed.
- On the mucous membranes can develop a special kind of inflammation - catarrhal.

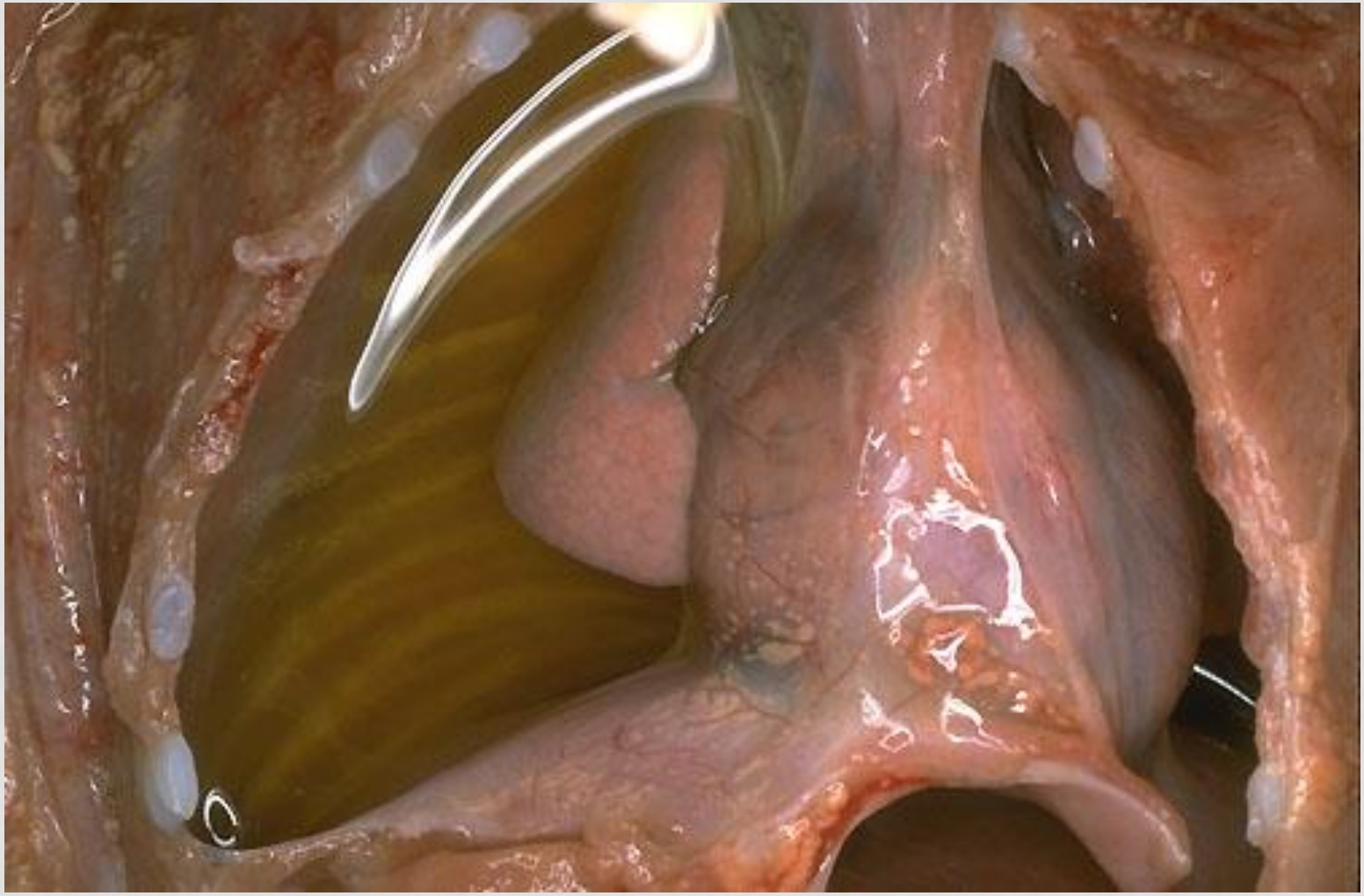
SEROUS INFLAMMATION

- Serous exudate contains up to 2% protein and a small number of cells (PNL, macrophages, depleted epithelium, etc.).
- It develops more often on serous membranes (polyserosites in rheumatic diseases, in uremia), mucous membranes, skin (streptococcal infection - bullous erysipelas, herpetic infection, burns), less often in internal organs (serous pneumonia in influenza, etc.).
- The outcome is usually favorable, the exudate resolves.

SEROUS INFLAMMATION (BURN)



SEROUS INFLAMMATION (PLEURITIS)



FIBRINOUS INFLAMMATION

- Exudate contains a large amount of fibrin, which is formed from fibrinogen under the influence of tissue thromboplastin.
- It can occur in infectious diseases (croupous pneumonia, diphtheria, dysentery, tuberculosis), infectious-allergic diseases (rheumatism), autointoxication (uremia).
- It usually develops on mucous membranes and serous membranes, forming membranes; rarely - in the organs (in the lung).

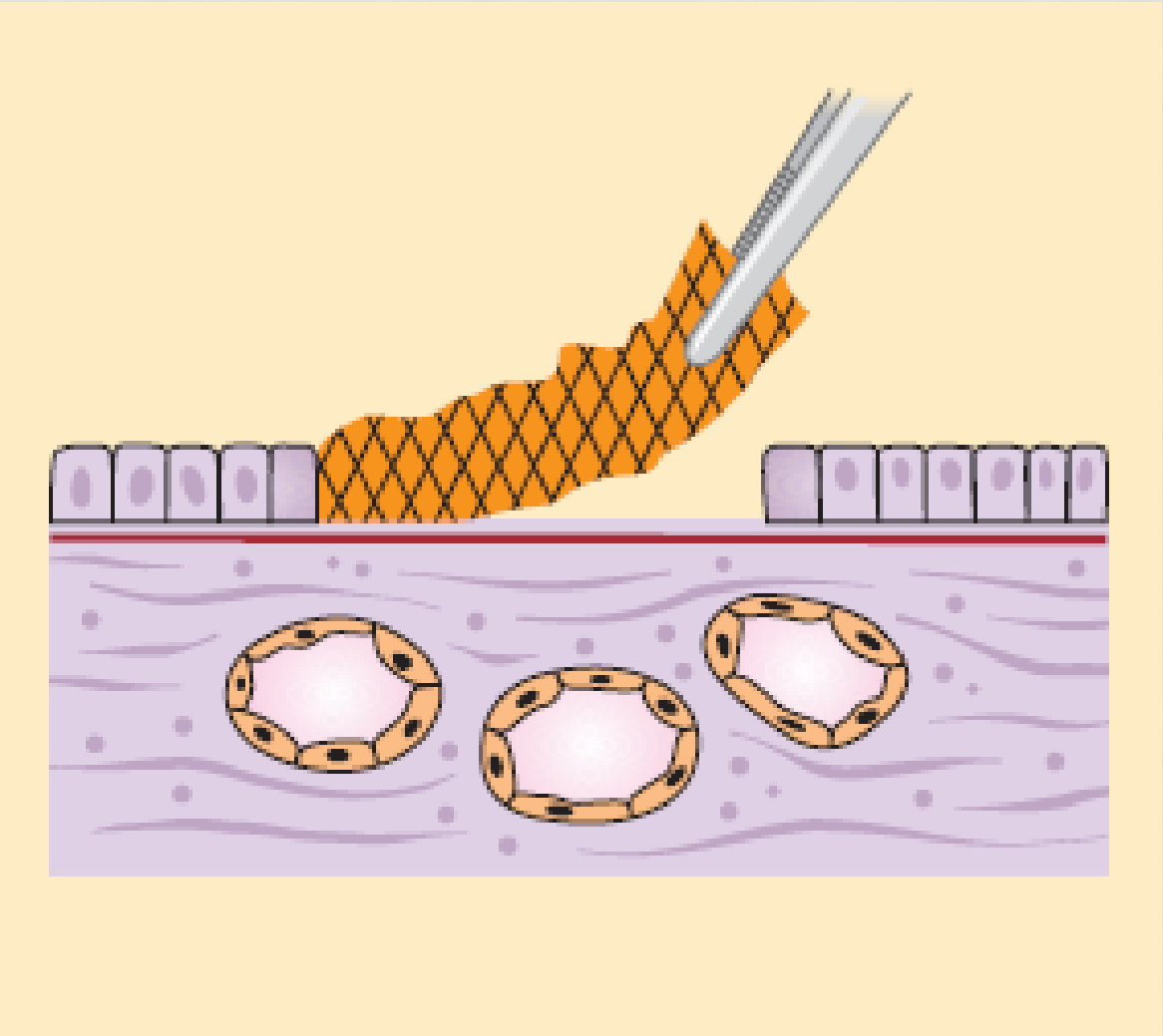
FIBRINOUS INFLAMMATION

- Depending on the nature of the attachment of fibrinous membranes to the underlying tissues, fibrinous inflammation can be:
  - Croupous,
  - Diphtheric.

CROUPOUS INFLAMMATION

- It develops on serous membranes, as well as mucous membranes covered by a cylindrical epithelium loosely associated with the underlying tissues.
- Fibrinous memebrane is thin (fibrin with an admixture of PNLs), easily torns away.

