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"Treatment of acute herpetic stomatitis in children"

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The monograph is based on the analysis of the research results, and the effectiveness of the drug "Citeal" in the treatment of acute herpetic stomatitis in children has been studied.

The monograph is intended for dentists and specialists dealing with this problem, as well as for pediatricians.

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LIST OF ABBREVIATIONS

- sJgA**- secretory immunoglobulin
HIV- human immunodeficiency virus
WHO- World Health Organization
- HSV**- herpes simplex virus
GI- hygienic index
GNL- helium-neon laser
DNA- deoxyribonucleic acid
IRL- interferon reaction of leukocytes
MMSI- Moscow Medical Dental Institute
- OGS**- acute herpetic stomatitis
SPL- Semiconductor laser stimulator
RMA- papillary-marginal-alveolar
- SOPR**- oral mucosa
AIDS- acquired immunodeficiency syndrome
UZ- ultrasound therapy
UZR- ultrasonic atomization
FP- phagocytic index
Gastrointestinal tract- gastrointestinal tract

INTRODUCTION

In recent years, there has been a steady increase in the number of diseases associated with disruption of the biological balance between the macroorganism and various populations of microbial flora. The microflora of the oral cavity is a highly sensitive indicator system that responds with qualitative and quantitative shifts to changes in the state of various organs and systems of the body [54]. The studies have shown that the barrier and protective mechanisms of the oral cavity are closely related to the microflora living in it. The variety and activity of microflora often predetermines the pathology of the oral cavity. Currently, fungal and herpes infections are among the most common and poorly controlled [46]. Thus, more than 400 species of fungi are known to cause various pathological changes in the body in humans, and diseases caused by the herpes virus are second only to influenza. According to WHO, from 90 to 100% of the world's population is infected with herpes simplex viruses (HSV) of the first and second types. This is mainly due to the introduction of new medical technologies and a significant increase in the number of patients with immunodeficiency, which manifests itself in children by the development of a dysbiotic state of the oral cavity [18]. Traditional methods of treating the oral cavity, when various chemicals such as potassium permanganate, menthol, and elixirs are used, do not have a pronounced bacteriostatic effect and aggravate the dysbiotic manifestation, in connection with which new drugs with a wide spectrum of action are being sought. One of such drugs that meets modern requirements for drugs used to treat oral mucosal diseases is the drug "Citeal".

Citeal is an antiseptic foaming solution. It is a synergism of three active components: chlorhexidine, hexamidine diisethionate, chlorocresol. The drug has a wide spectrum of action: antiparasitic, antibacterial, antiviral, fungicidal.

Good tolerance - does not irritate the skin of the face, mucous membranes, children's skin, has a pleasant smell, forms foam, does not cause photosensitivity, does not disturb the ecology of the skin and mucous membranes.

In the treatment of acute herpetic stomatitis in children with the drug "Citeal", we substantiated the effectiveness of its use, since in the process of work:

1. Having studied the state of non-specific factors of oral cavity protection at various stages of the clinical course of acute herpetic stomatitis in children in the dynamics of treatment with the drug "Citeal", and also compared with the traditional method of treatment.

2. A comparative assessment of the effect of the drug "Citeal" on the quantitative and qualitative indicators of the oral microflora in the treatment of patients with acute herpetic stomatitis was carried out.

3. A correlation was established between the indicators of clinical effectiveness of treatment methods and the state of microflora, non-specific factors of oral cavity protection in patients with acute herpetic stomatitis.

4. The most effective method of using Citeal for oral mucosal diseases has been established.

This work examines the effect of the drug "Citeal" on the microflora of the oral cavity in acute herpetic stomatitis in children.

The effect of the drug on local immunity of the oral cavity was revealed.

Based on clinical, laboratory and bacteriological studies, a method for using the drug "Citeal" in the treatment of acute herpetic stomatitis (AHS) stomatitis in children has been developed.

The existence of direct and inverse relationships between quantitative parameters of microbiocenosis and immunological indices of the oral cavity in

children suffering from herpetic stomatitis before and after treatment with the drug "Citeal" was established.

Based on clinical and immunobacteriological studies, qualitative and quantitative shifts in the composition of the oral microflora, as well as in the local immune system in children with AGS, have been identified. It has been revealed that traditional treatment of AGS does not contribute to the final elimination of the identified shifts in the immune and microbial balance of the oral cavity, which is the cause of relapses and chronicity of the disease.

A method for using the drug "Citeal" for the treatment of acute herpetic stomatitis in children has been developed.

The cost-effectiveness of treatment with Citeal compared to the traditional method consists in reducing the duration of treatment by 1-2 days with monotherapy with Citeal.

Chapter I. Modern methods of treatment of acute herpetic stomatitis in children

Acute herpetic stomatitis.

Herpes infection is currently the most common and poorly controlled [48,50].

According to WHO, diseases caused by the herpes virus are second only to influenza among viral diseases. Herpes simplex viruses (HSV) types 1 and 2 infect 90 to 100% of the world's population. There are about 80 known representatives of the Herpesviridae family, eight of which are pathogenic for humans [48].

Herpes [herpes] – from Greek means creeping. This virus is polytropic and can infect all human organs and systems, causing acute, recurrent and chronic infection. It can cause intrauterine damage to the fetus, be the cause of pathology in newborns, often with a fatal outcome, act as a cofactor of carcinogenesis, induce the process of atherosclerosis, change the course of other diseases, in particular activate the HIV genome, which is in the provirus stage, and be a cofactor in the progression of HIV infection [1, 16, 17, 20, 27].

The leading place among oral mucosal diseases in children is occupied by herpetic stomatitis, which occurs in 80-85% of cases [20, 48, 50, 10]. In recent years, relapses of this disease with transition to a chronic form have been increasingly observed. This is due to the fact that herpetic stomatitis occurs and develops, as a rule, in weakened children under conditions of a sharp decrease in the natural protective and adaptive reactions of the body. The formation of chronic forms of the disease is one of its most unfavorable outcomes, having not only clinical, but also social and epidemiological significance [4, 15, 11].

The herpes simplex virus (HSV) belongs to the subfamily Alpha Herpes Viridae and has two antigen types. Previously, it was believed that HSV-1 affects the oral cavity, nasopharynx, eyes, skin (infection above the waist); HSV-2 - the urogenital tract, skin (below the waist). In recent years, it has been

established that both types of the virus can cause lesions in both localizations [16, 27].

HSV is sensitive to heating and is inactivated at 500 C for 30 minutes. At the same time, the virus is resistant to low temperatures: at 240 C, HSV persists for several years. Due to the fact that the virion membrane contains a significant amount of lipids, HSV is easily destroyed by ether. Alcohol, chloroform, phenol, formalin, proteolytic enzymes, and bile are virus inactivators. The virus quickly dies under the influence of ultraviolet radiation and X-rays [6, 14].

The pathogenesis of herpes infection is determined by the ability to persist in nerve ganglia throughout a person's life. The "silent" genome cannot be removed from ganglion cells by any known antiviral chemotherapy drugs.

In parallel with this, cells of the granulocyte-monocyte and lymphocyte series become infected, which is accompanied by disorganization of the receptor apparatus of immune component cells and disruption of the production of many immunocytokinins, which leads to the development of systemic immunodeficiency, which largely determines the further course of the disease [40].

In case of OGS, the herpes simplex virus gets on the oral mucosa and if there are areas of damage to the integrity of the cover, it penetrates inside, and if there are no damages to the epithelial lining, it is adsorbed and attached to the integumentary cells. At the site of adsorption, the cell wall forms a "pocket" that turns into a vacuole and the virus ends up in the cytoplasm. Inside the epithelial cell, HSV reproduces with the help of nuclear DNA. Every 12 and 18 hours, viral particles leave the cells, which is accompanied by the destruction of cells and the formation of multinucleated giant cells [16, 17].

Antonelli C., Vigneli (1968) believed that the virus is present in the places of rashes. Then the virus passes through the basement membrane and enters the connective tissue and enters the blood vessel - primary viremia. The

blood of patients with acute gastritis contains specific antibodies and a rather weak production of interferon. Erythrocytotropism of the virus is noted. HSV disseminates to all organs and tissues through the bloodstream and is excreted in the urine.

HSV - penetrates organs and tissues through capillary barriers by diapedesis. Settling in the liver, spleen and other tissues, the virus quickly multiplies. Secondary viremia is observed in the prodromal period of the disease and in the first days of its peak. It is characterized by the appearance of a large amount of the virus in the blood after its increased reproduction in the organs.

In secondary viremia, viruses rush to the skin and mucous membranes, where they multiply, which leads to repeated rashes of disease elements and a deterioration in the general condition of the patient (malaise, fever, loss of appetite, headaches, etc.).

HSV is spread in 3 ways:

- a) extracellular pathway
- b) via intercellular bridges
- c) during cell division and viral genome

There are several methods of immune lysis of HSV-infected cells [22, 59].

1. Chemotaxis is the attachment of virus particles to a cell and entry into a phagocyte. Phagocytosis of HSV by a macrophage can delay virus assembly and limit reproduction.

2. The resulting HSV-antibody complex cannot destroy the virus without complement.

3. Direct cytotoxicity of sensitized lymphocytes (T-killers). In herpes, the interaction of sensitized lymphocytes with virus-infected cells leads to lysis of HSV-infected cells.

4. Antibody-dependent cellular cytotoxicity, which plays a primary role in host defense against the virus. Antibodies, adhering to target cells, contribute to their destruction.

5. Humoral immunity.

Synthesis of antibodies is of crucial importance against envelope antigens of the virus and membrane antigens of infected cells. In humans, antibodies in the form of Ig M are detected within 1-3 weeks, which quickly disappear. Later, antibodies A appear, the mechanism of action of antibodies on infected cells is associated with the suppression of the release of the virus into the environment. Antibodies can lyse infected cells in combination with complement. HSV infection is maintained in a complex with the antigen. Neutralization of the virus is achieved with the help of complement in combination with T-lymphocytes, macrophages and polymorphonuclear leukocytes of both immune and non-immune individuals [25, 141].

Lymphokines (cell-mediated immunity factors) are released by immune T-lymphocytes and infected cells. Cell-mediated immunity factors cause lysis of the infected cell, which releases the virus for subsequent neutralization by antibodies [26, 141].

The leukocyte interferon reaction (ILR) test proposed (1970, 1981) by V.D. Solovyov and T.L. Bektemirov notes rare relapses in individuals with active inducing capacity of leukocytes (ILR>40 units). With IRL <10 units, herpes relapses were recorded every 5 weeks [20].

Thus, according to the researchers, the importance of interferon is not limited to its role as an inhibitor of viral reproduction; it is more important as an immunomodulator of protective reactions.

Sharp Herpetic stomatitis (HS) most often affects children of nursery and preschool age, most often from 1 year to 3 years old. HS has 5 periods of development: incubation, prodromal (catarrhal), the period of development of the disease (rashes), fading and clinical recovery (reconvalescence). Depending

on the severity of general toxicosis and local manifestations in the oral cavity, the disease can occur in mild, moderate and severe forms. During the development of the disease, two phases are distinguished - catarrhal and rashes of the affected elements. During this period, symptoms of damage to the oral mucosa appear. Initially, intense hyperemia of the entire mucous membrane occurs, and after a day, less often two, elements of damage are usually found in the oral cavity. The severity of HS is assessed by the severity of toxicosis manifestations and the nature of the lesions of the oral mucosa [20, 41, 7, 8].

Mild form.The child's general condition is normal, the body temperature is subfebrile. The first clinical signs are pain when eating. Objectively, hyperemia and swelling of the oral mucosa, individual rounded erosions covered with plaque are noted. The rash is single, no new elements appear in the following days, the duration of the disease is 4-5 days.

Moderate and severe forms.The onset of the disease is acute, the body temperature rises to 38-40 degrees. The intoxication process is pronounced: the child is lethargic, capricious, sleeps poorly, complains of headache. Some children experience decreased appetite, nausea, vomiting, diarrhea. Examination of the maxillofacial region reveals painful submandibular, chin, cervical lymph nodes and initial signs of catarrhal gingivitis. On the 2nd-3rd day of the disease, rashes appear on the oral mucosa, red border of the lips and skin of the face. On the inflamed oral mucosa, there are from 2-3 to several dozen closely located groups of blisters that quickly open. In their place, erosions with necrosis in the center of the aphtha measuring 0.5 - 1 cm appear. Aphthae are extremely painful, they are localized on the tongue, mucous membrane of the lips, cheeks, less often on the palate, arches, gums. The oral mucosa is edematous, hyperemic, the tongue is coated. The gingival margin is edematous, hyperemic, erosions form along the edges of the gum. Saliva becomes viscous and stringy, there is an unpleasant odor from the mouth (halitosis). The period of rashes lasts 2-4 days. A secondary infection may join. A left shift in band nuclei and

esinophilia are detected in the blood of children. Protein appears in the urine. At the onset of the disease, a shift in pH to the acidic side is determined in saliva, then to the alkaline side. At the same time, there is no interferon in saliva, and the lysozyme content is reduced. The diagnosis of AGS is established based on the clinical picture and epidemiology of the disease.

