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**FEATURES OF THE COURSE OF ERYTHEMA MULTIPLE  
FORM ASSOCIATED WITH HERPES VIRAL INFECTION**

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## LIST OF ABBREVIATIONS

HSV - herpes simplex virus

GAME - herpes-associated exudative erythema

DTH - delayed type hypersensitivity

HIT - immediate type hypersensitivity

GCS - glucocorticosteroids

PG - herpes simplex

IR - immune complexes

IFS - interferon status

IF-interferon

IL-interleukin

IRI - immunoregulatory index

NBT-test with nitrosine tetrazolium



## **Introduction.**

Soon after the first reports of the association of erythema multiforme and "lichen pimple" published in Urbach, Anderson already called the herpes simplex virus a "time bomb" in relation to this. The 70 years that have passed since then have not only not changed the situation, but have given it a special urgency. If at the initial stages of studying this process the main issue was the search for causal factors, today there are other tasks related to the study of pathogenesis and the selection of therapy. Many pathogens have already been identified that can serve as an impetus for the development of a more common variety of exudative erythema of its infectious-allergic form. Including in many studies using modern diagnostic technologies, the etiological role of the herpes simplex virus, its direct connection with both the onset of the disease and subsequent relapses has been proven. According to the statistics of the availability of specialized clinics, the proportion of erythema multiforme caused by the herpes simplex virus among all its forms reaches 80%, which is about % of all patients who visit dermatovenereologists and dentists.

The urgency of the problem is given by the increase in the incidence of herpes simplex, which has taken one of the first places among the problem areas of the World Health Organization, along with such infections as the human immunodeficiency virus and influenza.

In the modern scientific literature, a large number of studies and, accordingly, publications are devoted to the characteristics of the herpes simplex virus, both clinical and immunological. However, there are no reports yet on the clinical features and immunological status of HS patients who develop GAME. However, upon receipt of such data, it becomes possible to predict the degree of probability of developing IGE. This, in turn, leads to the prevention of this dermatosis through active therapy of patients at risk. To date, there are many drugs for the treatment of herpes simplex. They can be divided into two main groups of etiological action (these are synthetic nucleosides) and agents aimed at immunostimulation, which are

a larger group. However, despite the wide choice of drugs for the treatment of herpes simplex, in the case of the development of exudative erythema against its background, recommendations are mainly reduced to the appointment of synthetic nucleosides. They are usually used to stop the current relapse. As a prophylactic method, most current guidelines recommend the continuous use of acyclovir. Unfortunately, to date, the development of acyclovir-resistant strains of the virus has been noted throughout the world. Thus, it is relevant to search for alternative methods for the prevention of herpes simplex recurrences leading to the development of GAME,

Among the latter, one can single out the herpetic vaccine as a drug with a specific immune effect, which has been widely used since 1933. According to the experience of treating patients with herpes simplex in different countries, its effectiveness ranges from 300/0 to 80%, that is, therapy using a herpes vaccine occupies a strong position in a number of immune-oriented drugs. The choice of nonspecific immunomodulators due to the lack of clear indications is often empirical. In such a situation, the use of a herpetic polio vaccine is relevant as a specific and affordable means of preventing recurrence of herpes simplex, leading to the development of erythema multiforme.

### **Purpose and objectives of the study.**

Purpose: Based on a comprehensive clinical and laboratory examination of patients suffering from GAME, to identify their characteristic clinical and immunological features and develop a pathogenetically substantiated differentiated approach to the treatment and prevention of this nosology.

In accordance with the goal, the following research tasks were set:

- 1) To identify the features of clinical manifestations of GAME.
- 2) Determine the level of phagocytosis, T- and B-lymphocytes, immunoregulatory index, circulating immune complexes and major immunoglobulins in patients with GAME, HS and other forms of MEE.

Formulate clinical and immunological parameters that increase the risk of developing GAME in patients with HS.

4) Develop a differentiated approach to therapy (both for relief of exacerbations and for prevention), adequate to the identified disorders and evaluate its effectiveness.

### **Scientific novelty of the research.**

1) For the first time, the features of the clinical picture of GAME were determined. This dermatosis develops on days 1-9 of PG recurrence. Elements of the GAME rash are solitary, congestive honey agaric, up to 4 cm in diameter and in less than 10% of cases affect the genitals, which distinguishes GAME from the toxic-allergic form of exudative erythema. GAME in 60% of cases occurs against the background of an increase in the frequency and (or) duration of relapses of HS, which in 93% of cases is localized on the face.

2) New data were obtained on a decrease in alpha- and gamma-interferon during GAME ( $55.0 \pm 9.2$  and  $714.0 \pm 21.2$ , respectively). In the humoral link, an imbalance in the production of immunoglobulins with a predominance of Ig E ( $462.0 \pm 20.0$ ) and a decrease in Ig A ( $1.5 \pm 0.5$ ) with an increase in the absolute number of B-lymphocytes ( $235 \pm 11.9$ ) was revealed.

3) A new concept of GAME pathogenesis has been formulated. Apparently, the basis for the development of GAME is a decrease in nonspecific antiviral mechanisms: the absence of an increase in the production of IL-2 and insufficient proliferation of natural killers, reduced production of Ig A. The lack of alpha interferon contributes to a long course of relapse, and gamma interferon - frequent exacerbations of HH. An increase in Th-2, along with an excessive presence of IL-4 and 6, causes an inadequate prevalence of the humoral type of response, which is

expressed by increased proliferation of B-lymphocytes, which is exacerbated by a deficiency of gamma-interferon and IL-2, the main mediators that polarize T-helpers towards the 1st subclass appropriate in this case. Th-2 and IL-4 mediate immediate-type hypersensitivity mediated through Ig E, also elevated in patients with GAME. In addition, the excess of spontaneous production of IL-6 can contribute to the homing of cytotoxic lymphocytes, their increased migration to the sites of rashes.

### **Practical significance.**

1) Clinical and immunological criteria for identifying a risk group for developing GAME among patients with HH are given. Clinical criteria: an increase in the frequency and (or) duration of relapses, its localization in the face. Immunological criteria: change in the production of IL-4 and IL-6 with the ratio between spontaneous and induced production. The predominance of Ig E with a decrease in Ig A against the background of an increase in the absolute number of B-lymphocytes. Decreased interferonogenesis and no increase.

2) A differentiated approach to the treatment of GAME relapses and a method of prevention are proposed. With the development of GAME against the background of the vesicular stage of PH, it is necessary to prescribe synthetic nucleosides, with the development in the crusty stage - synthetic nucleosides and 2 ml of diprospan intramuscularly once. Further, prolonged intake of synthetic nucleosides until the spontaneous and induced production of IL-4 and 6 is normalized. Antibiotic therapy for GAME is indicated in case of signs of secondary bacterial infection: symptoms of intoxication, impetiginization. As a prophylaxis of GAME, the use of a herpetic polio vaccine is used, the criterion for starting vaccination is the normalization of the production of IL-4 and IL-6

## **CHAPTER 1. LITERATURE REVIEW.**

### **Part 1. Multiform exudative erythema.**

#### **1.1 Classification, etiology, clinical manifestations.**

Erythema multiforme exudative (EEE) has been known as an independent disease for more than 100 years. Since F.Hebra in 2010, summarizing several previously described skin erythema under a single name, gave it this designation. In the process of studying the etiology of the disease, the heterogeneity of the causes of MEE was revealed. To date, it is generally recognized to divide it into two forms: idiopathic (that is, occurring without an apparent reason) and symptomatic, including toxic-allergic and infectious-allergic varieties (A.M. Alikhanov, 1986). introduction of an additional distinction. The "small" form is limited to lesions of the skin and mucous membranes, sometimes mild prodromal phenomena are observed, subjective symptoms are absent or are represented by moderate itching or burning. This form matches the description of Hebra. Severe multisystem involvement is called the "large" form or, more commonly, Stevens-Johnson syndrome (S. Mochella, H. Harley, 2011). MEE is characterized by certain age and sex characteristics. Mostly young people are ill (L.N. Mashkilleison, N.S. Potekaev, O.L. Ivanov and other Yu.K. Skripkin,). Symptomatic MEE develops more often in young men after a herpetic or mycoplasmal infection (D.K. Novikov, Yu.V. Sergeev, 2001). In general, the contingent of patients with any form of MEE is mostly represented by men, with half of the patients younger than 20 years old (T. Fitzpatrick, ). There have been reports on the relationship of dermatosis with diphtheria, nephritis, gastrointestinal pathology (L.N. Mashkilleyson,). The association of MEE exacerbations with histoplasmosis, mycoplasmosis, adenovirus infection, mononucleosis, Coxsackie B5 virus, and milker nodules was revealed. In addition to the basic etiological agent, physical factors (hypothermia, insolation, X-rays) and endocrine factors (menstruation, pregnancy) are responsible for the occurrence of MEE (M.A. Samgin, O.L. Ivanov, S.A. Kuzheleva, A.V. Biryukov, N.D. Lviv, ). Such a wide range of triggers, with the constancy of clinical manifestations due to

the unity of pathohistological mechanisms, indicates the possible presence of a constitutional predisposition to the development of hypersensitivity in the form of MEE.

The clinical picture of MEE in most cases is quite typical. The prodromal period, as a rule, is not characteristic or does not take a long time. After the end of the prodromal period, or against the background of general well-being, rashes appear. The favorite localization of rashes is the extensor surface of the limbs, to a greater extent the hands and forearms. To a lesser extent, the face, neck, shins, rear of the feet are affected. The oral mucosa, lips, and genitals are often affected. The rash with symptomatic MEE is more common, affecting the skin of the face and trunk to no lesser extent (EM. Abramova, N.L. Reznikova,). For MEE, lesions of the lips and oral mucosa are quite characteristic. This localization of efflorescences takes place in approximately one third of patients (R.A. Baikova,). Eruptions typical for MEE at different stages of dermatosis development are in most cases erythematous, erythematous-bullous or papular elements that have a pink-red color with a purple-cyanotic tint. The elements are arranged symmetrically, have different sizes, usually 1-2 cm in diameter. They are characterized by eccentric growth with resolution in the center, and in some cases new elements may appear in the center, going through the same cycle of development. Due to the difference in the color of the peripheral rim, which takes on a cyanotic hue, and the brighter color of the center, a characteristic appearance is formed, which has received the figurative name of two "color spots" or "target". As the disease progresses, a hemorrhagic component may be added. Several cases of hemorrhagic exudative erythema multiforme have been described in the literature. In the presence of cavity elements, the lid of the blisters or blisters is dense, which is associated with the subepidermal localization of the blisters. Over time, they subside or open. Then the central part of the elements is eroded, quickly covered with crusts. The contents of the cavity elements are mainly serous, less often hemorrhagic. In rare cases, vegetations form at the bottom of the cystic eruptions. According to the elements, erythematous, papular, erythematous-

popular, vesiculobullous, bullous forms are distinguished (L.N. Mashkilleyson, B.G. Belkin, E.Sh.Sanyan).

MEE is characterized by a chronic relapsing course, sometimes long-term. In some cases, there is a seasonality of exacerbations, mainly in spring and autumn. Cases of the permanent presence of MEE rashes on the oral mucosa are described. The outcome with MEE is usually favorable (L.N. Mashkilleyson,).

Thus, MEE is characterized by rash polymorphism with frequent development of typical elements in the form of "targets", a tendency to recurrence with varying frequency, and frequent lesions of young people.

## **1.2 Concepts of pathogenesis**

To date, mixed, immediate and delayed hypersensitivity reactions are recognized as the main process occurring in MEE. The cellular infiltrate is dominated by lymphocytes. They cause apoptosis and death of epithelial cells by expressing perforin proteins (D.K. Novikov, Yu.V. Sergeev et al., 2011). In the monograph "Private Dermatology", 2010, L.N. Mashkilleison evaluates the pathogenesis of the infectious-allergic form as an infectious allergy, and in later publications a detailed approach is developed to assess the pathogenesis from the position of immunology. The reaction of the immune system of the macroorganism to the foci of chronic infection is taken as the basic concept. According to A.L. Mashkilleison and A.M. Alikhanov, they are detected in 70% of patients with MEE, in half of the patients relapses occur after colds, including 24% after tonsillitis. R.A. Baykova, emphasized in her work the importance of bacterial infection in the development of MEE. Many authors point to the presence of foci of chronic infection in almost all patients, on the basis of which A.L. Mashkilleison and A.M. Alikhanov in 1983 proposed calling the idiopathic form infectious-allergic, emphasizing the importance of infectious allergy in the pathogenesis of the disease, and the symptomatic form - toxic-allergic. The presence of bacterial allergy is confirmed by the work of L.V. Popova, where skin tests and laboratory immunological reactions revealed hypersensitivity to staphylococci and streptococci in more than 70% of MEE patients. The state of the

immune system in patients with MEE was studied. Changes in the system of T- and B-lymphocytes, peripheral blood neutrophils, immunoglobulins A, M, G in patients with various etiologies of dermatosis were studied. It was shown that in patients with the toxic-allergic form, there is a decrease in the relative number of B-lymphocytes and immunoglobulin A; in the infectious-allergic form, these indicators were normal. In both forms, there was a decrease in the percentage of T-lymphocytes and neutrophils at their high absolute values. The isolated use of decaris, as well as in combination with ethacridine lactate, made it possible to normalize the indicators (A.M. Alikhanov, 1986). The difference in the levels of T and B-lymphocytes and immunoglobulins in different forms of MEE makes it reasonable to evaluate these parameters in GAME.

### **1.3 Treatment of MEE**

Treatment of MEE depends on the form of the disease. In the toxic-allergic form of the disease, therapy includes a standard set of measures used for toxicemia. In the presence of an infectious pathology of viral or bacterial origin, etiological treatment is carried out. Antibacterial drugs were successfully used in combination with antihistamines or glucocorticosteroids (A.A. Kalamkaryan, V.A. Samsonov, 2012; E.I. Abramova, L.S. Reznikova, 2010). There is some discrepancy in the recommendations regarding the topical use of glucocorticosteroids. The American Dermatovenereological School considers erythema multiforme as a disease that is intractable or aggravated by local corticosteroid therapy (L.MacDonald, 2012; S.Mochella, H. Harley, 1987). Domestic dermatologists consider it expedient to use topical steroids (O.L. Ivanov, 2012; Yu.K. Skripkin, 1998). Historically, salicylic acid preparations, quinine bromide, novocaine blockade, large doses of ascorbic acid (L.N. Mashkilleyson, 2015) were used in the treatment of MEE, which currently does not find wide practical application.



Thus, the MEE treatment method is determined by the trigger factor, which emphasizes the relevance of studying approaches to GAME therapy, due to the wide range of possibilities and ambiguity of approaches to the treatment of HH.

## **PART 2 HERPES SIMPLEX: IMMUNOGENESIS AND THERAPY**

### **2.1. Immunogenesis.**

Currently, the incidence of PG is very high and second only to influenza (A. Lassus, 1. Bergelin, 2015).

The herpes simplex virus belongs to the family of DNA viruses and consists of three main components - the nucleoid, the capsid and the outer shell. The virus reproduction cycle is about 10 hours. In infected cells, viral proteins are detected after 2 hours, their maximum amount accumulates after 8 hours. After about an hour, viral DNA is detected. Free mature virions appear after 10 hours (I.F. Barinsky, A.K. Shubladze, A.N. Fomina et al., 2010).

The reaction of a macroorganism to a virus is determined by a complex of factors. In particular, the ability of HSV to exist in a latent state. Over the years, studies have been conducted to identify the ways and reasons that allow the virus to maintain asymptomatic persistence in the recipient's body.

For the first time, the hypothesis of the constant persistence of the virus in the body in a latent state was put forward by R. Goodposture in 2010, which was confirmed by research by F. Horing in 2010. One of the confirmations of this hypothesis is the fact that antibodies to HSV remain at a sufficiently high level throughout life. Latency ensures the "escape" of the virus from the protective properties of the body (A.G. Bukrinskaya, V.M. Zhdanov, 2012) and has two varieties:

- 1) latent state of the virus genome,
- 2) the body's ability to prevent repeated clinical manifestations of infection.

Both species directly depend on the state of the immune system (I.F. Barinsky et al., 2012). Works by F. Bastain, 2010; J. Baringer, 2010; E. Smith,

L. McLaren, D. Galloway, according to the cultivation of SHIH from the trigeminal, lumbospinal and sacral ganglia, allowed us to state that the virus is in a latent state

in the sensitive paravertebral ganglia of the autonomic nervous system. The exit of the virus from the state of latency with the development of relapses occurs due to functional immunodeficiency, affecting many components of antiviral protection. In the future, work was carried out to clarify the specific manifestations of the immunodeficiency state.

The components of the immune defense system against the virus are currently being actively studied. Due to primary infection, virus-neutralizing and complement-fixing antibodies to the virus are formed. They appear in the blood 4-7 days after infection and reach a peak by 2-3 weeks, then persisting throughout life (G.J. Buddingh, 1953). Complement-dependent antibodies - Ig G and M have the maximum effect, their activity correlates with the level of production of antibodies to the membranes of HSV-infected cells. The consequence of their formation is the inhibition of the reproduction of SHIH at the site of its penetration, as well as the prevention of its further dissemination.

It was revealed that the synthesis of immunoglobulins is observed in the following sequence: UDM-IgG-IgA, and with relapses of PG, the same sequence of antibody production is observed against the background of those already present in a certain amount (A.Namians, B.Roizman).

According to the results of various studies, even a sufficiently high level of antibodies to HSV does not prevent the recurrence of infection and complete control over the replication of the virus (C. Daniels, M. Amstey, J. Rajjani.).

In general, the reaction of the immune system to a virus is not limited to the production of antibodies, it is known that in the reaction to any viral agent, there is a combined action of several main groups of immunocompetent cells and mediators: B- and T-lymphocytes, macrophages, the interferon system (R.V. Petrov, F.I. Ershov). A lot of attention has been paid to the study of various components of antiviral protection in different years.

The fact of activation of phagocytosis and stimulation of interferonogenesis under the influence of antibodies to SHIH was confirmed (P.Grauballe, D.Fanta).

Over the years, hypotheses have been expressed about the predominant suppression of certain immune factors in relapses of PH, including attention was paid to a decrease in the level of cellular factors associated with the production of T-lymphocytes (C. Lopes, R. O Relly). However, now most researchers note that the cause of the development of relapses of the viral process lies in varying degrees of severity of disorders of the immune system, affecting all links of antiviral protection (M.A. Samgin, A.A. Khaldin, 2002).

One of the deeply studied mechanisms of immunoresistance is interferonogenesis in HH.

If L. Ramussen notes that frequent relapses of the disease develop in individuals with low interferon-synthesizing ability of leukocytes, then in subsequent years, details of the violation of interferon status and their impact on other parts of the immune system are being developed. In combination with the assessment of interferon status, most studies assessed the activity of natural killers (Nk), as a factor interconnected with the level of interferon and playing an important role in the system of antiviral resistance. As a result of numerous works, the following approach to this problem has crystallized. The increase in the production of alpha-interferon by leukocytes occurs mainly during infection or during a relapse of HIG, respectively, it provides relief of relapse. Gamma-interferon produced by lymphocytes is of decisive importance in preventing relapses, while a decrease in the CAEK index, being a consequence of inferiority of cellular immunity, contributes to the loss of control over virus replication (F.I. Ershov, .V. Malinovskaya, K.N. Kudratullaev, I F. Barinsky, A.K. Shubladze, V.N. Greenyuk, M.A. Samgin, A.A. Khaldin). Based on the above facts, M.A. Samgin and A.A. Khaldin, 2002, conclude that, apparently, gamma-interferon and the degree of functional activity of NK are the most important factors controlling the latency of HSV.

Another important component of antiviral resistance is the monocyte-macrophage system (R.V. Petrov, G.T. Sukhikh et al.). The first group of components of this

system are macrophages located in the tissues, which mainly carry out the absorption and lysis of VGT with the induction of a further antiviral defense system. Another group is represented by cells of the monocytic series, carrying out a whole range of mediator interactions, covering the stimulation of T- and B-lymphocytes, the regulation of the level of EC and gamma-interferon (R.V. Petrov, 1970; B.F. Semenov, 1982). Accordingly, the functioning of the MFS system can be disrupted at two main stages. First, there may be a decrease in the level of virus uptake and stimulation of the next stages of the immune response at the initial stages of virus replication. Secondly, a decrease in mediator activity in the control of reproduction and spread of infection (G.T. Sukhikh et al., 2010; V.I. Pokrovsky et al., 2011; B.F. Semenov et al., 2012). The work of Yu.S.

The ratio among the components of the cellular link of immunity (T- and B-lymphocytes) was also studied. These indicators were evaluated in the work of T.B. Semenova et al., 1987, they revealed a decrease in the level of T-lymphocytes with an increase in the level of their activity against the background of a decrease in the level of B-lymphocytes.

The assessment of the level of T- and B-type lymphocytes is currently supplemented by an assessment of their subpopulation composition. So, in the group of B-lymphocytes, only a part of the cells has the main function of producing immunoglobulins, separate populations carry out antigen-presenting and mediator functions (M. Bumett, 1959;

J. Playfair, 1998). The clone of T-lymphocytes is also heterogeneous in composition. Different subpopulations perform different functions in the antiviral response system. The CD-8 positive subpopulation has mainly a suppressive effect on immune responses, in particular by suppressing the production of antibodies. The CD-4+ subpopulation is also subdivided into two groups: Th-1 and Th-2 types. Each possessing its own range of produced mediators (cytokines), they direct the development of the immune response in a predominantly cellular or humoral type. Accordingly, to assess the immunostatus, a quantitative relationship between

various subpopulations is determined. The ratio between CD-4+ and CD-8+ clones is called the immunoregulatory index. The ratio between Th-1 and Th-2 types is also estimated (J.F. Sheridan, 1985; A.A. Yarilin, 1999).

In the structure of the immune system, there is a group of so-called mediators of the immune response, or cytokines, which carry out intercellular cooperation. This group is represented by a large number of substances and is currently less studied in the context of herpes simplex immunogenesis than previously presented factors. Despite the multifunctionality of most cytokines, there are certain systems of their cooperation aimed at performing a particular function in the immune system. In the work of A.A. Haldina, 2000, analyzed the change in the ratio of cytokine production, which is normally characteristic of the antiviral response. It was found that there are several groups of immune status disorders in PH, corresponding to varying degrees of severity of clinical manifestations. Transient immune disorders correspond to rarely recurrent PG (1-2 times a year); the recurrence rate of 6 or more times a year corresponds to 3 types of disorders: A - immunodeficiency with a predominance of the T-cell response (the prevalence of IL-6 production),

B- immunodeficiency with a predominance of the humoral response (the prevalence of IL-4 production),

B- pronounced immunodeficiency of the undifferentiated type (decrease in the production of all immune mediators and the number of immunocompetent cells).

With a combination of types of immunogenesis (transient disorders, types A and B), herpes simplex often recurs 3-4 times a year.

Thus, the spectrum of disorders occurring in recurrent SH-forms a set of parameters, the assessment of which will be carried out in patients with PH, GAME, and other forms of MEE will make it possible to find out which of the possible immune defects in HT contribute to the formation of GAME. This includes T- and B-lymphocytes, among the first CD4+ and immunoregulatory index, specific antibodies, natural killers, alpha and gamma interferons, interleukins 4 and 6, phagocytosis.

## **2.2. Therapy for herpes simplex.**

There are several treatments for herpes simplex. Priority are two: etiotropic and immunocorrective. Preparations of immunocorrective action can be divided into two groups: 1st - immunomodulators (interferon and its inducers) and 2nd specific immunotherapy (herpetic polio vaccine) (A.A. Khaldin, 2002). Currently, extensive experience has been gained in the use of interferon and its inducers in the treatment of herpes simplex, their effectiveness has been repeatedly proven (M.A. Samgin, A.A. Khaldin, 1996). However, there is no evidence that this class of drugs has an effect on the allergic component inherent in the herpes-associated form of MEE, as synthetic acyclic nucleosides do not.

The antiherpetic vaccine was first made by L.Foumier and C.Levaditi in 1928, the first clinical trials were carried out in the mid-30s of the twentieth century. Currently, a herpetic polio vaccine is used in practice, containing the most common strains of HSV, inactivated by formalin. Based on the works of A.K., Shubladze, T.M. Mayevsky, R.M. V.N. Grebenyuk, 2013, the following scheme of vaccine administration was formed. At a dose of 0.1-0.2 ml subcutaneously, with an interval between injections of 2-3 days, a total of 5 injections. Re-vaccination according to the same scheme after 2-3 weeks. The expediency of repeated vaccination with an interval of 5-6 months was also shown. Changes in the immune status of patients who received a course of vaccination were assessed by several parameters.

S. B. Frank; E. Javets et al., P. Lepine et al.; M.A. Samgin, noted the absence of a pattern between the increase in titers of antibodies to HSV and the effectiveness of therapy with a specific vaccine. I.F. Barinsky in the early 70s and A.K. Shubladze in 1978 showed an increase in cellular immunity reactions under the influence of vaccination. W.O.N. Grebenyuk in 1983, comparing the effect of the vaccine and lyophilized interferon on IFS and CAEK in patients with HH, found that, unlike interferon, the vaccine does not increase the production of alpha interferon by leukocytes, but its main effect is associated with the activation of T-lymphocytes and cells of the monocyte-macrophage series, According to the data obtained as a

result of summing up the experience of treatment with various modifications of herpes vaccines in different countries, the clinical efficacy of specific immunotherapy in the form of persistent remissions during the year is from 30 to 80% among patients who have completed the full course of treatment (J. Whitley B. Meigner, 2014). Thus, the use of a herpes polio vaccine is effective in the treatment of herpes simplex and can be used against the background of functional disorders in antiviral immunoresistance. At the same time, a method of specific immunotherapy of allergic diseases by fractional administration of low doses of an allergen is known. The introduction of low doses of inactivated virus increases the immunogenicity of HHV in the patient's body, enhancing the response of cellular immunity. An increase in the immunogenicity of an allergen can contribute to a change in the balance of production of specific antibodies from class E immunoglobulins to class G immunoglobulins (A.A. Yarilin, 2014). Accordingly, the use of a herpetic polio vaccine can serve simultaneously as a method of anti-relapse therapy and a means of hyposensitization to herpes.

### **Part 3 Herpes-associated erythema multiforme**

#### 3.1. The etiological role of HSV: statistics and methods of laboratory verification.

The first publication on the association of MEE with the herpes simplex virus (SHTG) appeared in 1933, when E. Urbach reported several cases of MEE caused by "lichen lichen". In the future, the number of publications of this kind increased. If J. Foerster and G. Scott ; W.Shelley in report isolated cases of MEE caused by herpes simplex virus, then in S.Moschella and H.Harley indicate that in approximately 15% of cases recurrent MEE is associated with herpes infection. The term herpes-associated erythema multiforme (HAME) has come into use. In the literature, there are indications that in 30% of cases the cause of the development of GAME in young people is HSV type I, some authors also consider type 2 hepatitis B as a probable cause of the development of the disease (M.A. Samgin, O.L. Ivanov et al. ). A number of works of various directions have been carried out, confirming the etiological role of IVH or investigating various links in the pathogenesis of

GAME. One of the first published observation, which describes the appearance of typical MEE rashes in a patient sensitized by the introduction of particles of formalin-inactivated herpes simplex virus (W.Shelly,). It has been repeatedly reported that HHV was isolated from the contents of the vesicles during MEE that developed after a relapse of a herpes infection, which was interpreted as a manifestation of viremia and hematogenous dissemination of the virus (R. Sonthimer, S. Showalter, The etiological role of HSV in the development of MEE is also confirmed by electron microscopy of the skin biopsy of two patients with a recurrent form of GAME (during an exacerbation): single epithelial cells were infected with the virus, in which viral particles were detected in the stage decay localized in cytoplasmic vacuoles (M.G. Tonnesen,) In some other studies, attempts to detect the virus by electron microscopy were unsuccessful (J. Huff,).