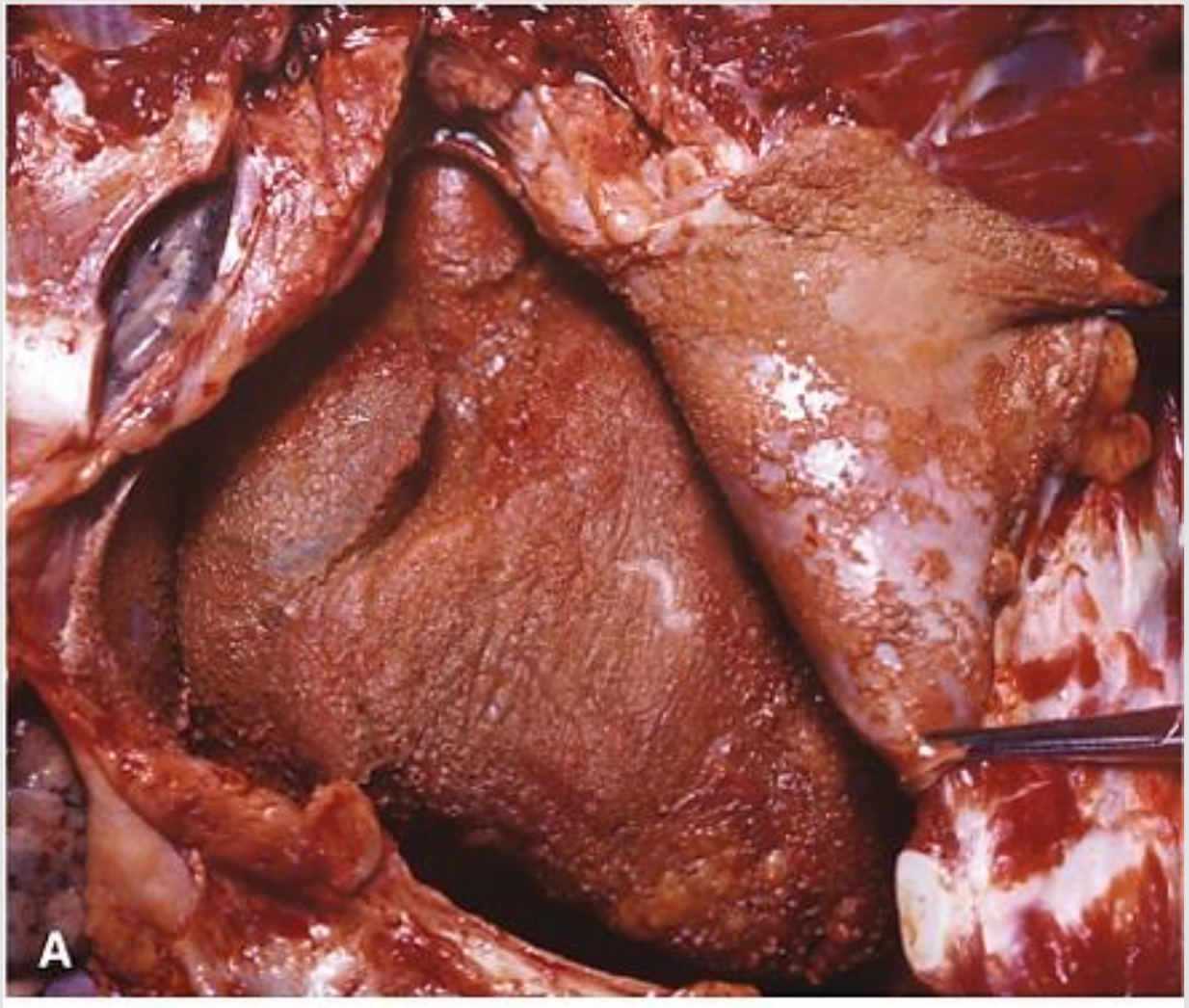
CROUPOUS INFLAMMATION

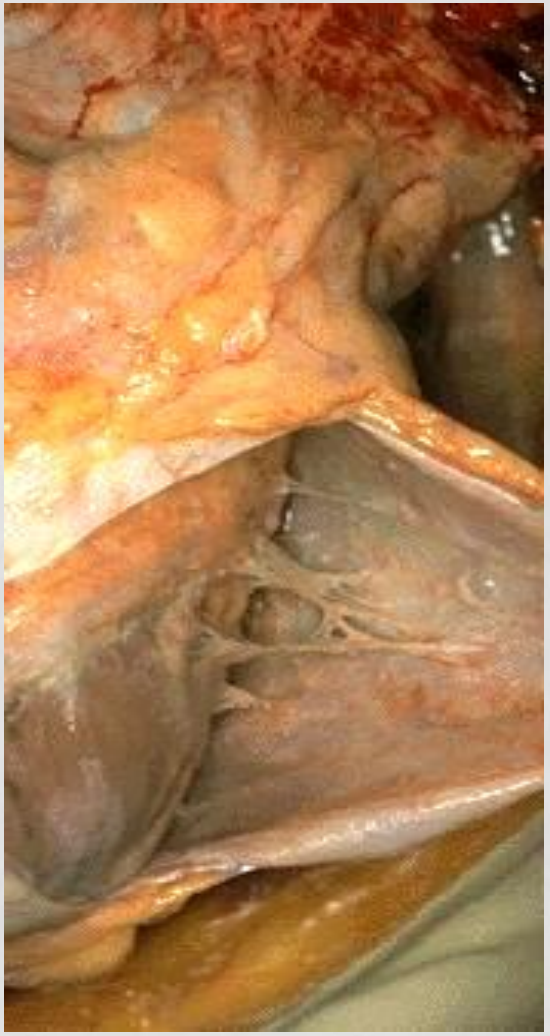


FIBRINOUS PERICARDITIS

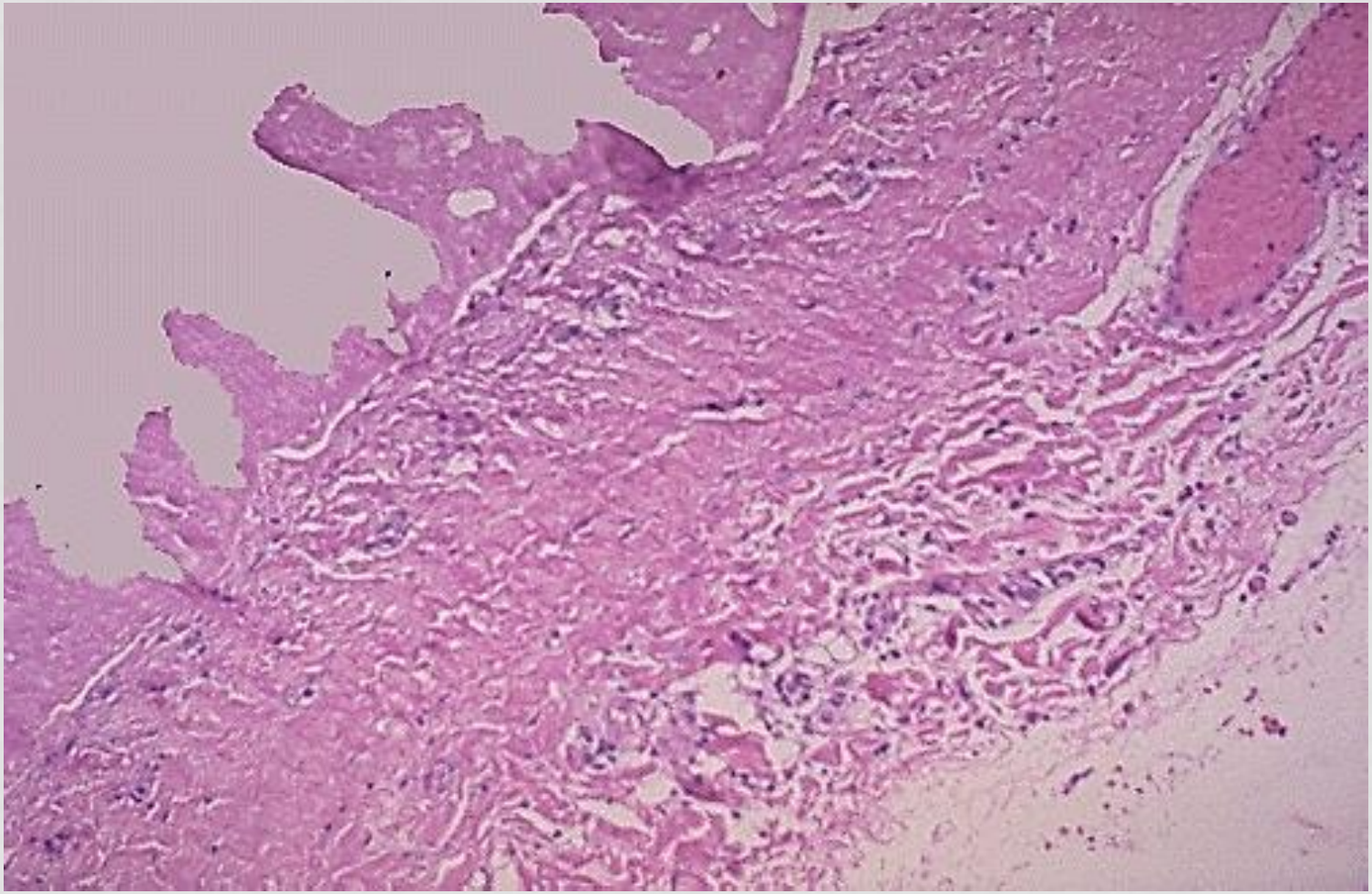
- It can occur in uremia, rheumatism, transmural myocardial infarction, croupous pneumonia.
- Macroscopic picture:
  - The epicardium is dim,
  - It is covered with grayish-yellow rough overlays in the form of filaments and resembles a hairy coat ("hairy heart").
  - Overlays can be easily removed.
- Outcome:
  - Adhesions between the leaves of the pericardium,
  - Often obliteration of the pericardial cavity,
  - Sometimes sclerized memebranes are petrified or ossified ("carapaceous heart").

FIBRINOUS PERICARDITIS





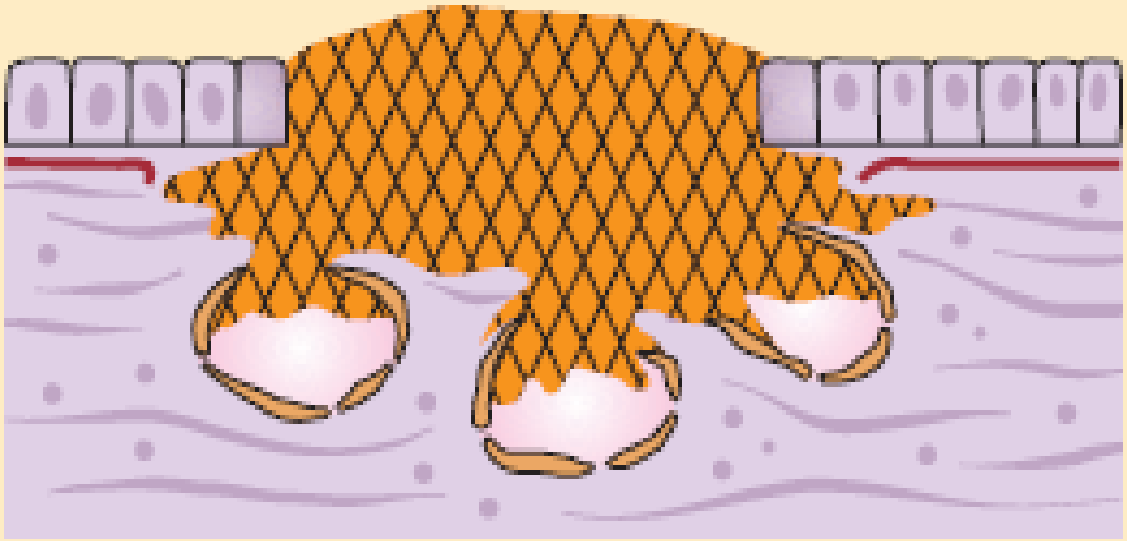
FIBRINOUS PERICARDITIS



DIPHTHERITIC INFLAMMATION

- It develops on the mucous membranes, covered by stratified squamous epithelium, which is tightly connected with the underlying tissues.
- In the presence of deep necrosis diphtheritic inflammation can also occur on mucous membranes covered with cylindric epithelium.
- The memebrane is thick (fibrin, leukocytes, necrotic tissue), torn with difficulty with the appearance of deep ulcers.
- Outcome: in place of deep ulcers that occur when the film is torn off, scars develop.

DIPHTHERITIC INFLAMMATION



PURULENT INFLAMMATION

- Characterized by the predominance of PNL in exudate (preserved and decaying).
- The most common cause is pyogenic microorganisms (staphylococcus, streptococcus, gonococcus, meningococcus, Pseudomonas aeruginosa, etc.).