Various drugs and methods are used in the treatment of diseases of the oral mucosa. However, despite the large number of available means, treatment measures are often ineffective and a chronic form of the disease is formed. Therefore, it is necessary to search for drugs with a wide range of action, which is the purpose of this work.

1.2. Microbiology and immunology of the oral cavity in children suffering from acute herpetic stomatitis.

The generally accepted position that it is easier to prevent a disease than to treat it remains relevant in the new economic conditions. A large economic effect can be achieved if disease prevention, including dental disease, begins in childhood. However, due to the transition of the Republic of Uzbekistan to market relations, dental care for children has found itself in a worse position. As is known, it has always been financed by the budget, and in the pre-perestroika period there was also a shortage of funds for it, and in our days the situation has worsened even more [6, 12].

Man and the environment represent a single ecological system in a state of biological equilibrium. Symbiont microbes that are part of the macroorganism's ecosystem not only form the normal composition of the child's microflora, but also take the most direct part in regulating many physiological reactions and processes to maintain homeostasis [32, 37, 39].

From a modern perspective, the normal microflora of a child is considered as a set of microbiocenoses of various parts of the body. The normal flora includes hundreds of different species with a total number of more than 10¹⁴ cells, which are capable of forming a stable structure of the microbial landscape, and their qualitative (species) and quantitative composition depends on localization [59, 3, 9].

In this case, the totality of microbiocenoses of a macroorganism is designated as normobiocenosis or eubiosis, although recently the term microecology has been more often preferred, which is a more capacious concept, since it includes not only data on the qualitative and quantitative balance of various populations of microbial flora of individual organs and systems of a macroorganism, but also their biochemical, metabolic and immunological state [46, 53].

However, it is necessary to remember that when the threshold value of exogenous and endogenous factors affecting the body is exceeded, microbiocenoses go out of the state of biological equilibrium, which, in turn, is accompanied by the emergence of microecological and immune disorders. This, in turn, leads to the dominance of potentially pathogenic microbes in the biotope, increased genetic exchange and the formation of altered clones, often including genes that determine the adhesive, cytotoxic properties of bacteria [23, 41, 53].

Research in recent years has shown that these processes can lead to serious consequences, both functional and structural, that is, to the development of dysbacteriosis [23, 53].

In turn, dysbacteriosis can develop due to direct ecopathogenic influence on the child's microflora with simultaneous disturbances in factors of the immunological aspect [13, 41].

Moreover, it has been proven that this involves species selection of microorganisms, as well as changes within the biological species due to the survival in the habitat of more resistant strains capable of causing or maintaining diseases [11, 41].

Microbiological studies conducted in recent decades show that bacteria occupy a dominant place both in terms of the diversity of species living in the oral cavity and in terms of quantity. Thus, according to various researchers, the number of bacterial species in this ecological niche in children ranges from 120 to 200. The number of bacteria in the oral cavity, in terms of the number of species and content per unit of material, competes with the gastrointestinal tract. The content of microorganisms in saliva (oral fluid) ranges from 4 million to 5 billion CFU / ml, in dental plaque (plaque) it is even higher and ranges from 10 to 100 billion per gram of material [23, 33].

According to various researchers, the share of anaerobic and microaerophilic flora of the oral cavity in children is from 60 to 80% of the

microbial landscape. The rest is made up of facultative species: staphylococci, streptococci, enterobacteria, neisseria, acinetobacteria and others [18, 19, 16, 23].

According to the results of research under the supervision of Academician N.N. Bazhanov (1985), Professor I.I. Oleynik (1990), conducted using anaerobic cultivation techniques, it was established that *Staph. aureus* accounts for no more than 15 percent of all strains isolated during inflammation of the oral mucosa, and coagulase-negative strains of staphylococci were isolated even less frequently: *St. epidermidis*, *St. saprophiticus*.

At the same time, the release of streptococci (*Str.pyogenes*, *Str.faecalis*, *Str.viridans*) during inflammatory processes in the oral mucosa is somewhat higher 20-30 percent. Although it is necessary to take into account separately the frequency of isolation of microaerophilic streptococci of the oral cavity in children, which occupy an intermediate position between anaerobes and aerobes [17, 16, 18].

It should be especially taken into account that microaerophilic streptococci: *Str.sanguis*, *Str.salivarius*, *Str.mitis*, *Str.mutans*, *Str.millari* are quite often found in pathological material in inflammatory diseases of the oral cavity in children, especially in periodontitis, abscesses, phlegmon, etc. [172,176,186].

It is well known that the mother's birth canal is not sterile and during birth the child receives the microflora located there. However, not all species of the mother's organism colonize the oral cavity of the newborn, which is determined by the characteristics of its genotype and physiology. 6-8 hours after birth, a rapid increase in the number of bacteria in the oral cavity is observed. During this period, as a rule, various aerobic and facultative-anaerobic species are determined: neisseria, sarcins, lactobacilli, streptococci, staphylococci, corynebacteria, etc. [17, 28].

At the same time, the oral cavity microflora reaches its maximum diversity at the age of 2-4 months of life. In this case, the following are isolated from the oral cavity: Neisseria, streptococci, including *Str.salivarius*, as well as yeast-like fungi of the genus *Candida*. Obligate anaerobes appear in the folds and crypts of the mucosa - these are *Veillonella* and some *Fusobacteria* [10, 18, 21].

An important stage in the dynamics of the formation of the oral microbiocenosis is the period of teething. Teeth create conditions for the growth of obligate anaerobic species and bacteria with high adhesive abilities in relation to enamel, these are streptococci (*Str.mutans*, *sanguis*, *actinomycetes*). In preschool children, the microflora of the oral mucosa and gingival groove resembles the microflora of adults and includes bifidobacteria, peptostreptococci, fusobacteria and spirilla. At the same time, most children, as a rule, do not have representatives of the bacteroides group, spirochetes, as well as protozoa [10, 18, 21].

The fact of interaction of normal microflora with the child's immune system is noteworthy, which is confirmed by the detection of antibodies to many types of microbes. Since these data mainly apply to age groups over 1 year, which coincides with the time of teething, it seems likely to us that this interaction is also associated with an inflammatory reaction in the gum during teething [13, 54, 46].

Many studies have established that saliva contains the most important molecular factors: lysozyme, lactoferrin, lactoperoxidase and other enzymes and cellular factors of non-specific resistance of the body. The protective activity of various substances in saliva is associated with both their direct effect on microbes and the inhibition of adhesion to tooth enamel or epithelium of the mucous membrane [19, 40].

It has been proven that lysozyme is an N-acetyl-muramyl hydrolase enzyme, active in a weakly acidic and neutral environment. It causes hydrolysis

of the glycosidic bond in the peptide glycan molecule of the bacterial cell wall. It is produced by lymphocytes, granulocytes, macrophages, and some types of bacteria [19, 49, 14].

At the same time, cellular factors of non-specific resistance – macrophages and microphages (granulocytes) – perform phagocytic function on the surface of the mucosa, in the gingival groove and submucosal layer. However, in children, due to the hypotonic environment of the oral fluid, the active role of leukocytes is significantly limited, and a picture of “incomplete phagocytosis” is often observed. Apparently, it is possible that such a mechanism is biologically justified from the point of view of maintaining equilibrium with the resident flora or stimulation of the antigen-presenting function of macrophages in the immune response [14, 28, 8, 35].

It is interesting to note that active contact with the environment, carried out by our body through the oral cavity, in particular the penetration of a wide variety of antigens, determines that it is a "theater" of action of various effector and effector mechanisms of the human immune system. It has been established that at the level of the mucous membrane, submucous layer of the oral cavity and the lymphoid apparatus of the maxillofacial region, all the most important functions of the immune system are realized to one degree or another [25, 53].

Undoubtedly, secretory IgA (sIgA) plays a particularly important role in this process; their concentration in saliva is 1000 times higher than their concentration in blood serum. sIgA is a dimeric or trimeric macromolecule protected from the action of proteolytic enzymes of saliva by a secretory component of glycoprotein nature. Due to these features, sIgA was considered the only antiviral and antibacterial factor of saliva for a long time. However, it has recently been established that IgM and IgG can also retain their activity in saliva, although their concentration is lower than sIgA [61, 22, 55].

Immunological studies have established that changes in the described defense systems are detected already in the first days of development of

opportunistic infections in the oral mucosa, and sometimes precede clinical manifestations of the disease. This gives grounds to consider defects in nonspecific resistance and immunological reactivity as a trigger factor for acute inflammatory diseases of the oral mucosa [9, 19].

As Loe H [19] notes, the most common cause of weakening human resistance to infection is considered to be a defect in the function of phagocytes. It turned out that the insufficiency of the cellular link of protection activates yeast-like fungi, some bacilli, streptococci, actinomycetes, protozoa, and the oral cavity; apparently, their population size is controlled by these mechanisms.

Loe H [19] also notes that lysozyme deficiency is accompanied by the activation of gram-positive obligate and facultative anaerobic bacteria: peptostreptococci, actinomycetes, staphylococci, streptococci, the peptide glycan herpes of which is destroyed with sufficient activity of this enzyme.

Thus, it is necessary to recognize that the nature of developing local disorders in the focus of inflammation also depends on the type of activated opportunist microbes, the breadth and possibility of realizing their pathogenic properties. This determines the need to consider individual genera and types of oral flora, their pathogenicity factors in the development of acute and chronic inflammatory diseases of the oral mucosa.

1.3. Modern approaches to the treatment of acute herpetic stomatitis in children.

Treatment of herpes simplex complex. It consists of general treatment and local treatment.

General treatment includes a high-calorie diet, plenty of fluids, and antiviral drugs are also widely used.

Antiviral drugs [59] – remantadine 0.05 g 3 times a day for 5-10 days, bonafton 0.1 g 3 times a day for 5-10 days. Kazantseva I.A. 2011 [40] believes

that the best therapeutic effect is provided by acyclovir (virolex, zovirax) and valtrex (valcyclovir).

Less active are bonafton, alpizarin, helipsin, flakozy

Interferon inducers [40] believe that it is better to use ridostin, cycloferon, worse - prodigioson, poludon, since these drugs can increase body temperature.

If other methods are ineffective and in severe cases, drugs such as comedon, aminsin, etc. are recommended [9, 7].

Immunomodulators - antiherpetic immunoglobulin - has a rapid positive effect within 1-3 hours after the administration of human immunoglobulin - the effect occurs on the 2nd day. Immunotherapy is prescribed for moderate acute herpes simplex virus infection in agreement with a pediatrician [48, 50, 51, 32].

Detoxification therapy – plenty of fluids, multivitamins, ascorbic acid. In case of severe intoxication – additional infusion therapy [51, 32].

Hyposensitizing therapy – diphenhydramine, suprastin, pipolfen, diprosin, diazolin, tavegil, fenkarol, etc. Autohemotherapy from 3-5 ml to 9 ml every other day intramuscularly, a course of 7 injections, according to the authors [31, 32, 47] gives a pronounced effect.

Antipyretic drugs are prescribed for temperatures above 38C.

Local treatment begins with application anesthesia of the mucous membrane with 3% anesthesin emulsion, 1% lidocaine solution, 0.5% trimecaine solution. Do not use aerosol preparations.

Vinogradova T.F., Lukinykh L.M. [31, 38, 65] suggest a 4% solution of pyromycaine. In pediatric practice, pyromycaine on glucose, novocaine with urotropin, anesthesin emulsion 5-10%, lidocaine-10%, 0.02% furacilin solution, 0.02% ethacridine lactate solution, 0.01% dimexide solution, 0.1% ethonium solution, etc. are used.

Lukinykh L.M. and co-authors [65] recommend using an antiseptic together with an anesthetic in a 1:1 ratio, the solution is prepared before use. It is used in the form of irrigation, baths, applications 3-4 times a day.

Kazantseva I.A. [6] does not recommend washing the mucous membrane, since this leads to the washing out of natural immunity factors. Strong antiseptics, irritants and cauterizing agents should not be used. Kazantseva I.A. and co-authors [40] recommend using a pale pink solution of potassium permanganate, a furacilin solution, a 1% hydrogen peroxide solution, a 0.02% chlorhexidine solution, and a dimexide solution.

Herbal infusions are also used for local treatment.

