МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
Харківський національний медичний університет

Module 1. Clinical immunology and allergology. Theme 8. IMMUNOLOGY OF SPECIFIC INFLAMMATORY PROCESSES IN MAXILLO-FACIAL AREA

Manual for practical lessons students having higher medical education in English majoring in dentistry

Модуль 1. Клінічна імунологія та алергологія. Тема 8. ІМУНОЛОГІЯ СПЕЦИФІЧНИХ ЗАПАЛЬНИХ ПРОЦЕСІВ ЩЕЛЕПНО-ЛИЦЕВОЇ ДІЛЯНКИ

Методичні вказівки до практичних занять студентів медичних вузів з англійською мовою навчання за спеціальністю "Стоматологія"

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Модуль 1. Клінічна імунологія та алергологія. Тема 8. Імунологія специфічних запальних процесів щелепно-лицевої ділянки : метод. вказ. до практ. занять для студентів мед. вузів з англ. мовою навчання за спеціальністю "Стоматологія" / упор. П. Г. Кравчун, В. Д. Бабаджан, І. І. Соколова, Ю. О. Ковальова. – Харків : ХНМУ, 2015. – 16 с.

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Subject: Immunology of specific inflammatory jaw – face area (tuberculosis, actinomycosis, syphilis, AIDS)

1. Background.

AIDS – a contagious viral disease immune etiology is relevant today. According to the literature dentists is second only to surgeons at the risk of contracting AIDS. Tuberculosis, actinomycosis, syphilis have not lost relevance today and can be detected in patients with deficiency of cellular immunity who seek dental care.

2. Tasks.

1. Know immunological features of delayed-type hypersensitivity reactions.

2. Know the immunopathology of genesis of AIDS, actinomycosis, tuberculosis, syphilis.

3. To be able to evaluate the clinical and anamnestic immune status of patients with manifestations of AIDS, actinomycosis, tuberculosis and syphilis.

4. Master the skills to evaluate immunograme patients with deficiency of cellular immunity.

The preparatory stage

At the beginning of class, the instructor reveals the importance of the subject, defines the main goals and objectives of the lesson, assess the initial level of knowledge by solving tests and oral interviews. Students are given a task to work with patients.

Literature

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Tests to check the initial level of knowledge

1. What type of immunity is formed with active syphilis?
A. acquired resistant *B. toxic* *C. non-sterile* *D. lifetime*

2. In the latent form of syphilis in blood prevail
A. IgA and IgM *B. IgG* *C. no antibodies* *D. IgAE. IgM*

3. Seronegative manifest course of syphilis occurs when
A. insufficient concentration of IgA and IgM to antigens pale treponema
B. high concentration of IgM
C. high concentration of IgG
D. absence of specific antibodies to the causative agent of syphilis

4. Lack of syphilis occurs when
A. activity of cellular immunity
B. sufficient activity of cellular and hum oral immunity
C. expressed antibody activity anti-treponemnyh
D. Tolerance of T- and B- lymphocytes

5. Treatment of primary syphilis involves the appointment
A. immunotropic drugs
B. drugs penicillin series
C. mandatory immunotropic combination preparations and penicillin
D. surveillance tactics

6. The mainstay of treatment of actinomycosis is
A. surgical treatment
B. immunotropic treatment
C. Surgical treatment and Immunotropic
D. surgical and antibacterial treatment
E. antibacterial treatment

7. For rapid diagnosis of actinomycosis used
A. polymerase chain reaction *D. histological response*
B. inhibition of leukocyte migration *E. serological tests*
C. cutaneous allergic reaction

8. For inhibition of actinomycytes is crucial
A. humoral immune response *D. complement system*
B. cellular immune response *E. factors of congenital and*
C. factors of innate immunity *acquired cellular immunity*

9. In the formation of anti-tuberculosis immunity play an important role
A. CD4 T-lymphocytes *C. antibodies IgG*
B. CD8 T cells *D. complement system*

10. Tuberculosis lupus patients is
A. with insufficient immune response to the pathogen
B. of agranulocytosis
C. with sufficient immune response to the pathogen
D. after immunosuppressive therapy

Correct answers to test questions: 1 – C. **2** – E. **3** –A. **4** – B. **5** – B. **6** – D. **7** – A. **8** – E. **9** – A. **10** – C.

BASIC CONTENT OF THEME
AIDS

Etiological factors of AIDS - a family of retroviruses, subfamily lento-viruses.Ways of viruses in the body:

1. through blood (lymphocytes, monocytes).
2. through the digestive canal in the lymph nodes, lungs, heart, retina, heart.
3. through blood, cerebrospinal fluid, vaginal secret saliva, secret tears, breast milk, sweat.

Transmission of the virus:

1. Sexual contacts.
2. Transfusion of blood and blood products, the use of non-sterile.
3. In utero from mother to fetus. Incubation period: 6–8 months – 4 years.