Another method that has been used to detect virus in the skin is immunofluorescence. In the reaction of direct immunofluorescence (DIF) with labeled rabbit antibodies to the VGT antigen, a characteristic luminescence was noted in the epidermal skin cells of patients with GAME. In the study of skin biopsy samples of patients with GAME in the reaction of indirect immunofluorescence using mouse monoclonal antibodies to the glycoprotein antigen of the virus, focal luminescence was detected in 12 out of 16 samples. In the material from the unaffected skin of patients with GAME and in control samples, including those using other monoclonal bodies, there was no luminescence (D.Cines, ). Thus, the etiological role of HSV has been proven in several independent studies using modern diagnostic technologies.

### **3.2. A modern view on the pathogenesis of GAME.**

The main issue that needs to be resolved is whether the herpes-associated variety of MEE belongs to one or another type of allergic reactions. The basic concept remains the presence of an infectious allergy, however, the microbiological features of VS-



can modify the process of the immune response. HSV refers to intracellular parasites that actively rebuild the cell's protein synthesis apparatus for the reproduction of its own nucleic acids, and at rest it is integrated with the cell genome, which imparts new properties to the antigens presented by the cell. In the process of studying the pathogenesis of GAME, attention was mainly paid to the pathogenic properties of the virus, which manifest themselves during its activation. In particular, several studies have examined the severity of immunocomplex reactions. The hypothesis was that GAME is an immunocomplex lesion resulting from the deposition of antigen-antibody complexes around dermal microvessels. Biopsy of GAME lesions revealed the deposition of immune complexes, the frequency of detection varied among different researchers. According to various sources, perivascular deposits are found in approximately half of patients with GAME and with MEE of an unspecified nature (P. Orton,). According to other researchers, peri- and intravascular deposits are found in 87% of cases (J. kazmierovski, ), in 30% of cases (L. Corciatti,), and even in 2 out of 24 patients (M. Feivell,). Elimination of RK from the body is facilitated by complement, phagocytosis by neutrophils and macrophages, and there is a sufficient amount of reactive oxygen species (ROS) in neutrophils. Therefore, the inclusion of these parameters in the spectrum determined during immunotesting will not only allow them to be compared with those in HH, but will also complement the understanding of the pathogenetic prerequisites for the formation of immunocomplex pathology.

Another aspect of studying the pathogenesis of GAME is the evaluation of the complement activation pathway. In the study of 10 biopsies of rash elements, in all cases, the luminescence of SC granules was determined, in 9 cases - properdin along the basement membrane.

All samples lacked C1q and C4 components characteristic of the classical pathway of complement activation (D. Chalmers, 1959). In recent years, the interaction of SHJH with dermal microvessel endothelial cells (EMRD) has been supplemented by more specific studies using monoclonal antibodies, with the determination of

differentiation clusters of adhesion molecules. During 12-hour cultivation of EMRD with native virus, a cytopathic effect is noted in 60-90% of cells. The surface expression of LA-class molecules and CD31 in infected cells was impaired, CD54 expression did not change. Another picture was observed when EMRD was exposed to blood mononuclear cells infected with HHJH. CD-54 increased by 5 times, CD31 did not change, HLA increased by 2 times. The change in adhesion molecules was confirmed by mRNA-Tect (C. Larcher, A. Gasser,).

These data characterize the susceptibility of the vascular endothelium to lymphocytes infected with the herpes simplex virus. An imbalance was also revealed among the lymphocytes themselves, reacting to VHH. An adequate immune response to IVH implies a predominant activation of cellular factors, with a predominance of type I T-helpers. However, it was found that type 2 T-helpers predominate in GAME, their increased number was also determined in the elements of the rash (H. kokuba, S. Imafucu, 1998). This subclass of T-helpers is typical for the implementation of immediate type hypersensitivity, which indicates the presence of an allergic component (O. Braae, 2003). Considering this, as well as the fact that the viral antigen is not found in the elements of GAME in 100% of cases, it can be concluded that GAME is not a purely infectious process, but rather an allergic one with a viral trigger, just as the mee induced by staphylococci is a consequence of the body's sensitization to him (L.V. Popova,).

A continuation of the study of the properties of immune response factors to IVH is the identification of heterogeneity of cytokines presented at the sites of rashes. It was found that in 16 out of 24 patients with GAME, gamma-interferon, a product of T cells involved in a delayed-type hypersensitivity reaction, is present in increased amounts at the sites of rashes. The presence of gamma-interferon was noted in blood mononuclear cells infiltrating the skin, in the inflamed epidermis in the intercellular spaces and in the dermal-epidermal junction. In places of rashes of herpes simplex in 10096 gamma-interferon was determined. There were no such changes in drug MEE. Also, in the affected skin with GAME, transforming growth factor-beta and

cyclin-dependent kinase inhibitor were determined in 61 and 67% of cases, respectively. In keratinocytes from skin directly affected by herpes simplex, these changes were found in 100% of cases and in no case in healthy skin. For comparison, cytokine disturbances were assessed in 11 patients with drug-induced MEE. Tumor necrosis factor alpha (TNF-alpha) was detected in 64% of cases, which was not observed in GAME (H. kokuba, L.)

These data indicate that the predominant production of certain cytokines plays a significant role in the pathogenesis of GAME. Therefore, studies of the immune status of patients should be carried out taking into account possible disturbances in the production of the most significant cytokines. Given the multicomponent nature of the cytokine profile, it is advisable to include IL-2 and

IL-1 R. IL-2, along with gamma-interferon, regulates the T-1 response according to the Th-1 type and stimulates the production of IL-1 R. It is one of the "main" cytokines that controls the process of interaction between Tel and V-1 during antibody genesis (A.A. Yarilin, 1998).

### **3.2. GAME treatment.**

Treatment of GAME is carried out according to the treatment regimens for the infectious-allergic form of MEE, that is, it includes the use of etiological drugs (synthetic nucleosides) and symptomatic action. In most literature sources, GAME therapy is presented mainly in the form of a continuous intake of synthetic nucleosides.

It is indicated that the treatment of GAME should include both the relief of an exacerbation of the infection and suppressive therapy aimed at preventing virus replication. Erythema multiforme appears to be a therapeutic dilemma. Along with the obligatory use of acyclovir in this situation, successful treatment of GAME with the use of systemic steroids has been reported. This observation suggests the possibility of using systemic glucosteroids (GCS), which in the case of severe forms is necessary to prevent the aggravation of epidermolysis against the background of the viral process. However, it seems important to evaluate the indications for the use

of steroids, since their administration to the stage of active viral replication may also worsen the patient's condition due to viral dissemination.

According to various sources, the treatment of a "small" form of MEE, including that caused by HSV, should include timely applied symptomatic drugs of local and systemic action. The main method for preventing erythema multiforme caused by HSV is the constant use of acyclovir (C. Leuete-Lambreze, 2000; Czubovska, 2000; Samgin M.A., Ivanov O.L. et al., J.T. Fitzpatrick. et al., ).

M.A. Samgin and A.A. Haldin, 2002, used a two-stage regimen for the treatment of GAME. The first stage consisted in the relief of exacerbations of GAME, the second in the prevention of relapses of PH, which is the trigger mechanism for this type of exudative erythema multiforme. Famvir or Valtrex was used to stop GAME. There were 16 patients under observation, including 10 women and 6 men, aged from 23 to 56 years. The main criterion for the diagnosis of GAME was a clear relationship between PH relapses and MEE exacerbations. The duration of the disease in them ranged from 6 months to 5 years, and relapses lasting up to 21 days occurred 4 to 6 times a year. Treatment of GAME exacerbations with synthetic nucleosides was started at the first clinical signs. Famvir was prescribed at a dose of 250 mg, Valtrex 500 mg twice a day for 5 to 7 days. Against the background of their intake, the appearance of new rashes stopped, and a pronounced regression of the manifestations inherent in both PG and MEE was observed. At the second stage, the purpose of which was to prevent relapses, an interferon inducer, ridostin (ds-RNA lysate of the killer yeast *Candida cerevisiae*), was used. He was prescribed 8 mg 1 time in 3 days, in the subscapular region, for a course of treatment - 4 injections. Observation of patients after the end of the proposed two-stage course of GAME therapy (in terms of 1 to 1.5 years) showed that 10 patients did not experience both manifestations of PH and exacerbation of GAME, 6 patients had relapses of HH in a much milder form, not accompanied by a rash characteristic of MEE. There was also a decrease in GHG manifestations. The success of this type of therapy speaks

in favor of the possibility of using immune-targeted drugs in GAME, which include the herpes vaccine.

It should also be noted the need for timely initiation of therapy and its application in the appropriate amount, since there are publications describing a clinical case of the development of Lyell's syndrome after an abortive attack of the MEE (L.A. Gusarenko, 2011). To this observation, we can add that insufficient use of steroids in the early stages of drug allergy can also lead to the development of Lyell's syndrome (D.K. Novikov, Yu.V. Sergeev). Drug allergy, which can be manifested by MEE, and infectious allergy have differences in pathogenesis: the manifestations of the former are more severe, but the main mechanisms and effectors of hypersensitivity are similar. We consider the foregoing in favor of the use of systemic corticosteroids in GAME, in order to prevent life-threatening conditions. Thus, the approach to GAME therapy to date has been based mainly on the episodic or chronic use of synthetic nucleosides. If necessary, it is possible to use systemic corticosteroids in GAME. Given the positive experience with the use of immune preparations, it seems relevant to search for new methods of immunocorrection, including the evaluation of the effectiveness of herpetic polio vaccine.

## **CHAPTER 2. MATERIALS AND METHODS**

The examination of patients was carried out on the basis of the dentistry of the regional dental clinic of the dental faculty of the Samarkand State Medical University for the period from 2021 to 2023.

### **2.1. Composition of patient groups**

48 patients were examined and divided into 3 clinical groups.

Group A (main group) is represented by 28 patients with herpes-associated exudative erythema.

Group B (the first group of comparison) included 10 people with multiform exudative erythema of another origin.

Group C (second comparison group) consisted of 10 people with herpes simplex. MEE was diagnosed on the basis of clinical data: the rash was acutely inflammatory, located on the skin of the trunk, face, extensor surfaces of the upper and lower extremities, oral mucosa, lips (in various combinations). The elements of the rash were represented by dark pink or pink red spots or papules, which in the process of development acquired the appearance of a “target” (regression from the center with preservation of the edematous ridge along the periphery). In the center of the elements, bubbles with a dense cap were formed in some cases. On the oral mucosa, the elements were represented by erosions covered with a fibrinoid film and surrounded by a halo of hyperemia.

The herpetic etiology of MEE was diagnosed on the basis of the following data. In all patients who were diagnosed with GAME, a typical rash developed within 24 hours to 8 days after the onset of herpes simplex lesions, which were grouped vesicles with serous contents, located on an edematous-erythematous base. The diagnosis of herpes simplex was confirmed by polymerase chain reaction (PhT).

In 10 patients with MEE included in the comparison group, the etiology of the process was as follows: 5 patients had a toxic-allergic form of MEE, with a clear indication in the history of taking antibiotics in six cases, in one patient - a sulfanilamide drug, in one case a non-steroidal anti-inflammatory drug. means and in one case a hypnotic benzodiazepine series. In 4 patients, an infectious-allergic form of the disease was diagnosed with the presence of active foci of bacterial or mycotic infection in the genitourinary or respiratory systems, which was confirmed upon examination by a therapist, gynecologist or urologist with the following laboratory tests. In 3 patients, MEE exacerbations were noted after ARVI and developed in spring and autumn.

To exclude the influence of HSV on the pathological process, the criteria for selection into the comparison group according to the MEE were the information that all patients had not suffered from herpes simplex for at least 2 previous years.

Patients with herpes simplex included in the control group (22 women and 18 men aged 16 to 60 years) noted the recurrence of herpes simplex from 4 to 12 times a year, the duration of relapses was from 7 to 20 days, disease duration from 4 months to 6 years.

Considering that among patients with GAME there was a different frequency of recurrence, in the control group for PH, for statistical analysis of immunological parameters, we included individuals whose recurrence rate corresponded to that in GAME.

Criteria for selecting patients in the main and control groups.

GAME	MEE	Simple Herpes
28 people	10 people	10 people
Selection criterion: MEE always develops up to 14 days after a typical recurrence of PCs, confirmed by GAD.	Selection criterion: has not bothered for the last 2 years and has never recurred more frequently before 2 times a year	Selection criterion: Relapse rate corresponding to that in the GAME group.
	Etiology: 4 people - toxic allergic form, 6 people - infectious allergic.	

## **2.2. Medicines and the main schemes for their appointment.**

Acyclic synthetic nucleosides.

1) Acyclovir-Akri manufactured by Akrikhin was prescribed 200 mg 4-5 times a day.

2) Valtrex (Valacyclovir), manufactured by Glaxo Smith Klain, was prescribed 500 mg 2 times a day.

H) Famvir (Famciclovir) manufactured by Novartis - 250 mg 2 times a day.

Herpetic polio vaccine, cultural inactivated dry, is prescribed according to the following scheme. 2 courses of vaccination with a two-week interval between them and revaccination after 6 months. The course includes 5 injections, made 1 time in 3 days. Injection technique according to the instructions for use.

Dosing regimen 0.1 -0.2 - 0.2 0.2 - 0.2 (in ml).

"Viferon", produced by LLC Feron, is a human recombinant alpha2-interferon in combination with antioxidants (tocopherol acetate and ascorbic acid). Release form - rectal suppositories. Dosing regimen - one rectal suppository containing 500 thousand units 2 times a day.

With herpetic eruptions on the skin and mucous membranes, it is important to choose an effective antiviral drug that will quickly eliminate discomfort and speed up the wound healing process. Today, the pharmaceutical market offers many products that successfully fight the manifestations of herpes. But which one to choose. The most popular drugs are Valacyclovir and Acyclovir. Let's try to figure out what helps better in the treatment of herpes, what is the difference between drugs.

Mechanism of action of Valaciclovir and Aciclovir



Acyclovir, after entering the systemic circulation, attacks the cells of the virus. As a result of the specific effects of drugs, a transformation of a special enzyme, thymidine kinase, into triphosphate is observed. When this substance penetrates into pathogenic DNA, the virus is completely paralyzed, due to which the infection stops spreading.

Valaciclovir can be considered a second-generation drug, it was developed on the basis of the drug Acyclovir. The mechanism of its action differs - when it penetrates into pathogenic cells, two components with antiviral activity are formed (valic acid and acyclovir). Valaciclovir is much better absorbed by the body, respectively, and the therapeutic effect occurs faster.

#### Main differences

Antiviral drugs differ in a number of ways:

- Dosage form
- Active ingredient
- Duration of antiviral treatment
- The frequency of use of the drug.

Acyclovir release form - tablets, injection solution, ointment. The medicine can be used to relieve the symptoms of herpes simplex, chicken pox and shingles. Quite often, the use of pills and ointments is prescribed. Usually the duration of antiviral treatment is about 10 days, but long-term medical therapy is also allowed. The difference between Acyclovir and Valaciclovir is the occurrence of addiction with prolonged use of ointment or tablets. The drug can be prescribed to children, as well as during pregnancy.

Valaciclovir is available only in tablet form, but contains an increased concentration of the active ingredient. The drug is classified as a semi-drug, since the main transformations of L-valine ester occur in the liver cells, it is there that acyclovir itself is formed. Due to this special property, the drug has a prolonged antiviral effect, while not addictive.

Valaciclovir is taken 1 tab. dosage of 500 mg twice a day. The regimen for taking Acyclovir is significantly different, the daily dose of the drug is 6 tab. dose of 200 mg. It should be noted that Valaciclovir is taken for only 5-7 days, during which time a pronounced therapeutic effect is manifested.

What is better to choose

To date, doctors are increasingly recommending the use of Valaciclovir, as it belongs to the group of modified antiviral drugs and does not have the disadvantages of the first generation of drugs. The main advantage is a high rate of digestibility - 75% (Acyclovir has only 15%), this effect is achieved due to the transformation of L-valine ester under the influence of liver enzymes (after absorption in the intestine) directly into acyclovir, as well as valine amino acid.

Valaciclovir is available in various dosages, which allows you to choose the optimal treatment regimen. Moreover, the drug is taken less frequently than the analogue, which reduces the likelihood of missing the drug. At the same time, the risk of developing side symptoms in the form of a headache, as well as disruption of the gastrointestinal tract, is minimal.

Valaciclovir is not prescribed for:

- Hypersensitivity to the main component
- Childhood (child less than 12 years old)
- Pregnancy and lactation period.

Ointment Acyclovir can be prescribed to pregnant women and children under 3 years of age.

The main disadvantage of Valaciclovir is its cost - 313 - 3840 rubles. and one dosage form - tablets.

### **Analogues**

There are several analogues of antiviral drugs that have similarities and differences with the drugs discussed above.

Famciclovir

It is prescribed to eliminate the manifestations of herpes zoster, as well as herpes simplex. The active ingredient is penciclovir.

The main advantages of Famciclovir:

- High bioavailability - 77%
- When using the cream, there is a rapid healing of wounds on the lips
- In the case of genital herpes, it reduces the stage of crust formation.

Famciclovir, like Famvir, is much more effective than Acyclovir, due to its low cost it is affordable.

Valtrex

This drug is a complete analogue of Valaciclovir, as it contains the same active ingredient. The medicine is produced in the UK, respectively, the price of tablets is quite high - 829-4045 rubles. If you choose between Acyclovir or Valtrex, then, of course, you should give preference to the latter, since it is much more effective.

Valvir

Valvir is another drug based on valaciclovir hydrochloride hydrate, which quickly eliminates manifestations on the skin and mucous membranes with herpes zoster, labial and genital herpes. It can also be used prophylactically to prevent the development of cytomegalovirus infection. Valvir's advantages are an acceptable price (585-2550 rubles), a convenient medication regimen.

## **CHAPTER 3**

### **3.1. Age and sex composition of patients.**

As a result of the analysis of the age and sex composition of patients with GAME, the following data were obtained. The group of patients under our observation included 16 men (69%) and 12 women (31 whose age ranged from 15 to 65 years.

Thus, the majority of patients with GAME (almost 70%) are men. Certain age patterns were also observed. In male patients, GAME develops mainly at a young age (17-30 years). Among women, GAME is observed with approximately the same frequency both in young (17-30) and middle-aged (30-40 years).

### 3.2. Clinical features of rashes of herpes simplex, which provoked the development of GAME.

#### Localization.

All patients had manifestations of herpes simplex, after which GAME, localized on the face. The most commonly affected lips were the upper or lower lip, the corners of the lips, and the skin of the perioral region.

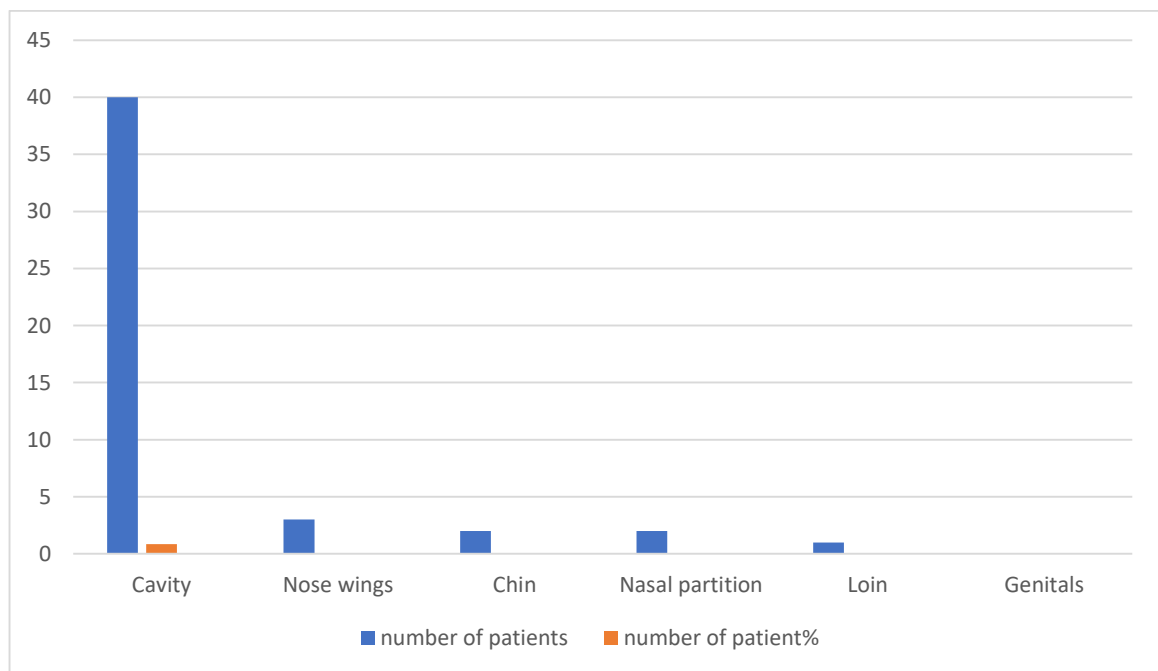
Somewhat less often - the skin and mucous membrane of the nose, least of all - the skin of the chin. In one case, HH was localized in the lumbar region, at the level of the 3rd lumbar vertebra, and in the other case, on the skin of the posterior-lateral surface of the right thigh. Nobody did not affect the genitals in isolation, although one patient had rashes both on the face and in the region of the labia majora. In this patient, previously recurring 3-4 times a year, herpes simplex was localized either on the genitals or in the face. The exacerbation, which entailed the development of GAME, manifested itself for the first time simultaneously with two "bipolar" foci of herpes simplex, in addition, it developed after a shorter time period (1 month after the previous exacerbation, when herpes simplex was localized only on the lower lip). The situation when the type of recurrence changes on the eve of the development of GAME was typical for most patients.

Table 22. Localization of rashes of herpes simplex.

	Number of patients, absolute indicator	Number of Patient,%

Cavity	40	85%
Nose wings	3	7,5%
Chin	2	4,2%
Nasal partition	2	4,2%
Loin	1	2,5%
Genitals		

Diagram : Localization of rashes of herpes simplex.

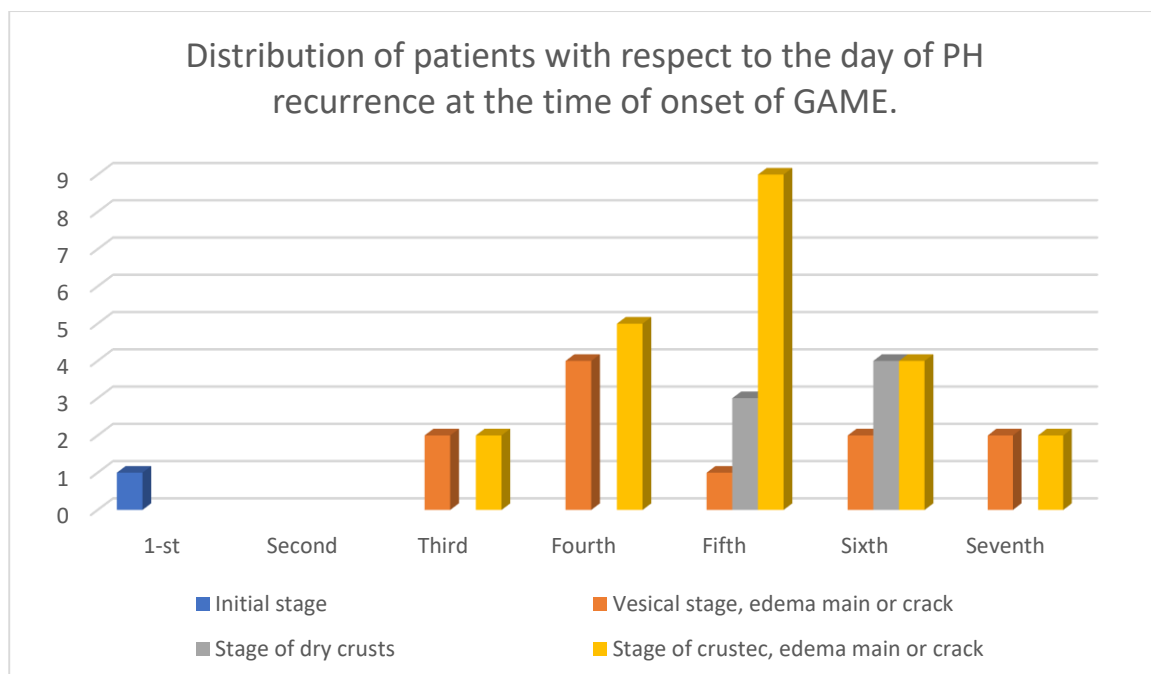


In 16 patients (60%), the development of GAME was preceded by a change in the severity of herpes simplex relapses. Of the 6 patients, 4 (noted an increase in the area of affected skin compared to previous relapses, on average by 10-20 percent. In 12 people (recurrent PH occurred for several years, but became accompanied by a widespread skin rash in the last 0.5- 1.5 years, and this fact took place against the background of an increase in the recurrence of herpes simplex, an average of 2 times and (or) an increase in the duration of a relapse, an average of 5 days. In addition, almost all patients (87%) noted that those who helped Previously, PG therapies are now ineffective or longer-term use is required. For example, ointment forms of synthetic nucleosides were previously effective, and later their tablet forms for oral administration began to be required, or longer than before the duration of the use of tablet forms. therapy in the same period of existence of herpes simplex as before. So, in most cases, GAME develops against the background of worsening of the course of PH: increased frequency, increase in the duration of relapse and (or) the area of the affected skin, resistance to previously effective therapy. Although the dynamics of exacerbation of herpes simplex did not differ significantly from the classical one, the following pattern was noted. In 15 people (55.6%), herpetic vesicles opened spontaneously or due to accidental injury within 4-5 days, after which wetting was observed in the area of erosion formed with an increase in the degree of edema of the base (an average of 30% of the original) and (or) the formation of layered loose crusts of yellow color. In 13 people (29%), on the 3rd-4th day of relapse, the appearance of a painful fissure with scanty serous-hemorrhagic discharge was noted (also with an increase in the degree of edema of the base). Thus, in more than 50% of cases, GAME is preceded by eczematization and (or) impetiginization of PG. According to Nikulin N.K., et al. 2012, local PG eczematization is observed in 30% of cases, and in patients with GAME, we observed this complication in more than half The duration of herpetic affect ranged from 4 to 20 days. At the same time, 19

patients (66.7%) noted that the development of a skin rash occurred against the background of the formation of a crust, that is, in the crusty stage of herpes simplex. What happened in most of them (more than 500/0 cases) against the background of an increase in edema of its base, along with the phenomena of weeping and (or) the formation of impetiginous crusts. In general, the characteristics of clinical severity at the time of development of GAME are presented in the following table. Distribution of patients with respect to the day of PH recurrence at the time of onset of GAME.

Day of recurrence	Initial stage	Vesical stage, edema main or crack	Stage of dry crusts	Stage of crustec, edema main or crack
First	1			
Second				
Third		2		2
Fourth		4		5
Fifth		1	3	9
Sixth		2	4	4
Seventh		2		2

Diagram M 4. Distribution of patients with respect to the day of PH recurrence at the time of onset of GAME.



So, in most cases, GAME develops on the 4-6th day of relapse, more often against the background of the crusty stage of PH.

