5.1. GENERAL ASPECTS

Inflammation is a complex local vaso-mesenchymal reaction of the body to alteration of tissue by various pathogenic factors. It is aimed to eliminate or inactivate and also to delimit the pathogenic agent with the subsequent structure and function reestablishment of the altered tissue. The causes of inflammation can be various physical, chemical and biological factors of exogenous or endogenous origin, which have a harmful action upon the tissues. Morphologically, the inflammatory process is manifest by alternative, exudative and proliferative modifications. In the first, alternative phase of inflammation, in the lesion site, dystrophic and necrotic modifications of the cellular and interstitial elements are observed. As a result of these modifications, chemical mediators of inflammation — biologically active substances are produced, which act upon the blood vessels, determining the evolution of the inflammatory process and encouraging the exudative reactions. According to their origin, the inflammatory mediators may be cellular (tissular) and plasmatic. The cellular mediators are eliminated by labrocytes, neutrophil and basophil leukocytes, thrombocytes, lymphocytes and monocytes (histamine, serotonin, heparin, acid lipids, lymphokines, monokines, etc.). Among the plasmatic mediators of greater importance are kinins (bradykinin and kalikrein) and some components of the complement and clotting / anticoagulating systems of the blood. The cellular mediators can be eliminated from the cells via 2 pathways: a) exocytosis — process that reminds secretion and is observed in leukocytes and b) degranulation, characterized by the elimination of granules from the cytoplasm and their subsequent desintegration in the extracellular space — processes that are observed in labrocytes.

Electromicrography “Degranulation of labrocytes” (fig. 105).

The left side (a) of the image contains the normal ultrastructure of the labrocyte. The cytoplasm contains multiple specific electronodense granules, which contain active amines: histamine, serotonin and heparin. The right side (b) of the image represents the elimination of the granules from the cytoplasm of the labrocyte by ruptures of the cellular membrane.

The second, exudative phase of the inflammation is determined by the chemical mediators (especially by histamine and serotonin) and is manifest by three important processes:

a) dilatation of the microcirculatory system vessels and the disturbance of the blood circulation (modification of the rheologic proprieties of the blood);

b) exudation (extravasation) of plasma

c) migration of blood cells.

The dilatation of the microcirculatory bed vessels, especially of the postcapillaries and venules under the action of histamine, causes an increased blood flow and active inflammatory hyperemia in the lesion site. This clinically is manifest by redness and local fever.
**Microspecimen “Inflammatory hyperemia of the skin in phlegmon”**.

In the dermis (fig.106) the dilatation and marked hyperemia of the vessels, edema with the dissociation of cellular and fibrillar elements, predominantly perivascular diffuse infiltration with neutrophil leukocytes. Macroscopically, the inflamed area of the skin is red and has a locally increased temperature.

Phlegmon is a purulent inflammation with no precise delimitation. It is characterized by the diffuse spreading of the exudate among tissue elements. It is more often localized in the cellular adipose tissue. In skin, the phlegmon can be caused by cutaneous wound supuration as a result of pyogenic bacteria (staphylococcus, streptococcus) invasion.

Exudation (extravasation) of the fluid components of blood with the formation of inflammatory edema and of local tumefaction of tissues represents an essential aspect of inflammation. The extravasation of plasma is determined by the increased permeability of the microcirculatory system vessels and is morphologically manifest by the intensification of pinocytosis processes.

**Electronmicrography “Pinocytosis in the capillary endothelium in inflammation” (fig.107).**

The cytoplasm of endotheliocytes contains multiple pinocytotic vesicles of small dimensions filled with plasmatic liquid. At the inner surface level of the endothelial cells there can be observed the inclusion of plasma by membrane invagination causing the formation of vacuoles. These vacuoles cross the cytoplasm of the endotheliocytes and eliminate their fluid content into the extracellular (extravascular) space.

Subsequently, plasma pass the basal membrane, which has an increased permeability due to the influence of chemical mediators. The mediators (especially histamine, bradykinin, hyaluronidase and other proteolythic enzymes) determine polysacharide depolymerisation of the ground substance, leading to the increased laxity and permeability of the capillary basal membrane. As a consequence, a transendothelial active transport of the blood plasma with the accumulation of fluid in tissues (extravascular spaces) and the appearance of inflammatory edema is observed. The liquid component of the exudate contains water, plasmatic proteins, electrolytes, salts, metabolic products, chemical mediators, antibacterial and antitoxic substances, etc. The quantity and quality of the inflammatory fluid depend on: pathogene agent peculiarities, the level of vasotissular permeability, and the localization of the process.

The migration of the blood cells represents the main aspect of the cellular phase of the inflammation. This process begins with the migration of the neutrophil leukocytes, when they detach from the axial zone of the blood column. The cellular elements move towards the vascular wall. Subsequently, the neutrophils adhere to the endothelial cells, give out cytoplasmic expansions (pseudopodes), and actively strain through the interendotheliocyte junctions into the subendothelial and interendothelial space. After this the neutrophils penetrate the basal membrane, due to the tixotropic phenomenon (the basal membrane ground substance colloidal state modification) and reach the perivascular connective tissue. The leukocytic diapedesis takes place predominantly in the postcapillaries and venules.

**Electronmicrography “Neutrophil leukocyte migration in inflammation” (fig.108 and 109).**

**Figure 108, a** contains neutrophil leukocytes which are attached to the vascular wall; the leukocyte from the lower part of the image penetrated partially into the subendothelial space of the wall, with the help of pseudopodes at the level of interendothelial junctions. On
the surface of the endotheliocyte there can be observed a pseudopod belonging to a third neutrophil leukocyte.

Fig. 108 represents some polymorphonucleated neutrophils, which are situated in the capillary wall, between the endothelium and the basal membrane. Exterior to the basal membrane, collagen fiber fascicles are observed.

Fig. 109 represents two neutrophil leukocytes, which have penetrated the basal membrane and have exited the lumen of the capillary into the perivascular connective tissue. The endothelial layer is unchanged, the contact zones of the endotheliocytes are observed. The lumen of the capillary contains a leukocyte ready to migrate.

Similar to this is the active migration mechanism of monocytes and eosinophils, while the lymphocytes cross the vascular wall through the cytoplasm of the endothelial cells (transendothelial); the erythrocytes cross the vascular wall passively, through the same holes as neutrophils do. After cell migration, the integrity of basal membrane is reestablished.

The polymorphonucleated neutrophils that have reached the perivascular spaces propel themselves actively towards the pathogenic agent through amoeboid movements of cytoplasmic expansions, whose length may be up to 10 times greater than the leukocyte diameter. The propulsion speed of the neutrophil is of about 0.02 mm per minute. This oriented (directioned) movement is due to the substances with positive chemotactic activity – so called attracting substances (immune complexes, some complement fractions, bacterial exotoxins, nucleic acid derivatives and other products from the lesion site).

The main function of polymorphonucleated leukocytes and monocytes in the lesion is phagocytosis – the engulfing of microorganisms, tissular remnants, foreign particles or other substances, with their subsequent intracellular digestion (destruction). Neutrophils are specialized cells, that have the ability to phagocyte small bodies, especially microorganisms (microphages). Monocytes and histiocytes phagocyte large, sizable particles, for example foreign bodies (macrophages). The phagocytosis process includes two main stages: I – the adhesion of the particles or microorganisms to the phagocyte membrane, the invagination of the membrane and their penetration into the cytoplasm; II – the forming of phagocyte vacuoles (digestion vacuoles) around the engulfed particles and their intracellular digestion under the influence of lysosomal enzymes.

Electronmicrography "Phagocytosis" (fig. 110).

The neutrophil leukocyte cytoplasm contains vacuoles with phagocyteded staphilococci, which are in different phases of desintegration.

Phagocytosis can be either complete or incomplete. Incomplete desintegration can encourage the dissemination and generalizing of the infection.