PERIODS OF DISEASE

Phase I. Phase acute fever. Asymptomatic phase. Persistent generalized lymphadenopathy

Phase II. Loss of body weight less than 10%, fungal, viral, bacterial skin lesions, ulcers of the mucous membranes, shingles for 5 years, recurrent upper respiratory tract infections (pharyngitis, sinusitis).

Phase III. Weight loss greater than 10%, unspecified chronic diarrhea, fever more than 1 month, oral candidiasis, hair leukoplakia of the mouth (Epstein-Barr). Pulmonary tuberculosis within the past year, severe bacterial infections (pneumonia).

Phase IV. Wasting syndrome caused by HIV, Pneumocystis pneumonia. Toxoplasmosis of the brain. Cryptosporidiosis with diarrhea more than 1 month. CMV infection (with involvement of other organs, except the liver, spleen, lymph nodes). Infections are caused by the herpes simplex virus from skin lesions and mucous more than 1 month or damage internal organs. Disseminated mycosis. Candidiasis of esophagus, trachea, bronchi and lungs. Atypical disseminated mycobacteriosis. Septicemia caused by salmonella. Extra pulmonary tuberculosis. Lymphoma, Kaposi 's sarcoma. Encephalopathy caused by the action of HIV.HIV infection :Bacterial infection (gingivitis, periodontitis, actinomycosis,)graviton of apical periodontitis, osteomyelitis, sinusitis, a disease of child scratches, abscess, cellulitis.Phlegm on not carious etiology immunopathology of genesis.In the blood of HIV-infected patients gradually reduced the number of CD-4 lymphocyte ratio and CD-4/CD8. In the early stages of HIV infection one infected lymphocyte present in 1000 to 10000 normal lymphocytes. As the disease progresses percentage and absolute number of lymphocytes infected CD-4 increases, leading to higher concentrations of viral RNA in plasma. Found that reducing the number of lymphocytes: autoimmune destruction CD-4 lymphocytes, direct destruction of lymphocytes, toxic effects of viral proteins urgent lymphocytes and bone marrow, lymphocyte apoptosis. Content lymphocyte CD4 (helper cells) in the blood serves as an important laboratory signs of immune system infected. The lower level of CD4 lymphocytes, the higher the risk of opportunistic infections. In CD4 lymphocytes an important role in the pathogenesis of HIV infection with other cells. HIV infects cells of innate immunity: monocytes,

macrophages, dendritic cells of lymph nodes, rarely affects the central nervous system cells and B-lymphocytes.

In the preclinical phase of the disease when there is no virus in the blood, the lymph nodes is active viral replication, decreased functional capacity (chemotaxis and intracellular destruction of microorganisms) infected macrophages. The release of cytokines, including tumor necrosis factor alpha positive macrophages is one of the reasons cachexia in the later stages of AIDS. According to the criteria of the Center for Disease Control U.S. diagnosed with AIDS exhibit, if the content of CD4 lymphocytes in the blood below 200 in 1 mcl. opportunistic infections and malignancies like Kaposi 's sarcoma and B-cell lymphoma, also confirmed AIDS. After infection, during the acute stage of fever, HIV is found in blood. After weeks of viraemia of carp runs, and increases in blood levels of cytotoxic T lymphocytes (CD8). After the disappearance of the virus from the blood in it appear neutralizing antibodies, but they do not play a role in the disappearance of viremia. The immune response that is mediated by antibodies directed against the virus proteins p24, r41 120 and other antigens. When polyclonal activation of B lymphocytes increases the overall level of immunoglobulins. Studies in rats show that these reactions contribute to the projective action, but due to antigenic variability of the virus are not effective enough. By leaving the bloodstream, the virus settles in the lymphoid organs, where it is replicated. During the asymptomatic phase the number of CD4 lymphocytes in the blood of every year is reduced by 50–100 in 1 mcl. End of the asymptomatic phase of the virus obtained from lymphoid organs. As the disease progresses in the blood increases levels of beta2-microglobulin, neopterin, tryhlytserydoi and HIV antigens (ie, p24). Stage of the disease is determined by the absolute number of CD4 and beta2-microglobulin levels in blood. Symptoms such as fever, sudden weight loss and sweating favor the drastic suppression of the immune system and poor prognosis**.**

Opportunistic infections

Up to 90% of deaths in HIV infection directly or indirectly caused by opportunistic infections, confirming the important role of prevention and treatment. Most common opportunistic infection caused Pneumocystis, Mycobacterium avium-intracellulare, Mycobacterium tuberculosis, Cryptococcus neoformans, Candida spp., Toxoplasma gondii, Histoplasma capsulatum.

