

Ministry of health care of Ukraine  
Highest state scientific institution of the Ukraine  
«Ukrainian medical stomatological academy»

"Approved"

at a meeting of the Department of Experimental  
and Clinical Pharmacology with Clinical  
Immunology and Allergology

**Head of the department**

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**Methodical guidance for students' self-directed  
work when preparing for practical session**

Academic subject	Clinical Immunology and Allergology
Semantic module №1	Immunological status. Immunodeficiency diseases and immune-pathology
Topic №7	<b>Immune aspects of autoimmune diseases</b>
Year of study	5
Faculty	medical

### 1. Relevance of theme:

Autoimmune disease can be characterized as those in which the result of the humoral or cellular immune responses of the body to normal structural components of different or functional damage of the latter. Attracted to an antigen called autoantigens. Antibodies that are able to react with autoantigens are defined as autoantibodies. This forms an immune response against its own tissues and organs. A significant role in the development of autoimmune processes is heredity. Genetic tendency is determined by MOE genes.

Autoantibody formation of one of the manifestations of the immune response in a number of chronic diseases. Distinguish organ-specific and non-specific disease. The former include gemocitopenia, immune thyroiditis, atrophic, immune endocrinopathies, CNS and eyes. By neorganospetsific include CAS and other "collagen". Patients produced autoantibodies to various intracellular and extracellular components (nuclei, mitochondria, microsomes, etc.). There is a first violation of T-cell function.

The most common rheumatoid arthritis (0.5-1%). In 100 cases, 25 cases of RA has to CAS, 15 - scleroderma, 10 - polimiiozita and 3 - periarteritis nodosa.

There is no doubt the fact that the immune system belongs to the prominent role of the fight against malignant tumors. It has been established that there are antigens that are associated with a certain type of tumor, but also interconnected between its development and the destruction of the immune system.

The tumor is formed and grows under the influence of opposing, but not mutually exclusive immune responses. The dynamics of tumor growth is determined by a balance between the factors of the immune supervision on the one hand, and problastomic factors that promote tumor growth, - the second.

The aim of immunodiagnostics of tumor process is the development of reliable tests in vitro, which can detect a tumor in the development of clinical symptoms and determine its location. Such tests are needed in early clinical diagnosis and differential.

According to conventional thinking, the success of immunotherapy of cancer must first reduce the size of tumors via a surgical operation, radiation or chemotherapy, or immune system, one can hardly cope with a large tumor mass and, moreover, a surplus of the tumor antigen can inhibit the immune response development, stimulating T -supressory.

### 2. Learning objectives:

1. Master the basic principles of diagnostics of autoimmune diseases by studying the pathogenesis of immune disorders.
2. Master the basic principles of the treatment of autoimmune diseases by studying the pathogenesis of immune disorders.
3. To master the concept of antigens associated with a tumor: antigens, virus-induced tumors and canserogenindutstretive, carcinoembryonic antigen, and others.
4. To know the role of T and B cells, macrophages, NK, LAK-cells, T-suppressor of tumor necrosis factor in the development and emergence of immunoproliferative syndrome.
5. To learn the principles of immunodiagnostics and immunotherapy for autoimmune diseases

### 3. Basic knowledge, skills necessary for studying the subject (interdisciplinary integration)

The name of the previous disciplines	These skills
Anatomy	Know the structure of the thymus, lymph nodes, peerovyh plaques, spleen, bone marrow. Spend examination of patients.
Normal physiology	To know the functioning of the central and peripheral organs of the immune system. Take hold of the basics of clinical and laboratory studies.
Biochemistry	Learn the basics of biochemical laboratory studies. Action and effect of cytokines of different groups of biologically active substances.

Microbiology and Virology	Know the immune response, diagnosis of bacterial and viral infections. Take hold of the basics of special microbiological methods.
Therapy	Know the pathogenesis and clinical manifestations of allergic diseases and secondary immunodeficiencies. To be able to collect immunological and allergic history.
phthisiatry	To master the mechanisms of the immune response cell dependence, course and clinical manifestations of tuberculosis.
Infectious diseases	Learn the pathogenesis, clinical manifestations of bacterial and viral infections. To be able to diagnose bacterial and viral infections.