After the phagocytic activity, the neutrophil leukocytes suffer dystrophic modifications, especially fat dystrophy, and die. Monocytes survive for a long time due to their ability of producing new lysosomes and new lysosomal enzymes.

As a consequence of these processes, especially of the plasma extravasation and of blood cells migration, the exudate (the inflammatory fluid) is formed in tissues as a final product of the inflammation.

The main components of the exudate are: a) the liquid part – water with proteins (albumin, globulin, fibrinogen; the liquid composition in proteins is more than 1-2%); b) cells of hematogenic (especially leukocytes and mononuclear phagocytes) and histogenic (local connective, epithelial and parenchymatous cells) origin; c) tissue destruction products (tissular detritus). The consistency, appearance, color and character of the exudate depend on the ratio
between its components. The accumulation of exudate in the inflammatory site leads to local tumefaction of the tissue (tumor) and pain (dolor) as a result of nerve termination compression with tissular tension (related to the inflammatory edema) and their excitement by the chemical mediators (kinins, histamine, various metabolites). The pain and local tumefaction lead to the functional disorder of the organ (tissue) affected by inflammation (functio laesa). The clinical (macroscopic) signs of the inflammation are schematically represented in fig. 111.

The proliferative phase (III) of the inflammatory process is manifest by cellular elements multiplication in the inflammatory site. Vascular hyperemia, extravasation of plasma and the migration of cells in tissues is gradually decreases, thus delimiting the altered zone from the adjacent tissues. The collection of cells in the inflammatory site is called inflammatory infiltrate.

Microspecimen “Cellular infiltrate in the inflammatory site (interstitial productive myocarditis)” (fig. 112). In the inflammatory site of the myocardial stroma there can be observed a localized collection of polymorphic cellular elements: lymphocytes, plasmocytes, macrophages. Leukocytes are rare; the vascular and exudative phenomena are insignificant.

The character of the inflammation depends on:
I) peculiarities of the causal factor (for example, in the lungs the pneumococcus causes fibrinous inflammation frequently, Staphylococcus aureus – purulent inflammation; flu virus – hemorrhagic inflammation);
II) the localization of the inflammatory process (the structural and functional peculiarities of the organ; for example, the lungs have a lax structure, while the bones have a hard, compact structure);
III) macroorganism reactivity (for example, in case of immune deficiency, the inflammatory reaction is more severe and extensive, tending to generalize the morbid process).

The morphologic particularities of the inflammatory process are determined by the relation between three major processes: necrosis of tissues under the action of pathogenic agents, the exudation of plasma and the proliferation of cells.

According to the morphologic criteria, inflammatory reactions are subdivided into exudative and productive.

5.2. EXUDATIVE INFLAMMATION

Exudative inflammation is characterized by the prevalence of microcirculatory bed vascular reaction and the formation of the exudate in tissues and in body cavities.

According to the peculiarities of the exudate the following varieties of exudative inflammation can be distinguished: serous, fibrinous, purulent, putrid, hemorrhagic, catarrhal and mixed. Their general characteristics are represented in table 21.

Serous inflammation (from lat. serum).

In this case, the exudate is a lemon-yellow, opalescent liquid. It contains 1-3% proteins (albumin), like the blood serum, being poor in cells. The localization of serous inflammation is various, the exudate can accumulate in the serous cavities, mucous membranes, meninx, skin and interstitial spaces of the parenchymatous organs (myocardium, liver, kidneys).
Microspecimen “Epidermal vesicle containing serous exudate”.

The specimen (fig. 113) contains a peripheral portion of a cutaneous vesicle formed as a result of epidermal detachment from the dermis by a serous exudates. It has a light eosinophilic color due to the presence of proteins and a reduced number of cells; the superficial zones of the dermis contain a relatively unexpressed cellular infiltration and edema.

Macroscopically, the skin displays swelling filled with yellowish, opalescent fluid; the adjacent zones are edematous and hyperemic (fig. 114).

Serous inflammation of the skin is seen in erysipelas (infectious disease caused by the hemolytic streptococcus – Streptococcus pyogenes), burns (in second degree burns the cutaneous vesicles contain serous exudate), allergic dermatitis, etc.

Microspecimen “Serous focal pneumonia” (fig. 115).

The alveolar lumen contains a pink (eosinophilic) fluid with rare polymorphonucleated leukocytes and desquamated alveolar cells. Clinically, wet rales are heard accompanying the normal respiratory sounds on auscultation of the chest. The most frequent etiology of focal pneumonia is infectious.

Consequently the serous exudate is reabsorbed and the altered tissue is completely reestablished. Serous inflammation evolves usually acutely (1-2-3 weeks), or even overacutely (2-3 days), having a light clinical evolution. Sometimes the serous inflammation can have major clinical manifestations by compression of parenchymatous organs (in pericarditis, serous pleurisy) or by their function disturbances (for example in myocarditis, hepatitis, serous glomerulonephritis).

Fibrinous inflammation

Fibrinous inflammation is characterized by the formation of an exudate rich in fibrin. It is more often localized on mucous and serous membranes, but it is also seen in some parenchymatous organs, for example in lungs (lobar pneumonia), kidneys (fibrinous glomerulonephritis), etc. It appears in cases when the pathogenic agent causes a significant increase of vascular permeability, which causes the extravasation of fibrinogen. After its extravasation fibrinogen coagulates into fibrin under the action of thromboplastin, which is eliminated as a result of tissular necrosis. It is met in infectious diseases (typical examples – diphtheria, dysentery, lobar pneumonia), intoxications (for example in uremia) or under the action of some physical factors (for example in burns).

The exudate is represented by whitish or yellowish membranes, localized on the surface of mucous and serous membranes, or by dense masses formed of fibrin meshwork localized in the respective parenchymatous organs.

Two forms of fibrinous inflammation my be distinguished: croupous and diphtheroid. In the croupous inflammation, the fibrin membrane is thin, weakly adhering to the adjacent tissue and can be easily detached. This is due to the fact that the necrosis of the underlying layers of the mucous and serous membranes is superficial.

Macrospecimen “Croupous tracheitis in diphtheria (diphtheric croup)”.

The mucous membrane of the trachea (fig. 116) is covered with a whitish-yellowish-gray membrane, which has a weak adherence to the underlying tissue. In some places the membrane detaches from the mucous membrane, causing superficial ulcerations.
Inflammation

It is more often seen in diphtheria, but can be also met in cases when some inhaled chemical substances or the cold air, etc. act harmfully upon the mucous membranes of the respiratory ways.

In croupous tracheitis, as a result of easy detachment of the fibrin membrane, stenosis or even obstruction of the respiratory ways and death due to asphyxia can occur.

**Macrospecimen “Lobar pneumonia (stage of gray hepatization)”**

The affected lobe is larger in size (fig.117), of an increased consistency (reminds the consistency of the liver) and without air. When sectioned has a gray color due to the storage in the alveoli of fibrinous exudate, rich in neutrophil leukocytes. On the pleural surface there can be observed fine depositions of fibrin (fibrinous parapneumonic pleuritis).

The most frequent causal factor of the lobar pneumonia is the pneumococcus.

In the evolution of the inflammatory process liquefaction of exudate under the action of leukocyte enzymes, elimination by expectoration, reabsorption by lymph drainage pneumatization of the altered lobe is involved. The pleural fibrinous exudate is usually organized with the formation of fibrous adherences in the pleural cavity.