Pneumocystis pneumonia - is the most common opportunistic infection of the respiratory tract in HIV-infected and occurs in 60–80% of patients with AIDS, but modern methods of prevention to minimize its severity. The risk of pneumonia is particularly significant when the number of CD4 lymphocytes reaches below 200 in 1 mcl. The disease is caused by re activation of latent infection. Such features as reducing the number of CD4 lymphocytes and the change in the ratio CD4/CD8, also indicate HIV infection, but nonspecific for her and observed in other diseases. The most common method for laboratory diagnosis of HIV infection – a solid phase ELISA. Its sensitivity and specificity reaches 99%. False positive results more often observed in populations with low HIV prevalence and may be caused by influenza vaccination. A positive

result obtained by solid phase ELISA should be confirmed by immunoblotting. Although immunoblotting – highly sensitive and specific method for the detection of antibodies to HIV, because of the cost and time for mass studies do not apply. The results of immunoblotting considered positive if antibodies be detected at least up to 3 proteins. When determining antibodies to one or two proteins considered doubtful result and one that requires clarification. Determination of antigen p24. Solid phase ELISA can detect even a few pictograms anty24. The formation of a complex between p24 and endogenous antibody reduces sensitivity. This method is used when examining patients with early HIV infection, when HIV antibodies are absent. 2. Virus isolation from blood – and very sensitive and specific method of diagnosing HIV infection. The virus may be determined in the culture of lymphocytes and monocytes patient. Because these methods are complex and require material expenditures, they are used for scientific purposes. 3. PCR – a relatively new method, based on the amplification of DNA and RNA. The main advantage of this method is its sensitivity, which allows to determine the minimum number of nucleic acids. However, the high sensitivity of the method does not allow the use of this method for the study of samples infested by other microorganisms. PCR was performed only in specialized laboratories under sterile. Referred to as quantitative PCR methods for the determination of viral genome, so it can be used to assess treatment efficacy. Another method of DNA analysis, the so-called branching DNA, which is based on the use of synthetic DNA that contains one region complementary fragments of viral RNA, and many areas on an artificial oligonucleotide probes, which labeled fluorescent dye. The method is less sensitive than PCR. Treatment of HIV-infection. Viral replication may stop at different stages of its life cycle. There are antiviral drugs that block attachment of the virus to the cell membrane, transcription of DNA from the viral RNA, assembly of viral RNA and proteins zidovudine – the first reverse transcriptase inhibitor approved for use in HIV infection. Initially, the drug was administered in high doses (more than 1 g/day orally or i/v), the development of neutropenia and severe anemia. Currently zidovudine administered at a dose of 400–600 mg/day orally or i/v, it does not reduce its therapeutic effect, but change risk of side effects. FDA approved and other reverse transcriptase inhibitors: zaltsytabin didanosine, stavudin, lamivudin, tryflurydyn.

1. **Zydovudin.** There is no consensus regarding the optimal timing of treatment zydovudin not. Now the drug is administered to all HIV-infected, in which the number of CD4 lymphocytes in the blood below 500 in 1 mcl (regardless of symptoms), and all patients with AIDS. Application zydovudin slows the development of AIDS and prolong the life of patients. Side effects of the drug – anemia and neutropenia – usually reversible. Prolonged use may cause myopathy and reduce antiviral efficacy. However, reducing the effectiveness of the drug may not lead to deterioration of the patient. When the resistance zydovudin remain effective and zaltsytabin

2. **Didanosine** – the second drug approved by the FDA for the treatment of HIV infection. Treatment of didanosine sometimes complicated acute pancreatitis, peripheral neuropathy is frequently observed. Didanosine inhibits disease progression in patients who were treated zydovudine. Change of antiviral drugs increases the effectiveness of treatment retroviral infection.

3. **Zaltsytabin Suitable** for intolerance or ineffectiveness zydovudinu. Side effects – stomatitis and peripheral neuropathy. At the end of XX century for the treatment of HIV/AIDS has been implemented in practice promising method «triple therapy». And it is the combination of three drugs: criksivan, Retrovir and Epivir – is the most effective current treatment for AIDS and HIV infection. criksivan (indinavir) – a new drug, a powerful protease inhibitor which inhibits the reproduction of HIV. Criksivan appearance in late 1995 changed the treatment strategy AIDS. It is known that HIV AIDS is restored when continuously and rapidly the whole period of the disease, producing approximately 10 billion new virus particles per day. New criksivane the treatment was: 1) reduce the concentration of virus (HIV) levels below the limit of determination and preservation of such an effect as the longest; 2) the significant recovery of the immune system by maximizing inhibition of virus replication.The result of this treatment was to improve the immune system of the patient, as evidenced by an increase in the number of immune cells – CD4 (within 100–500 in 1 mL). The optimal treatment regimen for AIDS «triple therapy»: criksivine to 800 mg every 8 hours starting treatment with CD4-lymphocytes of less than 300 per 1 ml. Today criksivine used as a basis for combination therapy in combination with retrovir (synonym: azydotimidin, zydovudin) and Epivir (synonym: lamivudin) – antiretroviral agents – reverse transcriptase inhibitors that penetrate the HIV cell block the synthesis of proviral DNA, replacing the original nucleosides under the synthesis.