Herbal preparations have always attracted the attention of modern medicine. These include naked licorice, which is one of the natural national treasures of our republic. In modern medicine, a number of preparations obtained from naked licorice are used, which have a wide range of pharmacological action. They are not toxic and do not cause side effects [34, 37, 47]. Thus, a group of scientists (Kurbanov G. I and Veliev P. M., 1997) used licorice root syrup in the treatment of acute gastritis. They prescribed licorice root syrup 1 teaspoon 3 times a day for 7 days. As a result of the study, it was found that the use of syrup leads to a reduction in the duration of treatment. Thus, the average time for epithelialization of lesions of the oral mucosa in a mild form was reduced by 2.6 days, in a moderate form - 2.8 days.

At the Department of Hospital Therapeutic Dentistry of the N.A. Semashko Moscow Medical and Dental Institute, lidoamidase was used to treat the oral mucosa. Enzyme preparations also have a good effect - 1-2% solutions of chymotrypsin, gypsin to cleanse erosion areas from necrotic tissue. [57], a 1% solution of lysoamedase or trypsin was used [37].

Lukinykh L.M. and his co-authors [65] used enzymes once a day for 15 minutes - lysozyme, pancreatin, deoxyribonuclease, which has not only a cleansing effect, but also an antiviral effect.

Applications of antiviral ointments are used 3-4 times a day for 20 minutes. E.A. Karmalkova 1990 [70] suggests treating OGS with 3% megasin ointment.

Makhsumova S.S., 1998 [10] suggests 0.75% glycerin ointment for local treatment of OGS.

Shukurova. G, 1999 [61] suggests 3% gosipol ointment for local treatment of OGS.

Vinogradova T.F., Maksimova O.P., Melnichenko E.M. [31] believe that a mixture of interferon with metacil not only has an antiviral effect, but also promotes epithelialization of the affected elements.

Lukinykh L.M. [65] recommends the use of 1% florenole ointment, 0.5%, 0.25%-1% ridoxol and 1-2% oxolinic ointment, as well as 3% gossypol liniment, 0.1% gossypol solution, 0.5% bonafthone ointment and 5% interferon.

They recommend acyclovir in the form of a 3% ointment (zovirax), phonophoresis with a 0.3% solution of acyclovir with 40% dimethyl sulfoxide, and DNase 1% solution. According to their data, the most effective treatment option is phonophoresis of acyclovir with dimethyl sulfoxide - 10 min., 4-5 procedures [40].

Treatment of OGS is aimed not only at reducing the duration of treatment, but also at preventing relapses of the disease.

V.P. Mikhailovskaya, A.G. Kolasheets, E.M. Melnichenko, N.D. Kolasheets. 1989 [15, 27] used specific immunoglobulin with a titer of antibodies to the herpes simplex virus in a dilution of 1:512 in the treatment of acute herpes simplex virus in children.

In connection with the immunological concept of the pathogenesis of AGS, immunocorrective drugs are of great interest. A representative of such drugs is Imudon.

The drug has an effect, it enhances phagocytic activity, increases the content of lysozyme and secretory immunoglobulins in saliva, and stimulates the activity of immune complex cells [48, 50, 32, 60].

A high effect when using agents that stimulate local immunity was obtained by Lukinykh L.M. (2000) - 1% sodium nucleinate solution, 5% methyluracil ointment, 10% methyluracil emulsion, 10% galaccorbin solution - 15-20 min. 3-4 times a day, the course is individual for each patient.

For local treatment of OGS, biological glue MK-7 is used. This glue is autosterile, non-toxic, moisture-resistant, accelerates wound healing, has a hemostatic effect, bactericidal and bacteriostatic properties [56].

Today, Elizarova V.M., Strakhova S.Yu., Dobrotenko L.N. 2003 [32] present new medicinal products: Solcoseryl dental adhesive paste, Mudizal-gel and Piralvex.

A.A. Kubanova, M.A. Gomberg, O.L. Lyazhen (1999) believe that solcoseryl adhesive paste gives a good effect for the complex treatment of stomatitis [82].

This group of drugs also includes "Holysol" - a combination gel that contains choline salicylate, which has an analgesic and anti-inflammatory effect, and an antiseptic - cetyl chloride - has an antimicrobial effect. The gel in the amount of 0.5 cm² - for children, rub into the affected area with light massaging movements 2-3 times a day [57].

From the moment of epithelialization of erosions, keratoplastic preparations are prescribed 2-3 times a day for 20 minutes: vit A in oil, vit E in oil, Shastakovsky's balm, Tezan emulsion, aloe juice and Kalanchoe juice, carotolin, rosehip and sea buckthorn oil. It is appropriate to use keratoplastic agents included in various aerosols - livien, levovinisol, olazol, hypozol, etc. [65].

Additional methods include physiotherapy according to indications.

The combination of physical factors of influence with means of drug therapy allows for a therapeutic effect both on the main manifestations of inflammatory and reparative changes in the tissues of the oral mucosa, and on general body factors that contribute to an increase in its immunobiological stability and normalize its homeostatic parameters.

A.F. Kuznetsova [48] used ultrasound therapy. Her studies showed that after the first exposure to ultrasound antibacterial therapy, inflammatory phenomena were clearly reduced, the subjective and objective condition of patients significantly improved, pain was reduced, the area of damage to the oral mucosa was reduced, the surface was cleaned, and conditions for normal food intake were created. After 2-3 ultrasound treatments, active epithelialization occurred.

When using HBO therapy in complex treatment [48], it was found that after 2-3 sessions, patients with acute forms of the disease noted significant improvements in their general condition.

When using helium-neon laser radiation [11] in patients with OGS, the inflammatory reaction disappeared on the 3-4th day; GNL was also used [22, 31, 32, 48].

S.A. Mamedova, R.G. Gashimov, R.M. Bikbulatov [11] used ultrasonic spraying of interferon and larifan solutions to treat acute gastritis in children. The studies showed that the therapeutic activity depended on both the selected drug and the method of its application. The use of ultrasonic spraying reduces drug consumption.

The mechanism of action of the semiconductor laser (SPL) is due to its positive effect at the cellular and tissue levels. SPL has a multifaceted clinical effect: anti-inflammatory, regenerative, analgesic, bactericidal, etc. SPL stimulates non-specific resistance factors, as well as cellular and humoral immunity [40]. They also used the drug "Optoren". The experience of using the

laser "Optoren" showed the expediency of its use due to the reduction of the pain period and the duration of treatment.

Laser therapy makes it easier for doctors to treat children who have contraindications to drug therapy.

Despite the rich arsenal of methods and means for treating oral diseases and the severe clinical course, the therapy of this pathology remains not yet fully resolved; a large percentage of chronic diseases leads to the search for and development of new methods for treating stomatitis, which is covered in this work.

CHAPTER II

Microbiological and immunological studies of children with acute herpetic stomatitis

2.1 General characteristics of clinical material.

We examined 105 children. The control group included 95 children with acute herpetic stomatitis (AHS) and 10 healthy children from kindergarten No. 419. The studies were conducted on children aged 3 months to 6 years, not burdened with any general diseases. There were isolated cases of 10, 11, 14 year old children. The examined children were divided into 2 groups and 3 subgroups:

Children with acute gastritis (OHS) 95 people were divided into three subgroups according to their clinical course:

Group 1 mild form - 22 children.

Group 2: moderate to severe form - 60 children.

Group 3, severe form – 13 children.

In all examined groups, children over 3 years of age were determined by the hygienic index using the Fedorov-Volodkina method and the PMA index (papillary-marginal-alveolar index). [Parma C., 1960]. The degree of inflammation of the gingival papilla, free marginal and adherent gum was determined by staining the vestibular surface in the area of all available teeth.

The severity of the inflammation process was assessed using the formula

The assessment was carried out according to the following codes

$$RMA = \frac{\text{sum of indicators}}{\text{number of teeth} \times 3} \times 100$$

0 points – no inflammation

1 point – inflammation of the gingival papilla

2 points – inflammation of the gum edge

3 points – inflammation of the alveolar gum

The severity was determined by the following criteria:

Up to 30% - mild degree

30-60% - average degree

more than 60% - severe degree

The degree of oral hygiene was determined using the method of Fedorov. Yu.A. and Volodkina. V.V, 1972; by staining the lower frontal teeth with Lugol's solution according to the following formula

$GI = \text{Total plaque score} / n \text{ number of teeth examined.}$

The intensity of staining of dental plaque on each tooth is assessed using the following codes:

1 point – no staining

2 points – staining of 1/4 of the tooth crown surface

3 points – staining of 1/2 of the tooth crown surface

4 points – staining of 3/4 of the tooth crown surface

5 points – staining of the entire tooth surface.

Scoring criteria

1.1-1.5 points – good oral hygiene

1.6 – 2.0 points – satisfactory oral hygiene

2.1 – 2.5 points – poor oral hygiene

2.6 – 3.4 points – poor oral hygiene

3.6 – 5.0 points – very poor oral hygiene.

AGS is an acute disease characterized by high temperature, general deterioration, increased ESR, leukopenia or leukocytosis. In the pathogenesis of the disease, 5 periods are observed:

- prodromal
- catarrhal
- period of rashes
- fading of the disease.
- clinical recovery.

1. Prodromal period - manifested by a feeling of burning, tingling, itching, a feeling of tension, numbness in the places of future appearance of the rash on the skin and mucous membrane. Poor sleep, malaise are observed.

2. Catarrhal period - characterized by hyperemia and swelling of the mouth and gingival margin. Patients complain of discomfort in the oral cavity when eating.

3. Period of rashes – single or multiple elements of the oral mucosa lesion appear – a spot, a vesicle, a blister and an erosion. The area of the oral mucosa lesion is associated with the severity of the disease.

4. The healing period is characterized by epithelialization of the affected elements. During this period, the affected elements are painless. After the affected areas are cleared of necrotic masses, active epithelialization begins.

5. The period of clinical recovery is characterized by complete restoration of impaired functions.

2.2. CHARACTERISTICS OF THE DRUG CITEAL.

Citeal– a foaming antiseptic solution with antibacterial, antifungal and antiparasitic effects.

The preparation contains chlorhexidine, a cationic antiseptic, a synthetic biguanide, hexamidine, a cationic antiseptic from the diamidine group, and chlorocreosol, an antiseptic from the halophenol group.

Due to the combination of three different components, Citeal has a wide spectrum of activity, which includes:

1. Gram-positive bacteria Streptococci, Staphylococci.
2. Gram-negative bacteria Proteus, Pseudomonas aeruginosa, E.coli, Neisseria gonorrhoeae.

Cyteal

ЦИТЕАЛ МЕХАНИЗМ ДЕЙСТВИЯ

Цитеал представляет собой пенообразующий раствор, который благодаря трем своим компонентам оказывает:

- ✓ бактерицидное действие
- ✓ фунгистатическое действие
- ✓ бактериостатическое действие

СИНЕРГИЗМ ТРЕХ АКТИВНЫХ КОМПОНЕНТОВ



Cytéal ЦИТЕАЛ

ИДЕАЛЬНЫЙ АНТИСЕПТИК ДЛЯ НАРУЖНОГО ПРИМЕНЕНИЯ



- ✓ Эффективен в биологических средах (гной, кровь, серозная жидкость и др.)
- ✓ Образует пену с приятным запахом
- ✓ Не раздражает кожу лица, детскую кожу, слизистые оболочки
- ✓ Уменьшает кожный зуд
- ✓ Не вызывает фотосенсибилизацию
- ✓ Не нарушает экологию кожи и влагилица
- ✓ Сохраняет терапевтический эффект в течении 18 часов

ТРИ АКТИВНЫХ КОМПОНЕНТА ЛУЧШЕ ЧЕМ ОДИН

3. *Candida albicans* fungi.

4. Protozoa *Trichomonas vaginalis*.

Citeal also inactivates the herpes simplex virus (type 1-2)

The drug retains its activity in the presence of biological substances (pus, keratin, blood, serous fluid).

Its effect lasts up to 18 hours after a single application. The drug also has an antipruritic effect.

The main active ingredient of Citeal is chlorhexidine.

Citeal does not irritate tissues and skin, does not cause photosensitivity or changes in skin color, and does not disrupt the ecology of the skin.

Citeal has both therapeutic and prophylactic effects.