**Table 21**

<table>
<thead>
<tr>
<th>Type of inflammation</th>
<th>Characteristics of the exudates</th>
<th>Macroscopic aspects of the organs (tissues)</th>
<th>Consequences</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Serous</td>
<td>The exudate is a yellowish opalescent fluid, containing 3-8% proteins (albumin) and a reduced number of cells (leukocytes, lymphocytes); the exudate reminds the blood serum</td>
<td>The tissue is tumefactated, hyperemic, without its characteristic shine, is warm at palpation, the serous cavities contain an accumulation of serous fluid</td>
<td>The process is usually reversible, the exudate is being reabsorbed</td>
<td>Serous pneumonia, myocarditis, hepatitis, peritonitis, etc.</td>
</tr>
<tr>
<td>b) Fibrinous</td>
<td>The exudate is rich in fibrin, has a whitish, opaque, dense appearance</td>
<td>The mucus and serous membranes are covered by whitish or yellowish membranes, which have a weak (croupous infl.) or strong (diphtheroid infl.) adherence to the underlying tissue; the affected zones lose their characteristic shine, and have a husk-like or sawdust-like aspect</td>
<td>On the mucous membranes - the detachment of the membranes with the formation of superficial or profound ulcerations, which subsequently undergo cicatrization. On serous membranes the organization of fibrin with the appearance of adherences in the serous cavities leading to their partial or total obliteration</td>
<td>Fibrinous trachitis, bronchitis in diphtheria; lobar pneumonia, fibrinous colitis in dysentery; and fibrinous pericarditis, pleuritis, peritonitis in uremia</td>
</tr>
<tr>
<td>Category</td>
<td>Description</td>
<td>Pathological Changes</td>
<td>Examples</td>
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<tr>
<td>c) Purulent</td>
<td>Pus is a viscous, dim fluid, of a yellowish-green color, composed of various</td>
<td>The affected zone represents a cavity in the parenchymatous organs or in the walls of cavitory and tubular organs; it is well delimited from the adjacent tissues and is filled with pus (abscess), or is tumefact, with an opaque aspect imbued with pus; the pus fluid diffusely spreading among the tissue elements, without precise delimitation (phlegmon); the inflamed tissue undergoes necrosis and lysis (melting); the cavitory and tubular organs contain accumulations of pus in the respective anatomical cavities (empyema)</td>
<td>Pulmonary, hepatic, renal, cerebral, subcutaneous, etc. – abscess; phlegmonous tonsillitis, appendicitis, gastritis, cholecystitis; phlegmon of the cellular adipose subcutaneous tissue; empyema of the vermicular appendix, bladder, pleural cavity, pericardial cavity, etc.</td>
<td></td>
</tr>
<tr>
<td>d) Putrid</td>
<td>The exudate is a green-gray mass, composed of necrotic, liquefied tissue</td>
<td>The inflamed tissue has a putrid dirty-gray color, with an ugly (fetid) smell</td>
<td>Sclerosis of the altered tissue</td>
<td></td>
</tr>
<tr>
<td>d) Gangrenous</td>
<td></td>
<td></td>
<td>Gangrenous – pneumonia, appendicitis, cholecystitis, endometritis, cystitis</td>
<td></td>
</tr>
<tr>
<td>e) Hemorrhagic</td>
<td>The exudate is rich in erythrocytes, like a hemorrhagic fluid</td>
<td>The inflamed tissue is opaque and has a reddish color</td>
<td>Focal hemorrhagic pneumonia in flu, plague; hemorrhagic meningitis in anthrax; purpuric hemorrhagic dermatitis in variola</td>
<td></td>
</tr>
<tr>
<td>f) Catarrhal</td>
<td>Initially, the exudate has a serous, lemon-opalescent appearance which gradually gets thicker, becoming seromucous (mucous), subsequently becoming mucepurulent</td>
<td>The mucous membranes are tumefact, hyperemic, covered with a serous (serous catarrh), mucous (mucous catarrh) or purulent (purulent catarrh) fluid, which drains on their surface</td>
<td>Catarrhal – rhinitis (cold), tracheitis, bronchitis, cholecystitis, endometritis</td>
<td></td>
</tr>
</tbody>
</table>
Inflammation

**Macrospecimen “Fibrinous pericarditis (villous heart)”**

The epicardium is opaque (fig.118), has an irregular surface, and is covered with villose-like yellowish-white deposits of fibrin, due to the movements of the heart. The heart gains a hairy or “cat tongue” appearance (villous heart). The fibrin deposits are flaccid and can be easily detached (croupous inflammation).

At clinical examination (auscultation) it is manifest by pericardial froutage.

It is seen in rheumatism, tuberculosis, transmural myocardial infarction, uremia, etc.

**Microspecimen “Fibrinous pericarditis”**

On the epicardium surface (fig.119) there can be observed fibrin deposits of a eosinophilic color. In the underlying layer - vascular hyperemia, edema, inflammatory infiltrate with neutrophil leukocytes, lymphocytes, macrophages are present.

Fibrinous pericarditis ends up more often with the organization of the fibrinous exudate and the formation of some adherences inside the pericardial sac, subsequently obliterating it.

With time, calcium salts are deposited in the serous membranes affected by sclerosis. These salts petrifry or undergo ossification (“heart in cuirass”), leading to a progressive chronic cardiac insufficiency.

In diphtheroid inflammation, the fibrin membrane is thicker, having a strong adherence to the underlying tissue. It can be hardly be detached because the necrosis in these regions is much more profound. Fibrin and the necrotic masses form a common compact membrane. If this membrane is detached, sometimes bleeding ulcerations occur.

The croupous or diphtheroid character of the fibrinous inflammation depends not only on the profundness of the necrosis, but also on the type of the mucous membrane epithelium. Diphtheroid inflammation usually affects the membranes covered with squamous epithelium (buccal cavity, tonsils, vocal plicae, esophagus, cervix uteri), while the mucous membranes covered with simple glandular epithelium and the serous membranes (mesothelium) are more often affected by croupous inflammation (superior respiratory ways, gastrointestinal tract, endometrium, pleura, peritoneum, pericardium).

**Macrospecimen “Diphtheroid fibrinous colitis” (fig.120).**

The large intestine wall is thickened and edematous. The mucousa is covered with a rough membrane of a yellowish-white membrane, which adheres to the underlying layer. At its detachment profound bleeding ulcerations remain.

It is frequently seen in severe, toxic forms of dysentery, it can also appear in uremia. The healing process of the ulcerations inside the intestine may result in stenosing and deforming fibrous scars, causing severe functional disorders (constipation, intestinal occlusion, etc.).

The consequences of the fibrinous inflammation can be various: in some cases the complete reabsorption of the exudate occurs due to the fibrinolytic action of the leukocytic enzymes. In other cases the fibrin is not reabsorbed, but organized causing mucous membrane scars or adhesions (also called symphyosis or synchecia). In the serous cavities (pericardial, pleural, peritoneal) causing their partial or total obstruction and the functional disturbance of the respective organs.
Purulent inflammation

Purulent inflammation is characterized by the predominance in the exudate of neutrophil leukocytes, by tissular necrosis and lysis (histolysis).

Pus is a viscous, dim, greenish-yellow fluid, composed of polymorphonucleated neutrophil leukocytes, which suffer dystrophic modifications (especially fat dystrophy) and are gradually desintegrated (so called pus globules or pyocytes), tissular detritus, and microbes. Purulent inflammation is most frequently caused by pyogenic bacteria (staphylococcus, streptococcus, meningococcus, coli bacillus, etc.).

Tissular necrosis in purulent inflammation is due to direct injurious action of pyogenic bacteria toxins on tissues, and to circulatory disorders (linked with vascular thrombosis or with their compression by the inflammatory edema). Histolysis (proteolysis) is produced by proteolytic enzymes (protease), which are eliminated by neutrophil leukocytes; a viscous semifluid mass appears as a result of lysis of the altered and necrotic tissues.

Two morphological variants are met: abscess and phlegmon.

Abscess is a circumscribed purulent inflammation, manifest by lysis of tissues and the formation of a cavity filled with pus.