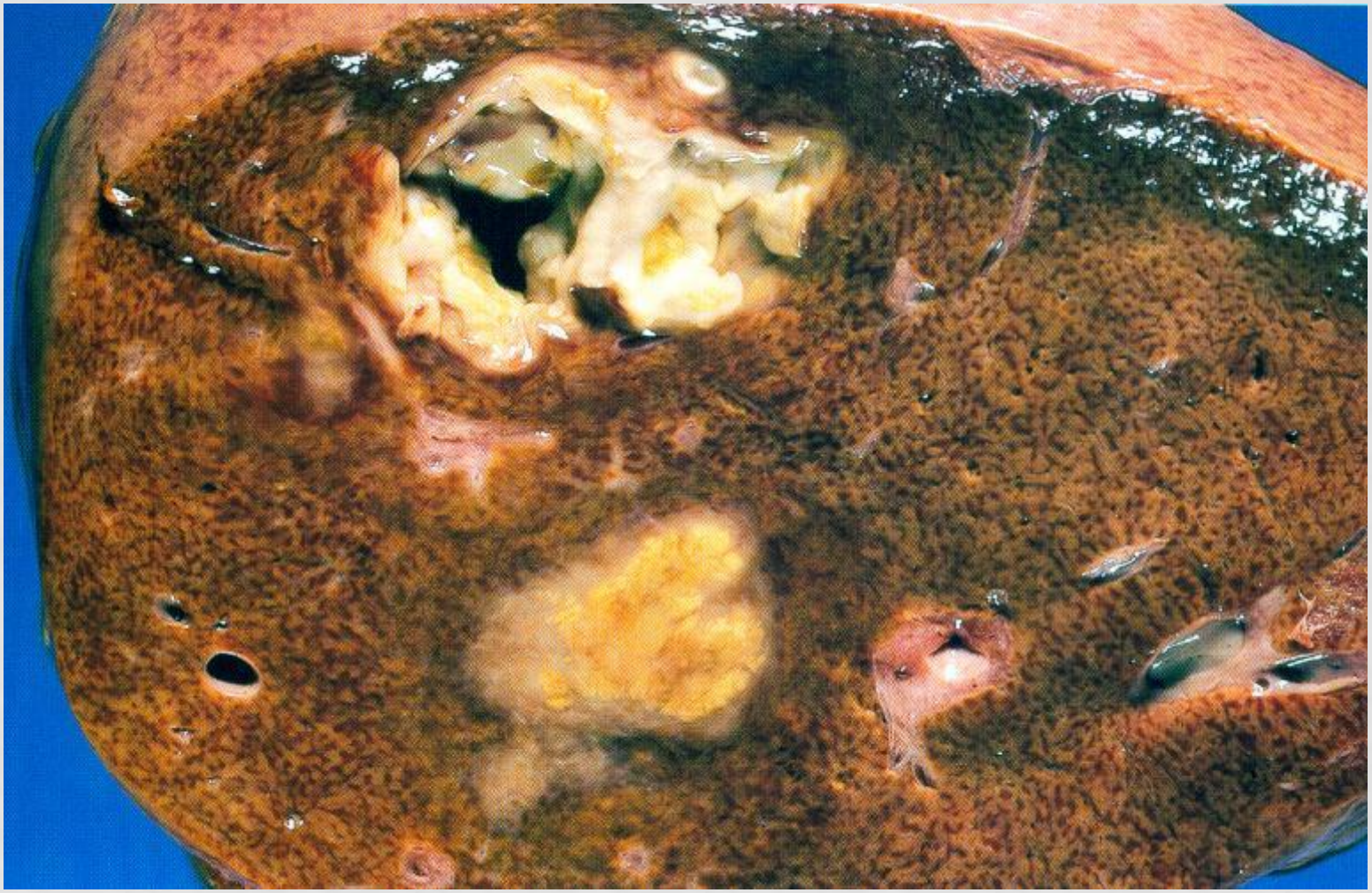
PURULENT INFLAMMATION

- A characteristic morphological feature is histolysis - melting of tissues by proteolytic enzymes of leukocytes.
- Purulent inflammation is of the following types:
  - Limited (abscess),
  - Diffuse (phlegmon),
  - Empyema.

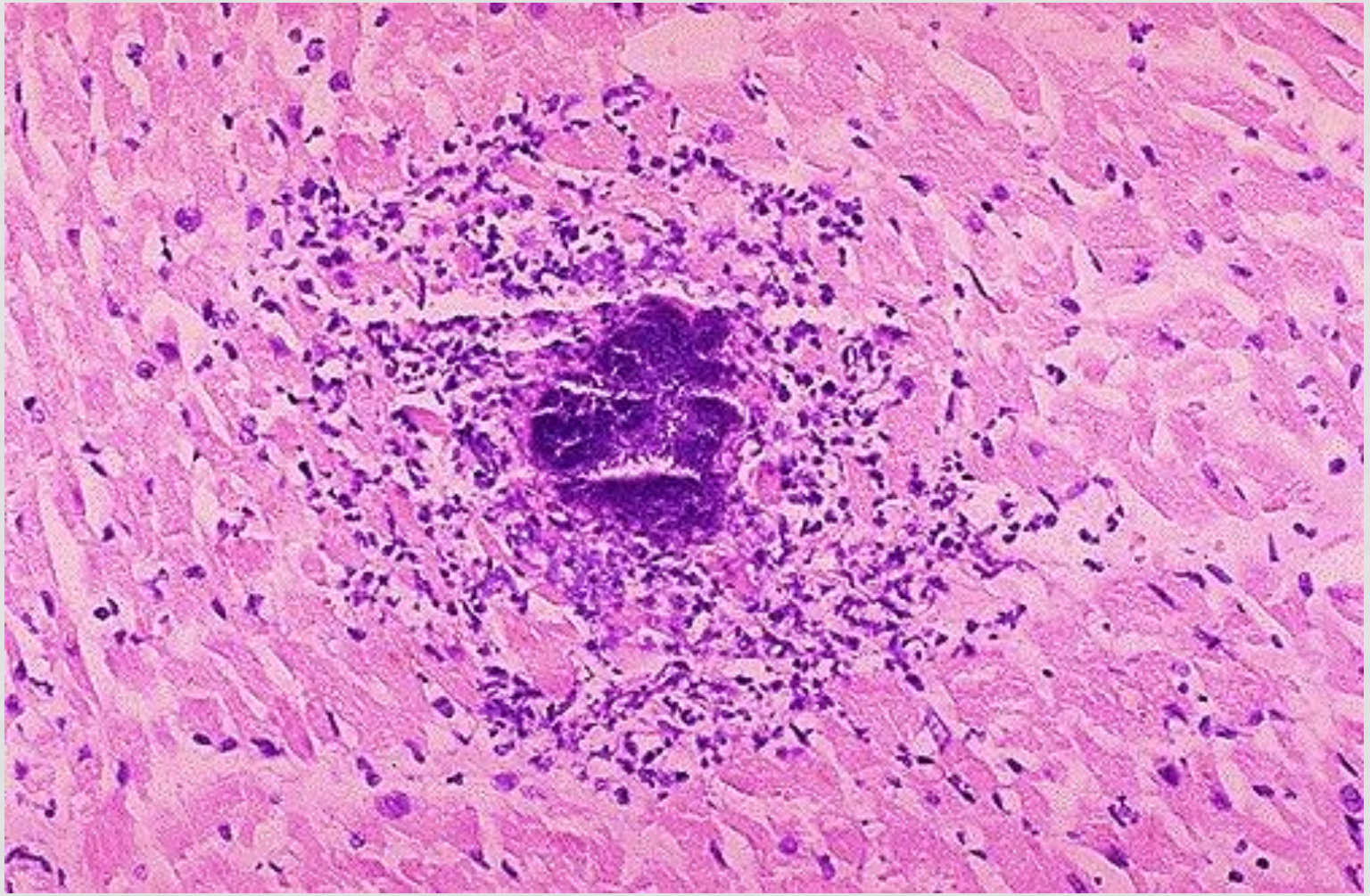
ABSCESS

- It is a limited purulent inflammation.
- Abscesses can be:
  - Single,
  - Multiple (often formed in septicopyemia due to microbial embolism).
- Outcome:
  - At the site of the abscess a scar is formed.
  - In some cases, the abscess takes a chronic course: it is formed a connective tissue capsule around it, the inner layer is represented by a granulation tissue (a pyogenic membrane).