These drugs were widely used before: Epivir 150 mg 2 times a day, azydotimidin (Retrovir) 150 mg 4 times a den. Known that the development of resistance to HIV azydotymidine, it can be replaced by didanozyn, zaltsitabin and stavudin. The consequence of the use of «triple therapy» in AIDS mortality has decreased by 30–40%. A steady decrease in the concentration of HIV-1 in blood improves immune system function: increasing the number of CD4-lymphocytes (within 100–500 in 1 ml) and decreased frequency of disease progression. The cost of «triple therapy» high, but such treatment prolongs life and dramatically reduces the potential risk of infection to others.

Immune-pathogenesis. In the blood of HIV- infected patients gradually reduced the number of CD-4 lymphocyte ratio and CD-4/CD8. As the disease progresses percentage and absolute number of lymphocytes infected CD-4 increases, leading to higher concentrations of viral RNA in plasma. Found that reducing the number of lymphocytes advantage : autoimmune destruction CD-4 lymphocytes, direct destruction of lymphocytes, toxic effects of viral proteins urgent lymphocytes and bone marrow, lymphocyte apoptosis.Content lymphocyte CD4 (helper cells) in the blood serves as an important laboratory signs of immune system infected. The lower level of CD4 lymphocytes, the

higher the risk of opportunistic infections. At the level of 0.2 per 109 lymphocytes/L should be administered prophylaxis pneumocystis pneumonia, and at the level of 0.05 to 109 cells/l increases the risk of CMV retinitis and infection caused by Mycobacterium avium-intracellulare. In CD4 lymphocytes an important role in the pathogenesis of HIV infection with other cells.

HIV infects cells of innate immunity: monocytes, macrophages, dendritic cells of lymph nodes, rarely affects the central nervous system cells and B-lymphocytes. In the study detect infected lymph node dendritic cells, around which contains a large number of viruses. In the preclinical phase of the disease when there is no virus in the blood, the lymph nodes is active viral replication, decreased functional capacity (chemo taxis and intracellular destruction of microorganisms) infected macrophages. The release of cytokines, including tumor necrosis factor alpha positive macrophages is one of the reasons cachexia in the later stages of AIDS. According to the criteria of the Center for Disease Control U.S. diagnosed with AIDS exhibit, if the content of CD4 lymphocytes in the blood below 200 in 1 mcl. Opportunistic infections and malignancies like Kaposi's sarcoma and B-cell lymphoma, also confirmed AIDS. After infection, during the acute stage of fever, HIV is found in blood. After weeks of viral of carp runs, and increases in blood levels of cytotoxic T lymphocytes (CD8). After the disappearance of the virus from the blood in it appear neutralizing antibodies, but they do not play a role in the disappearance of viral. The immune response that is mediated by antibodies directed against the virus proteins p24, r41 120 and other antigens. Polyclonal activation of B lymphocytes increases the overall level of immunoglobulin's. Studies in rats show that these reactions contribute to the projective action, but due to antigenic variability of the virus are not effective enough. By leaving the bloodstream, the virus settles in the lymphoid organs, where it is replicated. During the asymptomatic phase the number of CD4 lymphocytes in the blood of every year is reduced by 50–100 in 1 mcl. End of the asymptomatic phase of the virus obtained from lymphoid organs. As the disease progresses in the blood increases levels of beta2-microglobulin, HIV antigens (ie, p24). Stage of the disease is determined by the absolute number of CD4 and beta2-microglobulin levels in blood. Symptoms such as fever, sudden weight loss and sweating favor the drastic suppression of the immune system and poor prognosis.

Basic principles of therapeutic strategies AIDS

Principle 1. Continuous HIV replication results in damage to the immune system and the development of AIDS. HIV infection is always dangerous for the organism survival cases of clinically significant immune damage observed rarely. Known statistics developed countries: the time from infection to the development of clinical symptoms without treatment is 10–11 years. In 20% of cases of AIDS symptoms develop in the first 5 years after infection. Thus, HIV viruses more than other viruses.

Principle 2. The level of HIV RNA in plasma reflects the activity of HIV replication and the associated rate of destruction of CD4-lymphocytes, and

the number of CD4-lymphocytes indicates the degree of damage to the immune system. Regular determine the number of CD4- lymphocytes and HIV RNA is needed to assess disease progression and the definition of starting or changing retroviral therapy.

Principle 3. Since HIV-positive rate of progression varies, the approach to the choice of therapy should be individualized and based on risk, which is determined by the level of HIV RNA and CD4-lymphocyte number.