#### **4. Tasks for work during preparation for the classes.**

##### **4.1. The list of key terms, parameters, characteristics which the student is to assimilate while preparing for the class:**

Term	Definition
Hybridoma	The hybrid cell line to the formed after the merger of the tumor and 1 MFIs and the bottom of the first cell with a normal lymphocyte.
Mitogen	The substance, which involves non-specific lymphocyte proliferation.
Idiotype	Portions of the amino acid sequences within antibody variable region or T cell receptor identification, which antibody production antiidiotyping
Tumor necrosis factor, F	F factor that is synthesized by monocytes and macrophages. Participates in the regulation of immune response, and destroy tumor cells
Myeloma	Tumor plasma B cells capable of indefinite proliferation in culture.

##### **4.2 Theoretical questions to the lesson:**

1. Definition of autoimmune reactions, autoimmune disease. The mechanisms of breakdown of immunological tolerance, the role of genetic factors. Immunological, immunopathogenesis.
2. The role of immunological methods of research in the early verification of the diagnosis of auto-immune diseases. Autoimmune component and immunopatogenesis in different human diseases.
3. Modern approaches to the use of their drugs munotropic new deer in the treatment of patients with auto immune pathology.
4. Antineoplastic problastomn and mechanisms of interaction between the immune system of the organism "host" and "tumor".
5. Factors immunological resistance of the tumor. The concept of a fluff of with social antigens. Immunosuppressive effect of tumors. Immune changes in cancer patients.
6. Immunodiagnostics, differential according to the CD -.. Phenotype of tumor cells. Modern approaches to the patient with cancer immunotherapy.

##### **4.3 Practical works (task) which are executed on lesson:**

1. Learn how to diagnose autoimmune disease, given the typical changes in the immune system..
2. Seize the skills to identify the type of immunotropic disorders in patients with auto immune Health issues arising, based on Dunn's immunogramm.
3. To be able to appoint a general clinical and immunological examination of patients with autoimmune diseases.
4. Seize skills assign specific immunomorfological therapy in patients with autoimmune disorders.
5. Master the skills of approx immunological, cytological cancer diagnosis methods, sensitization reactions of cellular type.
6. Seize the skills to apply biological medicator immune response to BCG, levamisole, interferon, IL-2 and others.

**Content of topic:**

**Autoimmunity** characterized by a loss of tolerance or natural mismatch to self antigens. As a consequence, the autoantibodies produced by cells with the cytotoxic or immune complexes predetermine disease development.

To auto immune disease (non-exhaustive list of which is intended to show the frequency of this pathology in almost all branches of medicine) include:

1. Systemic lupus erythematosus.
2. Rheumatoid arthritis.
3. Scleroderma.
4. Dermatopol.
5. Mixed connective tissue disease.
6. Sjogren syndrome
7. Psoriasis.
8. Vitiligo.
9. Dermatitis herpetiformis.
10. Pemphigus is common.
11. Disease (syndrome) Reiter.
12. Ankylosing spondylitis.
13. Scattered multiple sclerosis.
14. Myasthenia gravis.
15. Thyroiditis and Moto Hush (auto immune).
16. Graves' disease (hyperthyroidism with diffuse goiter).
17. Insulin-dependent diabetes mellitus (and type).
18. Auto immune of adrenal lesions (The add and sone disease).
19. Auto immune to the floor and endocrinopat.
20. Sarcoidosis.
21. Idiopathic pulmonary fibrosis.
22. Nonspecific ulcerative colitis.
23. Crohn's disease (regional enteritis).
24. Auto immune gastritis type A.
25. Primary biliary cirrhosis.
26. Chronic active hepatitis.
27. Autoimmune to enteropathy.
28. Enteropat gluten.
29. Glomerulonephritis.
30. Goodpasture's syndrome.
31. Auto immune uveitis.
32. Pernes anemia.
33. Auto immune hemolytic anemia to me.

The pathogenesis of these diseases play a major role in the pathological changes in the immune system, the data of which are given in the further information.

**Rheumatoid arthritis (RA)**

**RA** - auto immune the disease, which is caused by immune-surrounding autoaggression relative tissue joints and manifests as erosive arthritis that leads to articular deformations, fibrosis and ankylosis. In RA, the possible development and stseropat and second, but the key is still there after the defeat of the joints.

There is no clear etiology of the disease to date is not set. Admit that cause the breakdown of tolerance in RA is a chronic (often - subclinical) infection (paramyxoviruses, Epstein-Barr virus, mycoplasma, chlamydia) in genetically susceptible individuals or under conditions of immune defects.

Theories of RA development. According to the T-cell theory, RA develops as a result of activation autoreaktiv governmental T lymphocytes under the influence of unknown etiology that primarily affects the joints will.