LIVER ABSCESSES



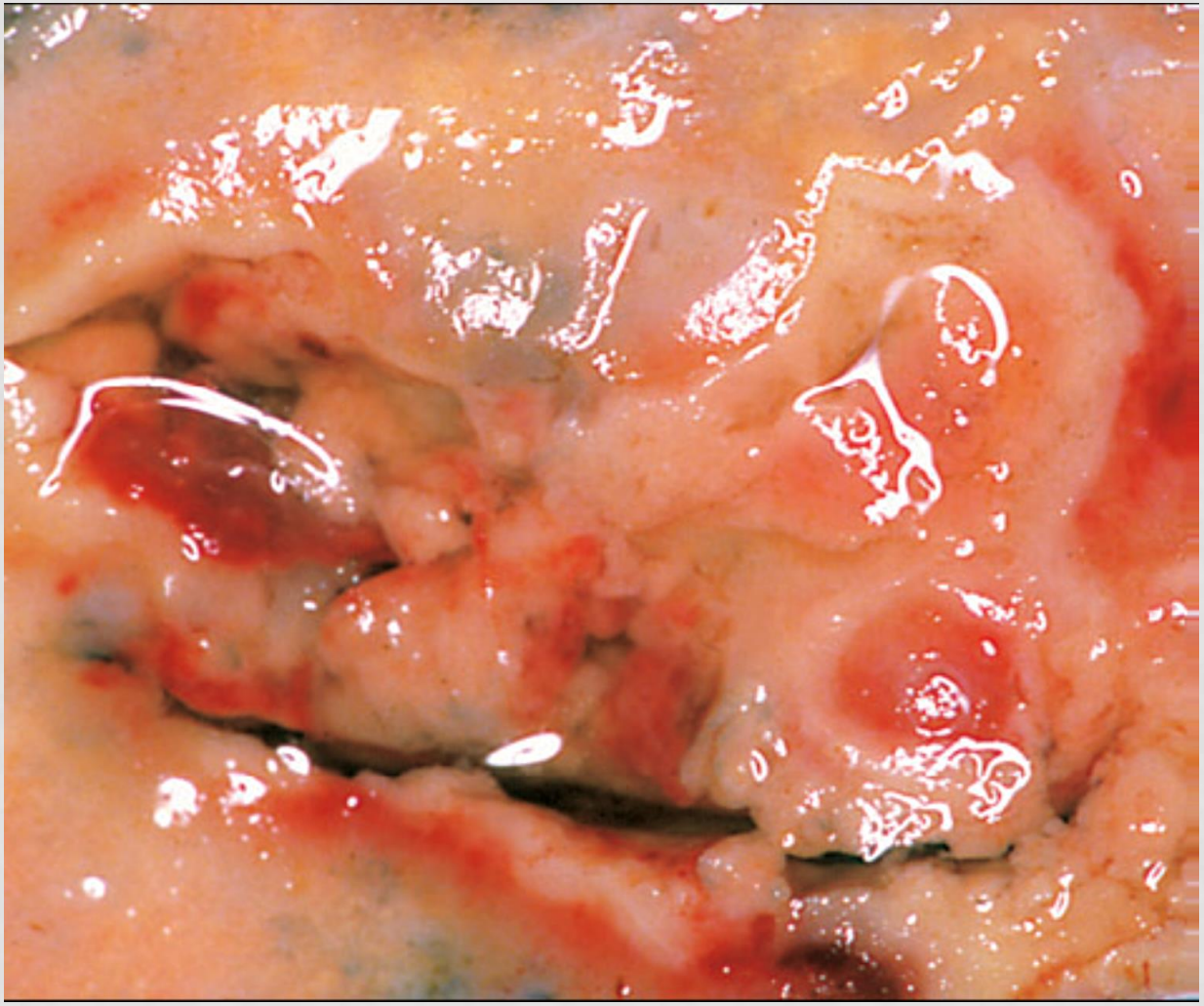
ABSCESS



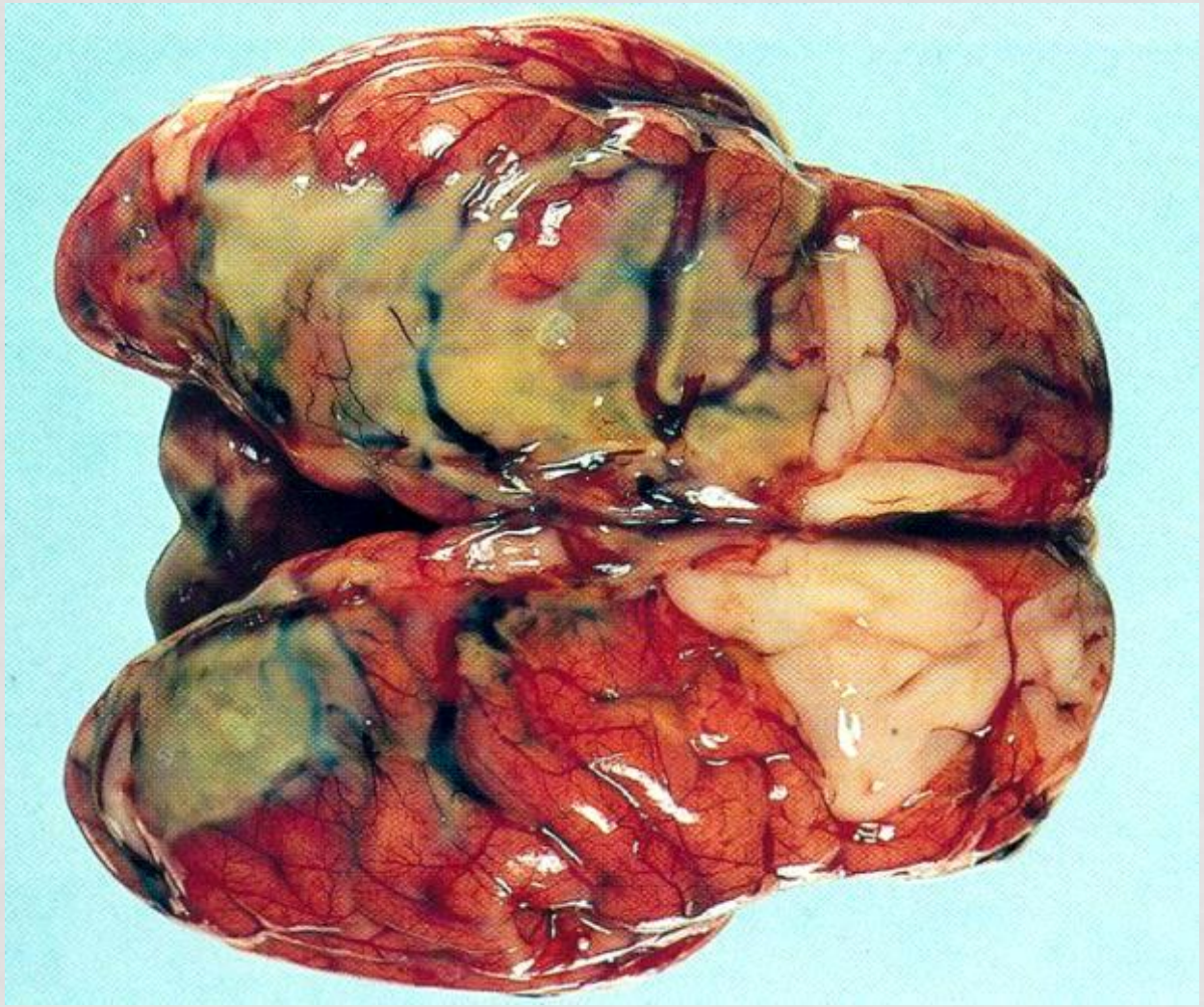
PHLEGMON

- Phlegmon - diffuse purulent inflammation.
- It often occurs in the subcutaneous tissue, in the area of fascia, along the course of the neurovascular bundles.
- Diffusive purulent inflammation can also occur in the parenchymal organs, in the pia mater (purulent leptomeningitis).

SOFT TISSUE PHLEGMON



PURULENT LEPTOMENINGITIS



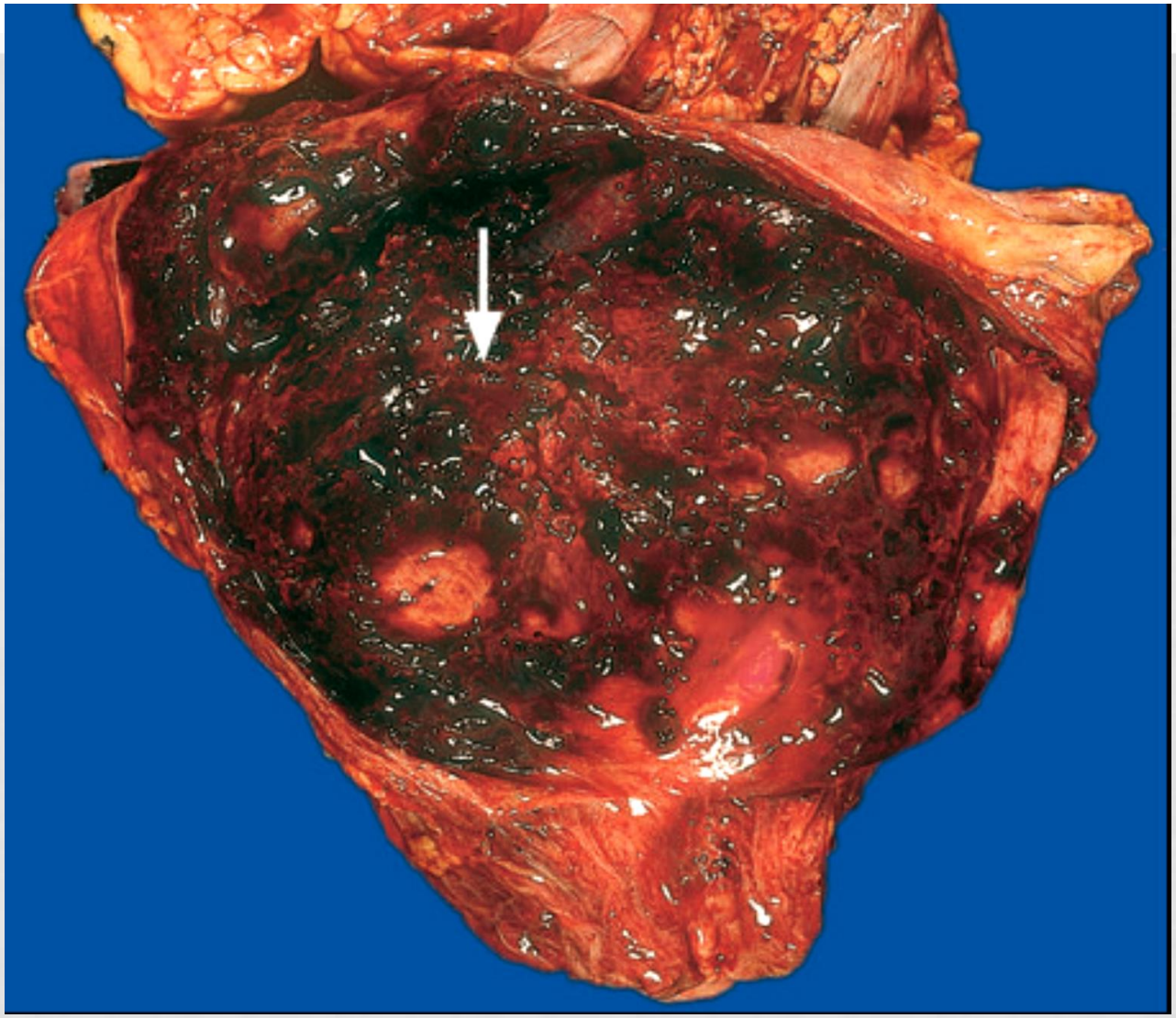
EMPYEMA

- Purulent inflammation in existing body cavities with accumulation of pus is called empyema.

HEMORRHAGIC INFLAMMATION

- It is characterized by the presence in the exudate of a large number of erythrocytes.
- The great importance in its development has vascular permeability
- It occurs in severe infectious diseases:
  - The plague,
  - Anthrax,
  - Influenza.

HEMORRHAGIC CYSTITIS



PUTREFACTIVE INFLAMMATION

- It often occurs in wounds with extensive crushing of tissue or when the wound is heavily contaminated with soil.
- It is more often associated with anaerobic clostridial infection in combination with pyogenic microorganisms.
- Characterized by extensive foci of necrosis.

CATARRHAL INFLAMMATION

- Occurs in the mucous membranes.
- It is characterized by an abundance of exudate that drains from the surface.
- Exudate always contains mucus.
- Can be serous, purulent and mucous.

CATARRHAL INFLAMMATION

- It can occur in infectious diseases (upper respiratory catarrh in ARI), allergic conditions, etc.
- The outcome is often favorable - complete restoration of the mucosa; sometimes can have a chronic course, which is accompanied by a restructuring of the mucosa and its atrophy.

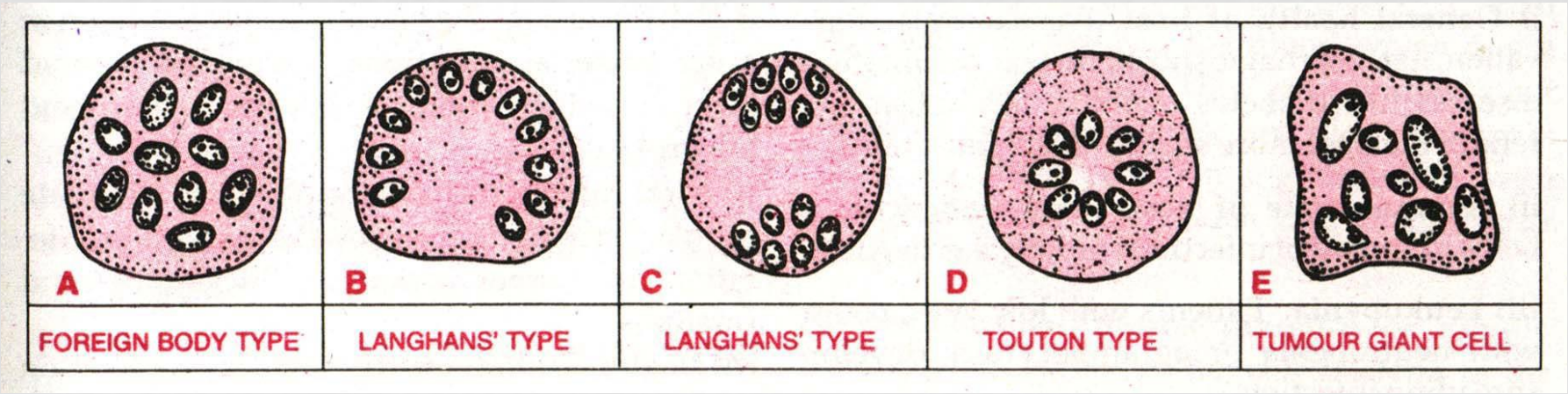
PRODUCTIVE INFLAMMATION

- Characterized by the prevalence of cell proliferation.
- Occurs in the case of a prolonged persistence of the damaging agent due to an imperfect exudative reaction or due to the specific properties of the pathogen itself (incomplete phagocytosis).