Principle 4. Combination therapy with highly active antiretroviral drugs that suppress HIV replication to a level that will not be evaluated even when using highly sensitive methods for the determination of HIV RNA, reduces the likelihood of HIV strains that are resistant to antiretroviral drugs. The presence of such strains is a major factor that limits the ability of antiretroviral drugs to suppress HIV replication and delay disease progression. Therefore, the goal of therapy is to maximize the reduction of HIV replication.

Tuberculosis

In Ukraine 781 thousand patients, representing 1.4% of the population. We know that a third of the population is infected with Mycobacterium tuberculosis. One patient with tuberculosis can infect the year 10–15 people, and the day he identifies up to 10 billion.

Tuberculosis – specific chronic infectious disease whose causative agent is Mycobacterium tuberculosis (MBT). At the dentist's reception is more common immune-compromised patients suffering from somatic diseases are radio and chemotherapy, are registered with the drug and TB dispensaries. These patients are at increased risk of transmission tuberculosis infection. The source of infection and spread of tuberculosis, in addition to sick people may be suffering from tuberculosis and animal food from them (meat, milk) that have not been sufficient heat treatment. Known disease in which the probability of the presence of tuberculosis increases. Refers to the patients: with chronic nonspecific pulmonary diseases (COPD) – a prolonged course of acute respiratory diseases; suffering from recurrent dry pleurisy; with diabetes; With high degree of reactions to tuberculin; the long-term hormone therapy; In chronic alcoholism, drug addiction, mental illness and AIDS. Diseases in history along with the appearance and identification of specific changes in the oral cavity must draw attention to the need for dental screening for tuberculosis. In the mouth tuberculosis occurs rarely, the mucous is not susceptible to mycobacteria. The originator can get on the mucous endogenous (lymph genetic) and exogenous way, while the agent is often dies. Reproduction probable pathogen at low immune status of the patient, the course of tuberculosis in the body due to neuro-endocrine changes and nutrition patient. Primary tuberculosis of the oral cavity is possible only after mucosal injury. Secondary tuberculosis occurs as a result of tuberculosis of the lungs or skin occurs as tuberculosis and lupus, ulcerative tuberculosis. Tuberculosis lupus occurs in patients with a sufficient immune response to the pathogen. TB patients are prone to intensive development of dental caries and chronic diseases. They often find chronic odontogenic infection, hard tissue of teeth, paresthesia oral mucosa.

Immune-pathogenesis

Infection occurs through inhalation of aerosols containing mycobacteria or after eating contaminated food. Further and pulmonary alveolar macrophages mycobacteria and transported them to the regional lymph nodes. Phagocytic reaction with an incomplete character, the agent remains in the cytoplasm of macrophages. Mycobacteria reduce the activity of phagocytes by products that enhance the toxic effect of cord factor (affects mitochondrial membrane) and inhibit fusion with lysosomes. Reproduction pathogen occurs within phagocytes in the lymph node sinuses. Phagocytes carry mycobacteria from lymph nodes in the bloodstream. Macrophages and dendritic cells are antigen activator of T cells in the lymph nodes para-cortical areas. In the course of regional lymph nodes formed the original complex, namely the formation of granulomas in the form of a protuberance. Granuloma in tuberculosis no characteristic properties is a cellular delayed type hypersensitivity reaction. The formation of granulomas promotes formation of large amounts of lactic acid, low pH and high concentration of CO2. In the center is region tubercle case us necrosis, where the sticks Koch. Around necrosis are giant cells Pirogov-Langhans behind them-lymphocytes, plasma cells and mononuclear cells. In granuloma multiplication of the pathogen is reduced or terminated. The primary focus heal the degradation of content, calcification and fibrosis of the parenchyma may pathogen of primary lesions (lymph nodes often) to form foci - screening. By reducing immune activation of the fire and develops secondary process. In debilitated patients and patients with immune deficiencies observed disseminated tuberculosis with the formation of granulomas in various organs after breaking content granulomas in the bloodstream. Study of immune status and non-specific reactivity with tuberculosis showed that the active progressive course of disintegration of tissue and bacterial occur: depression of T-cell immunity, the displacement ratio CD4/CD8 subpopulations in favor of the latter, amplification products of interleukin IL-1, tumor necrosis factor TNF, IL-6, is the suppression of cellular immunity and activation of anti-TB products antibodies. In contrast with a favorable course of tuberculosis, the absence of bacteria, closure of decay cavities, reducing infiltrative events subpopulations increases the ratio CD4/CD8, decreased production of macrophage IL, increasing the production of interferon (IFN)-γ, activates specific cellular immunity and antibody production of antibodies are decreased. In patients with acute forms of the disease plays a significant role immunodeficiency disorders with structural lymphocytes and apoptosis, leading to a decrease of T regulatory cells and their subpopulations, reducing their functional ability. Structural and metabolic cells of monocyte-macrophage series leading to a decrease in their function and rapid degradation in the area of inflammation with case of formation of destructive changes in the lungs. In the formation of anti-TB immunity are important CD4 T-lymphocytes. Their role has become particularly clear after the increase in tuberculosis among persons infected with the AIDS virus. In these patients have reactivated latent form of tuberculosis. Pathogenesis role of subpopulations of T-helper cells is determined by their ability to recognize major histocompatibility complex antigens (HLA II class). So recognizable