In the pathogenesis of rheumatoid arthritis usually distinguished main of the first and

secondary mechanisms of self-aggression. The first involves a violation of tolerance to autoantigens articular cartilage tissue, which is why in the joints is carried out antigen presentation of self antigens and activation peptide Ia autoreactive governmental T lymphocyte proliferation with the following last and differentiation primarily to T-helper type 1 as well. In the role of antigen presenting cells (APC) in favor of the RA macrophages, dendritic cells and chondrocytes. The last expression of the molecules begin HLAII class under the influence of pro playback and Lita cytokines.

A massive infiltration and synovitis shell lymphocytes in lymphoid last formed clusters that resemble follicles peripheral organs of the immune system. It is believed that the above changes result in the transformation of synovitis and joint cially second shell into a kind of authority immunogenesis where reactions occur antigen-differentiation of autoreactive lymphocytes (B-cells etc). Thus, at a certain stage opatogeneza immune disease, not only the immune system as a whole, but are themselves damaged joints can fully support the move autonomously auto immune action process.

Note that autoreactive lymphocytes which mature in the joint tissue or coming from the vascular here, do not have direct access to the cartilage, since the latter is devoid of blood vessels. In this regard, initially they accumulate in the synovium of joints. Therefore, the first signs of inflammation are swelling and cell infiltration and synovitis was cially shell. Due to the proliferation of fibroblasts, endothelial cells multiplication, increasing I and MFIs and the bottom and article infiltration and synovitis, and I shell transformed into the affected joints pannus - in a special way hypertrophied connective tissue that holds at least two key properties. Firstly, pannus cells lack sensitivity chalones (natural agents which limit proliferation), because the latter has the ability to increase steadily progressing. The reason for reducing the sensitivity to chalones poorly understood. I admit that this is due to the part of the divided cells and altered microenvironment. Secondly, pannus tissue is extremely aggressive, as produces high concentrations and is called metalloprote and free radicals. These factors contribute to the development of erosive changes in RA. Aggressive properties pannus due to its cellular structure - primarily by macrophages, and activated NF- $\gamma$  and Myth, and neutrophils and fibroblasts. Last begin production of proteolytic enzymes under the influence prozapal cytokines. The figure shows that of synovitis and cially shell on articular cartilage grows pannus (granulation tissue incendiary), which has an aggressive effect on the cartilage tissue. The structure includes an active pannus Strait fibroblasts, lymphocytes, macrophages (histiocytes); tight an intensive angiogenesis by endothelial cells actively reproduce.

Depending on the presence or absence of RF distinguish seropositive and seronegative form of the disease. At the same time more aggressive forms of seropositive as rheumatoid factor promotes faster generalizing auto immune action process and the development and stseropat and minutes. Sometimes RA runs across for Seronegative option, but later transformed into seropositive form, which is regarded as a poor prognostic sign. It should be noted that the RF can occur in other auto immune diseases, but in lower concentrations (i.e., it is not to patognomic RA). Very often the Russian Federation is the second in systemic lupus erythematosus and periarteritis nodosa.

#### **Phase immune of opatogeneza rheumatoid arthritis**

The name of the phase	Immunopathological hours and change RP G
1. Start	Disruption of immune tolerance to autoantigens articular cartilage the influence of unknown factors, the development of incendiary changes in the joints, migration autoreactive governmental T-cells
2. Honey and I Athorne	The action of cytokines secreted by immune cells and APC
3. Lymphoid	The formation of lymphoid follicles in the joint tissues, ie the transformation of the latter in a unique body immunogenesis, where the local differentiation of antigen autoreaktiv governmental B-lymphocytes. Mature plasma cells produce autoantibodies (including RF) and T-helper 1 type immune mediate auto deployment action process through the synthesis of cytokines

4. Aggressive	It linked to the aggressive action of the pannus, which builds on the cartilage tissue
5. Payload	The pannus is almost completely erodes the articular cartilage, which leads to fibrosis and ankylosis of the articular surfaces, joint deformity

#### **Indicators of humoral immunity.**

1. Determination of rheumatoid factor (RF), which is an antibody to the Fc fragment and Ig. "Classic" Russian is an Ig M, described the Russian Federation, which belongs to the other Ig. RF in RA is in the so-called seropositive type.

2. Positive reaction Vaaler-Rose. Diagnostic considered titer of 1:80 or more. High titers of reaction in the early stages of the disease indicate a progressive and severe its course with possible further destruction and deformity of the joints.