Macrospecimen “Hepatic abscesses” (fig. 121).
The liver contains multiple cavities of various dimensions, which are well delimited from the surrounding tissue. These cavities contain pus which has a yellowish color.

It most frequently appears after the spread of infection into the liver by the hemogencic way through the portal system (for example, pilephlebitic abscesses in destructive appendicitis), as a complication of severe purulent cholangitis (cholangitic abscesses) or of purulent pancreatitis (infection propagation by lymph vessels), etc. Besides these, liver can be infected by the blood stream through the hepatic artery system in cases of septicemia (pyemic abscesses).

The hepatic abscess can be complicated by fistulization, causing the exiting of pus into the abdominal cavity leading to the appearance of diffuse purulent peritonitis; this process is encouraged by the increased osmotic pressure in the abscess cavity due to the proteolytic processes and to the water absorption from the surrounding tissues. In cases of benign evolution of the abscess, the pus becomes more dense, then subsequently substituted by connective tissue or undergoes calcification (petrification).

Macrospecimen “Metastatic abscesses in kidneys” (fig. 100).
The surface, cortical and medullary layers of the kidney contain multiple small foci, with a yellowish-gray color, filled with pus (abscesses).

Microspecimen “Metastatic abscesses in kidneys (purulent embolic nephritis)”.
The renal cortex and medulla (fig. 122) contain multiple foci of purulent inflammation or abscesses. These are represented by neutrophil leukocyte collections. The renal tissue is destroyed. In the center there are bacterial colonies (bacterial embolus). The tubules and the adjacent glomerules are necrosed, the vessels are dilated and hyperemic. Metastatic abscesses in kidneys appear more often as a result of bacterial embolism seen in septicopyemia (a form of sepsis).
Inflammation

Microspecimen “Acute cerebral abscess” (fig. 123).

The cerebral tissue contains a well outlined focal collection of desintegrating neutrophil leukocytes; the encephalic substance in the purulent site is necrosed and liquefied. In the surrounding tissue dystrophic modifications and pericellular edema is observed.

The cerebral abscess is a complication of purulent leptomenigitis, pneumonia, purulent otitis and mastoiditis or of septicopyemia. Clinically, it is manifest by paresis or paralysis. Small cerebral abscesses can heal resulting a fibrogial cicatrix, while larger abscesses form a cystic cavity.

Acute abscesses are delimited from the adjacent tissue by a fibrinoleukocytic exudate or by granulation tissue. The chronic abscess is delimited by a pyogenic membrane, consisting of granulation tissue rich in capillaries from which an intense migration of leukocytes takes place. On the outer side, the membrane consists of fibrous connective tissue.

According to its clinical evolution, the abscess can be either acute or chronic. The consequences of abscesses can be:

a) Organization (cicatrization);

b) Petrifaction (condensation and calcification of the pus);

c) Fistulization – formation of fistulas, through which the pus drains to the exterior or into a preformed bodily cavity. The pathologic channel through which the pus drains from the abscess cavity to the exterior or onto the surface of the organ, or can penetrate into a neighboring organ is called a fistula. If the purulent site contains tissue fragments, which can not undergo autolysis or organization, or are unable to exit the cavity due to their excessive dimensions, then this substance is called sequestrum (for example, bony sequestrum in fistulized purulent chronic osteomyelitis).

Phlegmon (phlegmonous inflammation). It is characterized by a diffuse spreading of pus, with no delimitation among tissular elements, along intermuscular spaces, adipose tissue and neuro-vascular trunks, etc. It is more often caused by streptococcus hemolyticus, which produces great amounts of hyaluronidase and fibrinolysin. These alter the ground (intercellular) substance, encouraging the spreading of the inflammatory process. It is seen in adipose tissue (subcutaneous, mediastinal, retroperitoneal), in muscles, in the walls of cavitory and tubular organs (vermicular appendix, gall bladder, stomach, intestine, etc.) and in leptomeningitis, etc.

Macroscopic “Purulent leptomenigitis” (fig. 124).

The leptomeninge from the convex surface of the brain, especially from the frontal, temporal and parietal zones, is thickened, edematous, imbued with a yellowish-gray purulent exudate. The inflamed zone does not have a precise outline. Most frequently the cause of purulent leptomeningitis is the meningococcus. In consequence, either the reabsorption of the exudate and the complete resolution, or the thickening of membranes and the formation of some adhesion between the membranes can occur on the brain surface, encourage the appearance of cystic cavities in the leptomeninges or internal hydrocephaly due to the stenosis or obstruction of Magendie and Luschka orifices.

Macroscopic “Acute phlegmonous appendicitis” (fig. 125).

The vermiform appendix is thickened, especially its distal portion, dilated, filled with pus (empyema). The serous membrane is opaque, hyperemic and covered with fibrinous
deposits of a whitish-gray color (periappendicitis). The wall of the appendix is thickened, imbedded diffusely with pus; the mesentery is thickened, edematous, hyperemic. The most severe complications of acute phlegmonous appendicitis can be: perforation of the wall causing peritonitis, gangrene of the appendix with its autoamputation, metastatic abscesses in the liver, etc.

**Microspecimen “Phlegmonous inflammation of the adipose tissue (phlegmonous cellulitis)” (fig.126).**

In this specimen there can be observed a diffuse infiltration of the adipose tissue with neutrophil leukocytes, most of which are in state of desintegration. The blood vessels are dilated and hyperemic.

Macroscopically, the inflamed zone is tumefected, warm at palpation and imbedded with pus. On section, it has a dim, yellowish-gray color. It can have either a hard, wood-like consistency (*hard phlegmon*) or a flaccid one (*soft phlegmon*), depending on the spreading and gravity of the tissular necrosis processes in the respective zone (in cases of diffuse tissular necrosis the consistency is harder).

Phlegmon of the subcutaneous adipose tissue (dermal phlegmon) of diverse localization can occur as a complication of purulent wounds, furunculus, carbuncle, dental caries, lymphadenitis, hydradenitis, osteomyelitis, etc.

According to its clinical evolution, the phlegmonous inflammation can be either acute or chronic. The acute phlegmon can be complicated with septicemia (when the inflammation spreads along veins and lymphatic vessels with the installation of thrombophlebitis and purulent lymphangitis). Secondary amyloidosis can occur as a complication of chronic forms of abscesses and phlegmons.

The site of purulent inflammation can be infected with putrefaction bacteria (*colibacilli, proteus vulgaris*, etc.), which cause putrid desintegration of the inflamed tissues, accompanied by gas formation having an unpleasant (putrid) smell. Such an inflammation is called a **putrid (gangrenous) inflammation**. It is localized in tissues that are in contact with the external environment (gangrenous - tonsillitis, stomatitis, pneumonia, appendicitis, colitis, endometritis, etc.).

**Hemorrhagic inflammation**

Hemorrhagic inflammation is characterized by the presence of a great number of erythrocytes in the exudate. It is seen in flu, plague, streptococci infection, anthrax, variola, especially in patients with hemorrhagic diathesis or cachexy.

**Microspecimen “Influenzal hemorrhagic bronchopneumonia”**.

The lung is diffusely hyperemic (fig.127), the alveolar and bronchiolar lumen contains an exudate composed mainly of erythrocytes. In some places there can be observed a serous eosinophilic fluid and a reduced number of macrophages and leukocytes. Macroscopically the sites of hemorrhagic pneumonia have a reddish color.

The hemorrhagic exudate usually is associated with another type of inflammation. It has to do with a significant increase of vascular permeability and/or with a negative chemotaxis towards leukocytes.
Catarrhal inflammation

It affects the mucous membranes of the respiratory ways (rhinitis, bronchitis), digestive tract (gastritis, enteritis, colitis, cholecystitis), urogenital ways (endometritis, salpingitis, cystitis). First the catarrhal exudate has a serious character, and yellow color when the mucous membranes drain an abundant liquid exudates. The exudate gradually gets thicker, gaining a mucous (seromucous) character, due to the excessive secretion of mucus, desquamation of epithelial cells and migration of neutrophil leukocytes. In the end the exudate may become purulent (mucopurulent).

