

Modern approaches to laboratory diagnostics of inflammatory conditions

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- Inflammation (lat. inflammatio) is a typical pathological process, a complex protective reaction of the body to the action of harmful agents, which was formed during long evolution and is a complex of tissue and vascular changes
   The biological meaning of inflammation is to prevent the spread of pathogens in the body, sometimes the inflammatory process contributes to their destruction
- Inflammation is a local adaptive response of the body in response to injury. This cyclic reaction ends with the elimination of the disease-causing cause, regeneration of tissues and restoration of organ function (I. V. Davydovskyi)
- Inflammation is a complex local vascular-mesenchymal reaction to tissues, caused by the actions of various agents and aimed at destroying the agent and restoring damaged tissue
- Inflammation is a reaction produced during the course phylogeny, has protective and adaptive character and contains elements not only pathology, but also physiology





#### Cells and molecular which involved in acute inflammation

https://www.creative-diagnostics.com/acute-inflammation.htm



Liu, C., Abrams, N., Carrick, D. *et al.* Biomarkers of chronic inflammation in disease development and prevention: challenges and opportunities. *Nat Immunol* **18**, 1175–1180 (2017). https://doi.org/10.1038/ni.3828

Various research methods are used to diagnose inflammatory conditions:

## clinical blood analysis:

one of the most common tests, it allows you to detect changes in indicators that indicate an inflammatory process, important markers: an increased level of leukocytes, a shift in the leukocyte formula, changes in the sedimentation rate of erythrocytes

biochemical blood analysis:

allows you to assess the level of certain substances, such as proteins, enzymes, electrolytes, gases, cytokines and other markers of inflammation

## urinalysis:

is used to determine inflammatory processes in the kidneys or urinary tract

secret analysis:

in case of localization of inflammation in specific areas of the body - analysis of secretions: sputum, mucus or others

immunological studies:

include studies of factors of cellular and humoral immunity, the presence of autoimmune antibodies or markers associated with specific diseases



# General changes blood analysis



 ESR is increased - in inflammatory conditions: infections, poisoning, inflammation of the lungs, tuberculosis, myocardial infarction, anemia, diseases of the kidneys, joints

physiologically during pregnancy

- ESR is reduced with blood clotting, polycythemia, anaphylactic shock
- Increased leukocytes (total number) in inflammatory processes, viral or bacterial infections, allergies, asthma, intensive training, severe stress
- Leukocytes are reduced (total number) with a lack of nutrients, autoimmune diseases, bone marrow dysfunction, severe infections, diseases of the immune system, HIV, AIDS, lymphomas
- Neutrophils are increased bacterial infections, trauma, burns, heart attack, inflammatory processes, rheumatoid arthritis, Cushing's syndrome, some types of leukemia, severe stress, intense training
- Neutrophils are reduced viral infections, drug reactions, autoimmune diseases, chemotherapy, radiation therapy, acute leukemia

- Lymphocytes are increased with viral infections chickenpox, rubella, herpes, tuberculosis, whooping cough, chronic inflammatory processes - ulcerative colitis, blood diseases (leukemias)
- Lymphocytes are reduced in immunodeficiency states, viral hepatitis, influenza, typhoid fever, HIV infection, rheumatoid arthritis, lupus
- Monocytes are increased tuberculosis, syphilis, fungal infections, bacterial endocarditis, collagen vascular diseases - lupus, vasculitis, rheumatoid arthritis, scleroderma
- Monocytes decreased bone marrow damage or failure, aplastic anemia, hairy cell leukemia, corticosteroids
- Eosinophils are increased helminthiasis, specific allergic reaction, bronchial asthma, drug intolerance, inflammatory bowel diseases, celiac disease, Addison's disease
- Eosinophils are reduced normally the concentration in the blood is very low
- Increased platelets blood clotting, ulcerative colitis, tuberculosis, liver cirrhosis, hemolytic anemia, iron deficiency anemia, treatment with corticosteroids, rheumatoid arthritis, lupus, inflammatory bowel disease



Platelets are reduced - in blood diseases - thrombocytopenic purpura, leukemia, some drugs, mononucleosis, hepatitis, measles, cirrhosis, leukemia, lymphoma

# Blood plasma proteins

More than 100 different species

Five fractions are distinguished according to mobility during electrophoresis: **albumin**,

 $\alpha$ 1-,  $\alpha$ 2-,  $\beta$ - and  $\gamma$ -globulins and fibrinogen Blood plasma proteins make up 8% of the plasma mass (65-85 g/l)

- **albumins** (60%) 38-50 g/l;
- globulins (30-40%) 20-30 g/l;
- fibrinogen (0.3-0.4%) 2-4 g/l

The level of blood proteins reflects: the state of protein synthesis in the body, the amount of oncotic pressure, the buffering properties of blood, the viscosity of plasma, the ability of blood to carry out transport function and immune protection

Albumins

hypoalbuminemia:

with alimentary dystrophy,

with secondary exhaustion as a result of severe general diseases, with liver and kidney diseases - with amyloid and lipoid nephrosis, with flu, croup pneumonia

- Globulins coarsely dispersed proteins with a molecular weight
  of more than 100,000 Da
- during electrophoresis are divided into α1-, α2-, β- and γ-globulin
  fractions



#### a1-globulins

α1-acid glycoprotein, α1-antitrypsin, thyroxine-binding protein, transcortin, erythropoietin, plasminogen, prothrombin

#### $\alpha 2$ -globulins

α2-macroglobulin, haptoglobin, ceruloplasminantithrombin III, retinol-binding protein, bradykininogen and kalidinogen