### 3.2. Clinical features of the course of GAME.

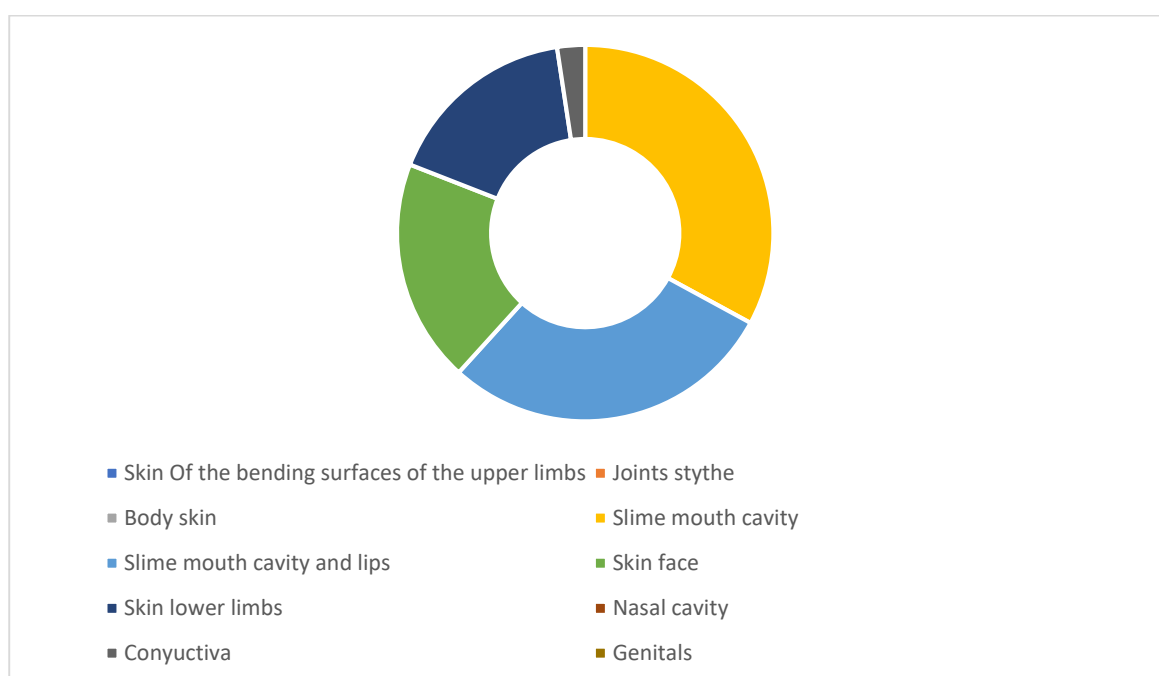
We analyzed the morphological composition and dynamics of the rash GAME. The localization of the rash generally corresponded to that of a typical MEE, but some peculiarities were noted. So, with 100% damage to the hands, frequent damage to the face and trunk, on the legs, the rash was less localized and in most cases was absent on the genitals. According to A. Hurley,

D. Moschella, 2010, as well as J. Fitzpatrick, 2011, the so-called "small" exudative erythema, that is, with minimal involvement of mucous membranes, is mainly associated with PG. This is consistent with our data, with a purely viral etiology (without secondary infection), if the mucous membranes are involved in the pathological process, then no more than 2 areas, in more than half of the cases - one area. In particular, a combined lesion of the oral cavity and the genital area is extremely rare.

Table . Localization of the rash in GAME.



Skin Of the bending surfaces of the upper limbs	
Joints stythe	
Body skin	
Slime mouth cavity	48 %
Slime mouth cavity and lips	42 %
Skin face	28 %
Skin lower limbs	24,3 %
Nasal cavity	
Conyuctiva	3,5 %
Genitals	

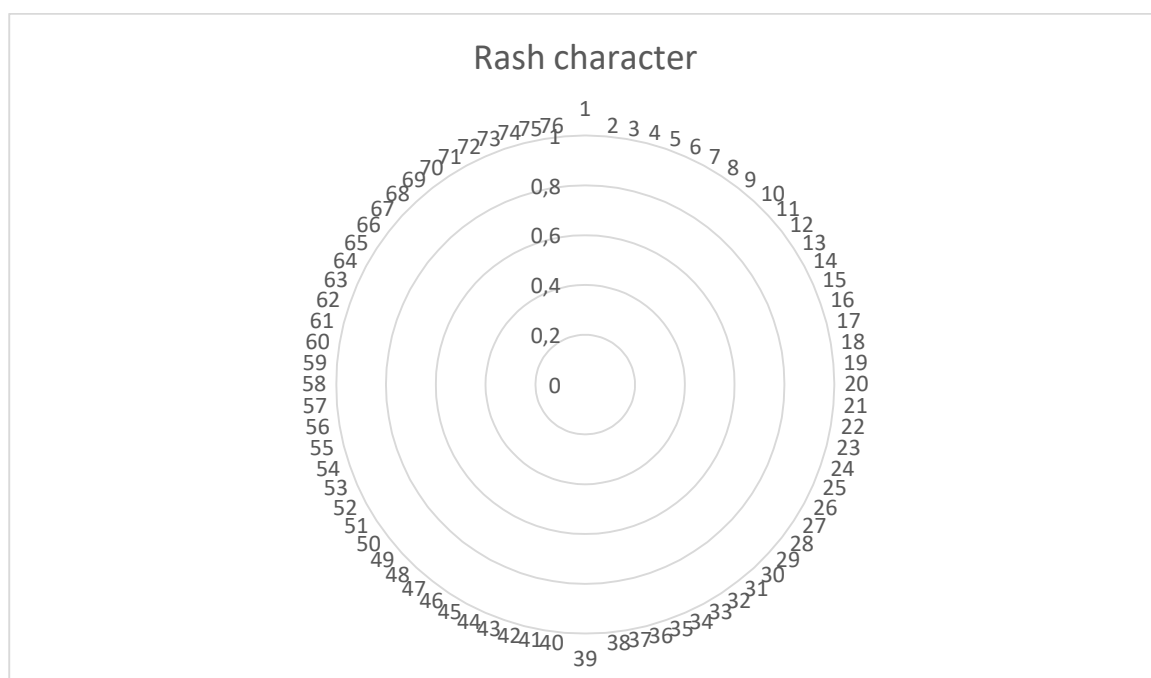


Rashes were represented by typical erythematous-edematous foci according to the type (“target”, up to 3 cm in diameter. In their center, in most cases, weakly tense blisters with a dense cover formed, which later tended to dry out with the formation of crusts. In a small part of patients the rash had a polymorphic character, was represented by erythematous-edematous and erythematous-bullous foci, single papules and pustules. In two people, erythematous-bullous rashes were combined with hemorrhagic elements, which accounted for about 30% of the entire rash. Monomorphic papular rash was noted in 5 people.

Table M5. Characteristics of the rash in GAME.

The nature of the rash	Number of patient	
Erimatous-edematous	4	8,9
Erimatous-edematous+buble	29	64,4
Erimatous-edematous +pustule +papules	5	
Erimatous-edematous+buble +hemorrhagia	2	
papules	5	

Diagram Correlation of erythematous-edematous and erythematous-bullous form of the rash with other varieties.



There is a clear predominance of erythematous-bullous and erythematous-edematous rash over other forms (in the absence of data for secondary bacterial infection, if it is present, the number of pustules increases.)

When evaluating the clinical picture of GAME, its differences from the toxic-allergic form of exudative erythema were found, while the infectious-allergic variety of dermatosis had features similar to GAME.

Such characteristics of the rash as localization, diameter and color of the elements, their tendency to grow and merge were analyzed. In addition, there were differences in the subjective feelings of patients. If the toxic-allergic variety was characterized by a feeling of heat in the skin and itching of varying severity (80% of patients), then with GAME such phenomena were observed rarely (less than 5% of cases) and were characterized by low intensity.

Table. Clinical differences between GAME and toxic-allergic form of exudative erythema.

	GAME	Toxic-allergic MEE
Localization Rashes	The extensor surface of the hands (palms affected in less than 5% of cases), face, torso. Rarely legs, extremely rarely genitals.	Any. When localized in ARM areas of the palm are involved in 70% of cases.
Involvement mucous	Minimum. Single elements in the mouth.	Depending on the route of entry of the allergen. There may be an isolated lesion of the oral mucosa and genitals, which is not observed in GAME.
Diametr	to 4 sm	In more than 73% of cases, lesions are 4 cm or larger.
Colour	stagnant, cyanotic .	Bright red, rose red.
trend towards growth and merger	Practically absent. May be observed slow peripheral growth (1-2 mm in 2-3 days).	Expressed.

The duration of GAME existence in patients varied from 3 months to 5 years. The frequency of recurrence of dermatosis also varied, from twice a year to monthly. The severity of the clinical symptoms in most cases did not depend on the frequency of recurrence. For ease of assessment and

clarity, the patients were divided into 3 groups. With a recurrence rate of 2-4 times per year (8 patients), the duration of relapse was 3-6 weeks, with a gradual onset of rash and spontaneous regression if untreated. Subjective symptoms were mild and mainly consisted of unpleasant sensations when eating (with the localization of elements in the mouth) and a feeling of slight malaise.

With recurrence 5-6 times a year (25 patients), subjective symptoms were observed in 9 people, the above symptoms were accompanied by a feeling of chills, low-grade fever. 17 people noted psychological discomfort. In the group with a frequency of recurrence 6 or more times a year (12 people), the manifestations of GAME were recurrent. Against the background of incomplete regression of old elements, new ones continued to appear. 4 people had symptoms of intoxication, a feeling of weakness, sweating, loss of appetite, fever up to 37.8 C. 9 patients had severe psychological discomfort associated with the almost constant presence of a rash on open areas of the body. In 8 people, despite the frequent recurrence of dermatosis, the rash was represented by a few elements, subjective symptoms were mild. The phenomena of intoxication syndrome took place with the phenomenon of secondary bacterial infection, which was also expressed by polyadenitis and pustulization of the rash. Thus, the severity of subjective symptoms in GAME does not depend on the frequency of recurrence, but on the presence of impetiginization. Thus, we can conclude that GAME is characterized by the following clinical features.

- 1) In more than half of cases, GAME develops against the background of a change in the course of relapses of herpes simplex: increased frequency, an increase in the duration of relapse and (or) a larger diameter of the herpetic focus, resistance to previously effective therapy. Local eczematization and

(or) impetiginization of herpes simplex occurs in more than 500/0 cases before the development of GAME.

2) Herpes simplex, which causes the development of GAME, is localized in the face.

3) GAME occurs twice as often in men than in women. In men, more often at a young age (17-30 years); in women with approximately the same frequency in young (17-30 years) and middle age (30-40 years).

4) GAME is characterized by damage mainly to the extensor surface of the arms, face and torso, the genitals are affected less than. Elements of a cyanotic rash, up to 4 cm in diameter, the tendency to merge and peripheral growth is not pronounced, which distinguishes GAME from the toxic-allergic variety of MEE.

5) GAME is characterized by frequent recurrence: 5-12 times a year.

6) The severity of subjective symptoms in GAME depends on the presence of secondary bacterial infection.

## **DATA OF IMMUNOLOGICAL EXAMINATION.**

Before the start of the examination of patients of the main and control groups, immunotesting of 10 healthy volunteers was undertaken to clarify the immunological norms. The results obtained were within the limits declared by the laboratory and the manufacturers of the test systems. To interpret the data of the immunological examination of patients, they were divided into groups: A, B, C.

Group A included patients suffering from GAME.

Group B consisted of persons suffering from infectious-allergic MEE, not associated with HSV and toxic-allergic variety.

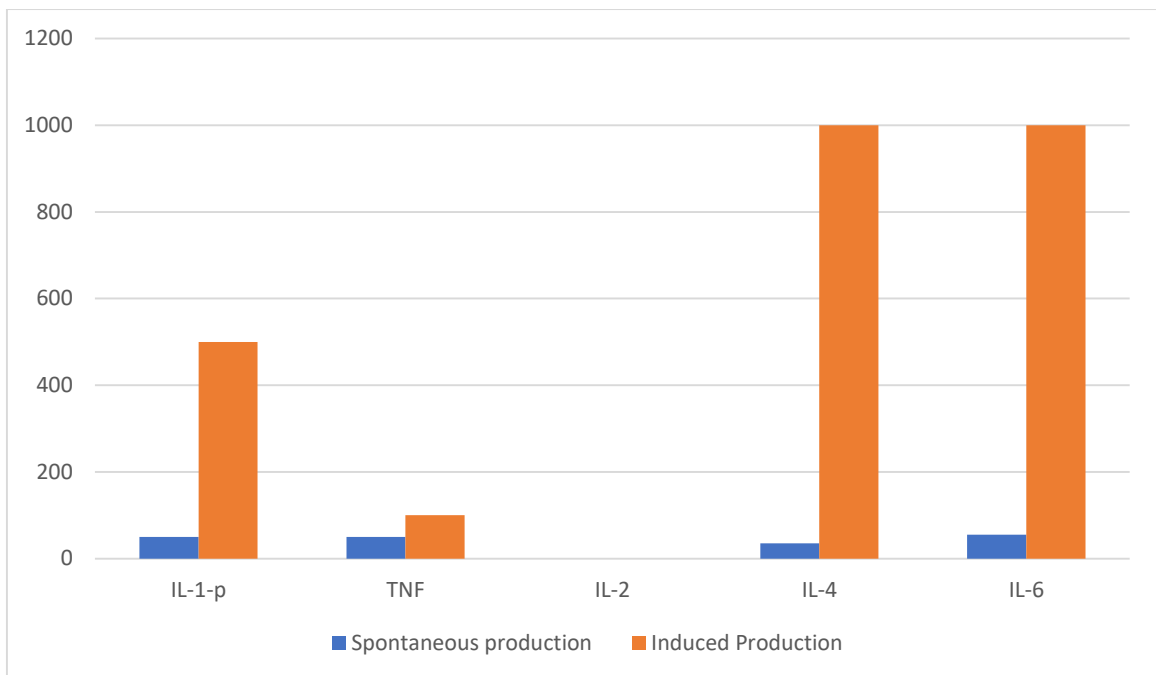
Group C included patients with moderately and frequently recurrent herpes simplex.

A comparative analysis of the indicators of all groups is presented separately for each link of immunity.

Table M7. The levels of the studied cytokines are normal.

Investigated cytokine	Spontaneous production, pg/ml	Induced production, pg/ml
IL-1-p	40 +10	More than 500
TNF	Less 50	More 1000
IL-2	Less 5 ME-ml	Less 20 ME-ml
IL-4	Less 30	More 1000
IL-6	Less 50	More 1000

Diagram Correlation between spontaneous and induced production of the studied cytokines in the norm.



In general, the change in production is characterized by a tendency to equalize between spontaneous and induced production. This happens for two reasons: an increase in spontaneous production of cytokines and a decrease in induced. The only cytokine that retained the ratio between spontaneous and induced production and remained within the normal range for both parameters is IL-2. IL-1-R, IL-4, IL-6 are united by a significant increase in spontaneous production and a decrease in induced. TNF-i, whose spontaneous production is also increased, retains the ability to respond to a stimulus close to normal. Spontaneous and induced production of IL-4 and IL-6 differs from the norm with a high degree of certainty (p). The main difference from group A is the less pronounced spontaneous production of IL-4 with a tendency to preserve its induced production, the bulk of the indicators remain close to normal. IL-6 in group B, although it is characterized by a large increase in spontaneous production, but its induced production tends to normal. In general, if GAME is characterized



by depletion of the induced production of IL-4 and IL-6, which is described as an immunodeficiency of the undifferentiated type, characteristic of PG immunogenesis with a high relapse rate (Khaldin A.A.2001), this is not observed in other forms of MEE. So, the main difference between other forms of MEE and GAME is the preservation of IL-4 values close to normal and the preservation of the induced production of IL-6 ( $p < 0.01$ ) Spontaneous production of IL-2 in the group of patients with PH exceeds that in patients with GAME and MEE ( $p < 0.05$ ), with approximately the same induced production. IL-4 indices do not have significant differences in patients with HH and GAME (increased spontaneous production, equal to reduced induced), which distinguishes them from close to normal IL-4 indices in the group of patients with other forms of MEE. The production of TNF- $\alpha$  does not have significant differences. In addition, the induced production of IL-6 was preserved. So, the main differences in the cytokine profile of patients with PH from patients with GAME are a higher spontaneous production of IL-2 ( $p < 0.05$ ), and the preservation of the ability to induced production of IL-6. If the intensity of TNF- $\alpha$  production, both spontaneous and induced, unites all three groups, then there are differences in other indicators. An increase in spontaneous production of IL-2 is observed in patients with HH, but does not occur in patients with GAME and in patients with other forms of MEE. The most indicative is the state of production of IL-4 and IL-6 in patients with GAME. Depletion of the induced production of both cytokines, which is characteristic of some patients with frequent recurrence of HH, occurs in almost all patients with GAME. It appears that individuals who are more likely to develop GAME are concentrated among patients suffering from a high recurrence rate and demonstrating this pattern of abnormal cytokine profile.

**INTERFERONS.** For the main evaluation criterion, we took the induced production as a parameter characterizing the prognosis of the anti-infective response (Khalidin A.A. 2001). Normally, there is the following ratio between alpha and gamma interferon. The production of gamma interferon is approximately 9 times predominant (alpha interferon  $141 \pm 15.0$  and gamma interferon  $1250 \pm 100$ ).

Table LF9. Interferons alpha and gamma in group A.

Alpha-interferon, pg/ml	Gamma-interferon, pg/ml
	800

Induced production of both gamma and alpha IF is reduced.

Table .M210. Interferons alpha and gamma in group B.

Alpha - interferon, pg/ml	Gamma-interferon, pg/ml
150	1300 +35,4

In group B, the production of gamma-IF and alpha-IF close to the norm was noted.

Table N211. Interferons alpha and gamma in group C.

alpha-interferon, pg/ml	Gamma-interferon, pg/ml
120	894

In group C, there was a lack of production of both alpha and gamma interferon. In all three groups, the production of gamma-interferon over alpha-interferon prevails. Considering that the variants of the norm of interphenogenesis in ELISA vary widely, we relied on a comparative assessment with group B and C. In the GAME group, the production of alpha-interferon and gamma-interferon is lower than in group B and lower than in group C ( $p < 0.05$ ).

Cellular immunity

Assessment of the level of T-lymphocytes.

Table M 12. The content of T-lymphocytes is normal.

Absolute number in $\mu\text{l}$ (abs)	
1600+100	70+5

Table . The content of T-lymphocytes in groups A, B, C.

Group A	Group B	Group C
Abs	Abs	Abs
1420+176      64+9,7	1435+145   61+9	1390+220 64+11

As can be seen from the presented results, the levels of T-lymphocytes do not have significant differences in different groups, remaining in the total mass within the normal range. Accordingly, disturbances in the number of CD-3+ cells do not affect the likelihood of developing GAME.

Immunoregulatory index (the ratio between the content of subpopulations of helper and suppressor cells).

Table . Immunoregulatory index in groups A, B, C.

Group A	Group B	Group C
-3		

While remaining normal in other forms of MEE, in PH and GAME, the immunoregulatory index varies widely, both increasing and decreasing in comparison with the norm, no significant intergroup differences were found. Apparently, IRI cannot be attributed to the factors that determine the likelihood of developing GAME. Among other factors of cellular immunity, changes were detected in the group of natural killers (Nk) with CD16+ differentiation clusters. Table . The level of natural killers FC) is normal.

Absolute amount in $\mu\text{l}$ (abs)	
350+50	14+3

Table. The level of natural killers (Nk) in groups A, B, C.

Group A	Group B	Group C
Abs	Abs	Abs

268+	11+3	370+3	14,1+	460+4	14+1
56	,8	9,7	1,2	7,4	,1

The absolute and relative Nk counts are lower in patients with GAME than in patients with other forms of MEE ( $p < 0.05$ ), although it remains near the lower limit of normal. We regarded this as a significant violation, since a decrease in the number of Nk is a relatively rare pathology accompanied by severe clinical manifestations (A.A. Yarilin 1999). Moreover, normally, in an acute infectious process, Nk should actively proliferate, which is observed in patients with other forms of MEE and HH. It can be concluded that the tendency to reduce the absolute and relative number of killers in the immunogram of a patient with HH increases the likelihood of developing natural HAME. The regulation of Nk proliferation is under the control of IL-2; accordingly, with an increase in spontaneous production of IL-2, the amount of Nk increases, which we observe in the patients examined by us with PC from the control group. The decrease in Nk in the GAME group is paradoxical and apparently plays one of the decisive roles. The insufficiency of their function at the earliest, non-specific stage of response to HSV replication may initiate the development of other mechanisms. Summation with a lack of alpha and gamma interferon exacerbates the situation.

### **HUMORAL IMMUNITY.**

To assess the B-lymphocyte link, we determined both the number of B-lymphocytes (CD23+) and the number of major immunoglobulins. According to R.Hamilton, 1980, the quantitative content of B-lymphocytes in the blood is a stable, practically unchanged indicator. However, given the indications of a possible role of excessive antibody genesis in the development of GAME, we considered this study appropriate.

Table .M217. The level of B-lymphocytes is normal.

Absolute amount in $\mu\text{l}$ (abs)	Percentage (%)
50+100	5 +3,0

Table . The level of B-lymphocytes in groups A, B, C.

Group A		Group B		Group C	
ABS		Abs		Abs	
95+100	17,0+ 3,5	39+50		27+47	9,7+1

The absolute number of B-lymphocytes was significantly higher in the GAME group.

Thus, an increase in the absolute number of lymphocytes increases the likelihood of developing GAME, while their decrease, on the contrary, decreases.

Table MT 9. The content of immunoglobulins in groups A, B, C.

Immunoglobulin	Normal	Group A	Group B	Group C
A general	5	1.6	5	2
E common	140	1.9	65+1 2	430

G common	14	2	4.2+0 8	2
M common		5	1+0.2	
G to HSV		5	1.1	0.9

Class A immunoglobulins are reduced ( $p < 0.05$ ) in groups A and B, while in group C they remain within the normal range. An increase in immunoglobulin E is observed in the GAME and MEE groups ( $p < 0.05$ ), although it is quite high in the PG group. Apparently, an increase in this immunoglobulin increases the likelihood of developing GAME, while at the same time being characteristic of frequently relapsing herpes simplex.

Diagram M 11.12. Immunoglobulin E and A in groups A, B, C and normal. The levels of production of total immunoglobulins G and M in all three groups do not have significant differences and cannot determine the prognosis for the development of GAME in patients with PH, and also do not contribute to the differential diagnosis between GAME and other forms of MEE. Class M antibodies to HSV 1 and 2 were not detected in any patient, which is associated with blood sampling in the remission stage, when at least 2 weeks have passed since the exacerbation of HSV. At this stage, class M antibodies are already eliminated from the circulation. So, a combination of a decrease in Ig A and an increase in IgE can serve as a feature of GAME,

the detection of this combination in patients with may increase the possibility of developing GAME.

all groups, there is a predominance of the spontaneous level over the induced one, which causes a decrease in the stimulation index, which does not reach the norm in any group. This situation is due not to a decrease in ROS production in response to a stimulus (it is within the normal range), but to an increase in their spontaneous production.

### **PHAGOCYTOSIS SYSTEM.**

The percentage level of phagocytosis is approximately the same in all three groups, remaining near the lower limit of normal. The phagocytic index of microbial bodies in Tayuke does not have significant differences in all three groups, however, being reduced, not reaching the lower limit of the norm in any case. The absolute phagocytic index varies widely and also has no intergroup differences. Thus, despite disturbances in the phagocytosis system, which consists in a decrease in the phagocytic index of microbial bodies, phagocytosis indices cannot serve as a criterion for predicting the development of GAME in patients with HH.

Table M21. Phagocytic indicators in groups A, B, C.

	Normal	Group A	Group B	Group C
Phagocytosis, %	60+ 10	57,7	60	74



Phagocytic index of microbial bodies, abs.				5
Absolute phagocytic index	8500	9000	8000	9000

If we evaluate the data on NBT and phagocytosis in general, it can be noted that the number of cells capable of phagocytosis is sufficient in all groups, and the level of absorption of microbial cells by one phagocyte also suffers in all cases. As for the further "processing" of the absorbed object with the help of reactive oxygen species, its increase in response to the stimulus was preserved in all groups. There is even some excess of ROS production in the absence of a stimulus. It should be noted that the methods used for assessing the functional state of phagocytes imply a suspension of *Staphylococcus aureus* as an inductor, therefore, they characterize antibacterial immunity to a greater extent. What in context and GAME matters when predicting the development of a secondary bacterial infection.

### **IMMUNE COMPLEXES.**

Normally, the amount of TsUK 6% PEG does not exceed 300.

Table M22. The level of immune complexes in groups A, B, C.

Group A	Group B	Group C
70,1 +25,3	08,9+ 11,3	01,8 + 24,1

In general, with the level of immune complexes is lower than with GAME and other forms of MEE. However, with GAME it still remains close to normal. Therefore, the change in the level of immune complexes 1-II•G 6% PEG cannot serve as a prognostic criterion for the development of GAME in patients with Summarizing the data obtained, it can be concluded that GAME is characterized by a change in the cytokine profile observed in patients with frequently recurrent herpes simplex. Namely: an increase in the spontaneous production of IL-4 and IL-6 (with higher levels of IL-6) in combination with the depletion of their induced production. GAME is characterized by an increase in the absolute number of B-lymphocytes and a decrease in natural killer cells. The humoral link in GAME is changed towards an increase in Ig E and a decrease in IgA. This condition is called dysimmunoglobulinemia and can be observed in various diseases. Probably, a decrease in the production of immunoglobulin A at the initial stages of antibody genesis contributes to a compensatory increase in the production of reagin antibodies.

## **DIFFERENTIATED APPROACH TO GAME THERAPY.**

### **CURED RECURRENCE.**

When stopping exacerbations, we initially took as a working hypothesis that the main role in the development of GAME is played by the replication of the virus that has emerged from the state of latency, and the background is the sensitization of the body to HSV, and not just a decrease in the antiviral immunity. This is consistent with the view of the problem by H. kokuba, S. Imafuku, J. Bumett, L. Aurelian, 1999: GAME is a combination of the direct cytopathic action of the virus, mainly its DNA polymerase, and immune reactions in the skin that occur in response to this impact. The mechanism of emerging immune responses, according to the same studies, is mainly mediated by two factors - the impact on the microcirculatory link of the dermis of mononuclear cells infected with IVH and the predominance of T-helper subclass type 2. On the basis of this hypothesis, we concluded that in the treatment of GAME, as an allergic reaction to IVH, the place of application of antibiotics is not well

defined. Of course, the decrease in anti-infective immunity is not strictly selective with a decrease in only antiviral protection, respectively, both PG and GAME can be complicated by a secondary bacterial infection. Therefore, it is advisable to formulate indications for the use of antibiotics in GAME, based on clinical data. Also, the dilemma was the use of hyposensitization agents. With widespread skin lesions and (or) a pronounced epidermolytic component, the use of systemic glucocorticosteroids (GCS) is justified. With insufficient prescription of drugs of this class in the early stages, the degree of sensitization may increase, up to the development of Lyell's syndrome (A.Yu. Sergeev, A.V. Karaulov, Yu.V. Sergeev, 2003). There are known cases of the development of Lyell's syndrome after abortive attacks of the MEE (L.A. Gusarenko, 1998). Considering the above, as well as the data available in the literature on the combined use of nucleosides and FS in GAME (J. Kats, A. Livhen, J. Shemer, Y. Danon, 1999), we considered it acceptable to use this approach. However, systemic corticosteroids have an active viral process among direct contraindications for use. Accordingly, the main issue in stopping GAME was the formulation of specific indications for the use of systemic TCS. It was necessary to correlate the potential harm from the use of corticosteroids against the background of an exacerbation of HH and the need for their use to prevent further hypersensitization. The basis for the decision was the heterogeneity of the pathogenesis of GAME. SHIG interacts with the tissues of the body with the development of a cytolytic effect during replication, this is manifested by the development of vesicles against an edematous-hyperemic background. However, in our patients, GAME in most cases developed into the stage of crusts. Of the 45 people in 30, the phenomena of exudative erythema appeared when the "fever on the lips" had already dried up in a crust, that is, there was a crusty stage of herpes simplex. Accordingly, control of the virus by the macroorganism has been restored. Apparently, at this stage, the phenomena of hypersensitivity come to the fore and drug correction should be directed to them. To confirm this hypothesis, we first used only synthetic nucleosides to stop the manifestations of GAME. However, a positive effect was not observed in all patients. If GAME followed immediately after the relapse of PH (against the background of the presence of

vesicles), the administration of nucleosides gave a positive effect within 2-3 days. It consisted of the following: drying of GH vesicles into crusts, cessation of the appearance of new GAME elements, a decrease in color intensity and flattening of old ones. On the contrary, with PH in the stage of crusts, in most cases, new GAME elements continued to appear or old ones increased. For the treatment of this group of patients, it was decided to use, in addition to synthetic nucleosides, systemic GCS betamethasone (Diprospan, manufacturer Shering-Plow) 2 ml intramuscularly once . The choice was due to the presence of two forms of betamethasone in this preparation: as an immediate action component and a delayed (up to 7 days) action component. This approach made it possible to achieve a clear trend towards regression of GAME rashes within a maximum of 3 days. Given the tendency of GAME to recur frequently and the decrease in antiviral immunity under the influence of betamethasone, we also prescribed synthetic nucleosides. In this case, the goal was not to stop GHG, but to prevent it. Despite the absence of visible signs of IVH replication in the form of vesicles, it was impossible to exclude the reactivation of the virus during the use of diprospan. Synthetic nucleosides were prescribed for various periods, depending on the immunoassay data during therapy. In general, such a differentiated approach was effective in 35 people (77.8%). In 10 patients, despite the ongoing therapy, new GAME elements continued to appear and (or) old ones increased. Of these, 7 people received therapy only with synthetic nucleosides, since they were in the vesicular stage, and 3 people with synthetic nucleosides and diprospan, against the background of the crustose stage of PH. Resistance to the therapy did not depend on the prevalence of the rash, if in 6 people about 20% of the body surface was affected, then in 4 it did not exceed 5%. The analysis of objective and subjective symptoms revealed the following. These patients were united by the presence of an intoxication syndrome in the clinical picture: fever 37.2 to 38, sweating, fatigue. All patients had polyadenitis of varying severity. In the picture of the rash, the phenomena of purulent exudation were noted at the site of the opened cavity elements, yellowish loose crusts were formed. The above clinical manifestations were regarded as manifestations of a secondary infection, impetiginization. Which, combined with the lack of effect of the

therapy, served as the basis for the appointment of broad-spectrum oral antibiotics for 7-10 days, and allowed all patients to achieve normalization of the general condition and a tendency to regress rashes within 2-3 days (Scheme 1).