3. An important feature of the immunological diseases is the presence of AT to collagen.

4. In some patients are antinuclear AT. They are most often found in the fraction of IgG. Antinuclear antibodies are typical for RA with a rapidly progressive course, and the impression of the joints. In some cases, RA TA detected to single-stranded DNA and histone.

5. Content of complement in serum of RA patients are usually in the normal range or slightly elevated. In severe forms an impression of the joints observed a moderate reduction of its correlation with high titers of RF, raising of Ig, behind joints manifestations. The synovitis and cial liquid contents complement always reduced.

6. A moderate increase in all classes of Ig, preferably IgG.

7. Increasing C and K, which are composed of all classes of Ig. You should always evaluate the quality C & K, that is, to give their characteristic components, particularly antigen, which will help clarify the pathogenesis of the disease.

#### **Indicators of cellular immunity**

1. A positive skin test of the IG.

2. Increasing RBTL with native or aggregated IgG, with autolog hours and minutes of the EQF serum from autological IgM, IgG.

3. Increasing RTML with native or aggregated IgG.

4. But reduction in the amount of T-lymphocytes (and most preferably T-lymphocytes).

RA treatment has pathogenetic orientation. There are means of basic therapy and anti-inflammatories (glucocorticoids and Nester and day anti-inflammatory drugs). The first help to halt immune pathological process, preventing disability of patients. The latter provide a reduction in pain and signs of inflammation in the joints, but the immune pathological process with their use continues to develop, which leads to the formation of ankylosis, contracture, joint deformities, ie disability. In accordance with the modern approach to the treatment of RA basic treatment facilities should be appointed no later than 3 months from the time of clinical diagnosis.

The therapeutic effect of gold drugs in RA is due to regenerating of their influence the last n and x the activity of neutrophils and macrophages, as well as violation of intercellular cooperation processes during the implementation of auto immune action response. Despite the high efficiency, the use of gold drugs is quite limited given the frequent severe complications of therapy (hepato- and nephrotoxicity, skin rash, neutropenia, and other).

Methotrexate. MTX treatment of RA is the "gold standard". The mechanism of the drug in doses, which are recommended for use in RA associated with oppression folatza pendent x enzymes blood cells, which leads to anti-inflammatory and mild immunosuppressive action. However, in recent audio studies it showed that methotrexate carries an immunomodulatory effect which is to increase the lymphocyte expression of genes that encode the structure of anti-inflammatory cytokines IL-4 and IL-10.

Traditionally, the efficiency drugs in RA is due to the ability of recent inhibit fibroblast proliferation, to reduce the activity of lysosomal enzymes, reduce the production of pro playback and Lita governmental on in and autoantibodies.

Cyclosporine A. The recently received given the effectiveness of Cyclosporin A (Sand immune) in RA. The drug has immunosuppressive effect by blocking the effects of IL-2 in connection with the violation of its synthesis of T-lymphocytes. Under the conditions of auto

immune action of the disease, most of activated T-cells have autoreactive. It is known that IL-2 activated used Autoreactive T cells for auto- and paracrine regulation of their proliferation.

Leflunomide is a synthetic drug (derivative of methotrexate). The mechanism of action of leflunomide and so associated with the blockade of tyrosine phosphorylation in the cytoplasm of T-lymphocytes, which leads to blocking signaling by IL-2 into the cell. With the ability of leflunomide to inhibit purine and pyrimidine synthesis, the spectrum of immune lyotropic activity of the drug is greatly extended.

The drug infliximab (Remicade) was established on the basis of monoclonal antibodies to the PNP-and that connect the latter to form inactive complexes, which are then phagocytosed by macrophages. In addition, such antibodies do cytostatic effect against neutrophils and macrophages, the cytoplasm of which at the time of the preparation etc. synthesis of this cytokine. Thus, the drug acts primarily on aggressive activated phagocytes and on cells that are not involved in the implementation of auto immune action process (inactive), provides a minimum overwhelming influence. These features provide a relatively selective action of infliximab. Recent studies indicate that under the influence of periodic injections of infliximab decreases swelling and pain in the affected joints, shortening the duration of morning stiffness, decreased levels of C-reactive protein and serum amyloid precursor decrease.

Inhibitors about Leflunomide established that the concentration of proinflammatory and Leflunomide elements cytokine and IL-1B in synovitis and a second fluid of affected joints in RA is directly correlated with clinical disease activity. According to the latest data, the parenteral administration of recombinant human receptor antagonist IL-1 n / a 1 times a day for 6 months is not only a decrease in clinical and serological evidence of disease, but also the positive dynamics of radiological changes.