All sick children were examined dynamically using clinical and laboratory methods. Dental examination of children was conducted on the first day of their admission. Concomitant and transferred diseases, duration of the main disease, to what extent the child owns and how individual hygienic care of the oral cavity is carried out were found out. Clinical examination of the oral cavity was conducted in the dentist's chair using dental instruments in natural light. When studying the dental status, the condition of hard tissues of teeth, periodontium, oral mucosa, the presence of rashes, aphthae, erosions, swelling, pastosity of plaque on the tongue, the condition of the papillae of the tongue were taken into account. The diagnosis of acute herpetic stomatitis was established on the basis of complaints of sick children, their parents, objective and laboratory data. The severity of the disease was determined by the severity of the temperature reaction, the presence of rashes on the oral mucosa, on the skin of the face and in the oral area. Sick children were divided into three groups according to the severity of the clinical course, and each group was treated using an individual method:

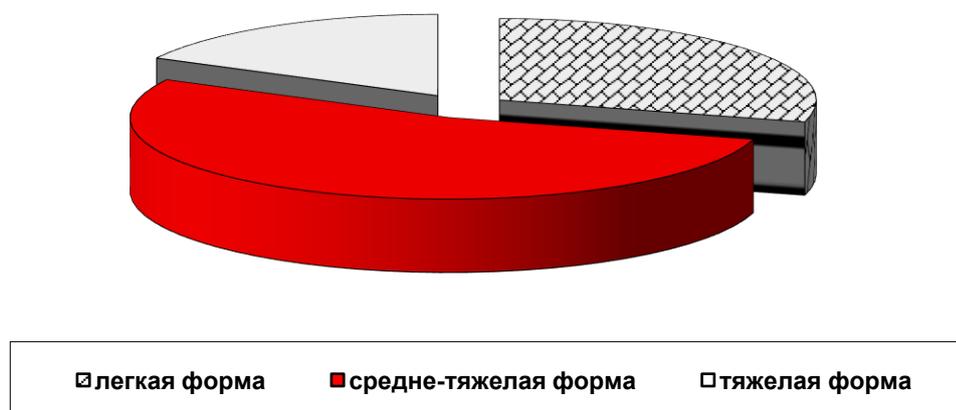
Group 1 mild form of the disease – 22 children. This group of patients was prescribed the drug Citeal in a dilution for local treatment. 1:10+2-3 drops of

2% novocaine 3-4 times a day. Keratoplasty – sea buckthorn oil on the 2nd day of treatment.

Group 2: moderate to severe form of the disease - 40 children. In this group, the drug Citeal was prescribed in a dilution 1:10+ 2-3 drops of 2% novocaine 4-5 times a day, and as for keratoplasty, sea buckthorn oil was prescribed on the 4th day of treatment.

Group 3 – 13 children – severe form of the disease. Against the background of general treatment, Citeal was prescribed in dilution 1:10 6-8 times a day, sea buckthorn oil, as keratoplasty on the 5th day of treatment. (Fig. 1).

Fig. 1 Distribution of patients with acute herpes stomatitis depending on the severity of the disease.



Most microorganisms do not have their own exchange system, but use the exchange system of the macroorganism's cell for vital activity and reproduction. At the same time, a number of new protein compounds are formed in the body, which cause intoxication and allergization of the macroorganism. Often there are also concomitant dyspeptic phenomena. Secondary infection also plays a major role.

In case of acute gastritis, antiviral drugs interferon, tebropfen, oxolinic and other ointments are indicated to suppress the development of the virus, and therefore to stop new rashes on the mucous membrane and skin. In case of mild

form, it is enough to use 0.25% oxolinic ointment, in case of moderate and severe forms, interferon and ointments with tebrofen are more effective. Interferon solution is instilled into the nose and mouth 2-3 drops several times a day. The use of 0.5-1% official tebrofen ointments is more convenient, 2-3% tebrofen ointments are diluted with sunflower or other oil before applying to the mucous membrane of the oral cavity and the child's skin, respectively, 1:1 or 1:2. On the 4-5th and subsequent days of the disease, antiviral drugs are ineffective.

Taking into account the concomitant allergization of the body, it is necessary to widely use desensitizing drugs: 5-10% solutions of calcium gluconate, one teaspoon, dessert spoon or tablespoon 3 times a day, diphenhydramine 0.01 g, suprastin or diprazin 0.005 g 3 times a day for children from one year to 3 years old. For older children, the dose is increased in accordance with age. In young children with acute gastritis, sodium salicylate gives a good effect, which is prescribed in a solution for children under 1 year - 1 ml, under 2 years - 2 ml, etc., but not more than 5 ml, from 6-7 years old, powder can be prescribed 0.5 g 3-4 times a day.

It is necessary to improve bowel function, ensure proper nutrition, prescribe gastric juice, vitamins, especially C and group B, and amidopyrine for neuralgic pain. In severe cases of the child's condition, as well as in cases of sluggish, prolonged course of the disease, general strengthening treatment is used.

2.3. Microbiological studies.

Along with dental research methods, we conducted microbiological and immunological studies on the same children.

For this purpose, oral fluid was collected from all examined children during the examination period 2 hours after meals in sterile test tubes. From the obtained material, serial dilutions were prepared in the laboratory, and a certain

volume of them was subsequently seeded onto the surface of differential diagnostic nutrient media: agar for anaerobes, Endo medium, milk-salt agar, Kalina medium, blood agar, MRS-4 medium, Sabouraud medium, and others.

It should be noted that the microbiology laboratory (TMA), since 2004, has been using new highly selective nutrient media obtained from the company "Hi Media", which opened the Uzbek-American joint venture "Phoenix International" in Uzbekistan.

Crops on blood agar, Endo, milk-salt agar, Saburo were cultivated under normal conditions. 18-24 hours, at a temperature of 37°C, and the cultivation of crops for the isolation of anaerobes was carried out using the method of "sealed" polyethylene bags (Somov L.A. et al., 1987) filled with natural gas (Adylov Sh.K., 1988). Cups with crops on MRS-4 were placed in a desiccator with a candle in a thermostat at 37°C for 24-48 hours. Bags filled with gas with crops on "Blaurocko", KAB were also placed in a thermostat at 37°C for 3-5 days. After the specified periods, the seeded dishes were removed from the thermostat, the grown colonies were counted, the group and species affiliation of the isolated microorganisms was determined based on the data of microscopy of smears stained according to Gram, the nature of growth on selective and differential diagnostic media in accordance with the order of the USSR Ministry of Health No. 535 dated 1985 "On the unification of microbiological research methods." Belonging to the Micrococcaceae family was determined by morphological features and the presence of catalase.

The genus affiliation of *Staphylococcus* and *Micrococcus* was determined by the following tests: the presence of pigment, microscopy data, and the breakdown of glucose under anaerobic conditions.

To differentiate *Staphylococcus aureus* and *Staphylococcus epidermidis*, the following tests were used: the ability to produce hemolysin, plasmacoagulase, lecithinase, and ferment mannitol under anaerobic conditions.

In the presence of all these properties, the studied cultures were classified as *Staphylococcus aureus*. Epidermal *Staphylococcus* did not have such properties.

We included strains that ferment mannitol, grow in 40% bile, 6.5% sodium chloride, and reduce 1% blueing in milk among group D streptococci.

Table 1. The volume of microbiological and immunological studies carried out.

N o.	Group of children	Total examined	Microbiologic al research	Immunologic al studies
1	Control group	10	10	10
2	Children with herpetic stomatitis with traditional therapy.	20	15	15
3	Children with oral candidiasis after traditional therapy.	20	18	17
4	Children with herpetic stomatitis after special treatment with "Citeal".	55	15	16
5	Children with oral candidiasis after special treatment with "Citeal".	40	20	20
Total		145	78	78

When working according to the modified method, the result was taken into account according to the last dilution in which bacterial growth was obtained; the number of microorganisms was calculated according to the following formula:

$$K = A \times 200 \times P \text{ (CFU/ml)}$$

Where, K is the number of bacteria of a certain type;

A – the number of colonies on the plate in the last dilution where there is microbial growth;

200 – coefficient that converts sowing with a loop (volume equal to 0.005 ml) into 1 ml;

P – degree of dilution.

The number of bacteria of each species was expressed as lg CFU/ml.

Taking into account numerous literary data on the pathogenic role of opportunistic autoflora, the presence of pathogenicity factors was determined in the isolated representatives of the salivary microflora.

To study pathogenicity enzymes, generally accepted methods were used; with their help, hemolytic properties, plasma coagulating capacity, fibrinolytic, lecithinase, and hyaluronidase activity were studied.

Cultures possessing two or more pathogenicity factors were considered the most likely agents in the realization of potential pathogenicity.

2.4. Immunological research methods.

In parallel with the microbiological studies, immunological parameters were studied in the same children. To determine the phagocytic activity of neutrophils in saliva, saliva was collected and processed using the method of M.A. Temurbaev (1984) as modified by A.V. Antonov (1996). For this purpose, the collected saliva was purified, washed with a buffered solution and centrifuged at 1000 rpm for 10 minutes: the supernatant was drained, and 0.5 ml of physiological solution was added to the sediment. To 0.2 ml of the resulting mixture, 0.1 ml of latex particle suspension (5×10^8 in 1 ml) with a diameter of 0.8 μm . The mixture was incubated in a humid chamber for 30 min at 37°C, shaking constantly. Subsequently, smears were prepared from this mixture and stained according to Romanovsky-Giemsa. At least 100 neutrophils were counted with and without latex in each preparation, the phagocytic index was determined, i.e., the % of phagocytosed leukocytes from those counted, and the phagocytic number - the average number of absorbed latex particles per phagocytosed cell.

The activity of lysozyme in saliva was determined by us using the method proposed by Aliev Sh.R. (1994), which included the use of sterile paper disks. For this purpose, saliva was collected on an empty stomach in sterile test tubes, then paper disks (similar to antibiotic disks) were taken with tweezers and carefully soaked in saliva, then these disks were placed on the surface of nutrient agar (Diffco agar) in Petri dishes seeded with a lawn of a daily culture of *Micr. lysodenticus* (strain 2665 of the State Clinical Institute named after L.A. Tarasevich), the crops were incubated in a thermostat at a temperature of 37°C, the activity of lysozyme in saliva was determined by the diffusion method in agar.

Determination of class A immunoglobulins of the secretory fraction. The method is based on the Mancini method (1964), which is based on measuring the diameter of the precipitation ring formed when oral fluid is introduced into wells cut in a layer of agar in which monospecific antiserum has been preliminarily dispersed. Under standard experimental conditions, the diameter of the precipitation ring is directly proportional to the concentration of immunoglobulin.

To determine the level of immunoglobulin in the test saliva, we proceeded as follows: the diameter of the precipitation ring of the test oral fluid was plotted on the abscissa axis, the perpendicular was restored to the intersection with the calibration curve, then the straight line was projected onto the ordinate axis. The resulting value corresponded to the level of immunoglobulin, which was expressed in IU/ml.

Chapter III. Clinical and laboratory evaluation of treatment results

3.1. Clinical study of the oral mucosa in acute herpetic stomatitis in children.

During the period of work, 105 sick children were under our observation. Of these, 95 children with acute herpetic stomatitis and 10 healthy children formed the control group. AHS was most often suffered by children aged 3 months to 6 years, but there was one case of a 20-day-old child with AHS – and 5 sick children older 10-13 years.

Children with acute herpetic stomatitis were divided into three groups according to severity – mild, moderate and severe:

OGS mild form of the disease. During examination, in the first days of the disease, locally in the oral cavity of sick children, all the signs of catarrhal gingivitis were observed - the gingival margin was brighter in color than the rest of the oral mucosa, the tops of the interdental gingival papillae were not sharp, but rounded. The oral mucosa was edematous, hyperemic, the gums were bleeding, and single or grouped small aphthae appeared in various areas (Fig. 2).

Eruptions 1-5 mm, single - characterized by the absence of symptoms of intoxication of the body, however, with a satisfactory general condition there may be a subfebrile temperature.

When determining the hygiene index in children of this group, we noted unsatisfactory oral hygiene, which corresponds to 2.1 - 2.5 points. When determining the RMA - characterized by a mild degree of inflammation, which corresponds to up to 30%.

The second group with a moderate form of the disease is the most numerous, since children most often suffer from a moderate form of the disease. Our observations have shown that the disease begins acutely, the body temperature is 38°C, and can reach 40°C. Intoxication is expressed, the child is

lethargic, capricious, sleeps poorly, complains of headaches, and has a significantly reduced appetite. Some children have



Fig. 2. Sick child with mild form of acute gastritis



Fig. 3. A sick child with moderate to severe acute gastritis

nausea, vomiting, bowel disorder. Catarrhal symptoms often join in - cough, conjunctivitis, runny nose. Examination of the maxillofacial region reveals enlarged and painful submandibular, submental, cervical lymph nodes. Locally on the mucous membrane of the oral cavity, we observed all three stages of rashes - vesicle - erosion - aphthae (Fig. 3).