Regression criteria: no complaints of weakness, sweating, no hyperthermia, flattening and blanching of existing rash elements, no new ones. From the foregoing, it follows that the indications for the use of broad-spectrum oral antibiotics in GAME are as follows:

1- No positive effect from therapy with synthetic acyclic nucleosides or synthetic acyclic nucleosides and diprospan for 3 days.

2- The phenomena of intoxication syndrome and impetiginization: subfebrile or febrile fever, polyadenitis of varying severity, feeling of weakness, chills, sweating, formation of purulent crusts on the elements of the rash.

## **PREVENTION OF GAME.**

When choosing a GAME prophylaxis agent, two issues had to be addressed. The first is a reduction in the frequency of recurrence of herpes simplex, and, accordingly, GAME, the second is a decrease in the body's hypersensitivity to HSV. Given the disturbances in interferonogenesis in GAME, it seemed appropriate to use interferon preparations or its inducers. However, their mechanism of action does not affect the allergic component of GAME. Among the features of immunity in GAME, we have identified hyperproduction of IgE (reagins), and this class of immunoglobulins is considered as a means of implementing immediate hypersensitivity (ITH). At the same time, a method is known to reduce the production of reagins by increasing the secretion of class G immunoglobulins, this is achieved by increasing the immunogenicity of the antigen. In allergological practice, this method is widely used, bearing the name of specific immunotherapy. (N.V. Medunitsyn, 1998). As a means of increasing

immunogenicity, low doses of the allergen are used. Among the currently existing HH therapies, low doses of inactivated virus are included in the herpetic polio vaccine. Therefore, as a method of prevention, we used herpetic polio vaccine. The main question that confronted us was the criterion for starting vaccination. As is known, in approximately 30% of cases with frequently recurrent PH, a humoral type of immunogenesis, which is uncharacteristic of chronic viral infections, is observed, and in approximately 10% of patients the immunoregulatory system is depleted. The appointment of an antiherpetic vaccine in such situations can further activate humoral factors with the development of autoimmune pathology or aggravate secondary immunodeficiency with the development of more severe manifestations. 2002). For the main criterion for its recovery, we took the level of cytokine production as an indicator characterizing the prognosis of the immune response, including the introduction of the vaccine (MA Samgin, AVA. Khaldin, 2002). High spontaneous levels of inflammatory cytokine production may contribute to the development of side effects or exacerbation of herpes simplex. Normally, a decrease in the stimulation of HH reagin antibodies and a shift in the ratio of immunoglobulin production towards immunoglobulin G, as in specific immunotherapy, are expected. However, the determination of the production of immunoglobulins is under the control of the cytokine link and an imbalance in it can serve as the development of an exacerbation. However, starting vaccination after the normalization of the cytokine profile, we received a positive effect in patients with a similar clinical picture. The next issue was the formulation of criteria for the effectiveness of vaccination. In medical vaccinology, there are two methods for evaluating the effectiveness of a vaccine: changes in antibody titer, including reagins in SIT, during treatment, and clinical effectiveness. (N.V. Medunitsyn, 1998). In our work, we did not aim to identify the mechanism of action of the herpetic polio vaccine in GAME,

since an adequate assessment of it would be possible by assessing the titer of specific Ig E in dynamics. However, today there are no test systems for assessing HSV-specific Ig E. Therefore, the main criterion for the effectiveness of the use of herpetic polio vaccine in the group of patients with GAME was the reduction in the frequency of relapses. In total, 45 patients with GAME received therapy with herpetic polio vaccine. Previously, all patients were prescribed synthetic nucleosides, under the control of monthly immunoassay. After the normalization of the cytokine profile, we proceeded to vaccination according to the scheme - 0.2 - 0.2 - 0.2 - 0.2 ml. One injection was made every 3 days, for a course of 5 injections. After a 2-week break, the course was repeated. To consolidate the results, revaccination was carried out after 6 months. Injections were made intradermally, in the area of the flexor surface of the forearm. The criterion for the correctness of the introduction was the formation of "orange peel" at the injection site. After completion of vaccination, we followed up the patients for a year, comparing the frequency of recurrence during the year before vaccination and after the 2nd course of revaccination (carried out 6 months after the end of the second course). To assess the effect, we used the scheme below, in which patients are divided into groups according to the frequency of recurrence. The frequency of recurrence was compared during the year before the start of vaccination and during the year after the second course of revaccination. When indicating "No relapses", we meant not only the complete absence of clinical signs and GAME, but also abortive relapses that appeared as swelling at the site of permanent localization and (or) papules 1–2 mm in diameter, regressing within 1–3 days. The absence of a positive effect from vaccination was observed in the group of patients with a recurrence rate of 5-6, as well as 6 or more times a year. If, with recurrence 5-6 times a year, 15% of patients had no effect, then in the group with a recurrence frequency of 6 or more times a year, out of 12 people, more than half did not show positive dynamics. In general, the method was ineffective in 11 patients.

The prevalence of the rash and the duration of the medical history did not affect the effectiveness of vaccination; no correlation was found in the statistical analysis. Also, no statistically significant differences were found in the immunological parameters of patients in the group with a positive effect from the use of polio vaccine and in the group with no such effect. The factor that united patients whose therapy with polio vaccine was not successful was resistance at the time of exacerbation to differentiated therapy with synthetic nucleosides or synthetic nucleosides in combination with diprospan. In the clinical picture of exacerbation of GAME in patients of this group, there were signs of intoxication syndrome (fever 37.5 - 39.0, sweating, weakness) and polyadenitis of varying severity, signs of impetiginization. Broad-spectrum antibiotics were added to the therapy, which gave a positive effect (which consisted in the absence of the appearance of new rashes, a decrease in the intensity of color and flattening of existing ones, the disappearance of symptoms of intoxication) within 2-3 days. Of the 11 people, 4 patients who demonstrated an exacerbation of herpes simplex after the first injection of the vaccine had no symptoms of bacterial infection earlier (with previous exacerbations of GAME). For the treatment of patients whose treatment with herpetic polio vaccine did not give a positive effect, we used prolonged administration of acyclic synthetic nucleosides. This approach led to the absence of relapses and GAME, or abortive course of exacerbations during the entire period of observation.

Scheme 22. The number of exacerbations (per year) in groups with different rates of GAME recurrence before and after treatment with herpetic polio vaccine.

## **DISCUSSION.**

So, as a result of the analysis of clinical manifestations, the immunological status of patients and the data obtained during therapy, criteria for the diagnosis and treatment of herpes-associated exudative erythema were formulated. Let's consider the obtained results.



According to J. Fitzpatrick, 2014, the majority of patients with erythema multiforme are men, and more than half of them are under 20 years old, these data refer to the EEC countries and the USA. Accordingly, it seemed relevant to study the age and sex composition of our patients. Among them, more than half (69%) were represented by men. As a reason for this, we can assume a more attentive attitude of women to the problem of recurrent herpes on the face. In addition, our patients were also characterized by a certain age composition. Despite the general trend towards the development of GAME in the range of 18-35 years, in middle and old age, GAME is observed more often in women than in men. Perhaps this is due to the age-related dynamics of immune reactivity depending on gender.

For GAME, some features of the clinical picture are characteristic, which distinguish it from the toxic-allergic variety of exudative erythema. First of all, this refers to the development of GAME after a recurrence of herpes simplex, it mainly occurs on the 5th-6th day of exacerbation of PH, and in most cases against the background of its transition to the crusty stage. This fact, in particular, served as the basis for formulating a hypothesis about the pathogenesis of GAME.

The frequency of recurrence of GAME was high, 5-12 times a year, due to the peculiarities of the etiological factor - herpes simplex, with violations of the antiviral immunity prone to frequent exacerbations (V.M. Zhdanov, I.F. Barinsky, G.A. Galegov, F.I.

Ershov, 2011).

Accordingly, the frequency of GAME recurrence depends on and is determined by the degree of decrease in antiviral mechanisms, both specific and non-specific.

The nature of the GAME rash differed from that in toxic-allergic exudative erythema (T-A MEE). The elements of the rash in T-A MEE are bright red, often larger than 4 cm, tend to merge with the formation of large foci, often localized on the mucous membranes of the mouth and genitals. With oral intake of the antigen, localization can be limited to the oral cavity and genital mucosa, which we have never observed in the herpes-associated variety. With GAME, the elements of the rash rather quickly (after

1-2 days of existence), acquire a stagnant shade, do not exceed 4 cm in diameter, and are not prone to merging. Another clinical feature of GAME was the rare involvement of the genital mucosa in the pathological process. This is probably due to the fact that labial herpes is almost always the cause of GAME. According to the dynamic theory of HSV replication, a virus localized in the spinal ganglia can migrate along the nerve trunks to their corresponding anatomical zones. It is possible that with labial herpes, local dissemination (and, accordingly, a hyperimmune response to its presence) occurs mainly in the mucocutaneous loci located above the midline of the body. Apparently, whether there will be a further spread of the rash depends on other factors, in particular, on the characteristics of the blood supply. The significance of the features of skin blood flow in the development of GAME is shown (H. kokuba, S. Imafuku, J. Bumett, L. Aurelian, 2012). In addition, the rare involvement of the genitals confirms the current opinion that HSV often causes a "small" form of exudative erythema, which affects the mucous membranes to a small extent (S.Mochella, H.Harley, 2012). erythema (I-A MEE) of other genesis, for example, after ARVI or tonsillitis caused by a bacterial pathogen, no differences were found. Probably, this is mainly due to differences in the pathogenesis of exudative erythema caused by infectious agents, and caused by drugs. As you know, the majority drugs are haptens, and allergic reactions to haptens (incomplete antigens) are more severe (D.K. Novikov, Yu.V. Sergeev et al., 2014). The above facts testify in favor of the possibility of diagnosing GAME on the basis of clinical data. The difference in the picture of the rash and anamnesis makes it possible to differentiate GAME from the toxic-allergic variety.

Before the onset of GAME, there is often a change in the type of HH recurrence. Basically, this is an increase in relapses, there may also be an increase in the duration of relapse or the area of skin affected by PG. In more than 90% of cases, herpes simplex, which initiated GAME, was localized on the face. Of undoubted interest is the clear priority of labial herpes, as a cause of GAME, over genital. If we consider global data as a whole, SHIG-1, which causes labial herpes in 90% of cases (A.Strand, 2010), is mainly the cause of herpes-associated diseases (Hwang Y.S., Spruance S.L., 2010). In our opinion, this is due to greater social focus on genital herpes. According

to patients, genital herpes is a dangerous sexual disease, and labial herpes is nothing more than a “cold on the lips.” Accordingly, in the presence of genital herpes, people immediately seek medical help, and labial herpes, even often recurrent, are treated independently with widely advertised creams and topical ointments that are not effective enough in the case of an increase in the severity of PH. This situation indicates the need for greater attention to the problem of recurrent labial localization and active therapy of patients at risk for the development of GAME.

The basis for formulating a hypothesis about the main stages of the pathogenesis of GAME was both its clinical features and the identified immunological disorders. Firstly, GAME develops on the 4-6th day of herpes simplex recurrence, and secondly, mainly against the background of the crusty stage. That is, there is an inhibition of HHH replication under the influence of some mechanism, the redundancy of which may lead to the development of GAME. Given the timing, it can be assumed that these are antibodies to HHH, since the peak of their production during exacerbations of HH falls on the 4-7th day of relapse (G.J. Buddingh, 1953). Further, the normal is the gradual elimination of antibodies. However, if the production of the corresponding mediators is disrupted, this may not happen. The question of the dynamics of the production of antibodies and their role in the relief of exacerbation of PH seems to be ambiguous. There is evidence of a possible attraction effect of antibodies to HSV (S.kohl, 1985; A.L Notkins, 1973; N.V Emanuele, 1991; K Jakel., T. Loning, 1993). Moreover, it was noted that during relapses, there is a gradual increase in the production of antibodies against the background of those already present in a certain amount (A.Namians, B. Roinnan, 1973). Considering these data, it can be hypothetically assumed that the accumulation of antibodies to HH, and against the background of insufficiency of other components of antiviral resistance, can initiate GAME. The complex of immune responses arising in response to viral replication is not limited to antibody genesis, many cells and mediators are involved in them. Their overreaction due to frequent relapses of IW may initiate hypersensitivity. Apparently, the phenomena of hypersensitivity develop against the background of a peak in the tension of anti-infective mechanisms. However, the number of patients with frequently

relapsing and therapy-resistant HH is incomparably greater than the number of patients with GAME. Therefore, the depression of specific and nonspecific antiviral mechanisms with compensatory tension of other parts of immunogenesis cannot be the only component of pathogenesis. The development of GAME against the background of worsening of the course of herpes simplex also does not allow reducing GAME to a monovalent allergic reaction to the viral antigen. As you know, allergic reactions are not dose-dependent, if they develop on a certain viral protein, for example, on viral DNA polymerase, which takes place according to Aurelian, 2010, the following would be observed. An immunological response would develop shortly after the onset of viral replication, minutes later in immediate hypersensitivity (HTH), or an appropriate period in delayed-type hypersensitivity (DTH). The development of GAME after an increase in the severity of herpes simplex testifies rather in favor of the immunocomplex mechanism, which has been repeatedly stated by various researchers. However, the presence of immune complexes in the histological picture of GAME ranges from 300/0 to 70%, according to various sources (L.Azinge, 2010; J.kazmierovsky, 2011; D.Cines, 2012; J.Immafura, 2012; K. Leigh, 2011 ), which does not allow us to fully accept this hypothesis. Probably, all three components are involved in the implementation of the pathogenesis of GAME, today the existence of hyperergic reactions of a mixed type is generally recognized (D.K. Novikov, Yu.V. Sergeev et al. 20012). The main reason, probably, lies in the violation of the immunoregulatory balance. Constant stimulation of T- and B-lymphocytes by the viral antigen (against the background of a decrease in nonspecific immune mechanisms) leads to hyperproduction (and then depletion) of a number of cytokine mediators. At a certain moment, their number can overlap the number of target cells, causing an inflammatory reaction that is inadequate to the strength of the original stimulus. Or there is hypersusceptibility of receptors, increased proliferation of adhesion molecules, which has been repeatedly detected in other dermatoses (N.K. Nikulin, I.A. Klemenova, T.Yu. Chernova, 2010). Let us consider in more detail, violations of the production of which cytokines can lead to the development of GAME. To date, there is a hypothesis that alpha-interferon is integrated into the mechanism of suppression of

viral replication at the time of exacerbation (F.I. Ershov 1984, T.Chard, P.Craig 2011), inhibition of the ability of leukocytes to produce alpha-interferon is observed mainly during prolonged exacerbations, more than 21 days (A.A. Khaldin, 2001). It can be assumed that the lack of alpha-interferon, in particular, causes compensatory proliferation of B-lymphocytes and further excessive production of antibodies. The production of interferon gamma is also reduced in patients with GAME and PG ( $p < 0.05$ ), remaining normal in other forms of MEE. As is known, gamma interferon is of decisive importance in preventing relapses of PH (I.V. Korobko, V.V. Malinovskaya, 1985), so its decrease in the GAME and HG groups is quite natural. The role of changes in the production of interferon gamma in the pathogenesis of GAME seems to be significant. GAME is characterized by the presence of gamma-interferon in the places of rashes of both GAME and GG (H. kokuba, L. Aurelian, 2013). The source of gamma interferon is MS cells and cytotoxic lymphocytes, it can participate in cytotoxic reactions. In addition, it suppresses the humoral cellular response, stimulates the cellular one, and reduces the proliferation of Th-2 cells (A.A. Yarilin, 1999) As is known, in GAME, the predominance of Th-2 cells (N. S. Imafuku, J. Bumett, L.Aurelian, 2015) and insufficient proliferation of Nk cells (O.L. Ivanov, M.V. Khaldina, 2012). Nk cells, or natural killers, are normally one of the first to respond to viral replication, ensuring the killing of cells affected by virions at the earliest stages of the immune response. When comparing the level of production of Nk cells in patients with GAME, PH and MEE of other genesis, the following was revealed. In PH and MEE, it increases, which is combined with an increase in the spontaneous production of IL-2, the main stimulator of Nk cell proliferation. However, in GAME, despite the frequently relapsing viral process, this does not happen, the Nk level remains at the lower limit of normal. In addition to the absence of an increase in the production of Nk cells and insufficiency of gamma- and alpha-interferon, the level of immunoglobulin A is reduced in patients with GAME. In addition, in patients of all three groups, a decrease in the phagocytic index of microbial bodies was noted, which corresponds to the data of I.V. Polesko and A. AND. Haldina, 2004, on the decrease in phagocytic activity in PH. Thus, for patients with GAME, there is a characteristic

decrease in interferonogenesis, phagocytosis, and immunoglobulin A. At the same time, some parameters of the immune status in GAME exceeded the norm. This is immunoglobulin E, mediating immediate hypersensitivity and absolute B lymphocyte count. There was also a sharp increase in the production of IL-4 and IL-6, combined with inhibition of their induced production. Summarizing the identified features, we can say the following. From the point of view of allergology, GAME is a mixed reaction that has features of both immediate hypersensitivity (HHT) and delayed hypersensitivity (HRT), as well as features inherent in immunocomplex pathology. From GNT - an increase in total (reagin antibodies) in almost all patients and the predominance of Th2 type cells among T-helpers, from HRT, the presence of CD8+ cytotoxic lymphocytes in the infiltrate (DK. Novikov, Yu.V Sergeev,). From immunocomplex pathology, the deposition of Ig M and C3 of the complement component (L.kazmierowsky,) in the places of rashes and the detection of IC with the herpes simplex virus in the blood. In any case, MEE is a manifestation of a shift in the adaptive mechanisms of the immune response towards hypersensitivity, that is, it is an allergic reaction, or, more correctly, a part of the atopic syndrome. Today, it is understood as a hereditary form of allergy, which is characterized by the presence of reaginic antibodies of the Ig E class. For GAME, their significant increase is characteristic (O.L. Ivanov, M.V. Khaldina, 2012), MEE was also found to be associated with certain HLA antigens (J. Malo, 2012), which indicates the genetic determinism of the disease. An interesting fact confirming this is the following clinical case. The patient, 0.26 years old, was admitted to the clinic of skin and venereal diseases of the Moscow Medical Academy named after. Sechenov with a diagnosis of exudative erythema. When collecting an anamnesis, food allergy was identified as the cause of MEE. The patient also suffers from mild bronchial asthma and allergic rhinosinusopathy. In the patient's children (4 and 5 years old) the phenomena of exudative diathesis. At the same time, GAME is a part of the herpes disease (M.A. Samgin, A.A. Khaldin. 2002), among our patients with MEE, 70% was represented by a herpes-associated form. Given that we included only obvious cases in the study, this figure could actually be even higher. That is, GAME develops in the case of the

development of frequently recurrent herpes simplex in individuals with a tendency to atopy. GAME is characterized by frequent relapses, 5-12 times a year, which is a direct consequence of the depression of antiviral mechanisms.

In addition, the immunologically detectable predisposition to GAME can, to some extent, speak in general about the predisposition to the development of herpes-associated diseases in patients with PH. After all, viral replication can change the gene apparatus of both resident cells (for example, epidermocytes), which leads to lesions limited to the epidermis, and immunocompetent cells, then systemic diseases, such as SLE, can be observed (this assumption is not ascertaining in nature, but once again speaks in favor of active therapy of patients with corresponding changes). According to the same hypothesis, both the receptor apparatus of cells and the enzymatic or immunomediator (cytokine) profile can change. In patients with GAME, there is a violation of the cytokine profile, causing, among other things, dysglobulinemia. And a violation of the production of antibodies in combination with an increase in the number of B-lymphocytes can directly lead to autoimmune diseases (Sokolov E.I., Glan P.V., Grishina T.I., Kuzmenko L.G. et al., 2016). Given this possibility, it is important to carry out their prevention. Therefore, when assessing the immunological parameters of GAME, we were interested in the totality of changes that make it possible to predict its development in patients with PH.

The most pronounced for GAME were the following changes in the immune status: a decrease in Ig A, an increase in Ig E, an increase in spontaneous production of IL-4 and IL-6 against the background of a decrease in their induced production, a decrease in the number of alpha- and gamma-interferon, an increase in the absolute number of B-lymphocytes . A decrease in the phagocytic index, which is not a distinguishing feature of GAME from PG, may acquire additional pathogenic significance. We regard a decrease in UD A, interferon alpha and gamma as factors contributing to frequent relapses of PH, and an increase in IL 4 and 6, Ig E and B lymphocytes as markers of hypersensitization to the virus. An increase in the number of B-lymphocytes in combination with the development of GAME on the 5th-6th day of relapse is largely consistent with the opinion about the alterative effect of antibodies and the

"paradoxical" humoral type of the immune response to HSV. As you know, specific viral antibodies begin to be produced on the 4th-7th day of the recurrence of herpes simplex. This observation indicates the inadvisability of using immunomodulators that activate the B-lymphocyte link for the treatment of GAME. In general, we assessed the changes in the immunogram in the context of a normal response to HBV. After the virus, due to any reason, has left the latent state, there are 4 main options for the interaction of the cell in which the virus began to replicate with the cells and mediators of the immune system. Interferons block the processes of translation and transcription of the virus, respectively, further replication does not occur.

1. A cell affected by a virus under the action (T-lymphocytes) expresses which, interacting with the initially present on the cell, starts the process of apoptosis.

2. The cell presents on its surface an antigen in combination with its own gene of the major histocompatibility complex type 1 (MHC1). They interact with the T-helper receptor (CD4+, Th1type), the production of which increases IL-2, and the cytotoxic production of which increases IL-6. As a result of this interaction, the cytotoxic lymphocyte destroys the cell with the help of a number of its own substances, without resorting to any humoral factors. This is the so-called cellular type of herpes simplex immunogenesis. With excessive production of IL-6, hyperproduction of cytotoxic lymphocytes involved in hypersensitivity reactions, in particular, of a delayed type, can be observed.

3. The cell presents on its surface the HSV antigen in combination with its own gene of the major histocompatibility complex type 2 (MHC2). They interact with the T-helper receptor (CD4+) and the HSV-specific immunoglobulin of the B-lymphocyte (Ig M or G). As a result of this interaction, complement (humoral non-specific immunity factor) is activated, attacking the cell membrane and causing its lysis. This is a humoral type of immunogenesis. During the production of immunoglobulins, an excess number

IL-4 may contribute to the production of types E and G4, mediators



Perhaps, at a certain stage, an increase in the synthesis of IL-4 and -6 overlaps the number of proliferating T- and B-lymphocytes that is adequate for the amount of antigen (SHIH). There is a shift in the adaptive immune response towards unregulated hypersensitivity: IL-4 potentiates the production of IgG4 and UDE, and IL-6 increases the production of cytotoxic lymphocytes that attack unaffected cells with a similar antigenic determinant. When analyzing the level of other cytokines: the amount of IL-2 was normal in all patients, but there were manifestations of insufficiency of one of its main effects: a decrease in the number. Normally, on the contrary, the receptor apparatus is activated and natural killers are produced during an acute infectious process. Indirect evidence of impaired functioning in GAME IL-2 may be the absence of an increase in its spontaneous production, in contrast to patients from the PG group. Apparently, the situation may be the result of receptor disorders and mediator imbalance, IL-2 and Nk seem to “ignore” viral aggression. This is probably a phenomenon of the same order as the depletion of the production of interleukins 4 and 6, that is, anergy that occurs during a long, often recurrent viral process. So, the main sequence of development of immune dysfunctions in GAME can be represented as follows. During HSV replication, against the background of the lack of adequate Nk proliferation, from the very beginning there is no complete lysis of virions and cells affected by them. In the future, alpha-interferon should be integrated into the process and impart non-permissiveness to IVH to neighboring infected cells. However, the amount of alpha-interferon is not enough and this does not happen. Then we should expect a compensatory increase in other factors. The preservation of the function of B-lymphocytes contributes to their enhanced proliferation. Normally, there should be a sequential change in the production of immunoglobulins A, M, G. However, the excess of spontaneous production of IL-4 contributes to a shift in the immunoglobulin repertoire towards reagents: Ig E and G4. Lack of production of gamma - interferon and IL-2 in combination with an excess of IL-4 contributes to the polarization of helper cells in a paradoxical direction, that is, according to the Th-2 type. The latter was not revealed by us, however, it has been repeatedly shown in other studies (H.KoKuba, S.Imafuku, S. Niapd, L. Aurelian, 2010). The Th-2 type is typical for the

implementation of hypersensitivity reactions and is often combined with an increase in IL-4 and UD E. Changes in local blood flow attract circulating immune complexes; they have been repeatedly found in MEE lesions. Probably, the component of immunocomplex vascular damage is present, but does not dominate. Since, firstly, highly pathogenic immune complexes are formed with an excess of antigen (which can be observed in patients with massive viremia and already suggests a primary deficiency of antiviral mechanisms, these are more often immunocompromised patients). At the final stage, there is a DTH component mediated by an excessive number of CD8+ cytotoxic lymphocytes, which are also found at the sites of MEE rashes and proliferate under the influence of IL-6 levels. The presented hypothesis, taking into account the multicomponent nature of the immune response, is schematic, but reflects the main key points. (Scheme MZ). The approach to the treatment of GAME includes both the relief of relapse and the prevention of further exacerbations.