### **Systemic lupus erythematosus (CAS)**

**CAS** - auto immune not disease associated with genetically caused by imperfection of immunoregulatory mechanisms, which leads to the production of numerous autoantibodies against antigens of various organs and tissues.

The etiology of the disease remains unknown. Admit that a role in the development of the CAS can play some RNA - containing viruses that persist in the long-term genetically prone body.

It was established that the development of symptoms resulting CAS genetically caused deficiency several complement components (C1, C2, C4). It is known that immune complexes, which are formed by antibodies to antigens (destroyed) by macrophages of the liver and spleen. At the same time they are recognized for fragments of complement components (opsonin), fixed to the immunoglobulin molecules. Yes, macrophages contain receptors for SZ i C\q components, allowing "caught" circulating immune complexes from the blood and neutralize them. At deficiency of complement proteins disrupted the natural clearance of immune complexes, which are formed in almost any infection. In connection with this last term circulate in the blood, causing the development damaged in H and I on the immune complex type. At the same time, not all patients with deficiency of the CAS is the complement proteins, because they find that other immune defects can be in the genesis of the disease. Also in the immune pathogenesis and systemically red lupus discusses the role of thymus as an organ, which is the formation of immune tolerance. There is thought that patients CAS occurs at the so-called elimination of pathogenic or "prohibited" clones of immune cells which respond from autoantigens presented in the thymus is, a large number of lymphocyte nuclei fragments (apoptotic run auto immune process).

Systemic lupus erythematosus were significantly more common in women. It is believed that female hormones contribute to the development of immune pathological process in the CAS. This is confirmed by the fact that during pregnancy and immediately after giving birth is usually marked aggravation of the disease. At the same time do androgens defined protective effect.

*Pathogenesis*. When CAS immunization occurs to autoantigens various organs and tissues. This auto immune reaction on the run across mostly humoral type that is associated with activation, proliferation and differentiation autoreaktiv GOVERNMENTAL T-helper type 2 and autoreaktiv GOVERNMENTAL B-cells. Recent as ripening transformed into plasma cells that produce a variety of autoantibodies.

If the CAS determines autoantibodies as organ antigens (against heart, against kidneys,

antibodies), and to individual cells and forming elements (such as white blood cells, smooth muscle, red blood cells, platelets), the inner content of cells (mitochondrial antilysosomal, antinuclear AVR antibodies ) or even the contents of the organelles (e.g., anti-DNA, nucleoprotein). Thus, when the CAS autoimmunity occurs at all levels: at the organ, cellular, subcellular (organelle) and molecular. Assume that initially implemented to surface structures autoaggression organs and cell destruction as the latter - to autoantigens organelles, and ultimately - molecules that are contained in organelles. Thus, the properties of the autoantigen and when CAS obviously did not play much importance as possible Autoimmunity virtually any structure to which the immune system has access. This indicates that CAS occurs at a very profound impairment of the immune tolerance (possibly deeper from all known auto immune diseases ).

#### **Indicators of humoral immunity.**

1. The definition of high titers of antinuclear AT .
2. Raising antibodies to specific antibodies cell nucleus :
  - a) AT to nucleoprotein and forth about
  - b) antibodies to DNA double-helix (native), single- and DNA (denatured)
  - c) ATRNA (antiribosomal AT )
  - g) antibodies to low molecular weight nuclear RNA.
  - d) antibodies to the neg and groans proteins.
  - e) AT to deoxyribonucleoprotein and forth and (histone-DNA complex)
3. Raising AT to the components of the cytoplasm : mitochondria, ribosomes, lysosomes.
4. Education organospecific AT , especially AT to the form GOVERNMENTAL blood elements.
5. Raising AT to components blood serum. Education is more common in the CAS which is accompanied by arthritis than in impressions.
6. In a significant number of cases, the CAS is a decrease complement activity, a sign of the rapid progress of the disease and the presence of a pathological process in the kidneys. Activity decreases C4, then C1, C2, C3. Determination of the concentration C1 and C3 may be used as a criterion for evaluating the effectiveness of the therapy.
7. Increased IgG and Ig M.
8. Increasing the amount of C and K. The level of C and K of the ESR, the amount of Ig and others. A clear correlation between the level of C and K, and clinical features of the disease is not present.
9. Second humoral components - not are real positive I Wasserman reaction (women more than 3: 1).