Macro- and microspecimen “Catarrhal tracheitis”.

The inferior portion of the trachea contains a yellowish-white viscous exudate, which drains on the surface of the mucous membrane (fig. 128). Microscopically, the exudate consists of mucus, serous liquid, desquamated epithelial cells and a reduced number of neutrophil leukocytes; the mucosecretory glands are larger in size, filled with mucus.

According to its clinical evolution, the catarrhal inflammation can be either acute or chronic. The acute catarrhal inflammation can heal in 1-2-3 weeks. Chronic catarrhal inflammation can lead to the atrophy or hypertrophy of the mucous membranes, causing function disorders in the respective organs (for example, the hypertrophic chronic rhinitis is manifest by nasal talking, while the atrophic rhinitis—by resonant voice). The most frequent causes of the catarrhal inflammation are: viral and bacterial infections, irritant gases, toxic substances (uremia), thermal factors, etc.

5.3. PRODUCTIVE INFLAMMATION

5.3.1. General aspects

Productive (proliferative) inflammation is characterized by the predominance of cell multiplication and transformation in the inflammatory site. The alteration and exudative modifications are insignificant. As a result of the proliferation processes, in the inflammation zone, diffuse or focal collections of cells appear, which are called inflammatory infiltrate. The cellular composition of these infiltrates can be various, but more often the predominance of 3 cell types can be observed: monocellular phagocytes (macrophages, epithelioid and gigantic cells), lymphoid cells (lymphocytes, plasmocytes, immunoblasts) and fibroblasts, and very rarely—leukocytes, especially eosinophils (in allergic inflammations). The predominance of different cell populations can vary depending on the stage of the inflammatory process. Most important are the macrophages and their derivations: epithelioid and polyeneated gigantic cells, which have the function of phagocytosis, which encourages the healing and regeneration processes.

Productive inflammation is usually chronic in nature, evolving for several months or even years. The chronic character of the inflammatory process is caused by the persistence of the pathogenic agent (infection or foreign body) in the lesion site. The inflammation persists as long as the irritant factor maintains its action. With elimination of the irritant, repair (regeneration) processes begin. The cellular composition of the inflammatory infiltrate gradually becomes homogeneous, and the predominance of only one cell is observed—the fibroblast. This cell participates at fibrillogenesis processes making the inflammation end with the neoformation of connective tissue (fibrosis, sclerosis and cirrhosis of the organs), (table 22).
Characteristic of connective tissue proliferation processes

<table>
<thead>
<tr>
<th>The name of the process</th>
<th>Characteristic</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrosis</td>
<td>The proliferation of connective tissue without the hardening of the organ</td>
<td>Pneumofibrosis, myofibrosis</td>
</tr>
<tr>
<td>Sclerosis</td>
<td>Pathological process, which leads to diffuse (microfocal) or local hardening of the internal organs, vessels, tissues, due to the excessive proliferation of the connective tissue</td>
<td>Cardiosclerosis, pneumosclerosis, nephrosclerosis, arteriosclerosis, phlebsclerosis</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>Sclerotic process, which leads to significant deformations of the organs</td>
<td>Hepatic, pulmonary, renal - cirrhosis</td>
</tr>
</tbody>
</table>

Chronic inflammation occurs in cases of:

- a) reduced pathogenicity (virulence) of the infection (for example, mycobacterium tuberculosis);
- b) physical factors, which can not be phagocytized (sand, talc, foreign bodies);
- c) small concentrations of chemical substances;
- d) repeated and prolonged action of harmful agents (for example of professional factors);
- e) circulatory disorders in the tissue that is affected by the action of the pathogenic agent.

Rarely the productive inflammation may have an acute evolution (for example in typhus fever).

So, the most frequent consequence of the productive inflammation is the neoformation of connective tissue in the place of the lesion site, causing the appearance of some more or less extended cicatrix, adherences, synechia, etc. More rarely the reabsorption of the inflammatory infiltrate can occur in productive inflammation, leading to the complete reestablishment of the altered tissue.

There can be distinguished 3 types of proliferative inflammation:

- a) interstitial;
- b) granulomatous;
- c) with the formation of the polypus and condyloma acuminatum.

5.3.2. INTERSTITIAL INFLAMMATION

The inflammatory process is localized in the stroma of the parenchymatous organs (myocardium, kidneys, lungs, liver).

Microspecimen “Interstitial myocarditis”.

The interstitial tissue of the myocardium (fig.112) contains infiltrates consisting of lymphocytes, monocytes, macrophages, plasmocytes, fibroblasts. The cellular infiltration is more prominent around the vessels (perivascular), especially in the subendocardial and subepicardial zones. In the sarcoplasma of the cardiomyocyte dystrophic lesions is observed. It is seen in viral infections (measles, rubella, influenza), bacterial infections (scarlet fever, typhus exantheticus, meningococcic infection, typhoid fever, brucellosis, septicemia, etc.), myotic and parasite infections. Clinically, it is manifest by signs of cardiac insufficiency,
rhythm and conduction disorders, etc. As a consequence of interstitial myocarditis, either the complete rehabilitation of the myocardium or cardiosclerosis can occur.

**Microspecimen "Interstitial pneumonia" (fig.129).**

The inflammatory process is localized in the pulmonary interstitium, the interalveolar septa are thickened, edematous, hyperemic and infiltrated with mononuclear cells (lymphocytes, monocytes, macrophages). The alveolar lumen contains an insignificant number of desquamated alveolar cells.

Interstitial pneumonia is more often seen in viral infections. Clinically, it is manifest by gas diffusion processes disorders (alveolo-capillary block). The severe forms can cause diffuse pneumofibrosis.

**Microspecimen "Productive vasculitis in periarteritis nodosa" (fig.130).**

The coronary artery wall is considerably thickened due to the diffuse inflammatory infiltration (lymphocytes, macrophages, plasmocytes), localized especially in the adventitia. In the stroma there can be observed a slight tendency towards basophilia and edema. The arterial lumen is thinner than normal. As a consequence, either acute coronary insufficiency, with the necrosis of the myocardium, or the chronic coronary insufficiency, with the beginning of cardiosclerosis can occur.

The periarteritis nodosa belongs to the rheumatic diseases group (collagenosis). Though the name of the disease indicates the localization of the inflammatory process in the adventitia, all the tunics of the arterial wall are affected, thus this is a panarteritis.

### 5.3.3. GRANULOMATOUS INFLAMMATION

Granulomatous inflammation is characterized by the formation of granulomas in the inflammatory site. The granuloma represents a circumscribed focal inflammatory infiltrate, which appears as a result of proliferation and transformation of phagocyte and lymphocyte cells of bone marrow origin. Usually a granuloma has a diameter of about 1-2 mm, but it can reach up to 3-5 cm. A tissue detritus (with a possible localization of the pathogenic agent) can be observed in the center of the granuloma; it is surrounded by cellular elements, especially by monocytes, lymphocytes and their derivations (macrophages, epithelioid and gigantic cells, plasmocytes).

According to their cellular composition, the following types of granulomas can be distinguished:

a) macrophagic granuloma (simple granuloma or phagocytoma);
b) epithelioidocellular granuloma (epiteliodocytoma);
c) giganticcellular granuloma (gigantocytoma).

Typical macrophagic granulomas are formed in rheumatism, especially in the tunics of the heart.