Also noted was the appearance of rashes on the skin of the face, on the red border of the lips and on the mucous membrane of the oral cavity. These rashes were in the form of blisters 1-3 mm in diameter, have transparent contents, after 1-3 days the contents become cloudy, the blister dries into a crust. If the blister cover is damaged, erosion is formed. Round erosions - aphthae, painful, localized on the tongue, mucous membrane of the lips, cheeks, less often on the palate, arches, gums. Fusion of aphthae with each other and the formation of extensive erosions of various outlines were observed. The mucous membrane is free of erosions, hyperemic and edematous, the tongue is coated, there are imprints of teeth along the edges of the tongue. The gingival margin is also sharply hyperemic and edematous, in places there are erosions. Salivation increases, saliva is viscous, stringy with an unpleasant odor.

In children of this group, the hygienic index GI was 2.6 – 3.4 points, which corresponds to poor oral hygiene, and RMA = 30-60%, which is typical for the moderate severity of the disease.

Group 3 – severe form of acute gastritisThe general condition of the children was characterized by the presence of all the signs of an infectious disease - apathy, adynamia, headache, nausea, vomiting, since the herpes virus is encephalotropic.

Body temperature is 39-40°C. When examining the oral cavity of sick children, the oral mucosa is edematous, hyperemic, covered with a large number of aphthous elements that recur. At the same time, the lips, mucous membrane of the cheeks, soft and hard palate, tongue, and gingival margin are affected. Ulcers, bleeding, swelling, and pain when touched are noted on the gingival

margin. In children with a severe form of the disease, the development of deep ulcerative-necrotic lesions of the oral mucosa is noted. Sick children completely refuse food. The disease lasts 7-15 days, the symptoms of gingivitis persist longer. The hygiene index in children with a severe form of the disease is very poor, which is equal to 5 points. RMA is characterized by 60% and more, corresponding to a severe degree of damage (Fig. 4, 5).

3.2. State of the oral microflora in sick children with herpetic stomatitis.

It is known that the oral cavity of a human body contains the largest number of bacterial species compared to other cavities, not including the large intestine. According to various authors, the number of bacterial species, including anaerobes, ranges from 100 to 200. This is explained not only by the fact that bacteria enter the oral cavity with air, food, water, etc., the so-called transit microorganisms, but here we are talking about the resident bacterial flora of the oral cavity, which forms a rather complex and stable ecosystem.

Numerous studies conducted both in our country and abroad have proven that in the vast majority of cases, pathological processes in the oral cavity are usually accompanied by dysbiotic changes in the microflora of the oral fluid, which in turn leads to a disruption of the immune system indicator.

According to modern data, human herpesviruses types 1 and 2 belong to Alphaherpesvirinae and are characterized by effective destruction of affected cells, a relatively short reproductive cycle and the ability to remain latent in the ganglia of the nervous system. The virus is found in saliva both in the presence of lesions of the mucous membranes of the oral cavity, and without them, when the disease is asymptomatic. Clinically expressed primary herpes infection is observed more often in children aged 6 months - 5 years and less often in adults. In children, the most common form of primary herpes is aphthous stomatitis, accompanied by extensive lesions of the mucous membrane of the oral cavity /Shuvalova E.P., 1999/.

Considering the associative nature of the "Microbial Landscape" in various pathological processes in the oral cavity, the question naturally arises about the role of individual representatives of the microflora in the development and course of the disease; in this we will be helped by studying the quantitative and qualitative ratio of individual representatives of the microbial flora.

Features of herpetic stomatitis.

Based on the above, we conducted a study of the quantitative and qualitative composition of the microflora of the oral fluid in children with herpetic stomatitis. The study was conducted taking into account the clinical course of acute herpetic stomatitis in children, which is classified into three forms: mild, moderate and severe.

Initially, we were interested in looking at the comparative aspect of the normal flora of the oral cavity in adults and children. We used the data of the normal flora of adults obtained at the Department of Microbiology of the TMA /Mukhamedov I.M., 2003/. The obtained data are presented in Table No. 2

As can be seen from the table, it is interesting to note that the healthy children we examined actually had the same types of microorganisms isolated from the children; moreover, microbes such as saprophytic staphylococci, lactose-positive *Escherichia coli*, which are not found in adults.

However, if we look at the obtained quantitative data, it is clearly visible. That in adults, the majority of microbial populations significantly prevail in comparison with the data in children. Here it is especially appropriate to note that these quantitative parameters are more related to anaerobic flora, while facultative flora in its quantities is not so significant. Apparently, this is a natural evolutionary process characteristic of a child's organism, since in their oral cavity, the necessary conditions for the development of anaerobic flora have not yet been created.

As stated above, we have conducted microbiological and immunological studies of sick children with acute herpetic stomatitis depending on the clinical form and severity of the disease. The information obtained from microbiological studies of sick children suffering from acute herpetic stomatitis in a mild form is given in Table 3. As can be seen from the table, dysbiotic changes in the microflora develop in children suffering from acute herpetic stomatitis in the oral cavity. Thus, in the flora of the oral fluid of children when visiting a polyclinic, it is clear that the most significant changes are observed in the anaerobic flora.

A characteristic trend of these changes is a reliable decrease in the total number of anaerobes, which amounted to $\lg 4.60 \pm 0.15$ CFU/ml with a normal \lg of 5.69 ± 0.15 CFU/ml ($P > 0.001$).

The same tendency to decrease is observed in lactobacilli cultures when their number was equal to $\lg 3.30 \pm 0.1$ CFU/ml, with a normal \lg of 4.60 ± 0.14 CFU/ml ($P > 0.001$).

Table No. 2. Characteristics of normal flora
oral cavity in children and adults.

N o.	Groups of microbes	Lg M±m CFU/ml	
		Number of microbes in 1ml of saliva	
		Norm in adults	Norm in children
1	Total number of anaerobes	7.60 ± 0.41	$5.69 \pm 0.15^{***}$
2	Lactobacilli	5.90 ± 0.14	$4.60 \pm 0.14^{***}$
3	Peptostreptococcus	6.00 ± 0.39	$3.77 \pm 0.11^{***}$
4	Total number of aerobes	6.30 ± 0.41	$5.30 \pm 0.17^*$
5	Staphylococcus aureus	-	-
6	Staphylococci saprophytic	-	2.15 ± 0.51
7	Staphylococcus epidermidis	3.15 ± 0.30	$4.15 \pm 0.14^{***}$

8	Streptococci group A.	-	-
9	Enterococci	4.30±0.19	5.15±0.15***
10	Escherichia coli Lp	-	2.30±0.17
11	Escherichia LN	-	-
12	Mushrooms of the r. Candida	1.30±0.25	2.15±0.18***

Note: *- presence of reliability (P>0.5) compared to control

***- presence of reliability (P>0.001) compared to control

Although it should be noted that among the anaerobic flora the number of peptostreptococci increased and amounted to lg 4.59±0.16 CFU/ml. Apparently, this is associated with compensatory adaptive processes in the oral cavity.

However, the most pronounced quantitative shift in the oral cavity in children occurred in the optional flora. Thus, as can be seen from the table, the total number of aerobes increased reliably by almost 2 orders of magnitude, which amounted to lg 7.15±0.31 CFU/ml, with the norm equal to lg 5.30±0.17 CFU/ml. reliability (P>0.5). In fact, most microorganisms studied in the oral cavity tend to increase, such as saprophytic staphylococci, Escherichia, fungi, while a decrease was noted only in epidermal staphylococci and enterococci.

It is also worth noting that children suffering from mild forms of acute gastritis had microbes in their oral fluid that were not cultured in healthy children; here we mean the detection of cultures of goldenseal.

staphylococcus (Fig. 8, 9) pyogenic streptococcus (Fig. 10, 11) and lactose-negative strains of Escherichia coli. It is appropriate to say that this is nothing more than strains with more pronounced aggressive properties and treating dentists must take this into account when providing medical care. It should be noted that the greatest quantitative shifts towards an increase were noted in Candida fungi, when their number was equal to lg 5.30±0.21 CFU/ml with control data lg 2.15±0.18 CFU/ml. reliability (P>0.001).

Table No. 3. State of the microflora of saliva in children with mild acute herpetic stomatitis.

Lg M±CFU/ml

N o.	Groups of microbes	Number of microbes in 1ml of saliva		
		Norm	Upon admission	After traditional treatment
1	Total number of anaerobes	5.60±0.15	4.60±0.15	6.11±0.32***
2	Lactobacilli	4.60±0.14	3.30±0.11	3.47±0.17
3	Peptostreptococcus	3.77±0.11	4.59±0.16	4.49±0.21
4	Total number of aerobes	5.30±0.17	7.15±,41	6.17±0.34
5	Staphylococcus aureus	-	2.30±,11	1.30±0.11***
6	Staphylococci saprophytic	2.15±0.51	3.15±0.17	3.00±0.15
7	Staphylococcus epidermidis	4.15±0.14	3.30±0.15	3.47±0.16
8	Streptococci group A.	-	1.15±0.05	1.30±0.07**
9	Enterococci	5.15±0.15	3.47±0.13	3.60±0.12
10	Escherichia coli LP	2.30±0.17	5.49±0.31	4.47±0.16***
11	Escherichia LN	-	4.30±0.22	2.30±0.10***
12	Mushrooms of the r. Candida	2.15±0.18	5.30±0.21	3.12±0.21***

Note: ** - reliability (P>0.01) compared to control

***- presence of reliability (P>0.001) compared to control



Fig. 8. Colonies of *S. aureus* growing on blood agar. Zones of hemolysis are visible around the staph colonies.

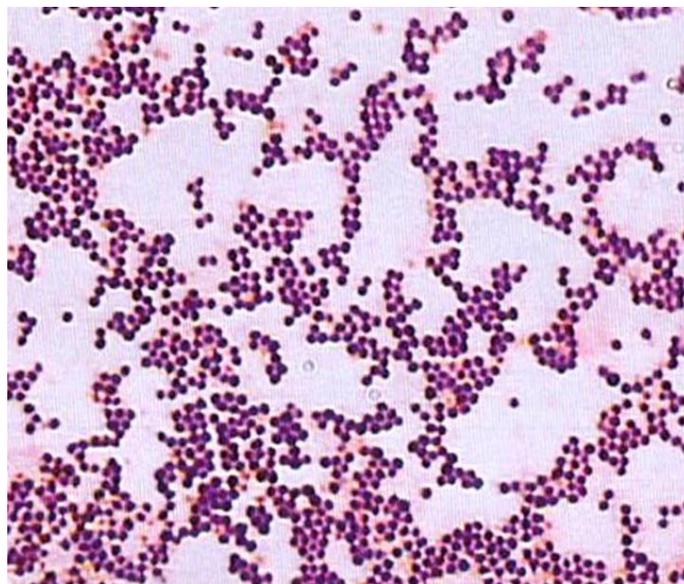


Fig. 9. Smear of pure culture of *S. aureus*. Gram staining

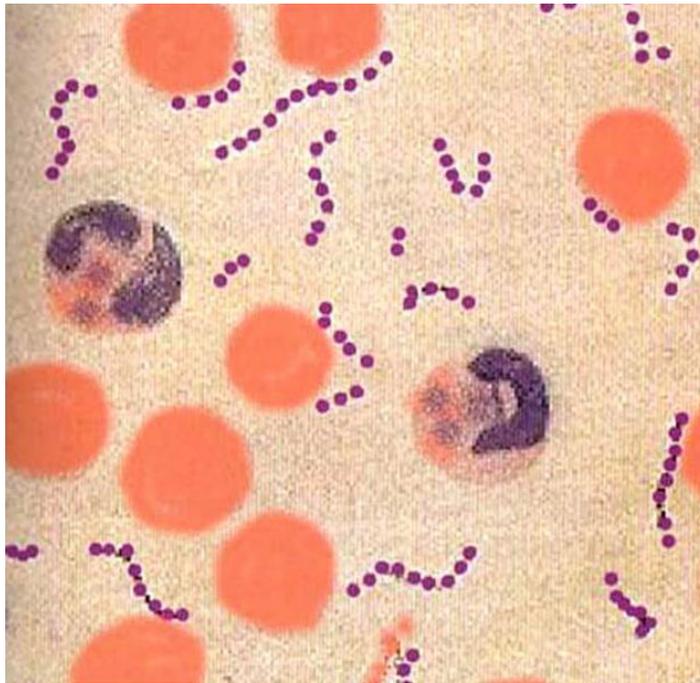


Fig. 10. Streptococcus in pus. Gram stain

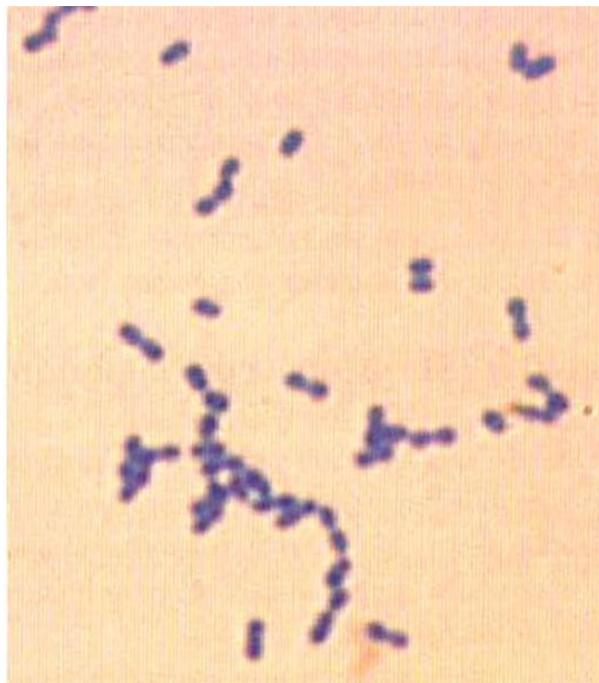


Fig. 11. *Streptococcus pyogenes*. pure culture. Methylene blue staining

One group of children suffering from mild forms of AGS underwent conventional treatment (the method of traditional therapy is given in the chapter Material and methods of research), after which they also underwent microbiological studies. The data obtained during these studies are given in Table 3. The table shows that in general the course of traditional therapy had a positive effect on the state of the oral fluid microbiocenosis, this information also correlates with the clinical picture in these patients. Thus, it can be noted that the total number of anaerobic microbes increased significantly and they amounted to $\lg 6.11 \pm 0.32$ CFU/ml, reliability ($P > 0.001$), which is slightly higher compared to data in healthy children.