#### **Indicators of cellular immunity**

1. Lymphopenia.
2. Identifying LE -cell - mature neutrophil cytoplasm which is filled with phagocytosed core of a dead white blood cell in the form of amorphous globule, which consist of DePaul Peninsula district but the second DNA.
3. Reducing the number of T-lymphocytes. Suppressor function is reduced, the helper I - increased .
4. Average amount, decrease or increase the number of B-lymphocytes.
5. The increased amount of on in and reduced the number of D-lymphocytes. Reducing AZKOTS.

### **Auto immune chronic active hepatitis**

#### ***Indicators of humoral immunity***

1. AT to Ag membrane of hepatocytes.
2. Antim AT .
3. Antibodies to smooth muscle tissues.
4. AT polymyositis .
5. AT to the nucleus of the cell structures.
6. Organospecific AT .
7. Russian Federation.



8. Increased C and K.

**Indicators of cellular immunity**

1. Positive RBTL and TMWG (with extracts of allogeneic and autologous liver tissue).
2. Reducing the function of T-suppressors.

**Glomerulonephritis**

**Indicators of humoral immunity**

1. AT to the glomerular basement membrane.
2. Activation of the complement system by the "classical" and "alternative" way.
3. Reduction of the synthesis of complement components
4. Increased C and K.
5. The increase in IgG, Ig A, IgM.

**Indicators of cellular immunity**

1. Reducing the T-lymphocytes.
2. Reducing the function of T-suppressors.
3. Positive RBTL with autologous kidney tissue.

**Question for self-control during the preparation of students :**

1. Define the concept of auto immune processes.
2. Mechanisms of development of auto immune diseases.
3. Immune disorders in RA (rheumatoid arthritis).
4. Immune disorders in CAS (systemic lupus erythematosus).
5. Immune disorders in NEC (ulcerative colitis).
6. Immune disorders in chronic glomerulonephritis.
7. Immune disorders with aggressive hepatitis.
8. Principles immune lyotropic correction in RA, CAS, NEC, chronic glomerulonephritis, aggressive hepatitis
9. Diagnose autoimmune disease, taking into account the typical changes in the immune system.
10. To be able based on data immune ogres we determine the type of immune disorders in patients with auto immune diseases.
11. Assign general clinical and immunological examination of patients with auto immune pathology.
12. Assign specific immune morphological therapy in patients with auto immune E infringements.

**Materials for self-control**

**A. Test for self-control**

**1. What is seronegative second option and seropositive rheumatoid arthritis?**

- a. RF absence
- b. RF positive
- c. RW positive result
- d negative result of RW

**2. Indicate which of the lower EPER including GOVERNMENTAL methods for the detection of antibodies, the most widely used in the diagnosis of auto immune diseases :**

- a immune fluorescencesera research on sections
- b . precipitation method in Gael
- c immune ofermentive second analysis
- d all of the above methods
- g., none of these methods

**3. Usually changes in the areas which may be made autoantibody Ig:**

- A. light level;
- B. a hinge zone;
- C. heavy management;
- D. zone fragment;

E. Fc fragment areas.

**4. In what diseases the method of choice in the treatment of a immunosuppressive therapy?**

- a. auto immune uveitis
- b. disease P
- c. insulin-dependent diabetes
- d systemic lupus
- g. rheumatoid arthritis
- e. when all these diseases

**5.** Patient 26 years old complains of significant weakness. Ill acutely with fever, malaise, joint pain, and the progress of the leg muscles. **OBJECTIVE:** violet-cyanotic erythema around the eyes and above the knee. HR -. 120 / minute, heart sound attenuated. What is the most likely diagnosis?

- A** Atopic dermatitis
- B** Systemic lupus erythematosus
- C** polymyositis
- D** Dermatome and ozit
- E** Reactive arthritis

**6.** The patient was 60 years old complains of pain in the interphalangeal joints of hands, which increases during operation. Objectively: the distal and proximal joints II-IV fingers def and gurovan us with heberden nodes, Bouchard, painful, with limited mobility.X-ray

Joints: joint space narrowing, marginal osteophytes, subchondral sclerosis. What diagnosis is most likely?