PRODUCTIVE INFLAMMATION

- It is accompanied by the appearance of focal or diffuse cellular infiltrates, consisting mainly of macrophages, lymphocytes, plasma cells.
- Is characterized by transformation of macrophages into epithelioid cells, and the latter - into giant cells (foreign bodies or Pirogov - Langhans), as well as increased activity of fibroblasts.

GIANT MULTI-NUCLEATED CELLS



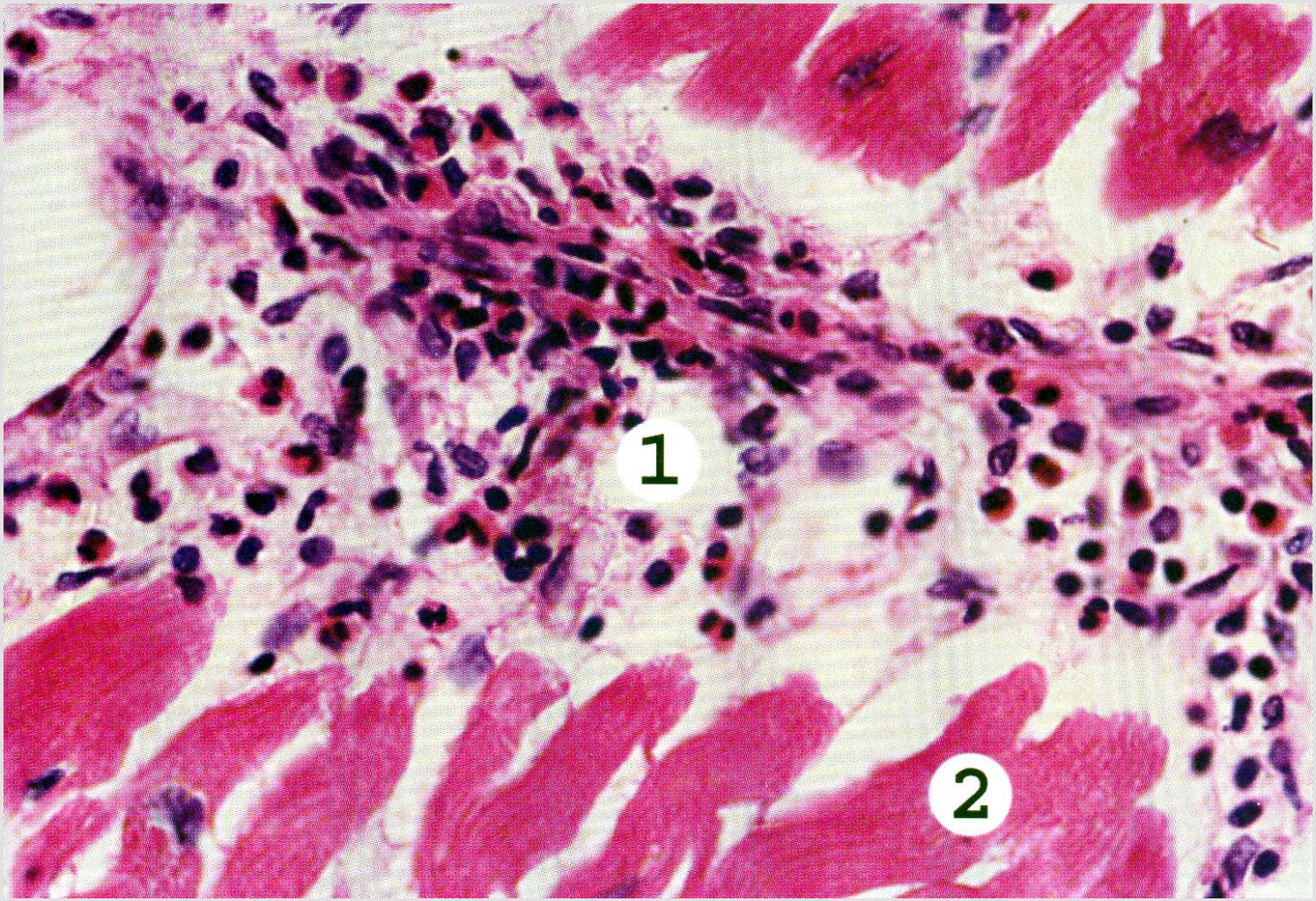
TYPES OF PRODUCTIVE INFLAMMATION

- Interstitial inflammation,
- Granulomatous inflammation,
- Inflammation with the formation of polyps and genital warts.

INTERSTITIAL INFLAMMATION

- Occurs in the stroma of the parenchymal organs (myocardium, liver, kidneys, lungs).
- Outcome: sclerosis of the organ.

INTERSTITIAL MYOCARDITIS



GRANULOMATOUS INFLAMMATION

- Is characterized by the formation of granulomas - cell clusters, which are based on monocytic phagocytes.
- In the development of granulomatous inflammation the resistance of the pathogen to phagocytes is crucial (phagocytic failure in relation to the pathogen - incomplete phagocytosis).

CLASSIFICATION OF GRANULOMAS

- On the etiology:
  - Infectious (tuberculosis granuloma, granulomas around parasitic animals (echinococcus, trichinella), etc.),
  - Non-infectious (granulomas of foreign bodies - around particles of organic and inorganic dust (silicosis, asbestosis)),
  - Unidentified etiology (with sarcoidosis, Crohn's disease, primary biliary cirrhosis, etc.).

CLASSIFICATION OF GRANULOMAS

- By pathogenesis:
  - Immune (reflect the reaction of HRT, most infectious granulomas),
  - Non-immune (most granulomas of foreign bodies).

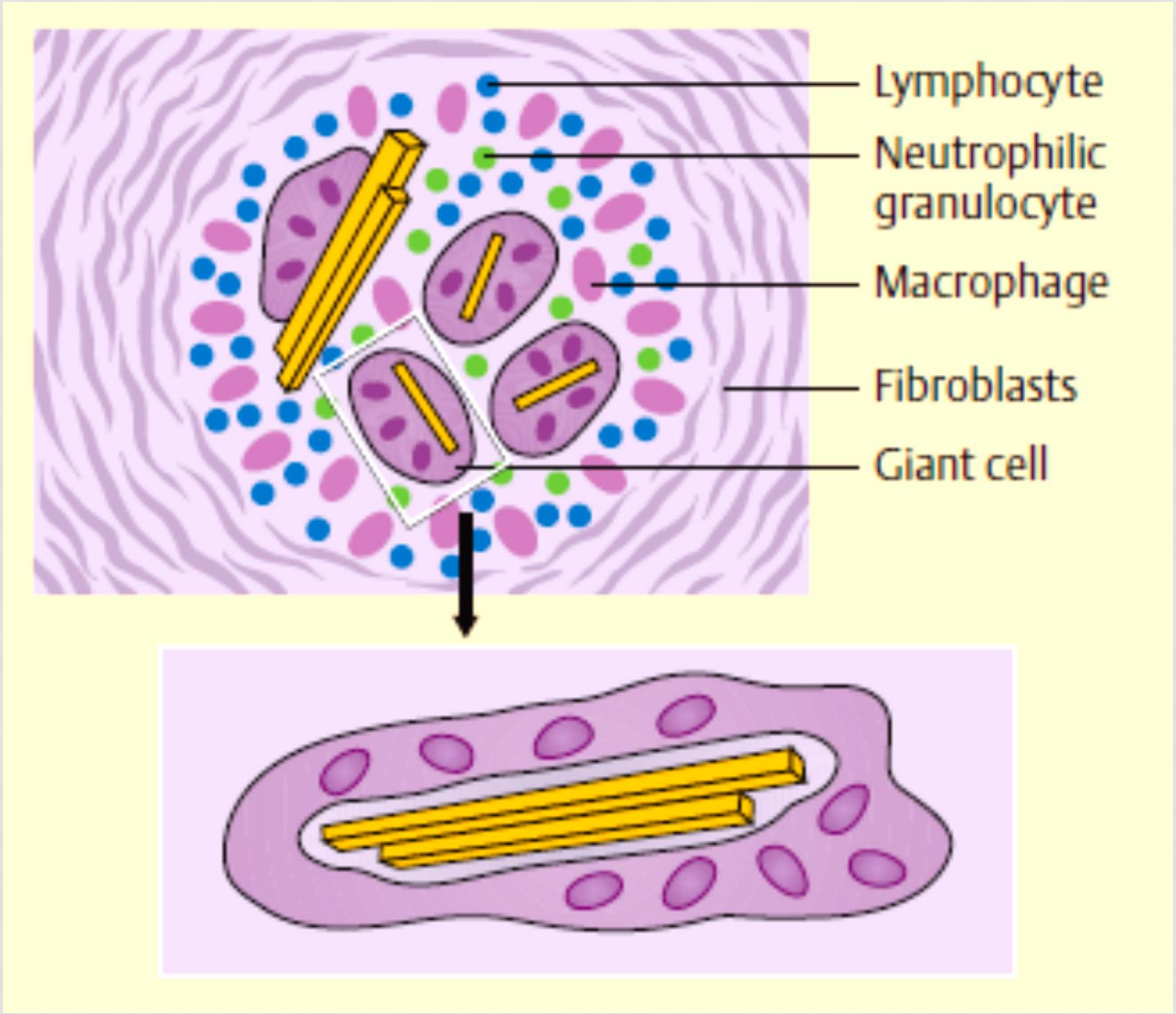
CLASSIFICATION OF GRANULOMAS

- By morphology:
  - Specific,
  - Nonspecific.

NON-SPECIFIC GRANULOMAS

- Do not have distinctive features.
- An example is inflammation around foreign bodies and animal parasites.