dendritic cells and macrophages in the vacuoles which are antigen peptide tuberculosis bacteria. Antimicrobial activity of CD8 T-lymphocytes may be achieved in several ways. Lymphocytes this population could be the source of production of cytokines, which are interferon-gamma (IFN-g) and TNF-a. CD8 T cells can induce projective direct effect on macrophages with M. tuberculosis, which are in the tissues. Production of cytokines plays an important role in the activation of macrophages. CD4, CD8 T cells INF-g and TNF-a, the concentration of which increases inflammation. Another mechanism by which macrophages are destroyed CD8 T lymphocytes, is associated with the ability to kill cells by macrophages perforines. Perforines - a protein that is synthesized granules of CD8 T lymphocytes. Perforines violates the integrity of the membrane of infected cells, therefore, fall into the cell toxic peptides Gransee and accelerate apoptosis in macrophages. Apoptosis of macrophages can be achieved through the mechanism of Fas-ligand that activates CD8 T cells. These cells can largely compensate for the functional deficiency of CD4 T lymphocytes. Ulcerative Tuberculosis is caused by Mycobacterium Koch hit in the lining in the field of personal injury. Tuberculosis affects the mucous cheeks lips, back, and side tip of the tongue, soft palate, hard palate at least, the bottom of the mouth. Characteristic of the inflammatory process is as follows: ulcerative lesion is deep, but painful, ragged edges, a bottom – grainy, rough, ulcers covered with yellowish-gray pus. Regional lymph nodes are enlarged, painful. Tuberculosis lupus affects both the skin and the oral mucosa. A typical element t – inflammatory lesion area and bubble size 1–3 mm in diameter. Affects primarily the mucous of the upper lip in the incisors and CTR, palate. At the confluence of vesicles formed from moderately painful ulcer edges. After ulcer healing form atrophic scars. With the localization of ulcers in the lip mucosa develops mikrostomiya.

Treatment.

Treatment takes place in a specialized medical facility. Local treatment includes exceptions traumatic factors, dental health, applique antiseptic and anti-inflammatory drugs.

Actinomycosis

Actinomycosis is a chronic, specific disease, which is caused by beam mushrooms, runs from lesions in various organs and tissues. Actinomycoses spread widely, and is 5–8% purulent processes of various locations. Radial fungi are always present in the human body. The basis of the pathogenicity of the fungus is their ability to secrete enzymes are hydrolases class. However, the role of aggression factor is not as significant compared with the change of the immune system microorganism. To their original places of localization include tonsils, carious mouth, gum pockets, upper respiratory tract, gastrointestinal tract. Development of the disease contributes to decreased immunity after the transfer of infectious processes. Peculiar role of the carrier beam mushrooms and traumatic factors which simultaneously play calculus. Found that actinomycytes constitute the bulk of the stroma stones saliva. Agents of actinomycosis - actinomycytes are part of the oral cavity and gastro-intestinal tract, they are regarded as opportunistic

pathogens. The main factors contributing to the development of disease: trauma mouth, periodontitis, dental manipulation. Most of the growth of the disease occurs in autumn and winter, respiratory infections, a favorable backdrop for pathogen multiplication actinomycosis (aerobic and anaerobic gram positive bacteria).

Pathogenesis. Lesions are endogenous (inflammation of the mouth and injury) and exogenous nature (with the introduction of the pathogen into the wound). Favorable factors – reduced immunity and local oral mucosa, the composition of the microbial flora, comorbidities (tuberculosis, diabetes, etc.). Around the pathogen in the sub mucosal membrane formed granuloma (aktynomikoma) containing colonies of the pathogen (friends). Then fire breaks with the development of purulent and farinose inflammation. The most common face of actinomycosis in 50–60% of cases of actinomycosis and in 6–10% of patients with inflammatory diseases of the jaws. Other diseases caused by actinomycetes are: dental caries, inflammation of the lacrimal gland infections resulting from the use of intrauterine contraceptive devices, mastitis, peritonitis, septic abortion, abscesses. In patients with a history of actinomycosis determine the destruction of tooth caries, tooth extraction, fractured jaw, periodontal abscess, foreign body lesions bodies (fish bones, corn stalks).Bone lesion and regional lymph nodes is rare and peryostit- and post-traumatic osteomyelitis often. Microorganisms Oral mechanisms contribute to the process by providing enzymes and toxins. Thus, actinomycosis is always a mixed infection in which actinomycetes are the leading pathogens that determine clinic and symptoms of the disease. Painting primary actinomycosis develops the mechanism delayed-type hypersensitivity (classification Gela ua Coombs) with the participation of innate immune factors. Around the mycelium of actinomycetes formed specific granuloma. In the basal layer of the epithelium observed leukocyte infiltration, accumulation of monocytes and lymphocytes are sub mucosal layer. On the periphery of the clusters formed granulation tissue with lymphocytes, plasma, fibroblasts, and giant cells. During necrobiosis in the center of granulomas is the accumulation of macrophages near the Druze actinomycetes. Macrophages are moving into the colony and capture spawn.