- A** rheumarthrosis
- B** Reiter's disease
- C** Deforming osteoarthritis
- D** The disease B
- E** Psoriatic arthritis

**7.** The patient was 45 years old complains of pain and weakness in the muscles of the arms and legs; redness, peeling and itching of the skin. **OBJECTIVE:** erythema and edema paraorbital fiber extremity edema. There painfull muscles of the shoulder and pelvic girdle on palpation. What research will establish the diagnosis with and used to it up

- A** Determining the blood levels of thyroid hormones. .
- B** Definitions blood stream level and called in the blood.
- C** Skin and muscle biopsies.
- D** rheotachygraphy
- E** LE-level definitions to notches in the blood

**8.** Male 42 years old complains of severe weakness, pain in muscles and joints, increasing the temperature to 38.6 ° C, emaciation. Acutely ill. 6 months ago suffered from viral hepatitis. Objectively: the state of moderate severity. Pulse - 80 / min, BP -. 175/95 mmHg The inner surface of the forearm palpable painful subcutaneous nodules up to 1 cm. On the upper extremities are marked sensory disturbances and type in "gloves". In the blood: mild anemia, leukocytosis, eosinophilia, accelerated ESR. Urine: moderate Prote and I microhematuria. What diagnosis is the most reliable?

- A** Rheumatism
- B** Systemic lupus erythematosus
- C** rheumatocelis
- D** Nodular arteritis field
- E** Dermatome

**9.** Patient 40 years, without complaint, during the passage of baseline medical examination passed urine on the overall analysis of the employment front. The results: the color; transparent; specific weight - 1008; pH - 6.5; Protein - 0.6 g / l: er. - 18-20 p / of changed; Lake. - 2-3 p / of; 2-3 cylinders , grainy. What is the most likely diagnosis?

- A** renal amyloidosis

- B** Acute glomerulonephritis
- C** Chronic pyelonephritis
- D** Chronic glomerulonephritis
- E** Urolithiasis disease

**B. Tests for control of the final level of knowledge**

1. Auto immune disease are divided into:
  - a. tumor
  - b. organospecific
  - c. system
- 2 Rheumatoid factor - is:
  - a. Class M antibodies directed against the Fc-fragment of Ig A
  - b. class antibodies in A, M, G directed against FAB fragment and Ig G
  - c. antibody classes A, M directed against the FAB fragment of Ig G
  - d. valve stem, the antibody G, M directed against the Fc fragment of IgG
3. Indicate which of nizhepere numerically 's methods of detecting antibodies, the most widely used in the diagnosis of auto immune diseases:
  - a. immune fluorescentic study sera slice
  - b. precipitation method in Gael
  - c. radioimmunoassay
  - d. all of these methods
  - d none of these methods
4. Specify which approaches to the treatment of auto immune disease currently exist.
  - a. regulation of metabolic processes in the body
  - b. Anti-inflammatory therapy
  - c. immunosuppressive therapy
  - d. immunostimulatory therapy
5. What drugs with anti-inflammatory effects are not applied in the treatment of auto immune diseases?
  - a. steroids
  - b. fats and Latin s , indomethacin, phenylbutazone
  - c. fenoprofen, ibuprofen
  - d. kordaron
  - e. all of the drugs
6. What types of immune responses often underlie the development of autoimmune process?
  - a. defects in C-1 and B the torus complement
  - b. cytotoxic immune responses
  - c. the reaction of immune complexes
  - d. cell responses
  - e. autoserotherapy caused by antibodies
  - g. None of these mechanisms
7. Which of the lower EPER by numerical 's products, which have immunosuppressive properties that are used for the treatment of auto immune diseases?
  - a. cyclosporin A
  - b. azathioprine
  - c. methotrexate
  - d. All of these drugs
  - e. Only nitrogen , methotrexate
8. In the girls 14 within about a year ago it appeared irritability and tearfulness. At the same time determined diffusely enlarged thyroid gland II degree. State regarded as a manifestation of puberty. The treatment was carried out. Irritability is gradually replaced by complete apathy. There puffiness of the face, pasty soft tissue, bradycardia, constipation. Appeared waxy pallor of the skin with a hint of the density of the prostate. What disease should be assumed?
 

**A** Subacute thyroiditis

- B** Diffuse toxic goiter
- C** Thyroid Cancer
- D** Autoimmune thyroiditis
- E** Puberty youthful basophilism

9. The baby 3 months after several days of concern, anorexia, subfebrile appeared jaundice, hepatosplenomegaly, dark urine and yellow discoloration of feces. At the age of 1m and were transfusion. What is the most likely diagnosis?

- A** Atresia of biliary tract
- B** Hemolytic anemia
- C** Viral hepatitis A
- D** Viral Hepatitis B
- E** conjugation jaundice

10. Male 42 years complains of severe weakness, pain in muscles and joints, raising the temperature to 38.6 ° C, emaciation. Acutely ill. 6 months ago suffered from viral hepatitis. Objectively: the state of moderate severity. Pulse - 80 / min, BP -. 175/95 mmHg The inner surface of the forearm palpable painful subcutaneous nodules up to 1 cm. On the upper extremities are marked sensory disturbances by type "gloves". In the blood: mild anemia, leukocytosis, eosinophilia, accelerated. Urine: moderate Prote I microhematuria. What diagnosis is the most reliable?