FOREIGN BODY GRANULOMA



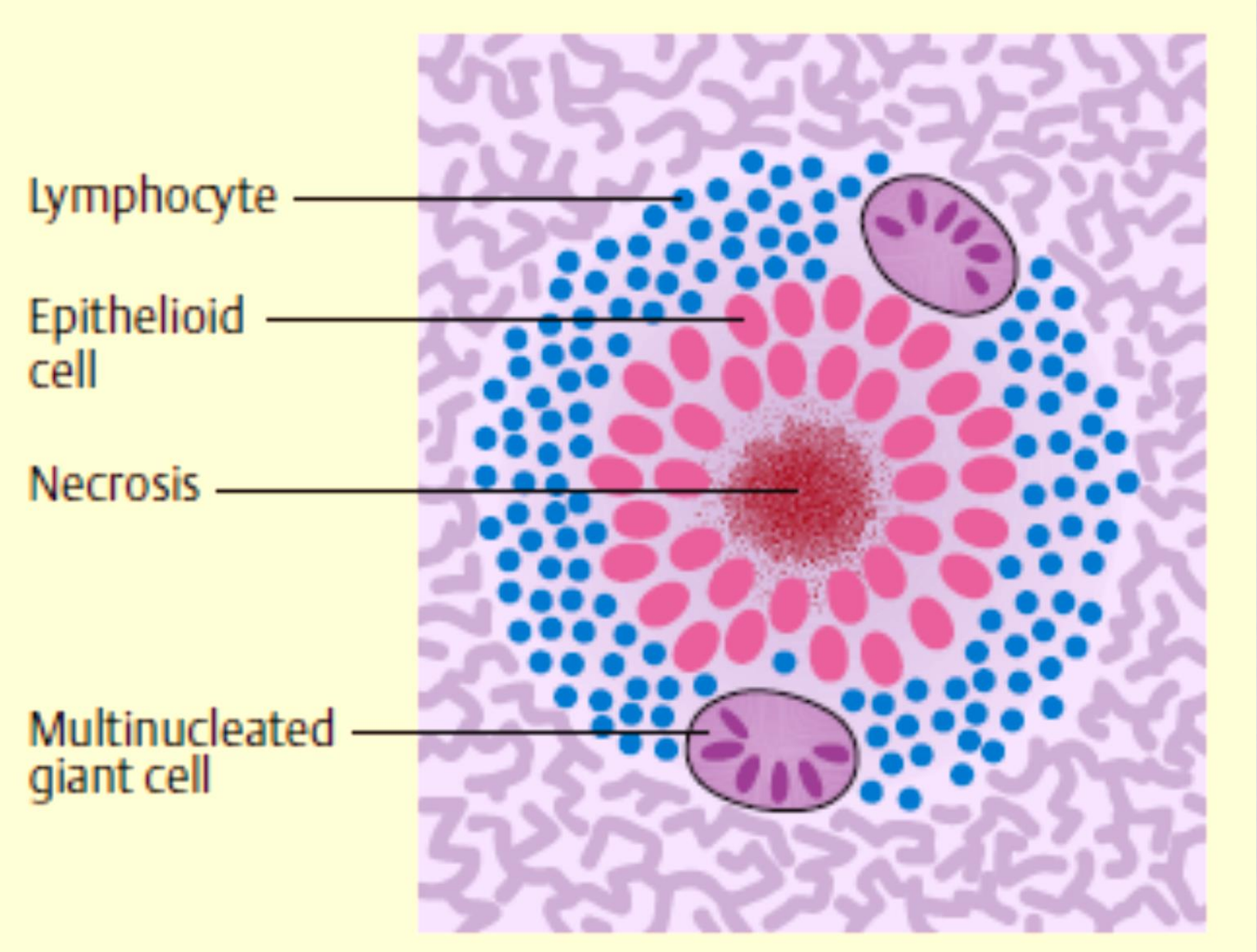
SPECIFIC GRANULOMAS

- They have a distinctive morphological picture, often allowing to establish an etiological factor.
- Discoverable with the following diseases:
  - Tuberculosis,
  - Syphilis,
  - Leprosy,
  - Scleroma.

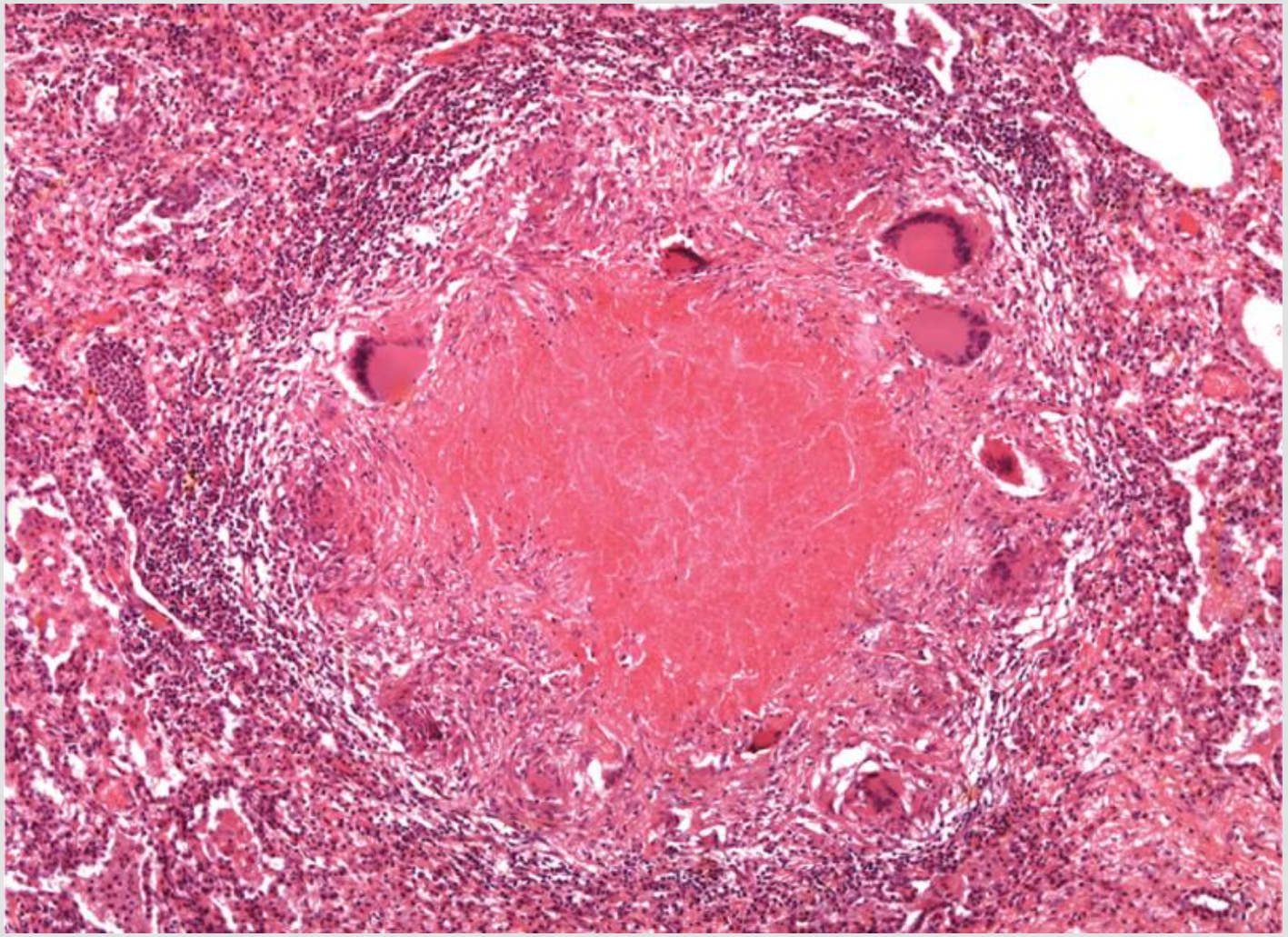
TB-GRANULOMA

- Tuberculosis granulomas are observed in miliary tuberculosis of the lungs and other organs.
- In the outcome of the tuberculosis granuloma, a small connective tissue scar is formed, more rarely petrification.
- Microscopic picture:
  - small foci of caseous necrosis;
  - a shaft from epithelioid cells, among which giant cells of Langhans are visible;
  - on the periphery - the shaft from the lymphocytes.

TB-GRANULOMA



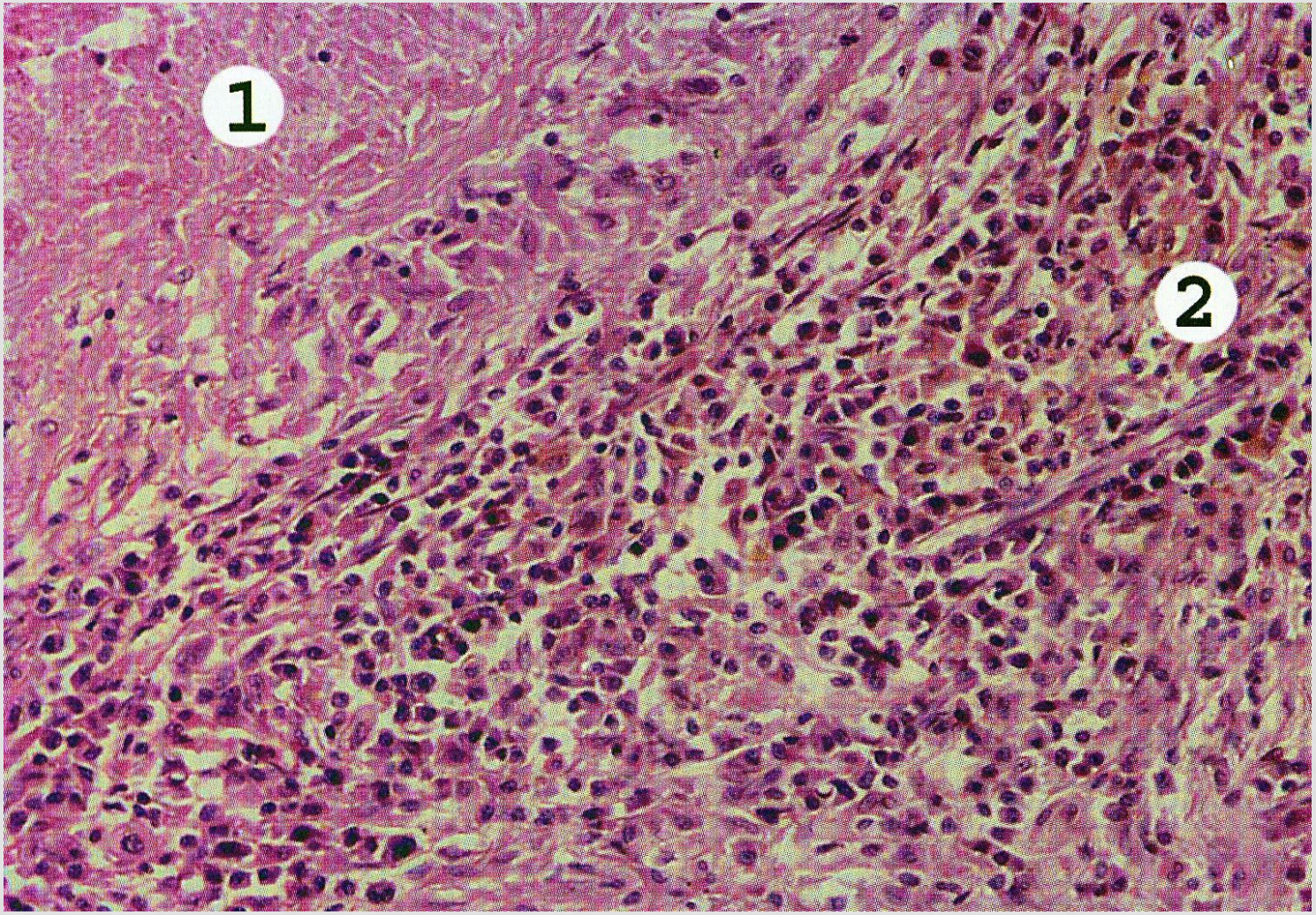
TB-GRANULOMA



SYPHILITIC GRANULOMA (GUMMA)

- Syphilitic granuloma (gumma) is characteristic of the tertiary period of syphilis.
- Localize in bones, skin, brain, liver, etc.
- Outcome: scar.
- Microscopic picture:
  - A large focus of caseous necrosis in the center of the granuloma,
  - Granulomatous tissue with numerous lymphocytes and plasma cells and an admixture of epithelioid cells, fibroblasts; Langhans cells are not characteristic.
  - Characteristic is the abundance of small vessels with the phenomena of productive endovascularity.
  - Connective tissue capsule on the periphery.