## β-globulins

- VLDL, VLDL, VLDL
- β1-globulin transferrin, antihemophilic globulin
- acute phase proteins: C-reactive protein, haptoglobin, C-Z complement component, cryoglobulins

#### $\gamma$ -globulins

- antibodies or immunoglobulins of 5 classes: Ig A, Ig G, Ig M, Ig D and Ig E  $\gamma$ -globulins  $\alpha$  and  $\beta$ -agglutinins of blood
- Hyperglobulinemia

in infectious diseases: croup inflammation, catarrhal pneumonia, liver diseases (acute parenchymal hepatitis, cirrhosis),

relative hyperglobulinemia - chronic debilitating diseases, alimentary dystrophy, wound exhaustion, inflammation, suppuration

#### Fibrinogen

- hypofibrinogenemia severe liver damage with prolonged jaundice, hemolytic anemia, pernicious anemia, severe forms of hepatorenal syndrome
- hyperfibrinogenemia malignant tumors, leukemia, hypothyroidism, amyloidosis, generalized tuberculosis, influenza, croup pneumonia

# PROTEIN FRACTIONS Alpha-1-globulins:

- increase in various inflammatory processes:
- acute, subacute and chronic exacerbation, liver damage;
- all processes of tissue decay or intensive cell division
- decrease with a lack of alpha-1-antitrypsin, hypo-alpha-1-lipoproteinemia Alpha-2-globulins:
- increase in all types of acute inflammatory processes, especially with pronounced discharge of fluid in the body cavity or purulent nature (pneumonia, empyema of the pleura, other types of purulent processes);
- connective tissue diseases (collagenosis, autoimmune diseases, rheumatic diseases);
- malignant tumors;
- in the recovery stage after burns;
- nephrotic syndrome
- decrease with diabetes, occasionally with pancreatitis, toxic hepatitis and congenital jaundice of newborns

## Beta-globulins

include transferrin, hemopexin, immunoglobulins and lipoproteins

- increase in primary and secondary hyperlipoproteinemias, liver diseases, nephrotic syndrome, bleeding stomach ulcer, hypothyroidism
- decrease with hypo-beta-lipoproteinemia

# Gamma globulins

# immunoglobulins Ig A, Ig G, Ig M, Ig D and Ig E

increase in the reaction of the immune system, when the synthesis of antibodies and autoantibodies occurs:

- in viral and bacterial infections, inflammation, collagenosis, tissue destruction and burnsactive hepatitis and cirrhosis
- rheumatoid arthritis, systemic lupus erythematosus, chronic lymphocytic leukemia, endothelioma, osteosarcoma, candidomycosis decrease physiological - in children aged 3-5 months
- congenital
- diseases and conditions that lead to exhaustion of the immune system and a decrease in the level of immune response

## Cryoglobulins

# Cryoglobulins belong to fractions of **y-globulins**

increase at -

- chronic kidney diseases, liver cirrhosis, tuberculosis, myocardial infarction, malaria,
- malignant neoplasms, myeloma, leukemia, Waldenström's disease
- Cryoglobulinemia occurs in patients with Waldenström's macroglobulinemia, myeloma, chronic kidney disease (uremia), liver cirrhosis, malignant tumors, leukemia, malaria, tuberculosis,
- myocardial infarction

# Acute phase proteins

a number of protective proteins that are intensively synthesized during the acute phase of any inflammatory process

• almost all acute-phase proteins are produced by hepatocytes under the influence of pre-immune cytokines, and are also produced by activated macrophages. In a state of rest, such proteins are either completely absent in the plasma, or are contained there in insignificant concentrations

Acute phase proteins include:

- C-reactive protein (CRP),
- serum amyloid A-protein, alpha-1-acid glycoprotein, alpha-1-antitrypsin,
- alpha-1-macroglobulin, fibrinogen,
- ceruloplasmin, C9 component of the complement system, haptoglobin, cryoglobulin, α2-macroglobulin, lactoferrin

Diagnostic value:

- interpretation of the result of infection, systemic connective tissue diseases, inflammatory bowel diseases, acute pancreatitis,
- myocardial infarction, postoperative period, malignant tumors insignificant, weight gain, atherogenic dyslipidemia,
- type 2 diabetes, hypertension, hormone replacement therapy, cardiovascular disease risk assessment

## Paraproteins

**Paraproteins** - are proteins of the acute phase of inflammation, which are formed in the body in some pathological conditions

- This is a type of immunoglobulins produced by pathological immunocompetent cells (pathological immunoglobulins PIg):
- tumor cells of the  $\beta$ -lymphocyte system,
- consist of structural units two H- and two L-polypeptide chains, which are contained in normal immunoglobulins

• With paraproteinemia, the number of normal immunoglobulins decreases sharply or they are not detected at all. A significant increase in the level of  $\beta$ -fractions with a low content of  $\gamma$ -globulins against the background of hyperproteinemia allows us to conclude about the appearance of paraproteins

#### Paraproteinemias:

- benign type collagenosis; chronic hepatitis; cirrhosis and other chronic inflammatory diseases, in healthy people after 60 years
- malignant type myeloma disease and its manifestation plasmacytoma, Waldenström's disease, heavy chain disease, other diseases of the lymphoplasmacytic system - malignant lymphomas, leukemias
- The number of paraproteins significantly increases in myeloma, chronic lymphocytic leukemia, Waldenstrom's disease,

endotheliomas, osteogenic sarcoma





https://www.bio-rad.com/enua/feature/flowimmunophenotyping.html