**Microspecimen "Granulomatous inflammation of the endo- and myocardium in rheumatism" (fig.131).**

The stroma of the endo- and myocardium contains multiple foci of productive inflammation. These are round or oval shaped granulomas, composed of polymorphous macrophages with big nuclei, intensively stained with hematoxyline, and having a basophilic cytoplasm. Among the granuloma cells there can be observed connective tissue desintegration
products, fibrinoid masses (fibrinoid intumescence) and tissular detritus (fibrinoid necrosis). In some granulomas the cellular elements have a palisade or fan disposition around the fibrinoid central masses (fig. 132).

The rheumatic granuloma appears as a disorganizing inflammatory reaction of the connective tissue. It is produced under the action of streptococcus-β hemolyticus from group A (the main causal agent of rheumatism). Macrophages posses a high phagocytic activity and are capable of fibrinoid mass reabsorption. Dynamically, as the fibrinoid masses are gradually absorbed, the prevalence of fibroblasts is becoming evident in the granuloma, as the collagen production increases and the granuloma undergoes cicatrization (substitution with connective tissue). The evolution in time of the granuloma from its debut until cicatrization lasts for about 3-4 months.

Granulomas appear in cases when the pathogenic agent is relatively resistant to phagocytosis, and can not be rapidly digested so that it persists for a long time in the inflammatory site. By granuloma formation, the harmful factor is isolated, outlined from the rest of the body, thus the pathological process being localized. Under the action of the granuloma cells, degradation and gradual destruction of the pathogenic agent occurs. Besides this, the cells of the granuloma possess the function of secreting various biologically active substances, which regulate the local tissular medium and contribute to the regeneration of the altered tissues.

Granulomatus inflammation reflects the reduced intensity of phagocytosis processes, and the body ability to outline and localize the pathogenic agent. It has been experimentally demonstrated that it is impossible for the inflammatory site that contains macrophages to get secondary local infection.

The formation of granulomas begins with a focal accumulation in tissues of young, inactive monocytes from the vascular bed. When these become mature, they transform into macrophages - cells with a pronounced phagocytic ability (so-called "sweeping cells" or "scavenger").

Those macrophages that can not phagocytize or the ones that have already engulfed particles, completely digested and eliminated them, transform gradually into epithelioid cells. The life duration of these cells is of 1-4 weeks. These cells can divide leading to the formation of new typical macrophages. If the phagocytized material can not be immediately digested or is hard to digest, the macrophages transform into gigantic polynucleated cells (macrophages suffering from "indigestion"). The gigantic cells subdivide into "foreign body" cells and Langhans type cells; they are formed as a result of incomplete fusion or division of epithelioid or macrophage cells. These are seen in tuberculosis, syphilis, mycosis, in cases of insoluble substances (ligatures, sutures, foreign bodies, talc, sodium urate crystals in gout, etc.). The gigantic cells can have a diameter of about 150μ and can contain up to 200 nuclei. In the gigantic cells of foreign bodies the nuclei have a chaotic distribution in the cytoplasm, while in the Langhans cells - a uniform distribution along the cellular membrane, in crown-like or horseshoe-like shapes occur.

Microspecimen "Foreign body granuloma in gout (gout tophus)".

The subcutaneous tissue (fig.30) contains deposits of sodium urate salts, surrounded by necrotic foci and perifocal inflammatory infiltrates with polynucleated gigantic cells - foreign body cells. These cells have the function of uric salts reabsorption. These macrophages surround the salt deposits, outlining and isolating them from the healthy adjacent tissues. The peripheral zones of the granuloma contain fibrous connective tissue fascicles. Macroscopically, these productive granulomatus have the appearance of painful nodules in articulation regions.
The granulomatous inflammation is seen in more than 70 diseases (granulomatous diseases). Usually, it appears in cases of: a) resistance to phagocytosis of the pathogen agent (incomplete phagocytosis); b) significant concentrations of the pathogen agent; c) the presence of factors that stimulate the maturation activity of the macrophages, for example, of corpuscular substances. The classification and most frequent etiology of the granulomatous inflammation is represented in table 23.

### Table 23: Classification of the granulomatous inflammation after etiologic criteria

<table>
<thead>
<tr>
<th>Granuloma group</th>
<th>Examples of granulomatous diseases</th>
<th>The most frequent localization of Granulomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Nonspecific infectious granulomas</td>
<td>Typhus fever</td>
<td>Lymphoid structures from the small intestine, mesenteric lymph ganglions, spleen, bone marrow</td>
</tr>
<tr>
<td></td>
<td>Exanthematic typhus</td>
<td>Brain, skin and other organs (excluding the liver, spleen, lymph nodes and bone marrow)</td>
</tr>
<tr>
<td></td>
<td>Tularemia</td>
<td>Skin, lymphatic ganglions</td>
</tr>
<tr>
<td></td>
<td>Brucellosis</td>
<td>Liver, heart, brain, meninx, kidneys, spleen</td>
</tr>
<tr>
<td></td>
<td>Rabies</td>
<td>Brain (medulla oblongata, Sylvian aqueduct zone, the wall of the third ventricle, Ammon’s horn)</td>
</tr>
<tr>
<td></td>
<td>Polyomyelitis</td>
<td>Spinal cord (anterior horns)</td>
</tr>
<tr>
<td></td>
<td>Cat scratch disease</td>
<td>Lymphatic ganglions - satellites of the pathogenic agent inoculation zone</td>
</tr>
<tr>
<td></td>
<td>Various mycosis:</td>
<td>Cervico-facial region, digestive tract, lungs</td>
</tr>
<tr>
<td></td>
<td>- actinomycosis</td>
<td>Digestive tract, urinary ways, lungs</td>
</tr>
<tr>
<td></td>
<td>- candidosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Parasitic diseases:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- echinococcosis</td>
<td>Liver, lungs</td>
</tr>
<tr>
<td></td>
<td>- trichinellosis</td>
<td>Skeletal muscles</td>
</tr>
<tr>
<td></td>
<td>- cysticercosis</td>
<td>Brain, eyes, skeletal muscles</td>
</tr>
<tr>
<td></td>
<td>- toxoplasmosis</td>
<td>Brain, eyes</td>
</tr>
<tr>
<td>II) Specific infectious granulomas</td>
<td>Tuberculosis</td>
<td>Characteristics given in table 24</td>
</tr>
<tr>
<td></td>
<td>Syphilis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Leprosy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rhinoscleroma</td>
<td></td>
</tr>
<tr>
<td>III) Rheumatic diseases granulomas</td>
<td>Rheumatism</td>
<td>Tunics of the heart</td>
</tr>
<tr>
<td></td>
<td>Rheumatoid arthritis</td>
<td>Periarticular tissues</td>
</tr>
<tr>
<td></td>
<td>Nodose periarteritis</td>
<td>Small and medium caliber arteries</td>
</tr>
<tr>
<td>IV) Noninfectious granulomas</td>
<td>Pneumoconiosis:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- anthracosis</td>
<td>Lungs</td>
</tr>
<tr>
<td></td>
<td>- silicosis</td>
<td>Lungs</td>
</tr>
<tr>
<td></td>
<td>Foreign bodies</td>
<td>Various localization</td>
</tr>
<tr>
<td></td>
<td>Suture material</td>
<td>Various localization</td>
</tr>
<tr>
<td></td>
<td>Oily substances (drugs)</td>
<td>Cellular adipose tissue</td>
</tr>
<tr>
<td>V) Granulomas of an unclear genesis</td>
<td>Sarcoidosis</td>
<td>Lymphatic ganglions, skin, lungs, liver, spleen</td>
</tr>
<tr>
<td></td>
<td>Crohn disease</td>
<td>Gastrointestinal tract</td>
</tr>
<tr>
<td></td>
<td>Horton disease</td>
<td>Temporal artery (temporal egantocellular arteritis)</td>
</tr>
</tbody>
</table>
The macro- and microscopic aspects of the granulomatous inflammation of different origin are illustrated in the anatomical and microscopic specimens described below.