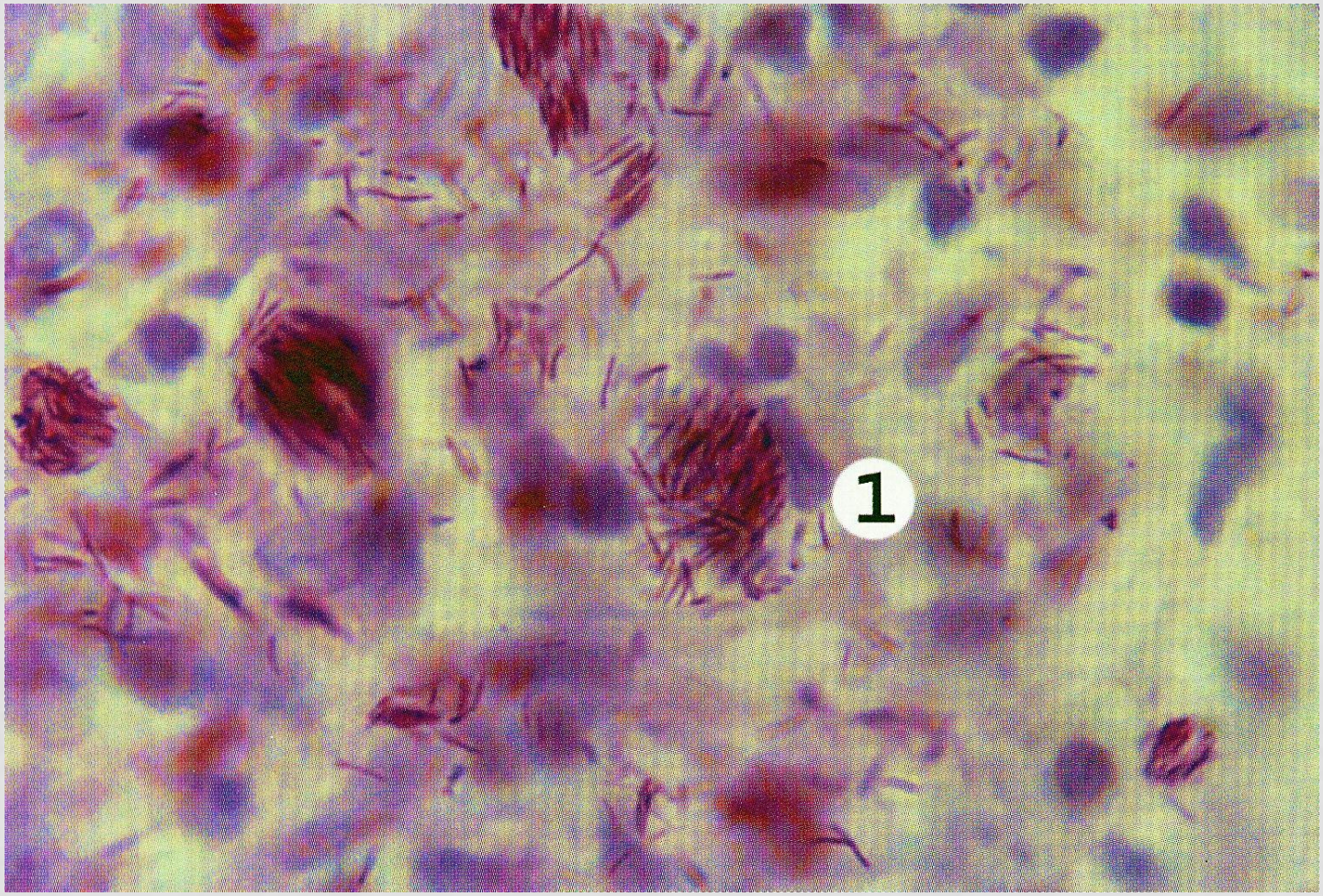
SYPHILITIC GRANULOMA (GUMMA)



LEPROSY GRANULOMA

- Often occurs in the skin.
- The microscopic picture in the lepromatous form of leprosy:
  - Granuloma consists of macrophages, epithelioid, plasma cells and lymphocytes.
  - Leprosy balls (Virkhov cells) are characteristic - giant cells, in the vacuolized light cytoplasm of which, in the Ziehl-Nielsen staining, mycobacteria leprosy (in the form of "palisade" or "cigarettes in a pack") are found.

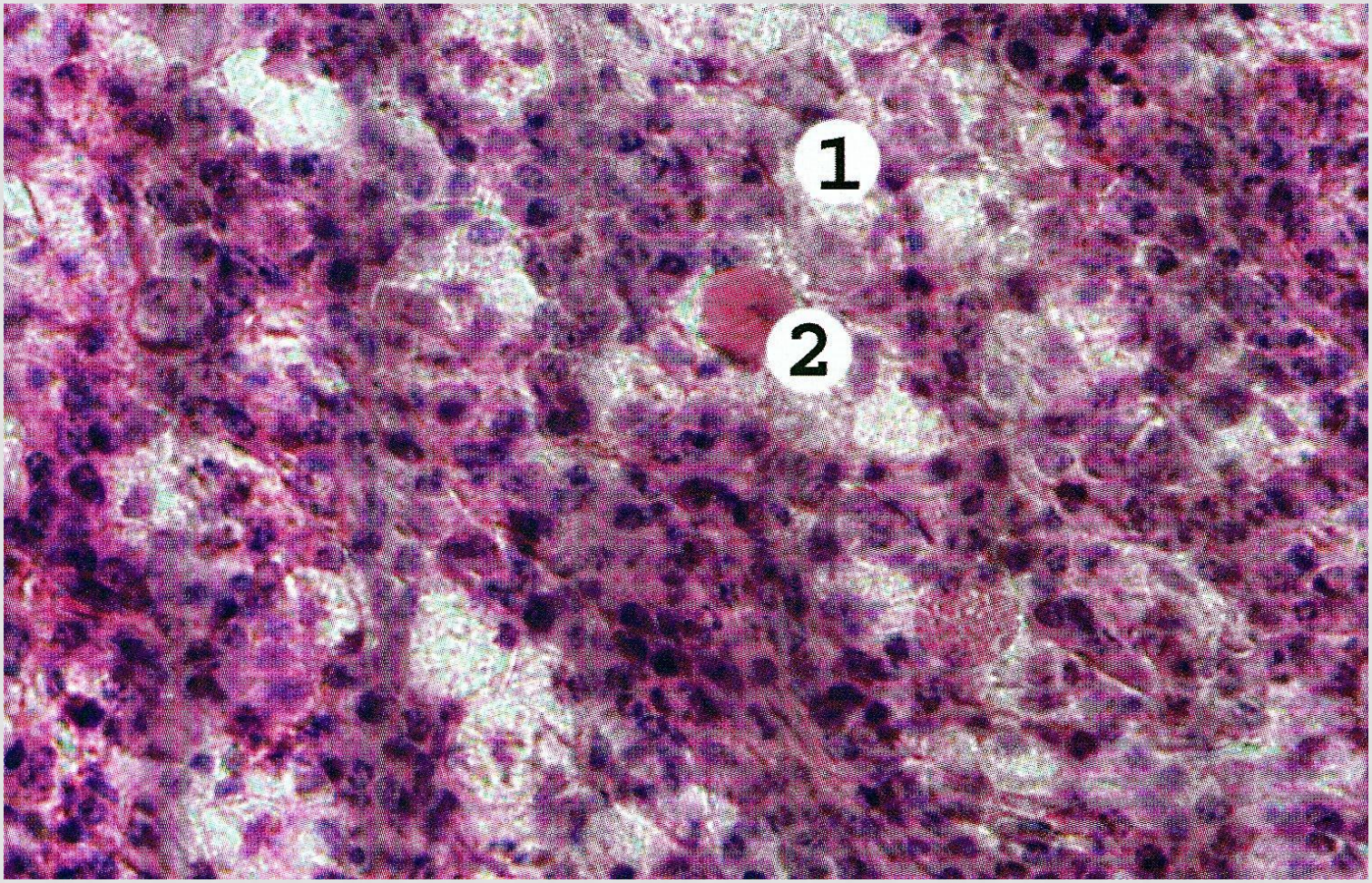
LEPROSY GRANULOMA



SCLEROME GRANULOMA

- They are located mainly in the mucous membrane of the upper respiratory tract.
- Microscopic picture:
  - The granuloma is constructed from lymphocytes, plasma cells and giant cells with a light cytoplasm (Mikulich cells), in which it is possible to detect the scleroma pathogen (Wolkowicz-Frisch sticks).
  - Among the cellular elements of the granuloma are many hyaline balls (Roussel's body), which are altered plasma cells.