It is noteworthy that against this background, when the number of anaerobes has increased, the quantitative indicators of facultative flora, on the contrary, have a tendency to decrease. Thus, the total number of aerobes has significantly decreased, and amounted to $\lg 6.17 \pm 0.37$ CFU/ml. We see the same tendency to decrease in quantity in microorganisms related to saprophytic staphylococci, enterococci, *Escherichia* and fungi.

At the same time, the quantitative parameters of pathogenic staphylococci and streptococci remained almost unchanged.

Thus, based on the obtained microbiological data, we can rightfully assert that the course of traditional therapy conducted in sick children suffering from mild forms of AGS generally had a positive effect on the state of the oral microflora. However, unfortunately, we cannot speak of a complete microbiological recovery, since the picture of dysbiotic shifts in the oral cavity still persists and requires additional intervention.

The next group of children consisted of children suffering from moderate acute gastritis. We also conducted microbiological studies of oral fluid in these children, these data are presented in Table 4. The table shows that dysbiotic changes were also detected in the oral cavity of these children at the stage of

visiting the clinic. These changes primarily concern the quantitative parameters of anaerobic groups of microbes.

Thus, in this study group we found a significant decrease in the total number of anaerobes and it amounted to $\lg 4.27 \pm 0.17$ CFU/ml with a normal \lg of 5.69 ± 0.15 CFU/ml. reliability ($P > 0.5$). Also, some decrease in the number of lactobacilli was noted, however, against this background, we see some increase in the number of peptostreptococci.

However, the most pronounced quantitative changes in these sick children were noted by us in the facultative flora of the oral cavity. Thus, the total number of aerobes increased by 3 orders of magnitude, and amounted to $\lg 8.11 \pm 0.57$ CFU/ml. In this group of children, we also see a tendency for such microbes as saprophytic staphylococci, *Escherichia coli* and *Candida* fungi to increase in the oral cavity.

It is interesting to note that in this group of children, as in the previous group of children with mild acute gastritis, we found the culture of microbes that are not found in the control group of children, these are such microbes as: *Staphylococcus aureus*, pyogenic streptococci and lactose-negative strains of *Escherichia*. The question naturally arises, then, how do these clinical forms differ from each other in the microbiological aspect.

Here, it can be clearly noted that with a moderate course of acute gastritis in children, compared with a mild form, it can be stated that dysbiotic changes differ in the degree of their expression, since quantitative parameters, especially for microbes with high aggressiveness, are more pronounced in patients with a moderate course compared with children who have a mild course.

This group of children with moderate acute gastritis also underwent traditional therapy /the treatment method is given in the section Material and Research Methods/. Upon completion of the traditional treatment course, we re-examined the state of the oral fluid microflora in these same children. These

studies showed that the traditional therapy course generally had a positive effect on the state of the oral microbiocenosis.

Table No. 4. Characteristics of the oral microflora in children with moderate acute herpetic stomatitis lg M±m CFU/ml.

No	Groups of microbes	The number of microbes in 1 ml of saliva in patients with moderate acute gastritis		
		Norm	Upon admission	After traditional treatment
1	Total number of anaerobes	5.60±0.15	4.27±0.25	5.47±0.37***
2	Lactobacilli	4.60±0.14	3.15±0.15	3.00±0.12
3	Peptostreptococcus	3.77±0.11	4.17±0.21	4.47±0.25
4	Total number of aerobes	5.30±0.17	8.11±0.57	6.49±0.41*
5	Staphylococcus aureus	-	2.60±0.11	2.00±0.11***
6	Staphylococci saprophytic	2.15±0.51	3.15±0.15	3.11±0.15
7	Staphylococcus epidermidis	4.15±0.14	3.30±0.12	3.30±0.17
8	Streptococci group A.	-	2.30±0.11	1.89±0.01***
9	Enterococci	5.15±0.15	4.59±0.27	4.60±0.31
10	Escherichia coli LP	2.30±0.17	4.47±0.26	3.60±0.02***
11	Escherichia LN	-	5.11±0.31	2.29±0.14***
12	Mushrooms of the r. Candida	2.15±0.18	4.30±0.23	3.47±0.13**

Note: *- presence of reliability (P>0.5) compared to control

** - presence of reliability (P>0.01) compared to control

*** - presence of reliability (P>0.001) compared to control

Thus, we have found an increase in the total number of anaerobes up to lg 5.47±0.37 CFU/ml reliability (P>0.001) and against this background a reliable decrease in the total number of aerobic microbes when their number was equal to lg 6.49±0.41 CFU/ml. reliability (P>0.5). And, what is especially important to note is that after the course of traditional treatment, most microbes that had a tendency to increase, significantly decreased in their quantities. However, we consider it important to note that traditional treatment had almost no positive effect on the quantitative parameters of microbes with a high degree of

aggressiveness. Based on these patterns, we are forced to state that although the course of traditional therapy generally has a positive effect on the state of dysbiosis, it is still too early to talk about complete microbiological recovery.

Apparently, in our opinion, this condition may subsequently serve as a cause for the relapse of the underlying disease, although it is possible that at the next stage it may lead to the transition of the moderately severe form of acute gastritis to a severe form.

The next group in the study consisted of children suffering from a severe form of acute herpetic stomatitis.

We also conducted microbiological studies of the oral cavity in this group of children; the data obtained from these studies are presented in Table No. 5.

From which it is evident that children suffering from a severe form of acute gastritis when visiting a clinic had a dysbiotic condition in the oral cavity.

At the same time, a significant decrease in the total number of anaerobic microorganisms is characteristic, among which the number of lactobacilli has decreased almost twofold, while the number of peptostreptococci, on the contrary, increased and amounted to $\lg 5.11 \pm 0.27$ CFU/ml with a normal \lg of 3.77 ± 0.11 CFU/ml. reliability ($P > 0.001$).

However, as expected, reliable shifts occurred in the optional group of microorganisms, as their total number reached the $\lg 8.57$ indicator. ± 0.53 CFU/ml with a normal \lg of 5.30 ± 0.17 CFU/ml. reliability ($P > 0.5$). That is, it increased by more than three orders of magnitude. In this group of patients, we also found a reliable increase in such microbes as *Escherichia* and fungi. Moreover, in this group of patients, microorganisms with a high degree of aggressiveness were also found, while it is alarming that their number significantly prevails compared to previous groups of patients.

Table No. 5. State of the microflora of oral fluid in children patients with severe acute gastritis

$\lg M \pm m$ CFU/ml.

N o.	Groups of microbes	The number of microbes in 1 ml of saliva in patients with severe acute gastritis		
		Norm	Upon admission	After traditional treatment
1	Total number of anaerobes	5.69±0.15	4.11±0.27	4.59±0.25
2	Lactobacilli	4.60±0.14	2.30±0.11	1.60±0.09***
3	Peptostreptococcus	3.77±0.11	5.11±0.31	3.27±0.21***
4	Total number of aerobes	5.30±0.17	8.57±0.57	6.85±0.37**
5	Staphylococcus aureus	-	2.59±0.15	1.47±0.09***
6	Staphylococci saprophytic	2.15±0.51	2.30±0.12	2.30±0.11
7	Staphylococcus epidermidis	4.15±0.14	3.15±0.15	3.30±0.21
8	Streptococci group A.	-	3.00±0.17	2.49±0.12*
9	Enterococci	5.15±0.15	3.60±0.17	4.11±0.27
10	Escherichia coli LP	2.30±0.17	5.87±0.41	4.29±0.29**
11	Escherichia LN	-	6.47±0.42	2.47±0.12***
12	Mushrooms of the r. Candida	2.15±0.18	5.30±0.23	3.11±,15***

Note: *- presence of reliability (P>0.5) compared to control

** - presence of reliability (P>0.01) compared to control

*** - presence of reliability (P>0.001) compared to control

Naturally, the question arises as to why such pronounced dysbiotic changes are observed in sick children suffering from OGS in all clinical forms of the disease. In our opinion, this is primarily due to the fact that OGS viruses, like other pathogenic viruses, have the ability to exert an immunosuppressive effect on the macroorganism, which leads to the activation of the normal flora of the oral cavity.

3.3. Immunology of oral fluid in children suffering from acute herpes infection.

The development and widespread introduction of immunological analyses into clinical practice in the last decade shows that the frequency of numerous diseases of the oral cavity, especially various inflammatory processes in children, is directly or indirectly dependent on the state of both general and local factors of immunity of the oral cavity.

According to modern data, mixed saliva and oral fluid are a colloidal solution built from micelles of phosphates and calcium hydrophosphates surrounded by dense water-protein membranes. Saliva contains the most important molecular: lysozyme, lactoferrin, lactoperoxidase and other enzymes, components of the complement system, and cellular: granulocytes and macrophages, which are factors of non-specific resistance of the body. The protective activity of various substances in saliva is associated with both their direct effect on microbes and inhibition of adhesion to tooth enamel or mucous membrane epithelium.

It should be noted that the exact mechanism that determines the causal role of opportunistic flora in inflammatory diseases of the oral mucosa has not yet been established. Although, the main postulate is the position on the determining role of regulatory immune and non-immune mechanisms in the balance of all components of the microbiocenosis of the disorder that leads to the development of the infectious process. Clear confirmation of this is the polyetiology of opportunistic infections, that is, from the inflammatory focus, as a rule, associations of several types are isolated, which is confirmed by the dynamics of the level of antibodies to their antigens.

At the same time, one cannot ignore the possibility of qualitative changes in the properties of the microorganisms themselves, that is, regulatory influences within the microbiocenosis - that is, the pathogenization of residents.

Apparently, and most likely, the first and second factors are closely related at the molecular level of biochemical regulation of microflora.

It is known that human herpes viruses are characterized by effective destruction of affected cells, a relatively short reproductive cycle and the ability to remain latent in the ganglia of the nervous system. Clinically expressed primary herpes infection is observed more often in children aged 6 months to 3 years.

Along with microbiological studies, we conducted immunological studies on the same sick children suffering from herpetic stomatitis. In this case, we paid much attention to the study of local factors of oral cavity protection, such as the level of lysozyme, the phagocytic index of leukocytes, the titer of the secretory fraction of immunoglobulin class A (s IgA) in oral fluid.

Initially, it seemed interesting to us to conduct a comparative analysis of these factors of non-specific protection in adults and children; this information is presented in Table No. 7.

The table shows that these indicators in adults and children are close to each other, although it should be noted that the level of lysozyme in saliva and the phagocytic index are somewhat higher, and the level of secretory immunoglobulin A is somewhat lower. Apparently, these states of non-specific protective factors in children are due to the anatomical and physiological characteristics of the child's body.

We studied the same parameters of non-specific protection of the oral cavity in sick children with acute herpetic stomatitis, taking into account the clinical course of these diseases, this information is given in Table No. 8. Analysis of the obtained data shows that in sick children suffering from herpetic stomatitis in all clinical forms of the disease, significant immunodeficiency is observed.

Table No. 7. Indicators of non-specific factors of oral cavity protection in healthy people.

No.	Indicators	Norm in adults	Norm in children
1	Lysozyme level, mg %	18.0±0.60	19.7±0.70*
2	Phagocytic index, %	55.3±1.20	58.1±1.50*
3	Level s Ig A, g/l	2.0±0.10	1.8±0.30

Note: * - presence of reliability (P>0.5) compared to control

It is noteworthy that the more severe the disease, the deeper the secondary immunodeficiencies. Moreover, the table shows that the traditional therapy we conducted for these patients does not give the desired results. Although, it should be noted that traditional therapy generally has a positive effect on the immune system indicators, but it is impossible to talk about a complete correction of the identified immunodeficiency disorders, which becomes one of the reasons for the chronicity of the disease.