**Macro- and microspecimen “Granulomatous productive inflammation in hepatic echinococcosis”**

Macroscopically (fig.133), the liver contains a cavity, (unicameral echinococcus or hydatid cyst) outlined by a whitish membrane - so called chytric membrane - filled with multiple daughter-vesicles. A fibrous capsule is formed around the echinococcic cyst, while the adjacent hepatic tissue is compressed and undergoes atrophy.

Microscopically (fig.134), the specimen contains small cavities delimited by chytric membranes, stained homogeneously with eosin (pink). Outside the chytric membrane, the hepatic tissue contains necrotic foci, and a zone of productive inflammation with a polymorphous cellular infiltrate. This infiltrate contains numerous eosinophil leukocytes. On the periphery the proliferation of fibrous connective tissue is observed; in the adjacent hepatocytes dystrophic and atrophic modifications are revealed. The infiltrate may contain unique gigantic cells (foreign body cells). These cells have the function of chytric and necrotic masses reabsorption. The presence of eosinophils indicates sensitivity to the toxic substances eliminated by the parasite. The fibrous capsule that is formed around the echinococcic cyst during the productive inflammation delimits the parasite, protecting the neighboring tissues from harmful action. If the echinococcus dies, the altered zone infiltrates with calcium salts (calcification and petrification).

**Microspecimen “Foreign body granuloma (suture granuloma)” (fig.135).**

The specimen contains unreabsorbed catgut sutures surrounded by a productive inflammatory reaction having great number of polymorphonuclear foreign body gigantic cells (reabsorption cells). The inflammatory reaction leads to the gradual reabsorption of the suture material. If this does not happen, than the encapsulation with fibrous connective (cicatrial) tissue and the isolation from the rest of the organ occurs, with the formation of a pseudotumoral nodule of a hard consistency.

**Microspecimen “Actinomycotic granuloma in the lung” (fig.136).**

The specimen contains an inflammatory focus with a central zone containing an actinomycotic druse (colony of actinomyces, intensely stained with hematoxylin, surrounded immediately by a neutrophil leukocyte collection (abscess). The next zone constitutes a inflammatory infiltrate made out of macrophages, plasmocytes, epithelioid cells, xanthomatos cells (these contain lipids, have a clear foamy cytoplasm, due to the fat being dissolved in alcohol), neoformed vessels, and young connective tissue cells. At periphery there is fibrous connective tissue.

Macroscopically, the actinomycotic sites are hard, yellow on section, with multiple small confluent abscesses. The affected zone looks like a honeycomb. It is most frequently seen in the cervico-facial region (buccal cavity, tonsils, cervical subcutaneous tissue). It often produces external fistuleae, while in chronic forms secondary amyloidosis may occur.

The most frequent consequences of the granulomas are:

a) the resorption of the cellular infiltrate;
b) organization;
c) incorporation;
d) calcification (petrification);
e) ossification;
f) secondary necrosis.
5.3.3.1. SPECIFIC GRANULOMATOUS INFLAMMATION

The specific inflammation differs from common (nonspecific) inflammation by characteristics of the granuloma, that make possible the morphological diagnosis of the respective disease without identifying the pathogenic agent. Most frequently specific granulomatous inflammation is seen in tuberculosis, syphilis, leprosy and rhinoscleroma. The productive inflammation in these diseases has usually an undulate chronic evolution and is accompanied by primary or secondary caseous necrosis of the altered tissue (primary necrosis appears at initial penetration of the pathogenic agent, while secondary necrosis is preceded by exudative or proliferative reactions). It must be mentioned that in these diseases, alterative, exudative and proliferative inflammatory lesions are observed. Productive inflammation characterizes the particular disease, a granuloma being the most eloquent morphologic sign of the specificity and of great significance for diagnosis.

The general characteristic of the specific granulomatous inflammation is summarized in table 24.

Tuberculous granulomatous inflammation

The macroscopic appearance of the tuberculous granulomas is clearly seen in the miliary tuberculosis of the lungs.

**Macroscopic “Miliary pulmonary tuberculosis”**

The sectioned surface of the lung (fig. 137) contains multiple whitish-gray lesions of a hard consistency. They are the size of a millet grain (lat. milium), 1-2 mm in diameter, uniformly spread through the lung parenchyma. These lesions represent tuberculous granulomas, which appear due to the spreading (generalizing) of the infection via hematogenous pathways.

**Microscopic “Tuberculous granuloma in the lungs”**

The pulmonary parenchyma contains tuberculous granulomas (fig. 138) that have a central zone of caseous necrosis (macroscopically, the necrotic masses has a “cheese-like” appearance), which is eosinophilic, amorphous (astructural) and anuclear. They are surrounded by a crown of cells placed in the following order: immediately surrounding the necrosis are the epithelioid cells, with enlarged, pale nuclei which have a radial distribution; they remind the cells from stratum spinosum of the epidermis (that is why they are called so), though they are of mesenchymal origin. Among these there can be observed the Langhans giant polynucleated cells, with eosinophilic cytoplasm and the nuclei placed in a horseshoe or crown-like pattern (fig. 139). The Langhans cells are typical of tuberculosis.

Their cytoplasm may contain phagocytosed Koch bacilli. At the periphery of the granuloma there can be seen a belt of lymphoid cells (small lymphocytes, macrophages and lymphocytes).

The absence of blood capillaries and the persistence of reticulin fibers are typical. Depending on the prevalence of specific cellular elements, tuberculous granulomas can be gigantocellular, epithelioid and lymphoid ones.

The tuberculous nodules can be of various dimensions, from the size of a pin head (in miliary tuberculosis) up to structures of several cm in diameter.
General morphopathology

The consequences of the tuberculous granuloma can be various. In cases of favorable evolution (tuberculostatic treatment, increased body resistance) resorption, organization, encapsulation or petrification and ossification of the lesion can occur. Unfavorable evolution can lead to secondary caseous necrosis and the softening of the granuloma.

Syphilitic (luetie) granulomatous inflammation

The inflammatory lesions characteristic of syphilis appear in the tertiary phase of the disease, which appear 3-6 years after contamination. They can have a nodular or diffuse character and are morphologically manifest by the formation of granulomas in organs and tissues. These are called syphilitic gummas or gummos (gumma type) infiltrates. Syphilitic gummas can be solitary or multiple. Their localization can be very diverse: in visceral organs (liver, heart, brain, kidneys), tegument, soft tissues, bones, cartilage, nasal septum, etc. The diameter of the gummas can vary from 1 cm to 5-6 cm (from the size of a pea to that of a hen egg).

*Macrospecimen “Syphilitic gumma in the liver” (fig.140).*

The liver section contains a well delimited node of affected tissue, having a pink-gray color and elastic consistency. With time the central zones of the gumma suffer necrotic modifications and the softening of the preexisting tissue. This zone is reminiscent of the arabic gum (that is where the name comes from: gr.kommi – gumma, rubber).

Microscopically (fig.141), the syphilitic gumma represents a necrotic site in the center, in which preexistent tissular structures can be seen (unlike in tuberculosis, where the caseous necrotic zone is amorphous, astructural). It is surrounded by a cellular wreath, consisting predominantly of lymphocytes and plasmocytes, though epithelioid and some Langhans type giant cells can also be seen, but are not characteristic of luetic inflammation. Blood vessels persistence is typically seen, with a productive inflammation (phlebitis and arteritis), leading to their narrowing and lumen obliteration. This obliteration explains in some degree the appearance of necrotic lesions.

The syphilitic gumma evolves more frequently into sclerosis and connective tissue cicatrization, with the formation of some retractile and deforming cicatrix in parenchymatous, cavitary and tubular organs. For example the deforming of the nose (“saddle nose”), liver (*hepar lobatum* – “rope-tied liver”), and lungs (*pulmo lobatus*), strictures of larynx, trachea, stomach, etc.