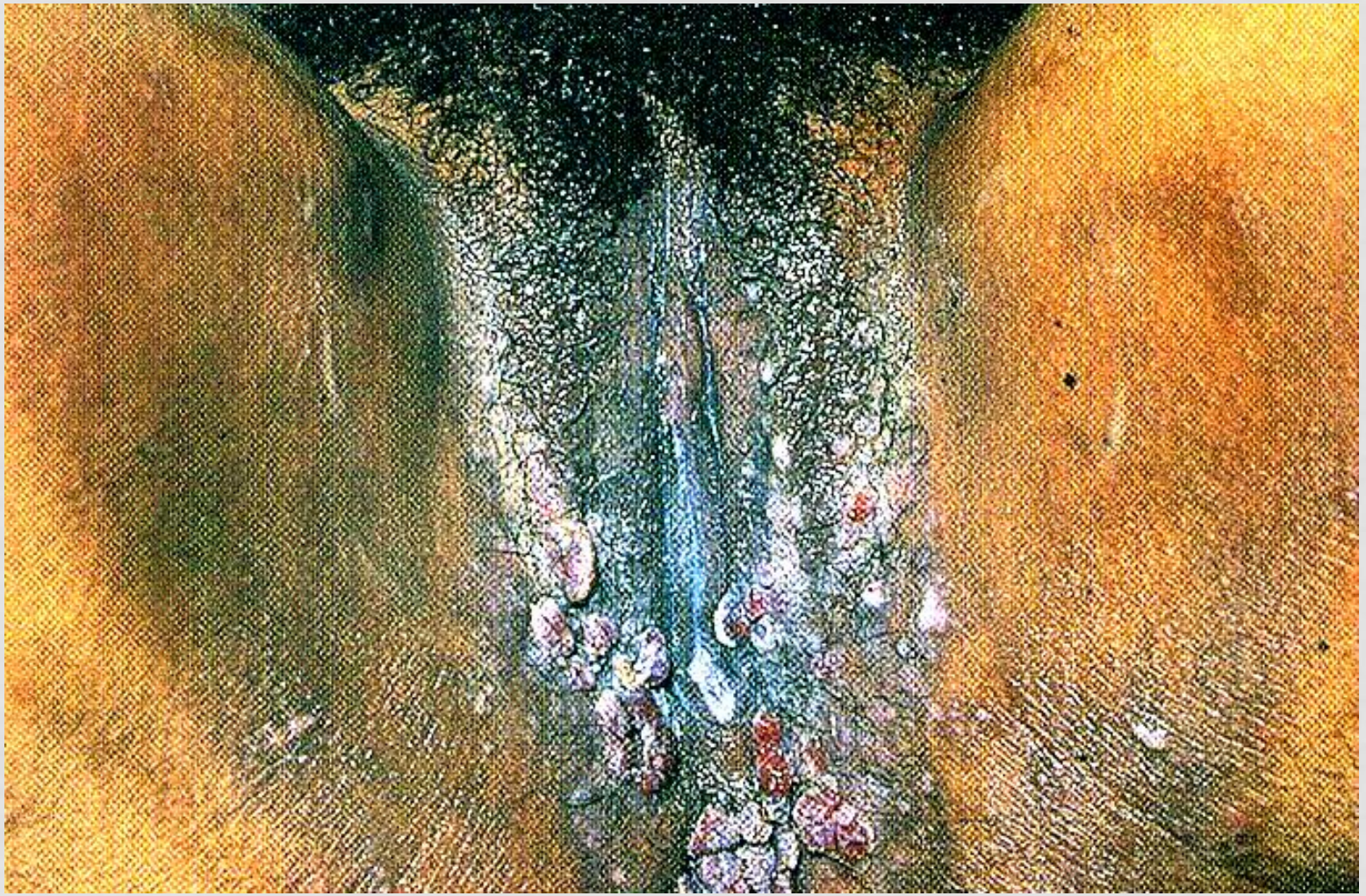
SCLEROME GRANULOMA



INFLAMMATION WITH POLYPS AND CONDYLOMAS

- **Polyps** - overgrowth of the integumentary epithelium as a result of hyperplasia.
  - Polyps appear on the mucous membranes of any organs (nasal cavity, sinus, bronchus, stomach, uterus).
- **Condyloma** - outgrowths formed at the junction of squamous and prismatic epithelium.
  - Condylomata often occur in the anus, the genitals.
  - The most frequent form of condyloma - spiky, is caused by the human papillomavirus.

SPIKY CONDYLOMAS



REGENERATION

- Регенерация – восстановление структурных элементов ткани взамен погибших.

FORMS OF REGENERATION

- The following forms of regeneration are possible:
  - Cellular,
  - Intracellular.

CELLULAR REGENERATION

- Characterized by the multiplication of cells.
- Occurs in the tissues:
  - Represented by labile, i.e. constantly renewed, cells (epidermis, mucous membranes of the gastrointestinal tract, respiratory and urinary tracts, hematopoietic and lymphoid tissue, loose connective tissue).
  - Presented stable, i.e. under normal conditions, possessing low mitotic activity and activation by fissionable cells (hepatocytes, epithelium of the renal tubules, epithelium of the endocrine glands, etc.); stem cells for these tissues are not identified.

INTRACELLULAR REGENERATION

- It is characterized by hyperplasia and hypertrophy of the ultrastructure of the cell.
- There is in all cells without exception.
- Under normal conditions, it predominates in stable cells.
- It is the only possible form of regeneration in organs whose cells are not capable of division (ganglion cells of the central nervous system, myocardium, skeletal muscles).

TYPES OF REGENERATION

- There are the following types of regeneration:
  - Physiological,
  - Pathological,
  - Reparative (restorative).

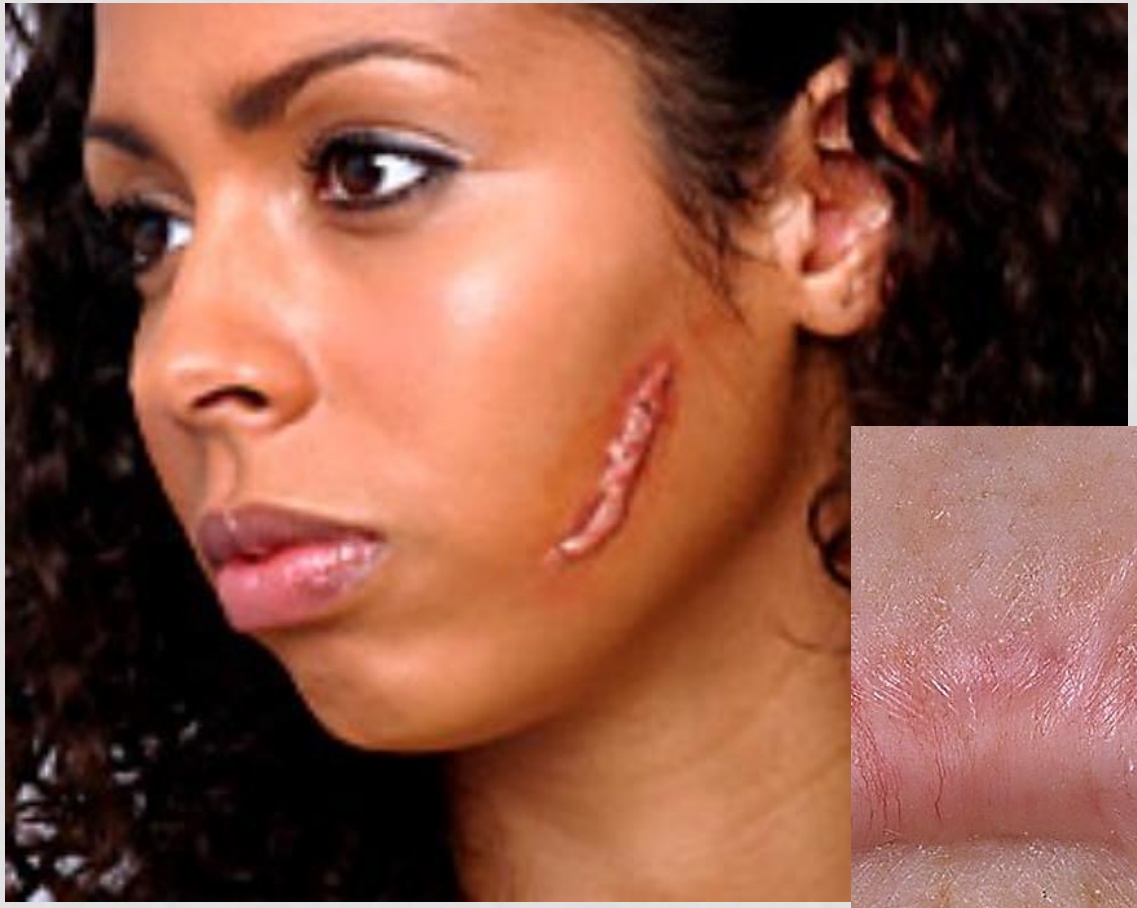
PHYSIOLOGICAL REGENERATION

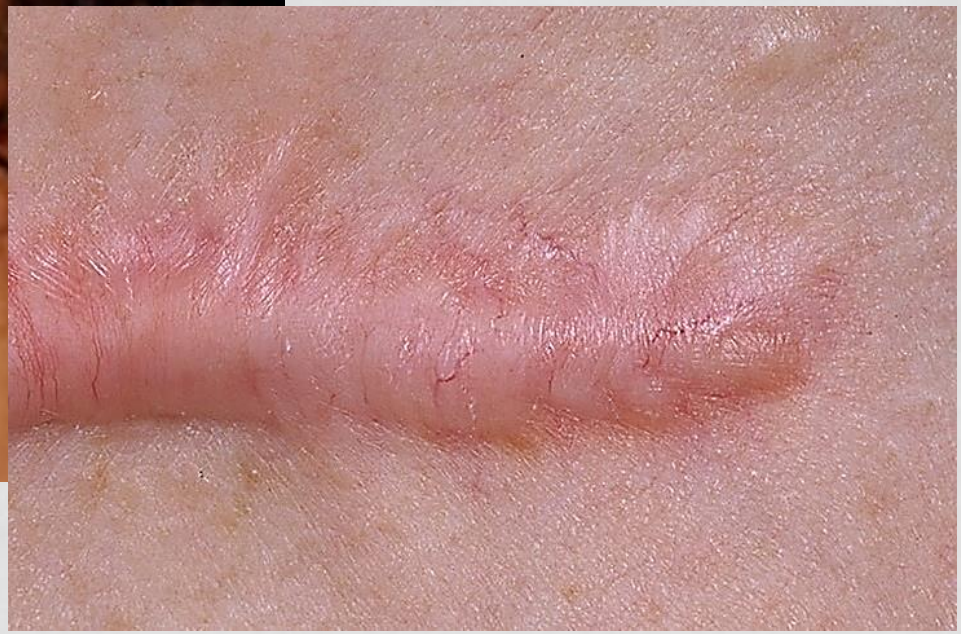
- Physiological regeneration is a constant renewal of the structures of tissues, cells that die in the process of vital activity.
- An example is the renewal of red blood cells every 120 days.

PATHOLOGICAL REGENERATION

- Pathological regeneration - the function of the regenerating tissue is not restored or distorted.
  - Hyporegeneration is a very slow recovery of lost tissue (trophic ulcer),
  - Hyperregeneration is an excessive regeneration, leading to the suffering of the function (keloid scar).

KELOID SCAR





REPARATIVE REGENERATION

- Reparative (regenerative) regeneration - observed in pathology with damage to cells and tissues.
  - Complete reparation - restitution,
  - Incomplete reparation - substitution.

COMPLETE REGENERATION (RESTITUTION)

- Characterized by the replacement of the defect with a tissue identical to the deceased;
- Occurs in tissues capable of cell regeneration (predominantly with labile cells);
- In tissues with stable cells it is possible only in the presence of small defects and with preservation of the basal membranes.

INCOMPLETE REGENERATION (SUBSTITUTION)

- It is characterized by replacement of the defect with connective tissue (scar);
- Hypertrophy of the remaining part of the organ or tissue (regenerative hypertrophy), through which the lost function is restored.

FORMATION OF GRANULATION TISSUE

- Cleansing:
  - It is carried out during an inflammatory reaction that occurs in response to damage;
  - With the help of macrophages, PMNs and enzymes released by them, melting and removal of necrotic detritus, fragments of cells, fibrin takes place;

FORMATION OF GRANULATION TISSUE

- Increased fibroblasts activity:
  - Proliferation of fibroblasts near the damage zone and their migration to the lesion site;
  - Further proliferation of fibroblasts and synthesis of proteoglycans, and then collagen;
  - Conversion of some fibroblasts to myofibroblasts (bundles of microfilaments that are capable of contraction in the cytoplasm);

FORMATION OF GRANULATION TISSUE

- Ingrowth of capillaries:
  - Endothelium in the vessels surrounding the damaged area begins to proliferate and, in the form of strands, grows into the zone of damage with subsequent sewage and further differentiation into arterioles, capillaries and venules;
  - Angiogenesis is carried out under influence of TGFb and FGF;

FORMATION OF GRANULATION TISSUE

- Maturation of granulation tissue:
  - Increase the amount of collagen and its orientation in accordance with the lines of greatest stretching;
  - Decreased number of vessels;
  - Formation of coarse-fibrous scar tissue;
  - Reduction of the scar (myofibroblasts).