Immune- pathogenesis. Protect the microorganism of fungal infection based on natural protective factors that are present continuously and specific immune factors that appear in response to pathogen invasion. The factors of innate resistance include: temperature and pH of the microorganism, competition with cells of normal micro flora, the integrity of the skin and mucous membranes. To antifungal innate humoral factors include: transfers, lysozyme, acute phase proteins. Deficiency of these factors and reduce competing microflora promotes proliferation of fungal infection. Major role in ridding the body of fungi played macrophages. System nitric oxide, which activates the selection pro-inflammatory cytokines is a major substances. The role of natural killer (NK) in the regulation of immune response to fungi is due to their secretion of interferon-gamma, TNF and IL-2 by activating Th1 type. Cells were acquired immunity CD-8 can destroy macrophages with incomplete phagocytosis and the presence of the fungus inside the phagocytes. CD-8 cells can inhibit Th 2 diabetes who do not provide an adequate immune response to fungi. CD-8 cells also have direct fungicidal effect.

Antibodies (IgG, IgA, IgM) against actinomycetes can be detected in serum by various methods, including ELISA. Humoral immune response in actinomycosis is critical for inhibition of the pathogen. The presence of antibodies is not sufficient protective effect in actinomycosis, their presence does not affect the cure of this infection. IgE detected in carriers and in infection. Activity IgE inhibits Th type 2 that inhibits fungal cell immunity and promotes disease progression.

Diagnosis

1. Diahnosis actinomycosis put in isolation and identification of the causative agent, the clinical symptoms are not very specific, histological and serological study of low specific and sensitive low. Presence of friends sometimes provide manure view "semolina", which may give rise to suspicion of actinomycosis.

2. Skin-allergic reaction not always decisive diagnostic test. This reaction gives a lot of questionable or negative results. Running it as follows: 0.3 ml aktynolizate injected into the skin on the flexor surface of the forearm. Along a 10 cm muscle administered 0.3 ml of broth. Soon blisters appear to disappear for 2 hours, erythema stored up to 12 hours. In the presence of actinomycosis erythema disappears 36–48 hours. But this reaction may be positive for tuberculosis and other inflammatory diseases.

3. More positive diagnostic results are obtained inhibition of leukocyte migration aktynolizatom as antigen.

4. For rapid diagnosis of actinomycosis are emerging as molecular diagnostic methods such as polymerase chain reaction. Lesion of the oral mucosa actinomycosis, especially in the localization process on the cheek and lateral surface of the tongue should be differentiated from tuberculosis chancre and lupus. Combination therapy of choice is protected from aminopenicillins metronidazole and gentamicin should be noted that a separate receiving clindamycin or metronidazole without prescription aminopenicillins or cephalosporin's are not effective

Treatment

Treatment can be designed in consultation immunologist and the immunological examination in case of failure of the above-mentioned treatments. Due to suppression of innate and acquired cellular immunity in actinomycosis is worthwhile destination immune-tropic drugs that act on these immunity. These include modern medications like Polyoxidonium, Imunofan, Nucleinat, Likopid.

4. For a comprehensive treatment of deep mycoses include immunotherapy aktynolizatom which is cooked fresh filtrate culture fluid actinomycetes. Aktynolizat administered 2 times a week for 3 ml. A course held from 10 to 25 injections**.**

Syphilis

Syphilis – a chronic infectious disease caused by the treponema pale. In congenital syphilis pathogen enters the body of the fetus through the placenta from an infected mother. In acquired syphilis infection occurs through the skin and mucous membranes by direct contact (usually sexual) and through objects contaminated with secretions of patients who have the pathogen. Infection can occur through medical instruments, including dental (tips and mirrors). If they were not sufficient disinfectant treatment. The condition is an infection of the

stratum cornea damage to the skin or mucosal epithelium. Infection can occur through direct contact with the pathogen in blood, for example through a wound at the hands of a physician during surgery. Dentists and gynecologists can get the treatment of patients. Is most contagious patients with active signs of syphilis in primary and secondary syphilis in the localization of periods in the mouth and on the genitals. Pale treponema quickly enters the body through the lymphatic system, and 1–2 days reach regional lymph nodes. The average incubation period of 21–28 days reach.

Clinic.