- A** Rheumatism
- B** rheumatocelis
- C** Nodular arteritis field
- D** Dermatome
- E** Systemic lupus erythematosus

11. Patient M., 31 year for 14 years suffers systemic scleroderma. Repeatedly treated in hospitals. He complains of periodic dull ache in the heart, palpitations, shortness of breath, headache, edema, emaciation, pain and deformation of the limb joints. The defeat, which body worsens the prognosis of the disease?

- A** Gastric tract
- B** hearts
- C** Easy
- D** Kidney
- E** Skin and joints

12 A patient of 35 years admitted to the hospital with complaints of pain in the left sternoclavicular, knee joints, lower back. Ill sharply with increasing temperature to 38 ° C. OBJECTIVE: Left sternoclavicular, knee with swelling, painful. The blood: leukocytes 9,5-D 1.5 mm-CRP, fibrinogen - 4.8 g / l acid, 0,28mmol \ l. As with the staples ie from the urethra - chlamydia. What is the most likely diagnosis?

- A** rheumarthrosis
- B** Gout
- C** Reiter's syndrome
- D** Rheumatoid arthritis
- E** disease B roar

### **B. Tasks for self-control**

**Task №1.** 19- year-old woman complains of pain ides and joints, erythema on the cheeks and nose, increasing the temperature to 38,5-39 ° C, shortness of breath, palpitations, and weakness. Sick 3 months. In the blood: leukocytes - 3.2 - 109 / L, platelets - 180 - 109 / L, erythrocyte - 3.0 10A12 / l. Urine: Protein - 0.66 g / l, erythrocyte - 2-5 in p/s, leukocytes to claim 5 in / sec . When X-ray studied underlined I pleura .

Your previous diagnosis.

What diseases will spend diagnosis? Enter the survey plan based on the most informative for detection of the disease is immune test

**Task №2.** A 52-year-old woman after hypothermia duty again began to disturb pains in the joints of the hands, expressed morning unfree, ESR - 26 mm / hours of your previous diagnosis and a plan of survey based on immunological parameters.

**Task №3.** In 30-year-old woman in the last year there has been progress following syndromes: symmetric polyarthritis, Raynaud's syndrome, the severity of swallowing solid food, ESR - 18 mm / hours of your previous diagnosis and a plan of survey based on immunological parameters

**Problem №4.** The patient was 22 years with complaints of decreased performance, emotional lability, expressive overall weakness, fatigue, diplopia. In reviewing: bilateral ptosis. Testing found pathological fatigue of facial muscles and limbs. In professional history - prolonged contact with toxic substances (formaldehyde, chlorine, aniline dyes). The presence of blood antibodies to atsetilhol and new x receptors in diagnostic titre. Suspected: **a syndrome** of chronic weariness, myasthenia gravis, sub-acute viral encephalomyelitis, chronic intoxication with formaldehyde, hysteria in the put the correct diagnosis, name the main elements of immune opatogenezis well and treatment.

**Task №5.** In 46-year-old woman with suspected breast cancer showed a significant reduction in weight, expressed muscle weakness, heaviness in swallowing liquid food experimental edema; ESR - 38 mm / yr Your early diagnosis and patient management plan.

**Answers** control the final level of knowledge -b 1 in; 2 -r; ; 3 - a, a; 4 c; 5 a, 6-b, c, d, e; 7 g; 8 - D; 9 - D; 10 - C; 11 - D; 12 - D; 13 - c.

**№6 tasks.** Systemic lupus erythematosus. The immune U : leukopenia, lymphocytosis; ESR acceleration; Th / Ts is greater than 3. a) glucocorticosteroids bottom I therapy.

b) another anti-inflammatory therapy.

c) the use of immunosuppressive drugs (chlorobut 5-15mg, cyclophosphamide 150-200mg, Azat 150-200mg)

№2 myasthenia gravis Immunopathogenesis: education "autoantibodies" complex - acetylcholine receptors activates complement, which leads to damage to the receptors, the blockade comes last and the violation of their functions. Treatment Antihol and neschterich RPG drugs, thymectomy, plasmapheresis, immunosuppression (corticosteroids, azatiopr).

№3 dermatome and ozit. After an active tumor treatment usually improves the condition in terms of the dermatome .

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