It is known that most pathogenic viruses have an immunosuppressive effect on our body; in fact, in our research we found complete confirmation of these postulates.

According to the opinion of the majority of well-known mycologists, the significant increase in the incidence of candidiasis, which has been observed in the last decade, is primarily due to the fact that this infection is opportunistic, and therefore primarily affects a weakened organism; this apparently explains the most frequent lesions of the oral cavity in children, whose immune system has not yet fully matured.

Table No. 2. Characteristics of normal flora
oral cavity in children and adults.

No.	Groups of microbes	Lg M±m CFU/ml	
		Norm in adults	Norm in children
1	Total number of anaerobes	7.60±0.41	5.69±0.15***
2	Lactobacilli	5.90±0.14	4.60±0.14***
3	Peptostreptococcus	6.00±0.39	3.77±0.11***
4	Total number of aerobes	6.30±0.41	5.30±0.17*

5	Staphylococcus aureus	-	-
6	Staphylococci saprophytic	-	2.15±0.51
7	Staphylococcus epidermidis	3.15±0.30	4.15±0.14***
8	Streptococci group A.	-	-
9	Enterococci	4.30±0.19	5.15±0.15***
10	Escherichia coli Lp	-	2.30±0.17
11	Escherichia LN	-	-
12	Mushrooms of the r. Candida	1.30±0.25	2.15±0.18***

Note: *- presence of reliability (P>0.5) compared to control

***- presence of reliability (P>0.001) compared to control

Thus, based on the conducted studies in sick children suffering from herpetic stomatitis and oral candidiasis, a comparative analysis shows that both with herpetic stomatitis and with candidiasis, dysbiosis and immunodeficiency are observed in the oral cavity, but the degree of expression of these changes is higher in patients with candidiasis. Apparently, these features are a natural evolutionary process that has become entrenched in the macroorganism, which must be taken into account in their practical work by pediatric dentists.

It should be especially emphasized that based on our studies of the microflora and immunology of the oral cavity in children suffering from herpetic stomatitis and candidiasis, all of the above postulates are confirmed. Nevertheless, from the information we have provided, it is clear that the entire set of microbial associations is determined in the microflora of the oral fluid of sick children, most of which are also cultured in healthy children. However, the whole interest of the studies is that there are reliable differences in both quantitative and qualitative parameters.

CHAPTER IV.

COMPARATIVE EVALUATION OF THE THERAPY

4.1. Evaluation of the clinical efficacy of using Citeal for acute gastric stomatitis in children.

Clinical effectiveness of the treatment determined by the following indicators: decrease in body temperature, acceleration of epithelialization, elements of damage to the oral mucosa, improvement in the general condition of the child.

Patients with OGS were divided into two groups:

1 A group of children with acute gastritis formed a comparison group and received traditional therapy.

2 A group of children - OGS, formed the main group and received the drug Citeal.

4.1.1 Comparative characteristics of the therapy carried out acute herpetic stomatitis.

We observed 95 children with acute gastritis. Against the background of general treatment, children with acute gastritis received local treatment. In the mild form of acute gastritis, children in group 1 were treated with a cotton swab soaked in 0.5% furacilin solution and applied with 0.25% oxolinic ointment. On the second or third day, children were able to eat freely, and their capriciousness and lethargy passed. Epithelialization of the elements began on the 2nd or 3rd day, which consisted of a decrease in the hyperemic rim around the aphthae, the aphthae became less painful to the touch, and decreased in size. With the onset of epithelialization, sea buckthorn oil was applied. Complete recovery occurred in 4-5 days.

In moderate to severe cases, local traditional therapy was used - children had a fever for 2 days, ate poorly, were adynamic, salivation continued for 4 days, lymph nodes were painful to palpation throughout

the treatment period. The lymph nodes decreased in size on the 5th-6th day after treatment. Gum bleeding disappeared on the 3rd-4th day. Epithelialization occurred on the 4th day after the start of treatment. Aphthae epithelialized slowly, the hyperemic rim around the aphthae decreased within 3-4 days. Aphthae began to decrease in size on the 4th-5th day, were painful for a long time.

Recovery occurred within 7-14 days

Against the background of general treatment of patients with a severe form of the disease using traditional therapy, children had a fever for 4-5 days, did not eat well, had headaches, salivation continued, the lymph nodes were painful when palpated throughout the treatment period. A decrease in the lymph nodes occurred on the 6th-7th day after treatment. Bleeding gums disappeared on the 5th-6th day. Epithelialization occurred on the 6th day after treatment. Aphthae epithelialized slowly, the hyperemic rim around the aphthae decreased within 5-6 days. The aphthae began to decrease in size on the 5th-6th day, were painful for a long time. Recovery occurred 10-14 days.

In the second group, with a mild form of acute gastritis, a diluted solution of Citeal was used. 1:10 and sea buckthorn oil. For pain relief, 2-3 drops of 2.0% novocaine were added to the solution. By evening, the children were able to open their mouths freely and eat without difficulty. Capriciousness and lethargy passed on the second day. Epithelialization of aphthae occurred on the second day after treatment. The aphthae significantly decreased in size, were painless when touched, and the hyperemic rim around the aphthae disappeared completely on the third day. Full recovery occurred on the 3rd-4th day.

Thus, in the mild form of the course of AGS, the use of the drug Citeal compared to the traditional method of treatment gave an earlier

improvement in the clinical condition of children. Clinical recovery occurred earlier by 1 - 2 days than with traditional treatment.

In the second group of children with a moderate form of the disease, when using the drug Citeal, children on the second day freely opened their mouths and ate food. Also on the second-third day after the treatment, salivation decreased. In older children, headaches and bleeding gums decreased. On the 3-4th day after the treatment, children began to epithelialize, the lymph nodes decreased in size, the hyperemic rim around the aphthae disappeared, the aphthae became less painful when touched, the mucous membrane acquired a pale pink color. Complete recovery occurred on the 5-7th day.

Thus, in moderate to severe cases of acute gastritis, the use of the drug Citeal compared to the traditional method resulted in an improvement in the clinical picture, i.e. the disease proceeded in a less severe form and gave earlier recovery times against the background of general treatment, which was confirmed by the general clinical condition of sick children. The results of our studies showed that Citeal has good antiseptic, bactericidal, antiviral and antimycotic action.

Children with a severe form of the disease were given the drug "Citeal". Children in this group were able to open their mouths freely on the 4th-5th day and began to eat. Salivation decreased on the 5th day. In older children, headaches and bleeding gums decreased. On the 5th day, children began to epithelialize after the treatment, the lymph nodes decreased in size, the hyperemic rim around the aphthae disappeared, the aphthae became less painful to the touch, and the mucous membrane acquired a pale pink color. Complete recovery occurred on the 7th-8th day.

Thus, the use of the drug "Citeal" in severe forms of the course of the disease of acute gastritis against the background of general treatment provides early recovery, compared with the traditional method of treatment. This is confirmed by the improvement of the clinical condition of sick children (Fig. 16).



Fig. 16. A sick child with OGS after treatment with Citeal.

4.2. Study of the effect of the drug "Citeal" on the parameters of salivary microflora in children with herpetic stomatitis of the oral cavity.

The barrier-protective mechanisms of the oral cavity are closely related to the microflora of the oral cavity. The variety and activity of the microflora of the oral cavity often predetermines the pathology of its hard and soft tissues. Unsatisfactory hygienic conditions of the oral cavity, especially in children, contribute to the development of a dysbiotic condition here. Traditional methods of treating the oral cavity, when various chemicals such as potassium permanganate, menthol, elixirs are used, do not have a pronounced bacteriostatic effect, in connection with which new antiseptic drugs are being sought.

It is well known that the oral microflora is diverse and difficult to study. Bacteria, fungi, viruses and protozoa inhabiting the oral cavity are no exception. The fact is that the oral cavity, its mucous membrane and the lymphoid apparatus of the maxillofacial region play a unique role in the interaction of the human body with the surrounding world of microbes.

Based on the above, it is logical to find preparations for treating the oral cavity that would have a wide range of antibacterial, antifungal and antiviral effects. The preparation "Citeal" meets all these properties.

The drug "Citeal" (Evromedex) was developed in 1954 in England, initially created as an antiviral agent. It is a foaming antiseptic solution used to treat mucous membranes and contains three sets: chlorhexidine, gypsamidine, chlorpresol, which are active against gram-positive, gram-negative bacteria, mycobacteria and fungi.

Initially, we studied the sensitivity of some types of microbes, taking into account their occurrence in the oral cavity, to the drug "Citeal" under in vitro conditions. For this purpose, certain types of

microbes were seeded in a "lawn" pattern on a Petri dish with a nutrient medium, then pieces of filter paper (similar to antibiotic disks) were taken, soaked in various concentrations of the drug "Citeal" and then placed on the surface of the nutrient agar with the seeding. The dishes were kept in a thermostat at a temperature of 37C for 24 hours. Then, the dishes were removed and the zones of inhibition of microbial growth around the piece of filter paper were measured.

The obtained data on determination of microorganism sensitivity to the preparation "Citeal" in various dilutions are presented in Table 10. It is evident from the table that the preparation "Citeal" in concentrated form has a pronounced antibacterial effect on both gram-positive and gram-negative microbes. It is also evident from the table that the preparation "Citeal" in concentrated form had the most pronounced effect on staphylococci, streptococci, Escherichia and lactobacilli, and the least effect on pathogenic staphylococci, lactose-negative strains of Escherichia and on the culture of Proteus.

At the same time, when diluting the drug, its antibacterial effect is significantly reduced, and as can be seen from the table, when diluting the drug in 1/5 and 1/10, the antibacterial effect, although reduced, is preserved against all studied microorganisms. However, in a dilution of 1/20, the antibacterial effect of the drug is sharply reduced, although it should be noted that in this dilution it continues to have an effect on gram-positive microorganisms.

Sensitivity of some oral microorganisms to Citeal under in vitro conditions.

No	Groups of microbes	Concentration of "Citeal"			
		1/5 20%	1/10 10%	1/20 5%	100%
1	Streptococci	15.1+1.2	10.2+0.8	5.4+0.6	17.1+1.4
2	Staffordshire Golden	-	-	-	5.1+0.4
3	Staff. Epidermal	16.1+1.3	11.1+0.9	5.7+0.7	21.1+1.6

4	Staff. Saprophyte	12.3+1.1	10.1+1.0	7.2+0.8	22.4+2.1
5	Escherichia LP	10.1+1.0	5.2+0.6	-	12.4+1.1
6	Escherichia LN	5.3+0.4	-	-	7.1+0.7
7	Klebsiella	11.1+1.2	5.6+0.7	-	13.1+1.2
8	Mushrooms of the r. Candida	7.1+0.6	5.4+0.7	-	8.4+0.8
9	Pseudomonas	-	-	-	9.2+0.7
10	Proteas	5.3+0.4	-	-	8.6+0.8
11	Lactobacilli	9.1+0.8	8.4+0.07	7.1+0.5	11.5+1.3

(M+m) mm – growth inhibition zone

Thus, our studies have fully confirmed the passport characteristics of the drug "Citeal" and we believe that it is best to use the drug in a dilution of 1/5 and 1/10, i.e. 10 and 20% concentration.

Based on the data we obtained and taking into account literary sources, we used the drug "Citeal" to treat sick children suffering from acute herpetic stomatitis, taking into account the clinical phases of the course. (The treatment method is given in the section Material and methods of research.)

The data obtained from these studies are presented in Table 11. The table shows that there is a significant difference in the treatment of children with mild forms of acute gastritis using the drug "Citeal" compared to traditional treatment.

This difference in treatment concerns the following issues:

- Firstly, treatment with Citeal almost completely normalizes the quantitative indicators of the anaerobic group of microbes;
- Secondly, a highly positive effect on the quantitative indicators of facultative flora is noted;
- Thirdly, the most important thing in our opinion is the complete elimination of microbes with aggressive properties;

Table 11

The state of the oral microflora in children patients with mild acute herpetic stomatitis after treatment with Citeal

lg M+m CFU/ml.