Primary syphilis. Primary occurs at the primary site of infection and is localized to the red border of lips, rarely on mucosa of the mouth (tongue, tonsils and other tracts). View chancre may be typical or have a small erosion, cracks with a small infiltrate at the base. In tonsils chancre may take the form of a smooth increase and consolidation of one tonsil, tongue look like a limited seal on gums – as erosion. Regional lymph nodes were enlarged, painless on palpation, not welded to each other and the surrounding tissues. In oral chancre may be complicated by a staph infection. In such cases, the clinical picture is no longer the default, there pain and purulent exudate.

Secondary syphilis. The mucous membrane of the mouth often affected with secondary syphilis. Manifestations in the mouth appear simultaneously with the skin, but can be isolated.

Papules syphilis – is the most common form of oral lesions, especially in smokers and injuries. Papules are easily eroded when trying to remove them. Papules and erosion are composed of many pale treponem.

Pustular syphilis rare in the mouth, usually sugar debilitated patients and shows infiltration that enters ulcer of necrotic- purulent coating.

Tertiary syphilis. It begins 3–5 years after infection and can last for decades. Mucosa is frequently affected in two forms: Gummy and bubbles-form syphilis. Gummy located on the soft and hard palate are rarely on the tongue. In center Gummy ulcer crater formed. Ulcers can become infected secondary streptococcal infection. Pain Gummy expressed moderately. Specific infiltrate is replaced by fibrous tissue, there are atrophic ulcers. Bubbles localized on the lips. Alveolar process and palate and has the form of small bubbles painless bluish-red. Syphilitic bubbles exist for years, but less than in tuberculosis. After healing scars do not appear on the new bubbles. Scars syphilis more serious than tuberculosis lupus. Regional lymph nodes with tertiary syphilis may not respond or give nonspecific response to activation of secondary infection. Identify pale treponemu in the centers of tertiary syphilis impossible.

Diagnosis. All serological tests for the diagnosis of syphilis and non-specific non- shared, as well as screening, diagnostic and supporting. For the production of non-specific reactions used nonspecific antigens: treponemnyy antigen derived from cultural treponem nonpathogenic strains (group identification of specific antibodies) antigen that is artificially made (detection of antibodies to lipid treponema antibodies).Selective reactions used for mass serological tests for syphilis persons decreed professions patient clinics and

hospitals. Most often used mikroreaktsiya precipitation (MRI). Diagnostic reaction used to confirm the clinical diagnosis in patients with suspected syphilis and for examination of sexual partners, to monitor the effectiveness of treatment (in combination with mikroreaktsiyeyu) to test donors and pregnant women. For diagnostic reactions also belongs complement fixation test (RSC). Abroad currently not using RAC. MR and RAC are positive at the end of the second week of primary syphilis. For the production of specific reactions using specific antigens derived from pathogenic strains pale treponema by culturing on experimentally infected animals (to determine the species-specific antibodies).

Primary humoral protection factor is an antibody that contribute to the elimination of the pathogen. In the early stages of syphilis significantly increased levels of IgM, and during the second stage of recurrent – IgG. Number of circulating immune complexes also increases the secondary period of syphilis. Specific treatment eliminates immune complexes only in 50% of patients.

Tests for verification final level of knowledge

1. Primary tuberculosis of the oral cavity is possible

A. only after mucosal injury *C. for airborne infection*

B. with intact mucous *D. only after immunosuppressive therapy*

2. The risk of pneumocystis pneumonia in HIV infection is particularly significant when the number of CD4 lymphocytes reaches

A. above 200 mcl^{-1}. *B. below 200 mcl$^{-1.}$* *C. below 500 mcl^{-1}* *D. below 1000 mcl^{-1}.*

3. Such features as reducing the number of lymphocytes CD4 and CD4/CD8 ratio change

A. indicate HIV infection, but nonspecific for her and observed in other diseases.

B. is a major diagnostic criterion HIV

C. not indicate HIV infection

D. indicate HIV infection to end-stage

4. Zydovudin drug administered to all HIV - infected, in which the number of CD4 lymphocytes in the blood

A. below 200 mcl^{-1} *C. below 1000 mcl^{-1}*

B. below 500 mcl^{-1} *D. not appointed because of the inefficiency*

5. Most common opportunistic infection in AIDS cause :

A. Pneumocystis carina,

B. Mycobacterium intracellular, Mycobacterium tuberculosis,

C. Cryptococcus neoformans, Candida spp.,

D. Toxoplasma gondii, Histoplasma capsulatum,

E. DNA viruses such as cytomegalovirus, herpes simplex virus

F. All answers are correct

6. Most effective in AIDS is

A. monotherapy antiretroviral drugs *D. symptomatic therapy*

B. dual therapy *E. immune-stimulating therapy*

C. triple therapy

Correct answers to test questions: 1 – A. **2** – B. **3** – A. **4** – B. **5** – F. **6** – C.

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IMMUNOLOGY OF SPECIFIC INFLAMMATORY PROCESSES IN MAXILLO-FACIAL AREA

Manual for practical lessons students having higher medical education in English majoring in dentistry