The approach to the treatment of exacerbation of GAME varies depending on the stage. With the development of GAME into the active (vesicular) stage, it is effective to take synthetic nucleosides according to herpes simplex treatment regimens, both in order to stop the recurrence of HAME and GAME and in the future, to prevent subsequent relapses. In those patients whose body has regained control over BIW (clinically they have a crusty stage of PH), the adaptive mechanism has already fulfilled its physiological purpose and has passed into the phase of uncontrolled hypersensitivity. These patients are shown diprosan in combination with synthetic nucleosides. In general, GAME is easier to prevent than to treat, and there have been numerous reports that long-acting nucleosides are effective in preventing it. We can add that it makes sense to take it on a continuous schedule, since the breakdown of the latency of the virus returns the immune system to its original level.

In the future, for the prevention of GAME, we used a herpes polio vaccine, 2 courses of 5 injections at a dose of 0.1-0.2-0.30.3-0.3 with a two-week break between courses, revaccination after 6 months, and repeating the vaccination course for next year to consolidate the result. We used normalization of the levels of spontaneous and induced production of IL-4 and IL-6 as a criterion for starting vaccination, which can take quite

a long time (6 months or more), during which we prescribed famciclovir 250 mg \* 2 times a day or valaciclovir 500 mg\*2 times a day or acyclovir 200 mg\* 4 times a day. According to our data, the levels of TNF-alpha and IL-1-beta were also disturbed in a number of cases, but there were no patients in whom the disturbances in the production of these cytokines would be selective, without changes in IL-4 and IL-6. Therefore, we considered it acceptable to use only IL-4 and IL-6 as a criterion for the normalization of the cytokine link. At present, it is known that the cytokine network, as well as all cells and mediators of the immune system in various pathologies, rarely changes strictly selectively. In this case, the changes are also of a compositional nature, however, the use of an assessment of the level of production of IL-4 and IL-6 as markers of the type of imbalance in the entire cytokine network reduces the cost of immunodiagnostics. The effectiveness of vaccination was 71%, which consisted in reducing the number of relapses and, accordingly, GAME by 2-4 times. These data coincide with the world data; in the treatment of recurrent herpes, the effectiveness of vaccination is from 30 to 80 percent. Several patients were relapse-free during the entire follow-up period (year)

## **FINDINGS**

1. With the general similarity of the clinical picture of GAME with other forms of exudative erythema, there are a number of features: development on the 4-6th day from the onset of the recurrence of herpes simplex. In 6.7% this interval is 3 days and in 4.5% 7-9 days. In contrast to the toxic-allergic form of exudative erythema, the elements of the GAME rash are solitary, congestive, up to 4 cm in diameter and affect the genitals in less than 10% of cases.
2. GAME in 60% of cases develops against the background of an increase in frequency and (or) an increase in the duration of relapses of herpes simplex, which in 93% of cases is localized on the face. Accordingly, an increase in the frequency of recurrence of herpes labialis requires active therapy to prevent the development of GAME.
3. Prognostic criteria that increase the risk of developing GAME is the presence of the following changes in the immune status of patients with herpes simplex. An increase

in the spontaneous production of IL-4 and IL-6 in combination with the inhibition of their induced production (the ratio of spontaneous: induced 1:1). In the humoral link, the imbalance in the production of immunoglobulins with a predominance of UD E (471.0+19.0) and a decrease in Ig A (1.2+0.4) with an increase in the absolute content of B lymphocytes (295.6+100.8). Decreased alpha and gamma interferon (63.0+8.6 and 720.0+19.4 respectively). No increase in Nk

The rest of the studied parameters turned out to be non-informative.

4. With the development of GAME against the background of the vesicular stage of PH, monotherapy with synthetic acyclic nucleosides is effective. With GAME that has developed into the crustous stage of PH, the administration of 2 ml of diprospan intramuscularly once in combination with the administration of acyclic nucleosides is effective. The use of broad-spectrum antibiotics is indicated in the case of secondary bacterial infection (the presence of an intoxication syndrome and impetiginization phenomena), which is observed in 22% of cases. As a secondary prevention of GAME, the use of herpetic polio vaccine in doses of 0.1-0.2-0.20.2-0.2, 1 injection in 3 days, revaccination after 2 weeks and after 6 months is effective. The criterion for starting vaccination is the restoration of the normal ratio between spontaneous and induced production of IL-4 and IL-6. The effectiveness of the vaccine is 71%, which is to reduce the frequency of relapses of PG and GAME by 2-4 times.

#### **PRACTICAL RECOMMENDATIONS.**

1. As criteria for the diagnosis of herpes-associated erythema, the following are used: dermatosis develops within 1-9 days from a proven recurrence of herpes simplex (HS). The diagnosis is made on the basis of the presence of typical vesicular lesions on an edematous-erythematous background or HYDR diagnosis in doubtful cases.

2. With an increase in the duration of HH relapses, resistance to earlier effective therapy and the presence of the following immunological criteria: inhibition of the induced production of IL 4 and 6, a decrease in UDD, alpha and gamma interferon, and an increase in the absolute number of B-lymphocytes, the method of treatment of HH is prolonged therapy with synthetic nucleosides.

3. With the development of GAME against the background of the vesicular stage of PH, it is necessary to prescribe synthetic nucleosides, with the development in the crusty stage - synthetic nucleosides and 2 ml of diprospan intramuscularly once. Further, a prolonged intake of synthetic nucleosides is required until the spontaneous and induced production of IL-4 and 6 is normalized. Antibiotic therapy for GAME is indicated in case of signs of secondary bacterial infection: symptoms of intoxication, impetiginization. As a prophylaxis of GAME, the use of a herpetic polio vaccine is used, the criterion for starting vaccination is the normalization of IL-4 and IL-6.

## **PROVISIONS FOR DEFENSE**

1. GAME has clinical and immunological differences from other forms of MEE.
2. There are immunological criteria to predict the development of GAME in patients with PH.
3. The tactics of arresting the recurrence of GAME depends on the stage of HH. Herpes vaccine can be used as a prophylaxis against GAME.

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## ОТЗЫВ

научного руководителя на выпускницу магистратуры  
направления 5A510401 - *Стоматология (ортопедическая стоматология)*

**Каки Худа Абдул Салам Хекмат**

Вскоре после того, как Урбах в 1933 году впервые сообщил о связи между многоформной эритемой и "пузыркоковый лишай", Андерсон уже описал вирус простого герпеса как "бомбу замедленного действия" этого кожного заболевания. Семьдесят лет спустя ситуация не только не изменилась, но и стала еще более серьезной. В первые годы главной задачей был поиск причинных факторов, но сегодня существует еще одна проблема, связанная с выяснением патогенеза заболевания и выбором лечения и вариантов лечения.. В частности, ряд исследований с использованием современных методов диагностики продемонстрировал роль следующих этиологических агентов. Многие исследования с использованием современных методов диагностики показали, что вирус простого герпеса имеет непосредственное отношение как к возникновению, так и к последующим рецидивам заболевания. Статистика количества обращений в клиники показывает, что доля многоформной эритемы, вызванной вирусом простого герпеса, достигает 80%, что соответствует примерно 1% всех пациентов, посещающих дерматологическую клинику. Простой герпес поднялся на первое место в списке проблем со здоровьем, составленном Всемирной организацией здравоохранения. Рост заболеваемости вирусом простого герпеса, который является одной из проблемных областей Всемирной организации здравоохранения, наряду с другими инфекционными заболеваниями, такими как вирус иммунодефицита человека и грипп, делает эту проблему актуальной.

Диссертация состоит из введения, обзора литературы, материалов и методов исследования, собственного исследования, списка результатов, практических советов и литературы. Основная часть диссертации отображается на письменном в виде, в таблицах и рисунках. Каки Худа Абдул Салам Хекмат 1974 года рождения, по национальности жительница ирака. Закончила в 2020

году стоматологический факультет Луганский государственный медицинский университет с 2021 по 2023 гг. проходила обучение в магистратуре Самаркандского Государственного медицинского университета на кафедре “Ортопедической стоматологии” по специальности 5A510401-Стоматология (ортопедической стоматология). В целом характеризуется как активный, исполнительный студент. Творчески и корректно решает поставленные перед ним задачи, которые всегда выполняются в срок. В полном объеме пользуется интернетом и современными компьютерными программами, много читает медицинскую литературу и монографии.

Согласно плану обучения в магистратуре прошла весь курс теоретической и практической программы, и в целом хорошо овладела основными навыками клинициста терапевта-стоматолога. Участвовала в приеме пациентов в разных отделениях согласно графику его ротаций. Участвовала на кафедральных собраниях кафедры ортопедической стоматологии. Проводила занятия со студентами 2-3 курсами стоматологического факультета на должном методическом уровне.

Выполнила научную работу по теме: «features of the course of erythema multiple form associated with herpes viral infection». По материалам диссертации опубликованы 6 научных работ, из них 6 журнальных статей.

Таким образом, представленная магистерская диссертация на тему: «features of the course of erythema multiple form associated with herpes viral infection» является завершенной магистерской диссертацией и может быть представлено к апробации и рекомендуется к публичной защите после сдачи итоговой аттестации и экзаменов.

**Научный руководитель:**

**Зав. Каф. Орт. Стом. СамГМУ**

**к.м.н. доцент Ахмедов А.А**



IMZOSINI  
«TASDIQLAYMAN»  
SamDTU Kadrlar bo'limi  
boshlig'i



**SAMARQAND DAVLAT TIBBIYOT UNIVERSITETI**  
**STOMATOLOGIYA (YO'NALISHLAR BO'YICHA) MUTAXASSISLIGI II KURS**  
**MAGISTRATURA REZIDENTI XUDA ABDUL SALAM XEKMAT 2022-2023 O'QUV YILI**  
**UCHUN SHAXSIY KALENDAR REJASI BO'YICHA**  
**IKKINCHI YARIM YILLIK HISOBOTI**

***I.O'quv va o'quv-uslubiy ish***

		<b>Hisobot davrida o'tilgan seminar darslar</b>	
<b>№</b>	<b>Mavzu</b>	<b>Soat</b>	<b>Dars o'tuvchi</b>
1	Kranio-mandibulyar ortodontiya. Moxiyati. Prikusni organizm bilan bog'liqligi. ALF apparati. Qo'llashga bo'lgan ko'rsatmalar. Xato va asoratlar	8 soat.	Assistent Axmadov I.N.
2	Splintoterapiya. Chakka pastki jag' bo'g'imlari va chaynov mushak kasalliklarida davolash uchun qo'llaniladigan ortodontik apparat va ularning turlari. Qo'llashga bo'lgan ko'rsatmalar	8 soat.	Assistent Axmadov I.N.
3	Yechilmaydigan ortodontik apparatlar. Edjuayz tizimini bevosita va bilvosita urnatish usullari	8 soat.	Assistent Axmadov I.N.
4	Twin Block yordamida davolashni asosiy moxiyati. Apparatni riivojlanish tarixi. Twin Block konstruktsiyalari. Kullashga kursatma va karshi kursatma. Twin Block bilan birgalikda kombirinirlangan xolda ishlatiluvchi apparatlar	8 soat.	Assistent Axmadov I.N.
5	Aktivatorlar. Konstruktsiyalari, Kullashga kursatma va karshi kursatma.	8 soat.	Assistent Axmadov I.N.
6	Elayner.Attachmenlar. Konstruktsiyalari . Kullashga kursatma va karshi kursatma. Ortopedik davolashdan olingi ortodontik davolash muolajalari. Uziga xosligi. Bolalarda ortopedik davolashni uziga xos xususiyatlari.	8 soat.	Assistent Axmadov I.N.
7	Ekzostozni xirurgik davolash. Yuqori lab, pastki lab va til yuganchalarida frenulotomiya o'tkazish. Yuz-jag' soxasidagi chandiqlarni olish.	8 soat.	Assistent Axmadov I.N.
8	Og'iz bo'shligida o'smasimon xosilalarni olish (fibroma, epulis) Yuzda yuza joylashgan O'smasimon xosilalarni olish (Ateroma, Lipoma)	8 soat.	Assistent Axmadov I.N.
9	Sinus lifting amaliyoti(ochiq va yopiq) Pastki jag'da o'tkaziladigan implantatsiya.	8 soat.	Assistent Axmadov I.N.
10	Yo'naltirilgan suyuk regeneratsiyasi (NKR). 3D kompyuter tomografiyani o'qish.	8 soat.	Assistent Axmadov I.N.
11	Retsessiyalarni erkin va oyoqchali laxtaklar bilan bartaraf etish. Retsessiyalarni koronar-apekal laxtaklar bilan bartaraf qilish. Paradontitlarda ochiq va yopiq kyuretaj	8 soat.	Assistent Axmadov I.N.
12	Bolalardagi stomatologik kasalliklarda morfologik va sitologik tekshiruv usullari, og'iz bo'shlik shilliq qavatining morfologik tuzulishi Bolalar yuz-jag' sohasi kasalliklarida rentgenologik tekshiruv ahamiyati, o'tkazish usullari va ularning o'ziga xosligi	8 soat.	Assistent Axmadov I.N.

13	Bolalar yuz sohasi suyaklarining anatomik tuzulishi. Bolalarda tish va jag'larining tuzulishi	8 soat.	Assistent Axmadov I.N.
14	Bolalar yuz-jag' sohasini chaynov va mimik mushaklarining anatomo-fiziologik xususiyatlari Bolalar ChPJB anatomo-topografik tuzilishi, funktsiyasi, o'ziga xosligi	8 soat.	Assistent Axmadov I.N.
15	Bolalar stomatologik kasalliklarida maxalliy o'tkazuvchan va infiltratsion og'riksizlantirishning o'ziga xos xususiyatlari	8 soat.	Assistent Axmadov I.N.
16	Tishlarning anomal joylashuvining' etiologiyasi, klinikasi va tasnifi. Tishlarning anomal joylashuvini tashxislash va davolash	8 soat.	Assistent Axmadov I.N.
17	Bolaning yoshiga bog'liq xolda klinik kechishi, tashxislash, operativ va umumiy davolash bosqichlari	8 soat.	Assistent Axmadov I.N.
18	Yuz va jag' suyaklarining yallig'lanish jarayonlari (spetsifik yallig'lanish jarayonlari: aktinamikoz, sil)	8 soat.	Assistent Axmadov I.N.
19	Yuz va jag' suyaklarining yallig'lanish jarayonlari(osteoartrit). Bolaning yoshiga bog'liq xolda klinik kechishi, tashxislash, operativ va umumiy davolash bosqichlari	8 soat.	Assistent Axmadov I.N.

#### Hisobot davrida o'tkazilgan amaliy ko'nikmalar

№	Amaliy ko'nikma nomi	Soni
1	Mandibulyar o'tkazuvchi og'riqsizlantirish	68
2	Mahalliy infiltratsion og'riqsizlantirish	125
3	Periostotomiya	7
4	Palatinal og'riqsizlantirish	14
5	Tuberal og'riqsizlantirish	23
6	Qayta bog'lam	3
7	Pastki jag'da tishni olish	32
8	Yuqori jag'da tishni olish	21
9	Ildiz uchi rezektsiyasi	3
10	Gistologik surtma olish	2
11	Distopiyalangan tishni olish	3
12	Olingan tish katakchasiga suniy suyak materialini qo'yish	1
13	Dental implantatga milk shakllantigich o'rnatish	3
14	Transfer yordamida qolip olish	3
15	Karioz kovakni ochish, charxlash, ishlov berish, finirlash	107
16	Karioz kovak plombalash, restavratsiya qilish	107
17	Tish ildiz kanallarini tozalash, kengaytirish, davolash,	73
18	Fissuralarni germetizatsiya qilish	18
19	Olinmaydigan protezlar uchun tishlarni charxlash	123
20	Standart qoshiq yordamida qolip olish	144
21	Individual qoshiq yordamida qolip olish	34
22	Tishlov balandligi va markaziy okklyuziyani aniqlash	167
23	Tish qatori anomaliyasi bor bemorlarni tashxislash	3
	<b>Жами:</b>	<b>879</b>



## II. Ilmiy- tadqiqot ishlari

1. Magistrlik ishim mavzusi **особенности течения многоформной экссудативной эритемы, связанной с герпесвирусной инфекцией** bo'yicha ilmiy rahbarim bilan xirurgik operatsiyalar o'tkazdik.
2. 5-fevralda **FRANCE international scientific-online conference: "SCIENTIFIC APPROACH TO THE MODERN EDUCATION SYSTEM"** da **особенности течения многоформной экссудативной эритемы, связанной с герпесвирусной инфекцией**

Hisobot oyida magistrlik ishim mavzusi « **особенности течения многоформной экссудативной эритемы, связанной с герпесвирусной инфекцией** » dissertatsiyamni yozib tugatdim .

## III. Ilmiy-pedagogik ish

№	Соат	Мавзу	Дарс утувчи
1.	8 soat	O'zbekiston Respublikasi "Ta'lim to'g'risida"gi Qonuni.Tadqiqot ishlarini rejalashtirish	Assistent Axmadov I.N.
2.	8 soat	Tadqiqot ishlarini o'tkazish bosqichlari. Muammoga to'g'ri yondashuv	Assistent Axmadov I.N.
3.	8 soat	Ilmiy- tadqiqot dizayni. Ilmiy izlanish materiali va uslublari	Assistent Axmadov I.N.
4.	8 soat	Ilmiy izlanish kartasini tuzish.Amaliy mashg'ulot tushunchasi, amaliy mashg'ulotni o'tkazish uchun zarur bo'lgan meyoriy hujjatlar	Assistent Axmadov I.N.
5.	8 soat	Ma'ruza tushunchasi, ma'ruzani o'tkazish uchun zarur bo'lgan meyoriy hujjatlar Joriy, oraliq va yakuniy nazorat tushunchalari, ularni o'tkazish usullari	Assistent Axmadov I.N.

## IV. Маънавият – маърифат ишлари:

O'tgan 5 oy davomida tashkil etilgan quyidagi ma'naviy-ma'rifiy tadbirlar va ilmiy-amaliy konferensiyalarda ishtirok etdim:

2023-yil 16-mart (bugun) soat 14:00 da Samarqand davlat tibbiyot universiteti rektori professor, Jasur Rizayevning "**LIDER-BU KIM?**" mavzusidagi mualliflik ma'ruzasiga

2023-yil 25-mart SamDTI kichik majlislar zalida "**КОНФЕРЕНЦИЯ ОБЩЕСТВА ПЛАСТИЧЕСКИХ, РЕКОНСТРУКТИВНЫХ И ЭСТЕТИЧЕСКИХ ХИРУРГОВ УЗБЕКИСТАНА**" ma'ruza va master-klass da ishtirok etdim

2023-yil 28-mart kuni soat 9:00da SamDTU ko'p tarmoqli klinikasi, morfologiya binosida "**БОЛЕЗНИ СОВРЕМЕННОЙ ЦИВИЛИЗАЦИИ: МЕЖДИСЦИПЛИНАРНЫЕ ИССЛЕДОВАНИЯ**" mavzusidagi xalqaro ilmiy-amaliy anjumanida

2023-yil 7-aprel kuni soat 8:30da SamDTU ko'p tarmoqli klinikasi, morfologiya binosida "**ИННОВАЦИОННЫЕ ТЕХНОЛОГИИ В ЗДРАВООХРАНЕНИИ: НОВЫЕ ВОЗМОЖНОСТИ ДЛЯ ВНУТРЕННЕЙ МЕДИЦИНЫ**" mavzusidagi xalqaro ilmiy-amaliy anjumanida

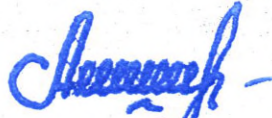
2023-yil 14-aprel kuni soat 9:30da SamDTU ko'p tarmoqli klinikasi, morfologiya binosida "СОВРЕМЕННЫЕ ПОДХОДЫ К ОБРАЗОВАНИЮ, НАУКЕ И КЛИНИЧЕСКОЙ ПРАКТИКЕ ВСТОМАТОЛОГИИ И ЧЕЛЮСТНО-ЛИЦЕВОЙ ХИРУРГИИ" mavzusidagi xalqaro ilmiy-amaliy anjumanida

2023-yil 28-aprel kuni. Soat:10-00 da "Karyera kuni" mehnat yarmarkasi

2023-yil 6-may kuni soat 10:00da Yoshlar markazida SamDTU BITIRUVCHILARI II FORUMIda

2023-yil 19 may kuni soat 9:00da SamDTU ko'p tarmoqli klinikasi, morfologiya binosida "Fundamental, amaliy tibbiyot va farmatsiya yutuqlari" nomli xalqaro ishtirokidagi tibbiyot talabalari va yosh olimlarning 77-ilmiy -amaliy konferensiyasida

Kafedra mudiri:



PhD Axmedov A.A.

Moderator



ass. Axmadov I.N.

Ilmiy rahbar:



PhD Axmedov A.A.

Magistratura talabasi:

Kaki Huda Abdul Salam Hekmat





**SAMARQAND DAVLAT TIBBIYOT UNIVERSITETI**  
**STOMATOLOGIYA (YO'NALISHLAR BO'YICHA) MUTAXASSISLIGI II KURS**  
**MAGISTRATURA REZIDENTI XUDA ABDUL SALAM XEKMAT 2022-2023 O'QUV YILI**  
**UCHUN SHAXSIY KALENDAR REJASI BO'YICHA**  
**YILLIK HISOBOTI**

***I.O'quv va o'quv-uslubiy ish***

		<b>Hisobot davrida o'tilgan seminar darslar</b>	
<b>№</b>	<b>Mavzu</b>	<b>Soat</b>	<b>Dars o'tuvchi</b>
1	Periodontitni davolashning fizioterapevtik usullari Fizioterapevtik uskunalar	8 soat.	Assistent T.f.n. Norbutayev A.B.
2	Xroniosepsisni davolash usullari	8 soat.	Assistent T.f.n. Norbutayev A.B.
3	Tish karashlarini bartaraf qilish va profilaktika usullari	8 soat.	Assistent T.f.n. Norbutayev A.B.
4	Milk qon tomirlari xolatini tekshirish, stomatoskopiya, kapilyaroskopiya, kapillyarlar turg'unligini Kulajenkoning dozalangan vakumi yordamida aniqlash	8 soat.	Assistent T.f.n. Norbutayev A.B.
5	Milk qon tomirlari xolatini tekshirish, stomatoskopiya, kapilyaroskopiya, kapillyarlar turg'unligini Kulajenkoning dozalangan vakumi yordamida aniqlash	8 soat.	Assistent T.f.n. Norbutayev A.B.
6	Parodontal chuntakning sitologik tekshiruvdagi milk suyukligini miqdori va sifatini, leykotsitlar migratsiyasini M.A. Yasinovskiy buyicha laborator tekshirish usullari	8 soat.	Assistent T.f.n. Norbutayev A.B.
7	Parodontal chuntakning sitologik tekshiruvdagi milk suyukligini miqdori va sifatini, leykotsitlar migratsiyasini M.A. Yasinovskiy buyicha laborator tekshirish usullari	8 soat.	Assistent T.f.n. Norbutayev A.B.
8	Sut va doimiy tishlarni davolashning o'ziga xosligi. Bolalarda kariesni davolashda qo'llaniladigan zamonaviy plomba ashyolari. Boshlangich (ok dog) va yuza kariesni maxalliy (ekzogen) va umumiy (endogen) davolash usullari. Bolalarda kariesni davolashda kumushlashning axamiyati	8 soat.	Assistent T.f.n. Norbutayev A.B.
9	Klinik kechishining o'ziga xosligi; Pul'pitni davolashda devitalizatsiyalovchi vositalarni qo'llash; Yallig'langan pul'pitni anesteziya orqali yo'qotish (vital ekstirpatsiya usuli). Pul'paning to'liq va qisman hayotiylik holatini saqlash;	8 soat.	Assistent T.f.n. Norbutayev A.B.
10	Bolalarda parodont kasalliklari. Parodont kasalliklari. Parodont kasalliklari etiologiyasi. Tasnif; Bolalar yoshida parodont tuzilishining o'ziga xosligi;	8 soat.	Assistent T.f.n. Norbutayev A.B.
11	Pubertat yoshida parodont to'qimasida uchraydigan o'zgarishlar..	8 soat.	Assistent PhD Axmedov A.A.
12	Parodontoz. Etiologiya. Patogenez. Klinika. Qiyosiy tashxis.	8 soat.	Assistent PhD Axmedov A.A.
13	Parodont kasalliklarini diagnostikasida qo'llaniladigan indekslar. Bolalarda umumiy somatik kasalliklarda (OIT, endokrin sistemasi,	8 soat.	Assistent PhD Axmedov A.A.



	QTS, asab sistemasi) parodontdagi o'zgarishlar. Etiologiyasi. Patogenezi.Klinikasi. Qiyosiy tashxisi.		
14	Parodont kasalliklarining mahalliy va umumiy profilaktikasi. Davosi. "Papiyon-Lefevr va x - gistiotsitoz sindromlarida parodontdagi uzgarishlar «Xend-Shyuller-Krischen, Osler, Itsenko-Kushing sindromida parodontdagi uzgarishlar».	8 soat.	Assistent PhD Axmedov A.A.
15	Tish qattiq tuqimalari patologiyasini ortopedik davolashda kiritmalarning qullanishi.	8 soat.	Assistent PhD Axmedov A.A.
16	Parodont kasalliklarini turlari. Tarqoq va maxalliy parodontit. Parodont kasalliklarida kompleks stomatologik davolashning ahamiyati. Doimiy va vaqtinchalik shinalarning bemorlarda ishlatilishini ziga xosligi.	8 soat.	Assistent PhD Axmedov A.A.
17	Tish qattiq tuqimasi nuqsonlarida lyumenir va vinirlarning axamiyati. Kursatma va qarshi kursatma. Lyumenir va Vinir uchun tishlarning charxlash taktikasi. Vinir tayerlash uchun klinik laborator usullari. Vinir va lyumenirni tish asosiga fiksatsiyalash. Xatoliklar va asoratlar.	8 soat.	Assistent PhD Axmedov A.A.
18	Immediat protezlarning olib qo'yilmaydigan va olib qo'yiladigan turlari. Immediat protezlarning konstruktiv tuzilmalari. Kursatma va qarshi kursatma, immediat protezni tayyorlashning klinik-laborator bosqichlari. Immediat protezlarning olib qo'yilmaydigan va olib qo'yiladigan turlari. Immediat protezlarning konstruktiv tuzilmalari. Klammer turlari	8 soat.	Assistent PhD Axmedov A.A.
19	Jag'larni to'liq adentiyasida tuliq olib quyiluvchi plastinkali tish protezlarni tayyorlashda yangi yondashuv. Klinik laborator tayyorlash boskichlari. Tuliq olib quyiluvchi protezlarni mukammallashtirish (metal asosli tuliq olib quyiluvchi protez, yumshoq asosli tuliq olib quyiluvchi protez).	8 soat.	Assistent PhD Axmedov A.A.
20	Onkologik kasalliklari bulgan bemorlarda turli asosli kiritmalarni tayyorlashning kliniko-laborator boskichlari.. Somatik va autoimmun kasalliklari bulgan bemorlarda og'iz bushlig'ida ortopedik davo utkazish taktikasi. Bu bemorlarda zamonaviy olib kuyilmaydigan tish protezlari. (oksid sirkon koplamalar) ularga bo'lgan ko'rsatmalar. Somatik kasalliklari bulgan bemorlarda zamonaviy qisman olib kuyilmaydigan tish protezlari. (oksid sirkon koplamalar) ularga bo'lgan ko'rsatmalar	8 soat.	Assistent PhD Axmedov A.A.
21	COVID 19. Kasalligi bilan kasallangan bemorlarda COVID 19 asorati tufayli yukori tanglay nekrozi bulgan bemorlarda protezlashni uziga xosligi	8 soat.	Assistent PhD Axmedov A.A.
22	Kranio-mandibulyar ortodontiya. Moxiyati. Prikusni organizm bilan boglikligi. ALF apparati. Qo'llashga bo'lgan ko'rsatmalar. Xato va asoratlar	8 soat.	Assistent Axmadov I.N.
23	Splintoterapiya. Chakka pastki jag' bo'g'implari va chaynov mushak kasalliklarida davolash uchun qo'llaniladigan ortodontik apparat va ularning turlari. Qo'llashga bo'lgan ko'rsatmalar	8 soat.	Assistent Axmadov I.N.
24	Yechilmaydigan ortodontik apparatlar. Edjuayz tizimini bevosita va bilvosita urnatish usullari	8 soat.	Assistent Axmadov I.N.