The syphilitic gumma-type inflammation has a more or less diffuse character; the infiltrate consisting of lymphocytes and plasmocytes mostly located perivascularly. It can be seen in aorta, liver, stomach, bronchi, intestines, etc.

*Microspecimen “Syphilitic mesoartitis” (fig.142).*

The medium layer of the aorta contains lymphoplasmonic infiltrates surrounding the vasa-vasorum. There is fragmentation of elastic fibers. The ascending portion of the aorta including the semilunar valves are most seriously affected. Gummatous inflammation can evolve into sclerosis and cirrhosis of the affected organs and tissues. Syphilitic mesoartitis leads to the installing of ascendent aorta aneurysm. Rupture of the aneurism is one of the frequent causes of death in syphilitic patients.
Leprous granulomatous inflammation

In leprosy the inflammatory lesions are more frequently localized in skin, subcutaneous tissue, superior respiratory ways, peripheral nerves, etc.

The specific granuloma — lepoma, appears in the lepromatous form of leprosy. It represents a inflammatory focus in the dermis of the skin. It is separated from the epidermis by a clear zone of connective tissue poor in cellular elements. The granuloma is made out of macrophages, lymphocytes, plasmocytes and giant cells with a foamy (vacuolar) cytoplasm due to the lipidic inclusions — so called leprous cells (leprous globes or Virchow cells). The latter are typical of leprosy and represent some macrophages, whose cytoplasm contains huge numbers of Hansen bacilli (leprous mycobacteria), closely packed like cigarettes in a box, which are made prominent by staining in the Ziehl-Nielsen test (fig. 143).

Macroscopically (fig. 144), the lepromas look like nodes of various shape and size located in the skin. The lepromas granulomas can become necrotic, subsequently organizing and forming mutilating scars, which distort the facial features (“leonine face”). As the disease evolves, trophic changes, cutaneous ulcerations, finger distortion, phalange mutilation, etc. may occur. The trophic disorders are due to the involvement of nervous trunks in the inflammatory process (demyelination and lysis of neurofibrilles takes place).

Granulomatous inflammation in rhinoscleroma

The inflammatory process is located in the mucous membrane of the superior respiratory ways, particularly in the nasal cavity. It can also extend to the larynx and trachea. Macroscopically, it is manifest by a pseudotumoral proliferation of hard granulation tissue, leading to the narrowing or obliteration of the respiratory tract. The inflammatory process can infiltrate the adjacent tissues of the upper lip. Clinically, it is manifest by chronic catarrh; it can produce respiratory disorders (asphyxia).

The microspecimen (fig. 145) shows a productive inflammation zone with granulomas consisting of plasmocytes, epithelioid cells and lymphocytes. Typical of the lesion is the presence of large macrophages, with clear foamy cytoplasm — Mikulicz cells. These cells contain a large number of Frisch bacilli, as well as fuxinophilic corpuscles (Russel hyalin spheres). They are caused by dystrophic lesions of the plasmocytes (containing γ-globulines — plasmocytes secretion product). The inflammatory process evolves into sclerosis and to the hyalinosis of the granulomatous tissues.

5.3.4. PRODUCTION INFLAMMATION WITH THE FORMATION OF POLYPS AND CONDYLOMA ACUMINATUM

Polyps. They represent pseudotumoral formations at mucous membranes level. They have a smooth or papillary surface, vary from 1-2 mm to several cm in size; they can be solitary or multiple. They are covered with glandular epithelium and are seen in the stomach, intestine, uterus, nasal meatus, bronchi and trachea. The appearance of polyps is determined by the productive inflammation of the mucous membranes accompanied by the proliferation of glandular epithelium and underlying connective tissue.
Macroscopic "Gastric polyposis" (fig. 146).
On the gastric mucous membrane multiple polyps of various dimensions can be seen. They have a broad or narrow base (pedicle), many of them having a cauliflower-like appearance.

Gastric polyposis can cause hemorrhage, secondary inflammation, circulatory disorders, stenosis of pylorus or cardia (depending on its location and dimensions).

Macroscopic "Endometric polyp" (fig. 147).
The bottom region of the uterus contains a polyp of relatively big dimensions, prominent into the uterine cavity. The color of the polyp is violet-brown due to the circulatory disorders.

Microscopically, the endometrial polyp is made from glands of various shapes and dimensions, some of them with cystic dilatations. The covering epithelium is cylindrical, the stroma contains a lymphoplasmocytic infiltration (fig. 148). Clinically, it is manifest by uterine hemorrhage (metrorrhagia), endometritis, etc.

Macroscopic "Tracheal polyp" (fig. 149).
The inferior portion of the trachea contains a polyp which obliterates the main bronchus, causing atelectasis of the respective lung. It can produce pulmonary hemorrhage and inflammatory processes.

The glandular polyps of various organs are considered precancerous conditions because they can undergo malignant transformation (from this background a cancerous tumor can evolve).

Condyloma acuminatum (gr. kondylos – prominence, lat. acumen – peak). These are papillary formations (sometimes with a cauliflower-like appearance), covered with pluristratified squamous epithelium (fig. 150). Hyperkeratosis, acanthosis, parakeratosis and koilocytosis of the epidermis is observed (koilocytes – cells with perinuclear cytoplasmic vacuolization and angulated nucleus). They are located on the skin from the perineal region, on the mucous membrane of the uterine cervix or of the urethra. Pathogenetically they depend on the irritant action of the genital tract secretions in gonorrhea, syphilis and other sexually contagious diseases. In the connective stroma of the condylomas a chronic inflammatory infiltration occurs (productive inflammation). Actually is proved that in majority of cases the anogenital condyloma acuminated is caused by human papilloma virus infection.
### General characteristic of the specific granulomatous inflammation

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pathogenic agent. The name of the granuloma</th>
<th>Most frequent location</th>
<th>Morphologic characteristics (structure of the granuloma)</th>
<th>Consequences</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tuberculosis</strong></td>
<td>Mycobacteria tuberculosis (Koch bacillus)</td>
<td>Can be located in all the organs and tissues</td>
<td>The center of the granuloma contains a focus of caseous necrosis, surrounded by a wreath of cells, composed of (from the center to the periphery): - epithelioid cells with a radial disposition, - giant polynuclear cells of Langhans type, - lymphoid cells</td>
<td>Reabsorption, organization (encapsulation, petrification, secondary necrosis, the softening of the granuloma leading to the formation of ulcerations or cavities)</td>
</tr>
<tr>
<td></td>
<td>Tuberculous granuloma (nodule, tubercle)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Syphilis</strong></td>
<td>Treponema pallidum</td>
<td>Subcutaneous tissue, liver, myocardium, brain, bones</td>
<td>The central zone contains a necrotic focus of a glue-like consistency, surrounded by lymphocytes, plasmocytes, epithelioid and solitary giant Langhans type cells</td>
<td>Organization, petrification</td>
</tr>
<tr>
<td></td>
<td>Syphilitic gumma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Leprosy</strong></td>
<td>Mycobacterium leprae (Hansen bacillus)</td>
<td>Skin, subcutaneous tissue, respiratory ways, digestive tract, nervous system</td>
<td>Nodular agglomerations of lymphoid cells, plasmocytes, macrophages, and Virchow cells</td>
<td>Necrosis, organization</td>
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<tr>
<td></td>
<td>Leproma</td>
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<tr>
<td><strong>Rhinoscleroma</strong></td>
<td>Frisch bacillus (Klebsiella rhinoscleromatis)</td>
<td>Nasal mucous membrane, larynx, trachea</td>
<td>Granulomas composed of lymphocytes, plasmocytes, epithelioid cells and Mikulicz cells</td>
<td>Sclerosis, hyalinosis</td>
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<tr>
<td></td>
<td>Rhinoscleromatous granuloma</td>
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