25	Twin Block yordamida davolashni asosiy mexiyati. Apparatni riivojlanish tarixi. Twin Block konstruktsiyalari. Kullashga kursatma va karshi kursatma. Twin Block bilan birgalikda kombirinirlangan xolda ishlatiluvchi apparatlar	8 soat.	Assistent Axmadov I.N.
26	Aktivatorlar. Konstruktsiyalari, Kullashga kursatma va karshi kursatma.	8 soat.	Assistent Axmadov I.N.
27	Elayner.Attachmenlar. Konstruktsiyalari . Kullashga kursatma va karshi kursatma. Ortopedik davolashdan olingi ortodontik davolash muolajalari. Uziga xosligi. Bolalarda ortopedik davolashni uziga xos xususiyatlari.	8 soat.	Assistent Axmadov I.N.
28	Ekzostozni xirurgik davolash. Yuqori lab, pastki lab va til yuganchalarida frenulotomiya o'tkazish. Yuz-jag' soxasidagi chandiqlarni olish.	8 soat.	Assistent Axmadov I.N.
29	Og'iz bo'shligida o'smasimon xosilalarni olish (fibroma, epulis) Yuzda yuza joylashgan O'smasimon xosilalarni olish (Ateroma, Lipoma)	8 soat.	Assistent Axmadov I.N.
30	Sinus lifting amaliyoti(ochiq va yopiq) Pastki jag'da o'tkaziladigan implantatsiya.	8 soat.	Assistent Axmadov I.N.
31	Yo'naltirilgan suyuq regeneratsiyasi (NKR). 3D kompyuter tomografiyani o'qish.	8 soat.	Assistent Axmadov I.N.
32	Retsessiyalarni erkin va oyoqchali laxtaklar bilan bartaraf etish. Retsessiyalarni koronar-apekal laxtaklar bilan bartaraf qilish. Paradontitlarda ochiq va yopiq kyuretaj	8 soat.	Assistent Axmadov I.N.
33	Bolalardagi stomatologik kasalliklarda morfologik va sitologik tekshiruv usullari, og'iz bo'shlik shilliq qavatining morfologik tuzulishi Bolalar yuz-jag' sohasi kasalliklarida rentgenologik tekshiruv ahamiyati, o'tkazish usullari va ularning o'ziga xosligi	8 soat.	Assistent Axmadov I.N.
34	Bolalar yuz sohasi suyaklarining anatomik tuzulishi. Bolalarda tish va jag'larning tuzulishi	8 soat.	Assistent Axmadov I.N.
35	Bolalar yuz-jag' sohasini chaynov va mimik mushaklarining anatomo-fiziologik xususiyatlari Bolalar ChPJB anatomo-topografik tuzilishi, funktsiyasi, o'ziga xosligi	8 soat.	Assistent Axmadov I.N.
36	Bolalar stomatologik kasalliklarida maxalliy o'tkazuvchan va infiltratsion og'riksizlantirishning o'ziga xos xususiyatlari	8 soat.	Assistent Axmadov I.N.
37	Tishlarning anomal joylashuvining' etiologiyasi, klinikasi va tasnifi. Tishlarning anomal joylashuvini tashxislash va davolash	8 soat.	Assistent Axmadov I.N.
38	Bolaning yoshiga bog'liq xolda klinik kechishi, tashxislash, operativ va umumiy davolash bosqichlari	8 soat.	Assistent Axmadov I.N.
39	Yuz va jag' suyaklarining yallig'lanish jarayonlari (spetsifik yallig'lanish jarayonlari: aktinamikoz, sil)	8 soat.	Assistent Axmadov I.N.
40	Yuz va jag' suyaklarining yallig'lanish jarayonlari(osteoartrit). Bolaning yoshiga bog'liq xolda klinik kechishi, tashxislash, operativ va umumiy davolash bosqichlari	8 soat.	Assistent Axmadov I.N.

<b>Hisobot davrida o'tkazilgan amaliy ko'nikmalar</b>		
<b>№</b>	<b>Amaliy ko'nikma nomi</b>	<b>Soni</b>
1	Mandibulyar o'tkazuvchi og'riqsizlantirish	81
2	Mahalliy infiltratsion og'riqsizlantirish	224
3	Periostotomiya	7
4	Palatinal og'riqsizlantirish	23
5	Tuberal og'riqsizlantirish	17
6	Qayta bog'lam	7
7	Pastki jag'da tishni olish	24
8	Yuqori jag'da tishni olish	26
9	Ildiz uchi rezektsiyasi	8
10	Gistologik surtma olish	4
11	Distopiyalangan tishni olish	9
12	Olingan tish katakchasiga suniy suyak materiali qo'yish	2
13	Dental implantatga milk shakllantigich o'rnatish	4
14	Transfer yordamida qolip olish	24
15	Karioz kovakni ochish, charxlash, ishlov berish, finirlash	232
16	Karioz kovak plombalash, restavratsiya qilish	212
17	Tish ildiz kanallarini tozalash, kengaytirish, davolash,	147
18	Fissuralarni germetizatsiya qilish	68
19	Olinmaydigan protezlar uchun tishlarni charxlash	256
20	Standart qoshiq yordamida qolip olish	240
21	Individual qoshiq yordamida qolip olish	63
22	Tishlov balandligi va markaziy okklyuziyani aniqlash	243
23	Tish qatori anomaliyasi bor bemorlarni tashxislash	17
	<b>Жами:</b>	<b>1871</b>

## **II. Ilmiy- tadqiqot ishlari**

1. **Magistrlik ishim mavzusi « особенности течения многоформной экссудативной эритемы, связанной с герпесвирусной инфекцией »bo'yicha ilmiy rahbarim T.f.n. Norbutayev A.B.bilan xirurgik operatsiyalar o'tkazdik.**
2. **5-fevralda FRANCE international scientific-online conference: "SCIENTIFIC APPROACH TO THE MODERN EDUCATION SYSTEM" da « особенности течения многоформной экссудативной эритемы, связанной с герпесвирусной инфекцией » maqolam bilan qatnashdim**
3. **« особенности течения многоформной экссудативной эритемы, связанной с герпесвирусной инфекцией »mavzusida dissertatsiyamni yozib tugatdim**



Hisobot oyida magistrlik ishim mavzusi « **особенности течения многоформной экссудативной эритемы, связанной с герпесвирусной инфекцией** » dissertatsiyamni yozib tugatdim .

### III. Ilmiy-pedagogik ish

№	Соат	Мавзу	Дарс утувчи
1.	8 soat	Ilmiy-pedagogik ish nima. Magistraturada ilmiy faoliyat yuritishda meyoriy hujjatlar va ularning mazmuni	Assistent T.f.n. Norbutayev A.B.
2.	8 soat	Pedagogikaning maqsad va vazifalari. Ilmiy mavzu tanlash	Assistent T.f.n. Norbutayev A.B.
3.	8 soat	Magistraturaning maqsad va vazifalari. Pedagogik texnologiyalar	Assistent T.f.n. Norbutayev A.B.
4.	8 soat	Ixtirolartushunchasi va ularning turlari. Patent izlanish.	Assistent T.f.n. Norbutayev A.B.
5.	8 soat	Kadrlar tayyorlash milliy dasturi. Ilmiy ishning annotasiyasi va referatlarga qo'yiladigan talablar	Assistent T.f.n. Norbutayev A.B.
6.	8 soat	O'zbekiston Respublikasi "Ta'lim to'g'risida"gi Qonuni. Tadqiqot ishlarini rejalashtirish	Assistent PhD Axmedov A.A.
7.	8 soat	Tadqiqot ishlarini o'tkazish bosqichlari. Muammoga to'g'ri yondashuv	Assistent PhD Axmedov A.A.
8.	8 soat	Ilmiy- tadqiqot dizayni. Ilmiy izlanish materiali va uslublari	Assistent PhD Axmedov A.A.
9.	8 soat	Ilmiy izlanish kartasini tuzish. Amaliy mashg'ulot tushunchasi, amaliy mashg'ulotni o'tkazish uchun zarur bo'lgan meyoriy hujjatlar	Assistent PhD Axmedov A.A.
10.	8 soat	Ma'ruza tushunchasi, ma'ruzani o'tkazish uchun zarur bo'lgan meyoriy hujjatlar Joriy, oraliq va yakuniy nazorat tushunchalari, ularni o'tkazish usullari	Assistent PhD Axmedov A.A.

**Umummetodologik modullar** doirasida o'tkazilgan quyidagi darslarda ishtirok etdim:

24,25,28,29,30 noyabr, 1,2,5 dekabr **Operativ xirurgiya va topografik anatomiya** jami 48 soat

30-31-yanvar 1-3 fevral kunlari **Nutq madaniyati** kursi 30 jami soat

Barcha fanlardan yakuniy nazoratdan muvaffaqiyatli o'tdim.

### IV. Маънавият – маърифат ишлари:

Yil davomida tashkil etilgan quyidagi ma'naviy-ma'rifiy tadbirlar va ilmiy-amaliy konferensiyalarda ishtirok etdim:

2022-yil 3-4 oktabr, SamDTU 1-sonli klinikaning majlislar zalida «**АКТУАЛЬНЫЕ ВОПРОСЫ УРОЛОГИИ: ЕДИНСТВО ТЕОРИИ И ПРАКТИКИ**» mavzusidagi ilmiy-amaliy anjuman

2022-yil 6-oktabr kuni Samarqand davlat tibbiyot institutini katta majlislar zalida Olga Kravets "Дисколориты зубов. Композитные виниры" mavzusida mualliflik kursi



2022- yil 10- oktabr, SamDTI 1 -sonli klinikasining majlislar zalida, “Osstem implant” kompaniyasi tomonidan “Dental implantologiya bilan tanishuv” mavusida ochiq ma’ruza

2022-yil 7 - oktabr kuni Samarqand davlat tibbiyot institutini 1-son klinikasida “Abu Ali ibn Sino va Buyuk Ipak Yo’li” I xalqaro xalq tabobati bo’yicha ilmiy-amaliy anjuman

2022-yil 12-oktabr Samarqand davlat tibbiyot instituti konferensiyalar zalida dotsent Lim Maksim Vyacheslavovich «Искусство доклада» mavzusida amaliy dars

2022 yil 14- oktyabr kuni Samarqand davlat tibbiyot institutida “Psixiatriya, nevrologiya, neyroxirurgiya va reabilitatsiya: integratsiya qirralari” mavzusidagi xalqaro ilmiy-amaliy anjuman

2022-yil 15 — oktyabr kuni Samarqand Davlat tibbiyot institutida morfologiya binosi kichik majlislar zalida мастер-класс от Помыткиной Татьяны Юрьевны- заведующей кафедрой педагогики, психологии и психосоматической медицины ФГБОУ ВО Ижевской государственной медицинской академии на тему: "Сообщение плохих новостей: навыки врача".

2022-yil 29-oktyabr kuni SamDTU ko’p tarmoqli klinikasi, morfologiya binosida “ИЧКИ KASALLIKLAR TIBBIYOTI SOG’LIQNI SAQLASH TIZIMIDA YETAKCHI O’RINLARDA” mavzusidagi xalqaro ilmiy-amaliy anjuman

2022 yil 8- noyabr, SamDTI 1-sonli klinikaning majlislar zalida professor Andrey Akulevich tomonidan o’tkazilgan «СОВРЕМЕННЫЕ ПОДХОДЫ К УСТРАНЕНИЮ ДИСКЛОРИТОВ ЗУБОВ» mavzusida mualliflik kusi va trening

2022-yil 9-noyabr SamDTI 1-sonli klinikaning majlislar zalida, "МЕДИЦИНСКОЕ ОБРАЗОВАНИЕ И СИСТЕМА ЗДРАВООХРАНЕНИЯ В США И УЗБЕКИСТАНЕ. ОБМЕН ОПЫТОМ В ФОРМАТЕ ДИАЛОГА" mavzusida Xalqaro ilmiy-amaliy konferensiya

2022- yil 21- noyabr, SamDTI 1 -sonli klinikasining majlislar zalida, “Osstem implant” kompaniyasi tomonidan “Dental implantologiya bilan tanishuv” mavusida ochiq ma’ruza

2022-yil 14-dekabr kuni SamDTU ko’p tarmoqli klinikasi, morfologiya binosida **“Высокие технологии в хирургии”** mavzusidagi xalqaro ilmiy-amaliy anjumani

2022- yil 21- dekabr, SamDTI 1 -sonli klinikasining majlislar zalida, “Osstem implant” kompaniyasi tomonidan “Dental implantatlar ustida ortopedik konstruksiyalar uchun qolip olish” mavusida ochiq ma’ruza

2022-yil 22-dekabrda Og’iz bo’shlig’i jarrohligi va dental implantologiya kafedrasida “Osstem implant” kompaniyasi tomonidan o’tkazilgan amaliy master klass

2023-yil 16-mart (bugun) soat 14:00 da Samarqand davlat tibbiyot universiteti rektori professor, Jasur Rizayevning **“LIDER-BU KIM?”** mavzusidagi mualliflik ma’ruzasiga

2023-yil 25-mart SamDTI kichik majlislar zalida **“КОНФЕРЕНЦИЯ ОБЩЕСТВА ПЛАСТИЧЕСКИХ, РЕКОНСТРУКТИВНЫХ И ЭСТЕТИЧЕСКИХ ХИРУРГОВ УЗБЕКИСТАНА ”** ma’ruza va master-klass da ishtirok etdim

2023-yil 28-mart kuni soat 9:00da SamDTU ko’p tarmoqli klinikasi, morfologiya binosida **“БОЛЕЗНИ СОВРЕМЕННОЙ ЦИВИЛИЗАЦИИ: МЕЖДИСЦИПЛИНАРНЫЕ ИССЛЕДОВАНИЯ”** mavzusidagi xalqaro ilmiy-amaliy anjumanida

2023-yil 7-aprel kuni soat 8:30da SamDTU ko’p tarmoqli klinikasi, morfologiya binosida **“ИННОВАЦИОННЫЕ ТЕХНОЛОГИИ В ЗДРАВООХРАНЕНИИ: НОВЫЕ ВОЗМОЖНОСТИ ДЛЯ ВНУТРЕННЕЙ МЕДИЦИНЫ”** mavzusidagi xalqaro ilmiy-amaliy anjumanida

2023-yil 14-aprel kuni soat 9:30da SamDTU ko’p tarmoqli klinikasi, morfologiya binosida **“СОВРЕМЕННЫЕ ПОДХОДЫ К ОБРАЗОВАНИЮ, НАУКЕ И КЛИНИЧЕСКОЙ ПРАКТИКЕ ВСТОМАТОЛОГИИ И ЧЕЛЮСТНО-ЛИЦЕВОЙ ХИРУРГИИ”** mavzusidagi xalqaro ilmiy-amaliy anjumanida

2023-yil 28-aprel kuni. Soat:10-00 da **“Karyera kuni”** mehnat yarmarkasi

2023-yil 6-may kuni soat 10:00da Yoshlar markazida SamDTU **BITIRUVCHILARI II FORUMI**da  
2023-yil 19 may kuni soat 9:00da SamDTU ko'p tarmoqli klinikasi, morfologiya binosida  
**"Fundamental, amaliy tibbiyot va farmatsiya yutuqlari"** nomli xalqaro ishtirokidagi tibbiyot  
talabalari va yosh olimlarning 77-ilmiy -amaliy konferensiyasida

Kafedra mudiri:



PhD Axmedov A.A.

Moderator



ass. Axmadov I.N.

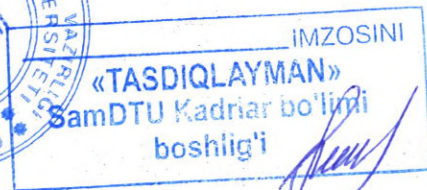
Ilmiy rahbar:



PhD Axmedov A.A.

Magistratura talabasi:

Kaki Huda Abdul Salam Hekmat





САМАРҚАНД ДАВЛАТ ТИББИЁТ УНИВЕРСИТЕТИ

ОРТОПЕДИК СТОМАТОЛОГИЯ КАФЕДРАСИ

КАФЕДРА ЙИЎИЛИШИНИНГ 6-СОНЛИ

БАЁННОМАСИДАН

КЎЧИРМА

7 Февраль 2023 йил

**ҚАТНАШГАНЛАР:** кафедра мудири т.ф.н. Норбутаев А.Б., PhD Ахмедов А.А., асс. Ортикова Н.Х., асс. Исламова Н.Б., асс. Иргашев Ш.Х., асс. Махмудова У.Б., асс. Ахмадов И.Н., асс. Санакулов Ж.О., асс. Бурханова З.К., асс. Давлатова С.М., Губаев М.С.

**КУН ТАРТИБИ:** Ортопедик стоматология кафедраси “Стоматология(йўналишлар бўйича)” мутахассислиги бўйича иккинчи йил магистратура талабаси Каки Абдул Салам Хекмат ярим йиллик аттестацияга тайёлиги тўғрисида муҳокамаси.

**ЭШИТИЛДИ:** Ортопедик стоматология кафедраси “Стоматология(йўналишлар бўйича)” мутахассислиги бўйича иккинчи йил магистратура талабаси Каки Абдул Салам Хекмат ярим йиллик аттестацияга тайёрлиги ва барча хужжатлари мавжудлиги тўғрисида И.Н.Ахмадов такидлади.

**ҚАРОР ҚАБУЛ ҚИЛИНДИ:** Юқорида қайд қилинган Ортопедик стоматология кафедраси “Стоматология(йўналишлар бўйича)” 2-босқич магистри Каки Абдул Салам Хекмат. Аттестацияга киришга рухсат берилсин.

/ Кафедра мудири, т.ф.н.

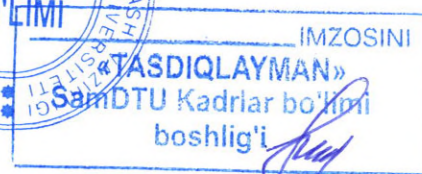


Норбутаев А.Б.

Модератор:



Ахмадов И.Н.



**Иммунологические исследования**

Лизоцим слюны (титры)	
SIgA слюны, мг%	
ФАН слюны, %	

**Бактериологическое исследование**

Стрептококки ки LgKOE/ml	
Стафилококки ки LgKOE/ml	
Лактобактерии LgKOE/ml	
Грибы рода Кандида	

**Состояние порога ощущения**

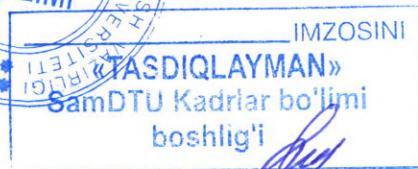
Норма	
Повышение	
Понижение	
Извращение	
Отсутствие	
Изм.иф порога	

Сонскатель:

Каки Худа Абдул Салам Хекмат

Научного руководитель

К.м.н Ахмедов А.А





**SAMARQAND DAVLAT TIBBIYOT UNIVERSITETI**  
**STOMATOLOGIYA (YO'NALISHLAR BO'YICHA) YO'NALISHI II KURS**  
**MAGISTRATURA REZIDENTI KAKI HUDA ABDUL SALAM HEKMATNING 2022-2023**  
**O'QUV YILI UCHUN SHAXSIY KALENDAR REJASI BO'YICHA NOYABR OYI**  
**HISOBOTI**

**I. O'quv va o'quv-uslubiy ish**

<b>Hisobot davrida o'tilgan seminar darslar</b>			
№	Mavzu	Soat	Dars o'tuvchi
1	Sut va doimiy tishlarni davolashning o'ziga xosligi. Bolalarda kariesni davolashda qo'llaniladigan zamonaviy plomba ashyolari. Boshlangich (ok dog) va yuza kariesni maxalliy (ekzogen) va umumiy (endogen) davolash usullari. Bolalarda kariesni davolashda kumushlashning axamiyati		Assistent Axmedov A.A
2	Klinik kechishining o'ziga xosligi; Pulbipitni davolashda devitalizatsiyalovchi vositalarni qo'llash; Yallig'langan pulbipitni anesteziya orqali yo'qotish (vital ekstirpatsiya usuli). Pulpaning to'liq va qisman hayotiylik holatini saqlash;	8 soat.	Assistent Axmedov A.A.
3	Bolalarda parodont kasalliklari. Parodont kasalliklari. Parodont kasalliklari etiologiyasi. Tasnif; Bolalar yoshida parodont tuzilishining o'ziga xosligi;	8 soat.	Assistent t.f.n. Axmedov A.A.
4	Pubertat yoshida parodont to'qimasida uchraydigan o'zgarishlar..	8 soat.	Assistent t.f.n. Axmedov A.A.

<b>Hisobot davrida o'tkazilgan amaliy ko'nikmalar</b>		
№	Amaliy ko'nikma nomi	Soni
1	Mandibulyar o'tkazuvchi og'riqsizlantirish	9
2	Mahalliy infiltratsion og'riqsizlantirish	18
3	Periostotomiya	4
4	Palatinal og'riqsizlantirish	3
5	Tuberal og'riqsizlantirish	4
6	Qayta bog'lam	2
7	Pastki jag'da tishni olish	11
8	Yuqori jag'da tishni olish	10
9	Ildiz uchi rezektsiyasi	4
10	Gistologik surtma olish	
11	Distopiyalangan tishni olish	1
12	Olingan tish katakchasiga suniy suyak materiali qo'yish	
13	Dental implantatga milk shakllantigich o'rnatish	2
14	Transfer yordamida qolip olish	
15	Karioz kovakni ochish, charxlash, ishlov berish, finirlash	20
16	Karioz kovak plombalash, restavratsiya qilish	16
17	Tish ildiz kanallarini tozalash, kengaytirish, davolash,	18



18	Fissuralarni germetizatsiya qilish	7
19	Olinmaydigan protezlar uchun tishlarni charxlash	26
20	Standart qoshiq yordamida qolip olish	24
21	Individual qoshiq yordamida qolip olish	15
22	Tishlov balandligi va markaziy okklyuziyani aniqlash	24
23	Tish qatori anomaliyasi bor bemorlarni tashxislash	2
	<b>Жами:</b>	<b>198</b>

## *II. Ilmiy- tadqiqot ishlari*

1. Noyabr oyida magistrlik mavzusi «**features of the course of erythema multiple form associated with herpes viral infection**» bo'yicha ilmiy rahbarim t.f.n Axmedov A.A. bilan ortopedik amaliyot o'tkazdik.

Hisobot oyida ilmiy ishimning mavzusiga aloqador bemorlarda o'tkazilgan operatsiyalar natijalarini tahlil qilishni davom ettirdim.

## *III. Ilmiy-pedagogik ish*

№	Соат	Мавзу	Дарс утувчи
1	4 soat	Magistraturaning maqsad va vazifalari.	Assistent t.f.n. Axmedov A.A
2	4 soat	Pedagogik texnologiyalar	Assistent t.f.n. Axmedov A.A

**Umummetodologik modullar** doirasida o'tkazilgan quyidagi darslarda ishtirok etdim:  
24,25,28,29,30 noyabr, 1,2,5 dekabr **Operativ xirurgiya va topografik anatomiya** jami 48 soat  
Barcha fanlardan yakuniy nazoratdan muvaffaqiyatli o'tdim.

## *IV. Маънавият – маърифат ишлари:*

Noyabr oyi davomida tashkil etilgan quyidagi ma'naviy-ma'rifiy tadbirlar va ilmiy-amaliy konferensiyalarda ishtirok etdim:

2022 yil 8- noyabr, SamDTI 1-sonli klinikaning majlislar zalida professor Andrey Akulevich tomonidan o'tkazilgan «**СОВРЕМЕННЫЕ ПОДХОДЫ К УСТРАНЕНИЮ ДИСКОЛОРИТОВ ЗУБОВ**» mavzusida mualliflik kusi va trening

2022-yil 9-noyabr SamDTI 1-sonli klinikaning majlislar zalida, "МЕДИЦИНСКОЕ ОБРАЗОВАНИЕ И СИСТЕМА ЗДРАВООХРАНЕНИЯ В США И УЗБЕКИСТАНЕ. ОБМЕН ОПЫТОМ В ФОРМАТЕ ДИАЛОГА" mavzusida Xalqaro ilmiy-amaliy konferensiya  
2022- yil 21- noyabr, SamDTI 1 -sonli klinikasining majlislar zalida, "Osstem implant" kompaniyasi tomonidan "Dental implantologiya bilan tanishuv" mavusida ochiq ma'ruza

**Kafedra mudiri:**



**t.f.n.Norbutayev A.B.**

**Moderator**



**Axmadov I.N.**

**Ilmiy rahbar:**

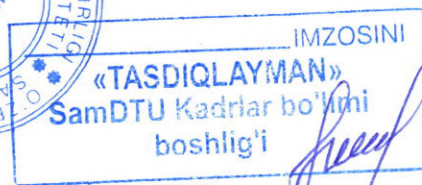


**t.f.n. Axmedov A.A**

**Magistratura talabasi:**



**Kaki Abdul Salam Hekmat**



**SAMARQAND DAVLAT TIBBIYOT UNIVERSITETI**  
**STOMATOLOGIYA (YO'NALISHLAR BO'YICHA) YO'NALISHI II KURS**  
**MAGISTRATURA REZIDENTI KAKI HUDA ABDUL SALAM HEKMATNING 2022-2023**  
**O'QUV YILI UCHUN SHAXSIY KALENDAR REJASI BO'YICHA YANVAR OYI**  
**HISOBOTI**

**I.O'quv va o'quv-uslubiy ish**

<b>Hisobot davrida o'tilgan seminar darslar</b>			
№	Mavzu	Soat	Dars o'tuvchi
1	Tish qattiq tuqimasi nuqsonlarida lyumenir va vinirlarning axamiyati. Kursatma va qarshi kursatma. Lyumenir va Vinir uchun tishlarning charxlash taktikasi. Vinir tayirlash uchun klinik laborator usullari. Vinir va lyumenirni tish asosiga fiksatsiyalash. Xatoliklar va asoratlar.	8 soat.	Assistent t.f.n. Axmedov A.A
2	Immediat protezlarning olib qo'yilmaydigan va olib qo'yiladigan turlari. Immediat protezlarning konstruktiv tuzilmalari. Kursatma va qarshi kursatma, immediat protezni tayyorlashning klinik-laborator bosqichlari. Immediat protezlarning olib qo'yilmaydigan va olib qo'yiladigan turlari. Immediat protezlarning konstruktiv tuzilmalari. Klammer turlari	8 soat.	Assistent t.f.n. Axmedov A.A
3	Jag'larni to'liq adentiyasida tuliq olib quyiluvchi plastinkali tish protezlarni tayyorlashda yangi yondashuv. Klinik laborator tayyorlash bosqichlari. Tuliq olib quyiluvchi protezlarni mukammallashtirish (metal asosli tuliq olib quyiluvchi protez, yumshoq asosli tuliq olib quyiluvchi protez).	8 soat.	Assistent t.f.n. Axmedov A.A
4	Onkologik kasalliklari bulgan bemorlarda turli asosli kiritmalarni tayyorlashning kliniko-laborator bosqichlari.. Somatik va autoimmun kasalliklari bulgan bemorlarda og'iz bushlig'ida ortopedik davo utkazish taktikasi. Bu bemorlarda zamonaviy olib quyilmaydigan tish protezlari. (oksid sirkon koplamlar) ularga bo'lgan ko'rsatmalar. Somatik kasalliklari bulgan bemorlarda zamonaviy qisman olib quyilmaydigan tish protezlari. (oksid sirkon koplamlar) ularga bo'lgan ko'rsatmalar	8 soat.	Assistent t.f.n. Axmedov A.A
5	COVID 19. Kasalligi bilan kasallangan bemorlarda COVID 19 asorati tufayli yukori tanglay nekrozi bulgan bemorlarda protezlarni uziga xosligi	8 soat.	Assistent t.f.n. Axmedov A.A

**Hisobot davrida o'tkazilgan amaliy ko'nikmalar**

№	Amaliy ko'nikma nomi	Soni



1	Mandibulyar o'tkazuvchi og'riqsizlantirish	10
2	Mahalliy infiltratsion og'riqsizlantirish	17
3	Periostotomiya	6
4	Palatinal og'riqsizlantirish	3
5	Tuberal og'riqsizlantirish	7
6	Qayta bog'lam	10
7	Pastki jag'da tishni olish	16
8	Yuqori jag'da tishni olish	18
9	Ildiz uchi rezektsiyasi	3
10	Gistologik surtma olish	6
11	Distopiyalangan tishni olish	15
12	Olingan tish katakchasiga suniy suyak materiali qo'yish	2
13	Dental implantatga milk shakllantigich o'rnatish	1
14	Transfer yordamida qolip olish	2
15	Karioz kovakni ochish, charxlash, ishlov berish, finirlash	12
16	Karioz kovak plombalash, restavratsiya qilish	18
17	Tish ildiz kanallarini tozalash, kengaytirish, davolash,	15
18	Fissuralarni germetizatsiya qilish	9
19	Olinmaydigan protezlar uchun tishlarni charxlash	28
20	Standart qoshiq yordamida qolip olish	25
21	Individual qoshiq yordamida qolip olish	5
22	Tishlov balandligi va markaziy okklyuziyani aniqlash	30
23	Tish qatori anomaliyasi bor bemorlarni tashxislash	3
	<b>Жами:</b>	<b>207</b>

## II. Ilmiy- tadqiqot ishlari

1. Yanvarda magistrlik ishim mavzusi «**features of the course of erythema multiple form associated with herpes viral infection**» mavzusida dissertatsiyamning 3-bobini yozib tugatdim

## III. Ilmiy-pedagogik ish

№	Соат	Мавзу	Дарс утувчи
	4 soat	Kadrlar tayyorlash milliy dasturi	Assistent t.f.n. Axmedov A.A.
	4 soat	Ilmiy ishning annotasiyasi va referatlarga qo'yiladigan talablar	Assistent t.f.n. Axmedov A.A.

**Umummetodologik modullar** doirasida o'tkazilgan quyidagi darslarda ishtirok etdim:

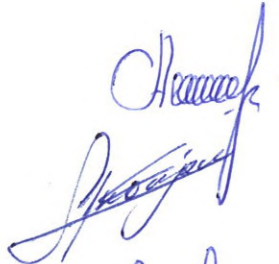
30-31-yanvar 1-3 fevral kunlari **Nutq madaniyati** kursi 30 jami soat

Barcha fanlardan yakuniy nazoratdan muvaffaqiyatli o'tdim.

**IV. Маънавият – маърифат ишлари:**


Yanvar oyi davomida tashkil etilgan ma'naviy-ma'rifiy tadbirlar va ilmiy-amaliy konferensiyalarda ishtirok etdim:

**Kafedra mudiri:**



**t.f.n. Normurad ov A.B.**

**Moderator**



**ass. Axmadov I.N.**

**Ilmiy rahbar:**

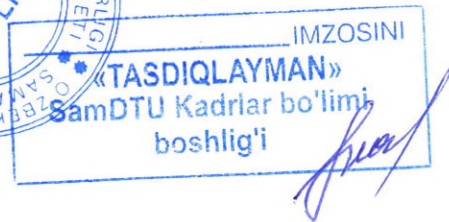


**t.f.n. Axmedov A.A**

**Magistratura talabasi:**



**Kaki Abdul Salam Hekmat**



**SAMARQAND DAVLAT TIBBIYOT UNIVERSITETI**  
**STOMATOLOGIYA (YO'NALISHLAR BO'YICHA) YO'NALISHI II KURS**  
**MAGISTRATURA REZIDENTI KAKI HUDA ABDUL SALAM HEKMATNING 2022-2023**  
**O'QUV YILI UCHUN SHAXSIY KALENDAR REJASI DEKABR OYI HISOBOTI**

**I.O'quv va o'quv-uslubiy ish**

<b>Hisobot davrida o'tilgan seminar darslar</b>			
№	Mavzu	Soat	Dars o'tuvchi
1	Parodontoz. Etiologiya. Patogenez. Klinika. Qiyosiy tashxis.	8 soat.	Assistent t.f.n. Axmedov A.A
2	Parodont kasalliklarini diagnostikasida qo'llaniladigan indekslar. Bolalarda umumiy somatik kasalliklarda (OIT, endokrin sistemasi, QTS, asab sistemasi) parodontdagi o'zgarishlar. Etiologiyasi. Patogenezi.Klinikasi. Qiyosiy tashxisi.	8 soat.	Assistent t.f.n. Axmedov A.A.
3	Parodont kasalliklarining mahalliy va umumiy profilaktikasi. Davosi. "Papiyon-Lefevr va x - gistiotsitoz sindromlarida parodontdagi uzgarishlar «Xend-Shyuller-Krischen, Osler, Itsenko-Kushing sindromida parodontdagi uzgarishlar».	8 soat.	Assistent t.f.n. Axmedov A.A
4	Parodontoz. Etiologiya. Patogenez. Klinika. Qiyosiy tashxis.	8 soat.	Assistent t.f.n. Axmedov A.A
5	Tish qattiq tuqimalari patologiyasini ortopedik davolashda kiritmalarning qullanishi.	8 soat.	Assistent t.f.n. Axmedov A.A
6	Parodont kasalliklarini turlari. Tarqoq va maxalliy parodontit. Parodont kasalliklarida kompleks stomatologik davolashning ahamiyati. Doimiy va vaqtinchalik shinalarning bemorlarda ishlatilishini ziga xosligi.	8 soat.	Assistent t.f.n. Axmedov A.A

<b>Hisobot davrida o'tkazilgan amaliy ko'nikmalar</b>		
№	Amaliy ko'nikma nomi	Soni
1	Mandibulyar o'tkazuvchi og'riqsizlantirish	7
2	Mahalliy infiltratsion og'riqsizlantirish	16
3	Periostotomiya	4
4	Palatinal og'riqsizlantirish	3
5	Tuberal og'riqsizlantirish	2
6	Qayta bog'lam	1
7	Pastki jag'da tishni olish	9
8	Yuqori jag'da tishni olish	12
9	Ildiz uchi rezektsiyasi	1
10	Gistologik surtma olish	



11	Distopiyalangan tishni olish	2
12	Olingan tish katakchasiga suniy suyak materiali qo'yish	
13	Dental implantatga milk shakllantigich o'rnatish	2
14	Transfer yordamida qolip olish	
15	Karioz kovakni ochish, charxlash, ishlov berish, finirlash	18
16	Karioz kovak plombalash, restavratsiya qilish	12
17	Tish ildiz kanallarini tozalash, kengaytirish, davolash,	18
18	Fissuralarni germetizatsiya qilish	7
19	Olinmaydigan protezlar uchun tishlarni charxlash	25
20	Standart qoshiq yordamida qolip olish	25
21	Individual qoshiq yordamida qolip olish	16
22	Tishlov balandligi va markaziy okklyuziyani aniqlash	24
23	Tish qatori anomaliyasi bor bemorlarni tashxislash	1
	<b>Жами:</b>	<b>201</b>

## II. Ilmiy- tadqiqot ishlari

1. Dekabr oyida magistrlik mavzusi «**Features of the course of erythema multiple form associated with herpes viral infection**» bo'yicha ilmiy rahbarim t.f.n.Axmedov A.A. ortopedik amaliyot o'tkazdik o'tkazdik.

Hisobot oyida ilmiy ishning mavzusiga aloqador bemorlarda o'tkazilgan operatsiyalar natijalarini tahlil qilishni davom ettirdim.

## III. Ilmiy-pedagogik ish

№	Соат	Мавзу	Дарс утувчи
1	4 soat	Ixtirolar tushunchasi va ularning turlari.	Assistent t.f.n. Axmedov A.A
2	4 soat	Patent izlanish.	Assistent t.f.n. Axmedov A.A
3	4 soat	Kadrlar tayyorlash milliy dasturi.	Assistent t.f.n. Axmedov A.A
4	4 soat	Ilmiy ishning annotasiyasi va referatlarga qo'yiladigan talablar	Assistent t.f.n. Axmedov A.A

**Umummetodologik modullar** doirasida o'tkazilgan quyidagi darslarda ishtirok etdim:  
24,25,28,29,30 noyabr, 1,2,5 dekabr **Operativ xirurgiya va topografik anatomiya** jami 48 soat  
Barcha fanlardan yakuniy nazoratdan muvaffaqiyatli o'tdim.

## IV. Маънавият – маърифат ишлари:

Dekabr oyi davomida tashkil etilgan quyidagi ma'naviy-ma'rifiy tadbirlar va ilmiy-amaliy konferensiyalarda ishtirok etdim:

2022-yil 14-dekabr kuni SamDTU ko'p tarmoqli klinikasi, morfologiya binosida "Высокие технологии в хирургии" mavzusidagi xalqaro ilmiy-amaliy anjumani

2022- yil 21- dekabr, SamDTI 1 -sonli klinikasining majlislar zalida, "Osstem implant" kompaniyasi tomonidan "Dental implantatlar ustida ortopedik konstruksiyalar uchun qolip olish" mavusida ochiq ma'ruza

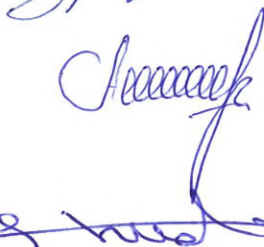
2022-yil 22-dekabrda Og'iz bo'shlig'i jarrohligi va dental implantologiya kafedrasida "Osstem implant" kompaniyasi tomonidan o'tkazilgan master klass

**Kafedra mudiri:**



**t.f.n.Norbutayev A.B.**

**Moderator**



**Axmadov I.N.**

**Ilmiy rahbar:**



**t.f.n. Axmedov A.A**

**Magistratura talabasi:**



**Kaki Abdul Salam Hekmat**





**SAMARQAND DAVLAT TIBBIYOT UNIVERSITETI**  
**STOMATOLOGIYA (YO'NALISHLAR BO'YICHA) MUTAXASSISLIGI II KURS**  
**MAGISTRATURA REZIDENTI KAKI HUDA ABDUL SALAM HEKMAT 2022-2023**  
**O'QUV YILI UCHUN SHAXSIY KALENDAR REJASI BO'YICHA SENTABR-OKTABR**  
**OYI UCHUN HISOBOTI**

**I.O'quv va o'quv-uslubiy ish**

<b>Hisobot davrida o'tilgan seminar darslar</b>			
№	Mavzu	Soat	Dars o'tuvchi
1	Periodontitni davolashning fizioterapevtik usullari Fizioterapevtik uskunalari	4 soat.	Assistent t.f.n. Axmedov A.A
2	Xroniosepsisni davolash usullari	4 soat.	Assistent t.f.n. Axmedov A.A
3	Tish karashlarini bartaraf qilish va profilaktika usullari	4 soat.	Assistent t.f.n. Axmedov A.A
4	Milk qon tomirlari xolatini tekshirish, stomatoskopiya, kapilyaroskopiya, kapillyarlar turg'unligini Kulajenkoning dozalangan vakumi yordamida aniqlash	4 soat.	Assistent t.f.n. Axmedov A.A
5	Milk qon tomirlari xolatini tekshirish, stomatoskopiya, kapilyaroskopiya, kapillyarlar turg'unligini Kulajenkoning dozalangan vakumi yordamida aniqlash	4 soat.	Assistent t.f.n. Axmedov A.A.
6	Parodontal chuntakning sitologik tekshiruvdagi milk suyukligini mikdori va sifatini, leykotsitlar migratsiyasini M.A. Yasinovskiy buyicha laborator tekshirish usullari	4 soat.	Assistent t.f.n. Axmedov A.A
7	Parodontal chuntakning sitologik tekshiruvdagi milk suyukligini mikdori va sifatini, leykotsitlar migratsiyasini M.A. Yasinovskiy buyicha laborator tekshirish usullari	4 soat.	Assistent t.f.n. Axmedov A.A

<b>Hisobot davrida o'tkazilgan amaliy ko'nikmalar</b>		
№	Amaliy ko'nikma nomi	Soni
1	Mandibulyar o'tkazuvchi og'riqsizlantirish	22
2	Mahalliy infiltratsion og'riqsizlantirish	24
3	Periostotomiya	5
4	Palatinal og'riqsizlantirish	3
5	Tuberal og'riqsizlantirish	3
6	Qayta bog'lam	4
7	Pastki jag'da tishni olish	18
8	Yuqori jag'da tishni olish	12
9	Ildiz uchi rezektsiyasi	3
10	Gistologik surtma olish	1
11	Distopiyalangan tishni olish	2
12	Olingan tish katakchasiga suniy suyak materiali qo'yish	1
13	Dental implantatga milk shakllantigich o'rnatish	

14	Transfer yordamida qolip olish	2
15	Karioz kovakni ochish, charxlash, ishlov berish, finirlash	26
16	Karioz kovak plombalash, restavratsiya qilish	20
17	Tish ildiz kanallarini tozalash, kengaytirish, davolash,	21
18	Fissuralarni germetizatsiya qilish	16
19	Olinmaydigan protezlar uchun tishlarni charxlash	44
20	Standart qoshiq yordamida qolip olish	44
21	Individual qoshiq yordamida qolip olish	25
22	Tishlov balandligi va markaziy okklyuziyani aniqlash	22
23	Tish qatori anomaliyasi bor bemorlarni tashxislash	2
	<b>Жами:</b>	<b>318</b>

## II. Ilmiy- tadqiqot ishlari

1. Oktabr oyida magistrlik mavzusi «**features of the course of erythema multiple form associated with herpes viral infection**» bo'yicha ilmiy rahbarim t.f.n.Axmedov A.A. bilan ortopedik amaliyotlar o'tkazdik.

Hisobot oyida ilmiy ishining mavzusiga aloqador bemorlarda o'tkazilgan operatsiyalar natijalarini tahlil qilishni boshladim.

## III. Ilmiy-pedagogik ish

№	Соат	Мавзу	Дарс утувчи
1.	4 soat	Ilmiy-pedagogik ish nima.	Assistent t.f.n. Axmedov A.A
2.	4 soat	Magistraturada ilmiy faoliyat yuritishda meyoriy hujjatlar va ularning mazmuni	Assistent t.f.n. Axmedov A.A
3.	4 soat	Pedagogikaning maqsad va vazifalari.	Assistent t.f.n. Axmedov A.A
4.	4 soat	Ilmiy mavzu tanlash	Assistent t.f.n Axmedov A.A

11-oktyabr 2022-yil “**Fixation of metal-ceramic prostheses**”

20-oktabr 2022-yil “**Partial removable arch prostheses**”

**Shu mavzularda ochiq darslar o'tdim**

**Umummetodologik modullar** doirasida o'tkazilgan quyidagi darslarda ishtirok etdim:

## IV. Маънавият – маърифат ишлари:

Sentabr-oktabr oyi davomida tashkil etilgan quyidagi ma'naviy-ma'rifiy tadbirlar va ilmiy-amaliy konferensiyalarda ishtirok etdim:

2022-yil 3-4 oktabr, SamDTU 1-sonli klinikaning majlislar zalida «**АКТУАЛЬНЫЕ ВОПРОСЫ УРОЛОГИИ: ЕДИНСТВО ТЕОРИИ И ПРАКТИКИ**» mavzusidagi ilmiy-amaliy anjuman



2022-yil 6-oktabr kuni Samarqand davlat tibbiyot institutini katta majlislar zalida Olga Kravets “Дисколориты зубов. Композитные виниры” mavzusida mualliflik kursi

2022- yil 10- oktabr, SamDTI 1 -sonli klinikasining majlislar zalida, “Osstem implant” kompaniyasi tomonidan “Dental implantologiya bilan tanishuv” mavusida ochiq ma’ruza

2022-yil 7 - oktabr kuni Samarqand davlat tibbiyot institutini 1-son klinikasida “Abu Ali ibn Sino va Buyuk Ipak Yo‘li” I xalqaro xalq tabobati bo‘yicha ilmiy-amaliy anjuman

2022-yil 12-oktabr Samarqand davlat tibbiyot instituti konferensiyalar zalida dotsent Lim Maksim Vyacheslavovich «Искусство доклада» mavzusida amaliy dars

2022 yil 14- oktyabr kuni Samarqand davlat tibbiyot institutida “Psixiatriya, nevrologiya, neyroxirurgiya va rehabilitatsiya: integratsiya qirralari” mavzusidagi xalqaro ilmiy-amaliy anjuman

2022-yil 15 — oktyabr kuni Samarqand Davlat tibbiyot institutida morfologiya binosi kichik majlislar zalida мастер-класс от Помыткиной Татьяны Юрьевны- заведующей кафедрой педагогики, психологии и психосоматической медицины ФГБОУ ВО Ижевской государственной медицинской академии на тему: "Сообщение плохих новостей: навыки врача".

2022-yil 29-oktyabr kuni SamDTU ko‘p tarmoqli klinikasi, morfologiya binosida “ICHKI KASALLIKLAR TIBBIYOTI SOG‘LIQNI SAQLASH TIZIMIDA YETAKCHI O‘RINLARDA” mavzusidagi xalqaro ilmiy-amaliy anjuman

**Kafedra mudiri:**

  
t.f.n.Norbutayev A.B.

**Moderator**

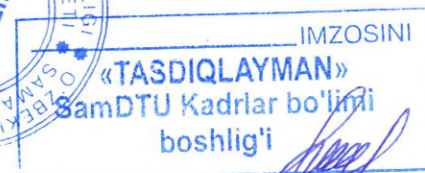
  
Axmadov I.N.

**Ilmiy rahbar:**

  
t.f.n. Axmedov A.A

**Magistratura talabasi:**

  
Kaki Abdul Salam Hekmat



**SAMARQAND DAVLAT TIBBIYOT UNIVERSITETI**  
**STOMATOLOGIYA (YO'NALISHLAR BO'YICHA) MUTAXASSISLIGI II KURS**  
**MAGISTRATURA REZIDENTI KAKI HUDA ABDUL SALAM HEKMATNING 2022-2023**  
**O'QUV YILI UCHUN SHAXSIY KALENDAR REJASI BO'YICHA BIRINCHI**  
**YARIM YILLIK HISOBOTI**

*I.O'quv va o'quv-uslubiy ish*

		<b>Hisobot davrida o'tilgan seminar darslar</b>	
№	Mavzu	Soat	Dars o'tuvchi
1	Periodontitni davolashning fizioterapevtik usullari Fizioterapevtik uskunalari	8 soat.	Assistent t.f.n. Axmedov A.A.
2	Xroniosepsisni davolash usullari	8 soat.	Assistent t.f.n. Axmedov A.A.
3	Tish karashlarini bartaraf qilish va profilaktika usullari	8 soat.	Assistent t.f.n. Axmedov A.A.
4	Milk qon tomirlari xolatini tekshirish, stomatoskopiya, kapilyaroskopiya, kapillyarlar turg'unligini Kulajenkoning dozalangan vakumi yordamida aniqlash	8 soat.	Assistent t.f.n. Axmedov A.A.
5	Milk qon tomirlari xolatini tekshirish, stomatoskopiya, kapilyaroskopiya, kapillyarlar turg'unligini Kulajenkoning dozalangan vakumi yordamida aniqlash	8 soat.	Assistent t.f.n. Axmedov A.A.
6	Parodontal chuntakning sitologik tekshiruvidagi milk suyukligini miqdori va sifatini, leykotsitlar migratsiyasini M.A. Yasinovskiy buyicha laborator tekshirish usullari	8 soat.	Assistent t.f.n. Axmedov A.A.
7	Parodontal chuntakning sitologik tekshiruvidagi milk suyukligini miqdori va sifatini, leykotsitlar migratsiyasini M.A. Yasinovskiy buyicha laborator tekshirish usullari	8 soat.	Assistent t.f.n. Axmedov A.A.
8	Sut va doimiy tishlarni davolashning o'ziga xosligi. Bolalarda kariesni davolashda qo'llaniladigan zamonaviy plomba ashyolari. Boshlangich (ok dog) va yuza kariesni maxalliy (ekzogen) va umumiy (endogen) davolash usullari. Bolalarda kariesni davolashda kumushlashning ahamiyati	8 soat.	Assistent t.f.n. Axmedov A.A.
9	Klinik kechishining o'ziga xosligi; Pul'pitni davolashda devitalizatsiyalovchi vositalarni qo'llash; Yallig'langan pul'pitni anesteziya orqali yo'qotish (vital ekstirpatsiya usuli). Pul'paning to'liq va qisman hayotiylik holatini saqlash;	8 soat.	Assistent t.f.n. Axmedov A.A.
10	Bolalarda parodont kasalliklari. Parodont kasalliklari. Parodont kasalliklari etiologiyasi. Tasnif; Bolalar yoshida parodont tuzilishining o'ziga xosligi;	8 soat.	Assistent t.f.n. Axmedov A.A.
11	Pubertat yoshida parodont to'qimasida uchraydigan o'zgarishlar..	8 soat.	Assistent t.f.n. Axmedov A.A.



12	Parodontoz. Etiologiya. Patogenez. Klinika. Qiyosiy tashxis.	8 soat.	Assistent t.f.n. Axmedov A.A.
13	Parodont kasalliklarini diagnostikasida qo'llaniladigan indekslar. Bolalarda umumiy somatik kasalliklarda (OIT, endokrin sistemasi, QTS, asab sistemasi) parodontdagi o'zgarishlar. Etiologiyasi. Patogenezi.Klinikasi. Qiyosiy tashxisi.	8 soat.	Assistent t.f.n. Axmedov A.A.
14	Parodont kasalliklarining mahalliy va umumiy profilaktikasi. Davosi. "Papiyon-Lefevr va x - gistiotsitoz sindromlarida parodontdagi uzgarishlar «Xend-Shyuller-Krischen, Osler, Itsenko-Kushing sindromida parodontdagi uzgarishlar».	8 soat.	Assistent t.f.n. Axmedov A.A.
15	Tish qattiq tuqimalari patologiyasini ortopedik davolashda kiritmalarning qullanishi.	8 soat.	Assistent t.f.n. Axmedov A.A.
16	Parodont kasalliklarini turlari. Tarqoq va maxalliy parodontit. Parodont kasalliklarida kompleks stomatologik davolashning ahamiyati. Doimiy va vaqtinchalik shinalarning bemorlarda ishlatilishini ziga xosligi.	8 soat.	Assistent t.f.n. Axmedov A.A.
17	Tish qattiq tuqimasi nuqsonlarida lyumenir va vinirlarning ahamiyati. Kursatma va qarshi kursatma. Lyumenir va Vinir uchun tishlarning charxlash taktikasi. Vinir tayerlash uchun klinik laborator usullari. Vinir va lyumenirni tish asosiga fiksatsiyalash. Xatoliklar va asoratlari.	8 soat.	Assistent t.f.n. Axmedov A.A.
18	Immediat protezlarning olib qo'yilmaydigan va olib qo'yiladigan turlari. Immediat protezlarning konstruktiv tuzilmalari. Kursatma va qarshi kursatma, immediat protezni tayyorlashning klinik-laborator bosqichlari. Immediat protezlarning olib qo'yilmaydigan va olib qo'yiladigan turlari. Immediat protezlarning konstruktiv tuzilmalari. Klammer turlari	8 soat.	Assistent t.f.n. Axmedov A.A.
19	Jag'larni to'liq adentiyasida tuliq olib quyiluvchi plastinkali tish protezlarni tayyorlashda yangi yondashuv. Klinik laborator tayyorlash bosqichlari. Tuliq olib quyiluvchi protezlarni mukammallashtirish (metal asosli tuliq olib quyiluvchi protez, yumshoq asosli tuliq olib quyiluvchi protez).	8 soat.	Assistent t.f.n. Axmedov A.A.
20	Onkologik kasalliklari bulgan bemorlarda turli asosli kiritmalarni tayyorlashning kliniko-laborator bosqichlari.. Somatik va autoimmun kasalliklari bulgan bemorlarda	8 soat.	Assistent t.f.n. Axmedov A.A.

	og'iz bushlig'ida ortopedik davo utkazish taktikasi. Bu bemorlarda zamonaviy olib kuyilmaydigan tish protezlari. (oksid sirkon koplamlar) ularga bo'lgan ko'rsatmalar. Somatik kasalliklari bulgan bemorlarda zamonaviy qisman olib kuyilmaydigan tish protezlari. (oksid sirkon koplamlar) ularga bo'lgan ko'rsatmalar		
21	COVID 19. Kasalligi bilan kasallangan bemorlarda COVID 19 asorati tufayli yukori tanglay nekrozi bulgan bemorlarda protezlashni uziga xosligi	8 soat.	Assistent t.f.n. Axmedov A.A.

**Hisobot davrida qayta ishlangan adabiyotlar ro'yxati**

<b>№</b>	<b>Nomi</b>	<b>Avtorlar</b>
1	Atlas off orthopedic stomatology	V.Kurlyandskiy
2	Polymers for Dental and Oprthopedic Applications	Shalaby W.Shalaby, Ulrich Salz
3	Orthodontics and Dentofacial Orthopedics	Gr.T.Пора Publisher U.M.F.lasi. 2013
4	Problem of Functional Measurement at full Adenti	Yuris Bayramov
5	Литье в ортопедической стоматологии	Т.Ф.Данилина, В.Н.Наумова

**Hisobot davrida o'tkazilgan amaliy ko'nikmalar**

<b>№</b>	<b>Amaliy ko'nikma nomi</b>	<b>Soni</b>
1	Mandibulyar o'tkazuvchi og'riqsizlantirish	34
2	Mahalliy infiltratsion og'riqsizlantirish	78
3	Periostotomiya	7
4	Palatinal og'riqsizlantirish	6
5	Tuberal og'riqsizlantirish	6
6	Qayta bog'lam	1
7	Pastki jag'da tishni olish	24
8	Yuqori jag'da tishni olish	16
9	Ildiz uchi rezektsiyasi	3
10	Gistologik surtma olish	4
11	Distopiyalangan tishni olish	2
12	Olingan tish katakchasiga suniy suyak materiali qo'yish	1
13	Dental implantatga milk shakllantigich o'rnatish	6
14	Transfer yordamida qolip olish	16
15	Karioz kovakni ochish, charxlash, ishlov berish, finirlash	98
16	Karioz kovak plombalash, restavratsiya qilish	98
17	Tish ildiz kanallarini tozalash, kengaytirish, davolash,	72
18	Fissuralarni germetizatsiya qilish	38
19	Olinmaydigan protezlar uchun tishlarni charxlash	112
20	Standart qoshiq yordamida qolip olish	118



21	Individual qoshiq yordamida qolip olish	48
22	Tishlov balandligi va markaziy okklyuziyani aniqlash	118
23	Tish qatori anomaliyasi bor bemorlarni tashxislash	9
	<b>Жами:</b>	<b>798</b>

## II. Ilmiy- tadqiqot ishlari

1. Magistrlik ishim mavzusi «**features of the course of erythema multiple form associated with herpes viral infection**» bo'yicha ilmiy rahbarim t.f.n. Axmedov A.A. bilan ortopedik amaliyotlar o'tkazdik.
2. **Noyabr oyida "Science and education" jurnalida «features of the course of erythema multiple form associated with herpes viral infection» mavzusida ilmiy maqolam chop etildi.**
3. **Dekabr oyida "International scientific research" jurnalida "Assesment and comparative analysis of the buccale epithelium and oral cavity health in persons having to smok tobacco" mavzusida maqolam chop etildi.**
4. «**features of the course of erythema multiple form associated with herpes viral infection**» mavzusida dissertatsiyamning 3-bobini yozib tugatdim

Hisobot oyida **Urgenchda o'tkazilgan xalqaro konferensiyada «features of the course of erythema multiple form associated with herpes viral infection» mavzusida ilmiy maqolam bilan ishtirok etdim.**

4. Hisobot oyida ilmiy ishimning uchinchi bobini yozib tugatdim. Mavzuga aloqador bemorlarda o'tkazilgan operatsiyalar natijalarini tahlil qilib chiqdim.

## III. Ilmiy-pedagogik ish

№	Соат	Мавзу	Дарс утувчи
1.	8 soat	Ilmiy-pedagogik ish nima. Magistraturada ilmiy faoliyat yuritishda meyoriy hujjatlar va ularning mazmuni	Assistent t.f.n. Axmedov A.A.
2.	8 soat	Pedagogikaning maqsad va vazifalari. Ilmiy mavzu tanlash	Assistent t.f.n. Axmedov A.A.
3.	8 soat	Magistraturaning maqsad va vazifalari. Pedagogik texnologiyalar	Assistent t.f.n. Axmedov A.A.
4.	8 soat	Ixtirolartushunchasi va ularning turlari. Patent izlanish.	Assistent t.f.n. Axmedov A.A.
5.	8 soat	Kadrlar tayyorlash milliy dasturi. Ilmiy ishning annotasiyasi va referatlarga qo'yiladigan talablar	Assistent t.f.n. Axmedov A.A.
6.	8 soat	O'zbekiston Respublikasi "Ta'lim to'g'risida"gi Qonuni. Tadqiqot ishlarini rejalashtirish	Assistent t.f.n. Axmedov A.A.
7.	8 soat	Tadqiqot ishlarini o'tkazish bosqichlari. Muammoga to'g'ri yondashuv	Assistent t.f.n. Axmedov A.A.
8.	8 soat	Ilmiy- tadqiqot dizayni. Ilmiy izlanish materiali va uslublari	Assistent t.f.n. Axmedov A.A.

9.	8 soat	Ilmiy izlanish kartasini tuzish. Amaliy mashg'ulot tushunchasi, amaliy mashg'ulotni o'tkazish uchun zarur bo'lgan meyoriy hujjatlar	Assistent t.f.n. Axmedov A.A.
10.	8 soat	Ma'ruza tushunchasi, ma'ruzani o'tkazish uchun zarur bo'lgan meyoriy hujjatlar Joriy, oraliq va yakuniy nazorat tushunchalari, ularni o'tkazish usullari	Assistent t.f.n. Axmedov A.A.

**Umummetodologik modullar** doirasida o'tkazilgan quyidagi darslarda ishtirok etdim:  
24,25,28,29,30 noyabr, 1,2,5 dekabr **Operativ xirurgiya va topografik anatomiya** jami 48 soat  
30-31-yanvar 1-3 fevral kunlari **Nutq madaniyati** kursi 30 jami soat  
Barcha fanlardan yakuniy nazoratdan muvaffaqiyatli o'tdim.

**IV. Ma'naviyat – ma'rifat ishlarini:**

O'tgan 5 oy davomida tashkil etilgan quyidagi ma'naviy-ma'rifiy tadbirlar va ilmiy-amaliy konferensiyalarda ishtirok etdim:

2022-yil 3-4 oktabr, SamDTU 1-sonli klinikaning majlislar zalida «АКТУАЛЬНЫЕ ВОПРОСЫ УРОЛОГИИ: ЕДИНСТВО ТЕОРИИ И ПРАКТИКИ» mavzusidagi ilmiy-amaliy anjuman  
2022-yil 6-oktabr kuni Samarqand davlat tibbiyot institutini katta majlislar zalida Olga Kravets “Дисколориты зубов. Композитные виниры” mavzusida mualliflik kursi  
2022- yil 10- oktabr, SamDTU 1 -sonli klinikasining majlislar zalida, “Osstem implant” kompaniyasi tomonidan “Dental implantologiya bilan tanishuv” mavzusida ochiq ma'ruza  
2022-yil 7 - oktabr kuni Samarqand davlat tibbiyot institutini 1-son klinikasida “Abu Ali ibn Sino va Buyuk Ipak Yo'li” I xalqaro xalq tabobati bo'yicha ilmiy-amaliy anjuman  
2022-yil 12-oktabr Samarqand davlat tibbiyot instituti konferensiyalar zalida dotsent Lim Maksim Vyacheslavovich «Искусство доклада» mavzusida amaliy dars  
2022 yil 14- oktyabr kuni Samarqand davlat tibbiyot institutida “Psixiatriya, nevrologiya, neyroxirurgiya va reabilitatsiya: integratsiya qirralari” mavzusidagi xalqaro ilmiy-amaliy anjuman  
2022-yil 15 — oktyabr kuni Samarqand Davlat tibbiyot institutida morfologiya binosi kichik majlislar zalida мастер-класс от Помыткиной Татьяны Юрьевны- заведующей кафедрой педагогики, психологии и психосоматической медицины ФГБОУ ВО Ижевской государственной медицинской академии на тему: "Сообщение плохих новостей: навыки врача".  
2022-yil 29-oktyabr kuni SamDTU ko'p tarmoqli klinikasi, morfologiya binosida “ICHKI KASALLIKLAR TIBBIYOTI SOG'LIQNI SAQLASH TIZIMIDA YETAKCHI O'RINLARDA” mavzusidagi xalqaro ilmiy-amaliy anjuman  
2022 yil 8- noyabr, SamDTU 1-sonli klinikaning majlislar zalida professor Andrey Akulevich tomonidan o'tkazilgan « СОВРЕМЕННЫЕ ПОДХОДЫ К УСТРАНЕНИЮ ДИСКОЛОРИТОВ ЗУБОВ» mavzusida mualliflik kusi va trening  
2022-yil 9-noyabr SamDTU 1-sonli klinikaning majlislar zalida, "МЕДИЦИНСКОЕ ОБРАЗОВАНИЕ И СИСТЕМА ЗДРАВООХРАНЕНИЯ В США И УЗБЕКИСТАНЕ. ОБМЕН ОПЫТОМ В ФОРМАТЕ ДИАЛОГА" mavzusida Xalqaro ilmiy-amaliy konferensiya  
2022- yil 21- noyabr, SamDTU 1 -sonli klinikasining majlislar zalida, “Osstem implant” kompaniyasi tomonidan “Dental implantologiya bilan tanishuv” mavzusida ochiq ma'ruza  
2022-yil 14-dekabr kuni SamDTU ko'p tarmoqli klinikasi, morfologiya binosida “Высокие технологии в хирургии” mavzusidagi xalqaro ilmiy-amaliy anjumani



2022- yil 21- dekabr, SamDTI 1 -sonli klinikasining majlislar zalida, “Osstem implant” kompaniyasi tomonidan “Dental implantatlar ustida ortopedik konstruksiyalar uchun qolip olish” mavusida ochiq ma’ruza

2022-yil 22-dekabrda Og’iz bo’shlig’i jarrohligi va dental implantologiya kafedrasida “Osstem implant” kompaniyasi tomonidan o’tkazilgan amaliy master klass

**Kafedra mudiri:**



**t.f.n. Norbutayev A.B.**

**Moderator**



**ass. Axmadov I.N.**

**Ilmiy rahbar:**



**t.f.n. Axmedov A.A.**

**Magistratura talabasi:**



**Kaki Huda A.S.**



## РЕЦЕНЗИЯ

на диссертационную работу магистра-резидента кафедры ортопедической стоматологии Самаркандского Государственного медицинского университета на соискание степени магистра Каки Худа Абдул Салам Хекмат на тему: «особенности течения многоформной экссудативной эритемы, связанной с герпесвирусной инфекцией» по специальности – «стоматология» - 5А510410

Диссертационная работа выполнена на актуальную тему. Вскоре после того, как Урбах в 1933 году впервые сообщил о связи между многоформной эритемой и "пузыркоковый лишай", Андерсон уже описал вирус простого герпеса как "бомбу замедленного действия" этого кожного заболевания. Семьдесят лет спустя ситуация не только не изменилась, но и стала еще более серьезной. В первые годы главной задачей был поиск причинных факторов, но сегодня существует еще одна проблема, связанная с выяснением патогенеза заболевания и выбором лечения и вариантов лечения. Уже выявлен ряд возбудителей, которые могут быть вовлечены в патогенез более частого варианта экссудативной эритемы - аллергической экссудативной инфекционной эритемы (*erythema exudativum infectiosum allergicum*). В частности, ряд исследований с использованием современных методов диагностики продемонстрировал роль следующих этиологических агентов. Многие исследования с использованием современных методов диагностики показали, что вирус простого герпеса имеет непосредственное отношение как к возникновению, так и к последующим рецидивам заболевания. Статистика количества обращений в клиники показывает, что доля многоформной эритемы, вызванной вирусом простого герпеса, достигает 80%, что соответствует примерно 1% всех пациентов, посещающих дерматологическую клинику. Простой герпес поднялся на первое место в списке проблем со здоровьем, составленном Всемирной организацией здравоохранения. Рост заболеваемости вирусом простого герпеса, который является одной из проблемных областей Всемирной организации здравоохранения, наряду с другими инфекционными заболеваниями, такими как вирус иммунодефицита человека и грипп, делает эту проблему актуальной.

Диссертантом поставлена цель: На основе комплексных клинических и лабораторных исследований выявить типичные клинические и иммунологические особенности пациентов, страдающих НАМЕ, и разработать патогенетически обоснованные дифференцированные подходы к лечению и профилактики данной патологии

Для достижения цели представлены четко и правильно сформулированные задачи. Объектом исследований явились пациенты – с герпес ассоциированной многоформной эритемой .

Диссертационная работа состоит из 4 глав, введения, обзора литературы, материалов и методов исследования, результатов исследования, их обсуждения, выводов, практических рекомендаций и списка литературы.

Во введении приведена актуальность и востребованность темы. Во главе обзора литературы приведены результаты изучения современной литературы, этиопатогенез GAME, МЕЕ, HS.

Во второй главе диссертации подробно описаны материалы и методы исследования. Приведены результаты обследования и лечения 45 пациентов, страдающих от вышеперечисленных патологий

В 3 и 4 главах приведены результаты собственных исследований и обсуждение полученных результатов. В них подробно описаны полученные результаты по отдельным группам исследований.

Результаты исследований имеют теоретические и практические значения, которые отражаются в том, что определено применение определенного подхода к лечению герпес ассоциированной многоформной эритемой, отдельно выделены препараты применяемые в купировании симптомов и профилактики данной патологии.

В процессе рецензирования возникли некоторые замечания, которые легко исправимы и они не умаляют ценность работы. В тексте диссертации имеются опечатки, орфографические, стилистические ошибки, в изложении имеются повторы которых необходимо тщательно отредактировать. Выводы и задачи исследования соответствуют друг другу.



Таким образом, диссертационная работа магистра-резидента кафедры ортопедической стоматологии Самаркандского Государственного медицинского университета на соискание академической степени магистра Каки Худа Абдул Салам Хекмат на тему: «особенности течения многоформной экссудативной эритемы, связанной с герпесвирусной инфекцией» по специальности – «стоматология» - 5A510410 соответствует выбранной специальности, является актуальной и законченной работой, отличается научной новизной и практической значимостью, может быть рекомендована для рассмотрения на последующих этапах.

Рецензент: PhD.

Кафедры ортопедической стоматологии



Ортикова Н.Х



Самарканд Давлат Тиббиёт Университети

«Ортопедик стоматология» кафедрасининг йиғилиши Баённома №8

КЎЧИРМА

15-май 2023йил.

**Катнашчилар:** Раис кафедра мудири: PhD. Ахмедов А.А., асс. PhD. Ортикова Н.Х., асс. Чакконов Ф.Х., асс. Давлатова С.М., асс. Исламова Н.Б., асс. Иргашев Ш.Х., асс. Нормуратов А.Н., асс. Бурханова З.К., асс. Махмудова У.Б., асс. Губаев М.С., асс. Санакулов Ж.О., асс. Ахмадов И.Н.

**Кун тартиби:**

1. Самарканд Давлат Тиббиёт университети «Ортопедик стоматология» кафедраси 2-курс магистранти Каки худа Абдул Салам Хекмат . (**Научный руководитель:** к.м.н. Ахмедов А.А.,) нинг “особенности течения многоформной экссудативной эритемы, связанной с герпесвирусной инфекцией” мавзусидаги магистрлик диссертациясини муҳокама қилиш.

**ЭШИТИЛДИ:**

Кун тартибидаги масала бўйича “Ортопедик стоматология” кафедраси 2-курс магистранти Каки Худа Абдул Салам Хекмат нинг “особенности течения многоформной экссудативной эритемы, связанной с герпесвирусной инфекцией” мавзусидаги магистрлик диссертациясини муҳокама қилинди. Кафедра ассистентлари Ортикова Н.Х., Чакконов Ф.Х., Давлатова С.М. лар томонидан саволлар берилди ва жавоблар қониқарли ҳолда қайтарилди ва шундан сўнг кафедра мудири PhD. Ахмедов А.А. томонидан мавзу юзасидан фикрлар билдирилиб, музокара қилинди.

Магистрлик диссертацияси маъқулланди ва кейинги босқичга ўтказишга тавсия қилинди

**МАЖЛИС ҚАРОРИ:**

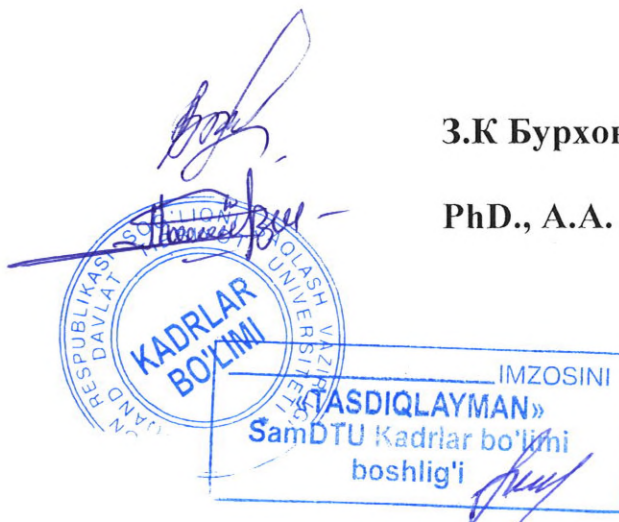
1 Каки Худа Абдул Салам Хекмат нинг “особенности течения многоформной экссудативной эритемы, связанной с герпесвирусной инфекцией” мавзусидаги магистрлик диссертацияси тасдиқлансин, кейинги босқичга ўтказишга тавсия қилинди.

Йиғилиш қотиби:

З.К Бурхонова

Йиғилиш раиси:

PhD., А.А. Ахмедов





## РЕЦЕНЗИЯ

на диссертационную работу магистра-резидента кафедры ортопедической стоматологии Самаркандского Государственного медицинского университета на соискание степени магистра Каки Худа Абдул Салам Хекмат на тему: «особенности течения многоформной эксудативной эритемы, связанной с герпесвирусной инфекцией» по специальности – «стоматология» - 5A510410

Актуальность проблемы обусловлена ростом заболеваемости вирусом простого герпеса, который, наряду с другими инфекционными заболеваниями, такими как вирус иммунодефицита человека и грипп, занимает одно из первых мест в списке проблем Всемирной организации здравоохранения. В современной научной литературе проведено и опубликовано множество клинических и иммунологических исследований, посвященных характеристикам вируса простого герпеса. Однако до настоящего времени нет сообщений о клинических особенностях и специфике иммунного статуса пациентов с ПГ, страдающих GAME. Однако, имея такие данные, можно прогнозировать степень вероятности развития GAME. Затем можно использовать активное лечение таких пациентов для предотвращения развития синдрома. В настоящее время существует ряд терапевтических средств применяемые при лечение данного недуга. Существует две основные группы препаратов для лечения простого герпеса: этиологические (синтетические нуклеозиды) и иммуностимуляторы (более многочисленная группа). Однако, несмотря на широкий выбор препаратов, доступных для лечения простого герпеса, основным рекомендуемым методом лечения простого герпеса является применение синтетических нуклеозидов. Они обычно используются для контроля текущих рецидивов. В качестве профилактической меры современные руководства рекомендуют продолжать использование ацикловира. Однако, к сожалению, во всем мире сообщается о появлении вирусов, устойчивых к ацикловиру. Поэтому важно изучить альтернативные методы профилактики рецидивов вируса простого герпеса, приводящих к GAMЭ,

Диссертантом поставлена цель: На основе комплексных клинических и лабораторных исследований выявить типичные клинические и иммунологические особенности пациентов, страдающих НАМЕ, и разработать патогенетически обоснованные дифференцированные подходы к лечению и профилактики данной патологии

Для достижения цели представлены четко и правильно сформулированные задачи. Объектом исследований явились пациенты – с герпес ассоциированной многоформной эритемой .

Диссертационная работа состоит из 4 глав, введения, обзора литературы, материалов и методов исследования, результатов исследования, их обсуждения, выводов, практических рекомендаций и списка литературы.

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Во второй главе диссертации подробно описаны материалы и методы исследования. Приведены результаты обследования и лечения 45 пациентов, страдающих от вышеперечисленных паталогий

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Результаты исследований имеют теоретические и практические значения, которые отражается в том, что определено применение определенно определенный подход к лечению герпес ассоциированной многоформной эритемой, отдельно выделены препараты применяемые в купировании симптомов и профилактики данной патологии.

В процессе рецензирования возникли некоторые замечания, которые легко исправимыми и они не умаляют ценность работы. В тексте диссертации имеются опечатки, орфографические, стилистические ошибки, в изложении имеются повторы которых необходимо тщательно отредактировать. Выводы и задачи исследования соответствуют друг другу.

Таким образом, диссертационная работа магистра-резидента кафедры ортопедической стоматологии Самаркандского Государственного медицинского университета на соискание академической степени магистра Каки Худа Абдул Салам Хекмат на тему: «особенности течения многоформной экссудативной эритемы, связанной с герпесвирусной инфекцией» по специальности – «стоматология» - 5A510410 соответствует выбранной специальности, является актуальной и законченной работой, отличается научной новизной и практической значимостью, может быть рекомендована для рассмотрения на последующих этапах.

Рецензент: д.м.н. проф.

Факультет последипломного образования



Назарова Н.Ш





**MINISTRY OF HEALTH OF THE REPUBLIC OF UZBEKISTAN**  
**SAMARKAND STATE MEDICAL UNIVERSITY**

**Faculty: Dentistry**

**Master's degree Resident: Kaky Huda Abdul Salam Hekmat**

**Department of Orthopedic Dentistry**

**Supervisor: PhD Akhmedov A.A.**

**Academic years: 2021-2023**

**Specialty: orthopedic dentistry**

**Relevance of the study:** According to statistical data, the prevalence of herpes simplex virus in all forms of erythema multiforme reaches 80%, which corresponds to about 1% of all patients visiting a dermatologist. Herpes simplex has risen to the top of the list of health problems of the World Health Organization. The urgency of the problem is due to the increase in the incidence of herpes simplex virus, which, along with other infectious diseases such as human immunodeficiency virus and influenza, occupies one of the first places in the list of problems of the World Health Organization. In the modern scientific literature, many clinical and immunological studies have been conducted and published on the characteristics of the herpes simplex virus. However, to date there have been no reports on the clinical features and specifics of the immune status of patients with PG suffering from GAME. However, with such data, it is possible to predict the degree of probability of the development of GAME. Then active treatment of such patients can be used to prevent the development of the syndrome. Currently, there are a number of therapeutic agents used in the treatment of this ailment. There are two main groups of drugs for the treatment of herpes simplex: etiological (synthetic nucleosides) and immunostimulants (a larger group). However, despite the wide range of drugs available for the treatment of herpes simplex, the main recommended method of treating herpes simplex is the use of synthetic nucleosides. They are usually used to control ongoing relapses. As a preventive measure, modern guidelines recommend continuing to use acyclovir. However, unfortunately, the appearance of viruses resistant to acyclovir has been reported worldwide. Therefore, it is important to study alternative methods of preventing recurrence of herpes simplex virus, leading to GAME.

**The aim of the study:** To identify typical clinical and immunological features of patients suffering from GAME on the basis of complex clinical and laboratory studies, and to develop pathogenetically justified differentiated approaches to the treatment and prevention of this pathology.

**Research objectives:**

1. To identify the features of clinical manifestations of GAME
2. Formulate clinical and immunological parameters that increase the risk of developing GAME in patients with HS.
3. Develop a differentiated approach to therapy (as for cupping exacerbations, and for prevention), adequate to the identified violations and evaluate its effectiveness

**The object of the study:** there were 48 patients aged 25-45 years in need of treatment who were divided into 3 clinical groups.

**Research methods**

1. Clinical examination (complaints, anamnesis, general and local condition)
2. Laboratory examination (functional and allergological methods).
3. Evaluation of the clinical effectiveness of treatment methods
4. Data registration.

**Scientific novelty**

For the first time, the differences between the clinical picture of GAME and the toxicallergic form of MEE were determined: the development of a recurrence of PG on day 1-9; the elements of the GAME rash are solitary, cyanotic, up to 4 cm in diameter. GAME in 60% of cases occurs against the background of an increase in the frequency and (or) duration of recurrent PG, which in 93% of cases is localized on the face. New data on the immunological features of GAME were obtained: an increase in spontaneous production of IL-4 and IL-6 in combination with inhibition of induced (the ratio between them is 1:1 instead of 1:20); alpha- and gamma interferon ( $63.0 \pm 8.6$  and  $720.0 \pm 19.4$ ); dysimmunoglobulinemia with a predominance of IgM E ( $471.0 \pm 19.0$ ) and a decrease in I<sup>A</sup> ( $1.2 \pm 0.4$ ) with an increase in the absolute number of B-lymphocytes ( $232 \pm 10.8$ ); no increase in the number of YK and spontaneous production of IL-2.

**Practical significance.** Clinical and immunological criteria for the identification of a risk group for the development of GAME among patients with HS are given. Clinical criteria: an increase in the frequency and (or) duration of HS, its localization in the facial area. Immunological criteria: changes in IL-4 and IL-6 production with the ratio of 1:1 between spontaneous and induced production. The predominance of Img E with a decrease in Img A against the background of an increase in the absolute number of B lymphocytes. A differentiated approach to the treatment of GAME relapses and a method of prevention are proposed. Antibiotic therapy for GAME is indicated in case of signs of secondary bacterial infection: symptoms of intoxication, impetigination.

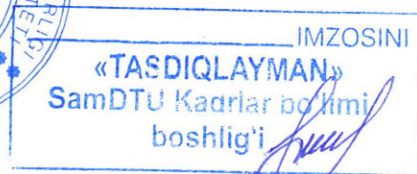
Supervisor:



PhD Akhmedov A.A

Resident of the magistracy:

Kaky Huda Abdul Salam Hekmat





**МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ УЗБЕКИСТАН**  
**САМАРКАНДСКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ**  
**УНИВЕРСИТЕТ**

**Факультет: Стоматология**

**Степень магистра ординатор: Каки Худа Абдул Салам Хекмат**

**Отделение ортопедической стоматологии**

**Научный руководитель: к.м.н. Ахмедов А.А.**

**Учебные годы: 2021-2023**

**Специальность: ортопедическая стоматология**

**Актуальность исследования:** Согласно статистическим данным распространенность вируса простого герпеса при всех формах многоформной эритемы достигает 80%, что соответствует примерно 1% всех пациентов, посещающих дерматолога. Простой герпес поднялся на первое место в списке проблем здравоохранения Всемирной организации здравоохранения. Актуальность проблемы обусловлена ростом заболеваемости вирусом простого герпеса, который, наряду с другими инфекционными заболеваниями, такими как вирус иммунодефицита человека и грипп, занимает одно из первых мест в списке проблем Всемирной организации здравоохранения. В современной научной литературе проведено и опубликовано множество клинических и иммунологических исследований, посвященных характеристикам вируса простого герпеса. Однако до настоящего времени нет сообщений о клинических особенностях и специфике иммунного статуса пациентов с ПГ, страдающих GAME. Однако, имея такие данные, можно прогнозировать степень вероятности развития GAME. Затем можно использовать активное лечение таких пациентов для предотвращения развития синдрома. В настоящее время существует ряд терапевтических средств применяемые при лечение данного недуга. Существует две основные группы препаратов для лечения простого герпеса: этиологические (синтетические нуклеозиды) и иммуностимуляторы (более многочисленная группа). Однако, несмотря на широкий выбор препаратов, доступных для лечения простого герпеса, основным рекомендуемым методом лечения простого герпеса

является применение синтетических нуклеозидов. Они обычно используются для контроля текущих рецидивов. В качестве профилактической меры современные руководства рекомендуют продолжать использование ацикловира. Однако, к сожалению, во всем мире сообщается о появлении вирусов, устойчивых к ацикловиру. Поэтому важно изучить альтернативные методы профилактики рецидивов вируса простого герпеса, приводящих к ГАМЭ,

**Целью исследования:** На основе комплексных клинических и лабораторных исследований выявить типичные клинические и иммунологические особенности пациентов, страдающих НАМЕ, и разработать патогенетически обоснованные дифференцированные подходы к лечению и профилактики данной патологии.

**Задачи исследования:**

1. Выявить особенности клинических проявлений ГАМЭ
2. Сформулировать клинико-иммунологические параметры, повышающие риск развития ГАМЭ у больных с ПГ.
3. Разработать дифференцированный подход к терапии (как для купирования обострений, так и для профилактики), адекватный выявленным нарушениям и оценить его эффективность

**Объектом исследования:** были 48 пациентов в возрасте 25-45 лет, нуждающихся в лечении которые были разделены на 3 клинические группы .

**Методы исследования**

1. Клиническое обследование (жалобы, анамнез, общее и местное состояние)
2. Лабораторное обследование (функциональные и аллергологические методы).
3. Оценка клинической эффективности методов лечения
4. Регистрация данных.

**Научная новизна**

Впервые определены отличия клинической картины ГАМЭ от токсикоаллергической формы МЭЭ: развитие на 1-9 день рецидива ПГ; элементы сыпи ГАМЭ солитарные, цинанотичного оттенка, до 4 см в диаметре. ГАМЭ в 60 % случаев возникает на фоне увеличения частоты и(или) продолжительности рецидивов ПГ, который в 93 % случаев локализуется на лице.



Получены новые данные об иммунологических особенностях ГАМЭ: увеличение спонтанной продукции ИЛ-4 и ИЛ-6 в сочетании с угнетением индуцированной (соотношение между ними 1:1 вместо 1:20); спад альфа- и гамма-интерферона (63,0+8,6 и 720,0+19,4); дисиммуноглобулинемия с преобладанием I<sub>g</sub> E (471,0+19,0) и снижением I<sup>A</sup> (1,2+0,4) при повышении абсолютного числа В-лимфоцитов(232+10,8); отсутствие увеличения количества ПГ и спонтанной продукции ИЛ-2.

**Практическое значение.** Даны клинические и иммунологические критерии по выявлению группы риска развития ГАМЭ среди пациентов с ПГ. Клинические критерии: нарастание частоты и(или) длительности ПГ, его локализация в области лица. Иммунологические критерии: изменение продукции ИЛ-4 и ИЛ-6 с соотношением 1:1 между спонтанной и индуцированной выработкой.

Преобладание I<sub>g</sub> E со снижением I<sub>g</sub> A на фоне увеличения абсолютного числа В лимфоцитов. Предложен дифференцированный подход к терапии рецидивов ГАМЭ и метод профилактики. Антибиотикотерапия при ГАМЭ показана в случае признаков вторичного бактериального инфицирования: симптомы интоксикации, импетигнизация.

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