No	Groups of microbes	Number of microbes in 1ml of saliva		
		Norm	After traditional treatment	After treatment with Citeal
1	Total number of anaerobes	5.69+0.15	6.11+0.32	5.19+0.17**
2	Lactobacilli	4.60+0.14	3.47+0.17	4.30+0.15***
3	Peptostreptococcus	3.77+0.11	4.49+0.16	3.47+0.12***
4	Total number of aerobes	4.30+0.17	6.17+0.34	4.89+0.15***
5	Staffordshire Golden	-	1.30+0.11	-
6	Staff. Epidermal	2.15+0.51	3.00+0.15	2.47+0.12**
7	Staff. Saprophyte	4.14+0.14	3.47+0.16	3.30+0.13
8	Strept. G. "A"	-	1.30+0.07	-
9	Enterococci	5.15+0.15	3.60+0.12	4.15+0.15**
10	Escherichia coli LP	2.30+0.17	4.47+0.16	2.19+0.11***
11	Escherichia LN	-	2.30+0.10	-
12	Mushrooms of the r. Candida	2.15+0.18	3.12+0.21	1.98+0.12***

Note: ** - presence of reliability (P>0.01) compared to control

*** - presence of reliability (P>0.001) compared to control

The data we obtained actually fully correlate with the data obtained during the testing of microbial sensitivity to the drug "Citeal".

We have also studied the effectiveness of using "Citeal" in moderate to severe acute gastritis in children. The microbiological indices obtained in these studies are presented in Table 12. The table shows that in fact, in these studies, as in the treatment of acute gastritis in a mild form, we have generally positive shifts. These shifts in quantitative parameters are observed both in the anaerobic and in the facultative group of microorganisms.

Table No. 12

Microbiological efficiency of treatment of children with moderate acute gastritis with the drug "Citeal"

lg M+m CFU/ml.

No	Groups of microbes	Number of microbes in 1ml of saliva		
		Norm	After traditional treatment	After treatment with Citeal
1	Total number of anaerobes	5.69+0.15	5.47+0.37	5.67+0.21
2	Lactobacilli	4.60+0.14	3.00+0.12	3.80+0.31**
3	Peptostreptococcus	3.77+0.11	4.47+0.25	4.41+0.25
4	Total number of aerobes.	4.30+0.17	6.40+0.41	5.00+0.31**
5	Staffordshire Golden	-	2.00+0.11	-
6	Staff. Epidermal	2.15+0.51	3.11+0.15	1.80+0.13***
7	Staff. Saprophyte	4.14+0.14	3.30+0.17	3.47+0.14
8	Strept. G. "A"	-	1.89+0.01	-
9	Enterococci	5.15+0.15	4.60+0.31	3.47+0.17**
10	Escherichia coli LP	2.30+0.17	3.60+0.20	1.69+0.11***
11	Escherichia LN	-	2.29+0.14	-
12	Mushrooms of the r. Candida	2.15+0.18	3.47+0.13	2.60+0.010***

Note: ** - presence of reliability (P>0.01) compared to control

*** - presence of reliability (P>0.001) compared to control

In conclusion, we studied the effectiveness of using the drug "Citeal" for the treatment of acute gastritis in children with severe clinical course. The data obtained in these studies are presented in Table 13. The table shows that the use of the drug "Citeal" had a generally positive effect. Thus, we see virtually complete quantitative restoration of both anaerobic and facultative groups of microbes. In these studies, it should be noted that the elimination of microbes with aggressive properties occurred, this indicates that the concentration of the drug "Citeal" used to treat children with acute gastritis in severe form was sufficient to provide therapeutic assistance.

Table No. 13

The effect of treatment with "Citeal" on the state of the oral microflora in children with severe acute gastritis lg M+m CFU/ml.

No	Groups of microbes	Number of microbes in 1ml of saliva
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.		Norm	After traditional treatment	After treatment with Citeal
1	Total number of anaerobes	5.69+0.15	6.59+0.25	5.87+0.17**
2	Lactobacilli	4.60+0.14	1.60+0.09	3.60+0.13***
3	Peptostreptococcus	3.77+0.11	3.27+0.11	3.11+0.15
4	Total number of aerobes.	4.30+0.17	6.85+0.37	4.90+0.16***
5	Staffordshire Golden	-	1.47+0.09	-
6	Staff. Epidermal	2.15+0.51	2.30+0.11	2.47+0.11
7	Staff. Saprophyte	4.14+0.14	3.30+0.21	3.85+0.21**
8	Strept. G. "A"	-	2.49+0.12	-
9	Enterococci	5.15+0.15	4.11+0.27	4.57+0.22
10	Escherichia coli LP	2.30+0.17	4.29+0.29	3.11+0.15**
11	Escherichia LN	-	2.47+0.12	-
12	Mushrooms of the r. Candida	2.15+0.18	3.11+0.15	2.60+0.12**

Note: **- presence of reliability (P>0.01) compared to control

***- presence of reliability (P>0.001) compared to control

It should be noted that the positive changes we identified during the study of microbiological indicators almost completely correlate with the data from clinical studies, which once again emphasizes the high efficiency of using the drug "Citeal".

4.3. Immunological effectiveness of the use of the drug "Citeal" in the treatment of acute gastritis in children.

Immunological studies have traditionally been considered as something very abstract from the point of view of specialists in the field of therapeutic dentistry. At present, this is a necessity, which is dictated by the increasing number of patients with aggressive forms that are resistant to traditional effects. Immunological studies are very relevant, since, on the one hand, in combination with microbiological data, they allow us to understand the features of pathogenesis, substantiate treatment and prevention methods in conditions of unfavorable effects of unfavorable factors.

However, when considering the triggers of the inflammatory process, we must also keep in mind the role of endogenous factors and, above all, the state of local and general defense systems and homeostasis maintenance. For example, it is known that with the development of inflammatory periodontal diseases, in particular with gingivitis, changes in the content of lysozyme and immunoglobulin A - secretory fraction (s IgA) in the oral fluid are observed, which are mutually compensating in nature.

Over the past decades, the idea has been formed that in inflammatory processes of organs and systems limited by mucous membranes, not general systemic factors, but also various local specific and non-specific resistance factors play an important role. Moreover, the immunity of the mucous membrane is not a simple reflection of general immunity, but has an independent system, in particular the production of sIgA, which also has a pronounced effect on the formation of general immunity. In this regard, a dentist, along with the general condition of the patient, including the systemic immune status, must be able to assess and correctly interpret the state of local resistance factors of the oral cavity. Knowledge of the state of the immune mechanisms in a particular patient will help not only in the treatment, but also in the prevention of dental diseases.

It is also obvious that, along with the increasingly widespread use of immunological methods for examining patients, it is necessary to more thoroughly study and take into account the influence on the patient's immunological status of not only internal but also external factors.

Along with microbiological studies of sick children suffering from acute gastritis and candidal stomatitis, we have studied immunological indices in the same children when using the drug "Citeal" for treatment.

The data obtained from these studies are presented in Table No. 15. Thus, in the mild form of acute gastritis, traditional therapy as a whole had a significant positive effect on all studied non-specific factors of oral cavity protection, although it should be noted that it is not necessary to talk about the complete elimination of immunodeficiency.

At the same time, after treating sick children with Citeal, we see that some indicators have become even higher than in a healthy group of children, although it should be noted that Citeal affects the state of secretory immunoglobulin (sIgA).

In the treatment of children with moderately severe acute gastritis with Citeal, we found that, as in the treatment of mild forms, a positive shift towards a decrease in secondary immunodeficiency was mainly observed. Thus, the lysozyme level was 18.7 ± 0.5 mg/%, reliability ($P > 0.01$), whereas after traditional therapy it was 15.7 ± 0.4 mg/.

At the same time, when treating sick children with Citeal OGS in severe clinical form, we noted the most pronounced positive changes in all the studied parameters. Thus, the level of lysozyme was 17.8 ± 0.6 mg% reliability ($P > 0.5$), the percentage of phagocytosis $52.3 \pm 1.1\%$ reliability ($P > 0.5$) and the titer of immunoglobulin class A (sIgA) was 1.59 ± 0.1 g / l reliability ($P > 0.001$), while in the healthy group these indicators were: 19.7 ± 0.7 mg%, phagocytic indicator $58.1 \pm 1.5\%$, the level of s Ig A 1.8 ± 0.30 g / l, respectively.

In recent years, there has been an increase in diseases of the oral mucosa in children. According to the results of numerous studies by domestic and foreign authors, the most common pathology in childhood is acute herpetic stomatitis.

According to WHO, diseases caused by the herpes virus are the second leading cause of death from viral infections after influenza. The herpes simplex virus affects the central and peripheral nervous system, parenchymatous organs, eyes, skin, oral mucosa, gastrointestinal tract, and genitals. HSV leads to intrauterine fetal pathology and spontaneous abortion (65). In young children, herpes infection most often causes acute herpetic stomatitis.

Treatment of diseases of the oral mucosa is diverse. But the disadvantage of these methods is that the treatment is aimed only at eliminating inflammation and affecting the immunity of the oral cavity. Although dysbiotic disturbance of the oral microflora has been noted more than once in the literature. In this regard, it is advisable to develop new methods of treating the oral mucosa, aimed at gentle impact on the normal flora of the oral cavity.

We observed 95 patients with acute herpetic stomatitis. Depending on the treatment administered, the children were divided into 2 groups: 20 children with acute gastritis received traditional treatment, 75 received treatment with the drug "Citeal".

The clinical diagnosis was established on the basis of anamnestic data, patient complaints, clinical manifestations and conducted index indicators of RMA and GI. The state of oral hygiene was determined by the method of Fedorov Yu.A. - Volodkina V.V. (1972)

Before treatment, saliva was collected from patients in sterile test tubes. Then, treatment was carried out with a solution of "Citeal" in a dilution 1:10 as follows:

Group I mild form - the drug "Citeal" in dilution 1:10 + 2-3 drops of 2% novocaine 3-4 times a day, sea buckthorn oil on the 2nd day.

Group II, moderate form - the drug "Citeal" in dilution 1:10+ 2-3 drops of 2% novocaine 4-5 times a day, sea buckthorn oil on the 4th day.

Group III severe form - the drug "Citeal" in dilution 1:10+ 2-3 drops of 2% novocaine 6-8 times a day, sea buckthorn oil on the 5th day.

The Citeal solution was given out for home use.

When determining the GI in children with a mild form of OGS, we noted unsatisfactory oral hygiene, which corresponded to 2.1–2.5 points. RMA corresponded to 30%, which characterized a mild degree of inflammation.

In children with a moderate form, the GI was 2.6–3.4 points, which indicates poor oral hygiene, and the RMA of 30–60% is typical for a moderate degree of inflammation.

In children with severe OGS, the GI was 5 points, which is very poor oral hygiene. RMA was 60% or more, which indicates a severe degree of damage.

When considering the dynamics of the hygiene index, we see the degree of disease damage. In children with moderate and severe forms of the disease, we see poor and very poor oral hygiene, which contributes to the aggravation of the clinical course of the disease.

In the laboratory, the oral microflora of patients with acute herpetic stomatitis was determined. Thus, dysbiotic changes in the microflora develop in the oral cavity of children with AHS. Significant changes are observed in the anaerobic flora. The total number of anaerobes decreases in the mild form to 4.60 ± 0.15 CFU/ml, 4.27 ± 0.25 – in the moderate-severe form, in the severe form – 4.11 ± 0.27 CFU/ml, and the norm is 5.69 ± 0.15 CFU/ml. Lactobacilli also decrease, their number is 3.30 ± 0.1 CFU/ml in mild form, 3.15 ± 0.15 CFU/ml in moderate form, 2.3 ± 0.11 CFU/ml in severe form, and the norm is 4.60 ± 0.14 CFU/ml. The number of peptostreptococci increased and was 4.59 ± 0.16 CFU/ml in mild form, 4.17 ± 0.21 CFU/ml in moderate form, 5.11 ± 0.31 CFU/ml in severe form, and the norm is 3.77 ± 0.11 CFU/ml.

Pronounced quantitative shifts also occurred in the optional flora. The number of aerobes in the mild form is 7.15 ± 0.31 CFU/ml, in the moderate-

severe form lg $8.11+0.57$ CFU/ml, in the severe form lg $8.57+0.57$ CFU/ml, and in the norm lg $5.30+0.17$ CFU/ml.

We observe an increase in such microorganisms as saprophytic staphylococci, Escherichia coli, fungi and a decrease in epidermal staphylococci and enterococci. Microbes that are not observed in healthy children appear in the oral fluid - these are Staphylococcus aureus, pyogenic streptococcus and lactose-negative strains of Escherichia coli. These are strains that have aggressive properties. The number of Candida fungi increases sharply in a mild form lg $4.00 + 0.21$ CFU / ml, in a moderate-severe form lg $4.30 + 0.23$ CFU / ml, in a severe form lg $5.30 + 0.23$ CFU / ml, while in healthy people it is lg $2.15 + 0.18$ CFU / ml.

Along with microbiological studies of oral fluid in sick children, immunological studies were also conducted.

Thus, in children with acute gastritis upon admission, the lysozyme level was: $16.1+0.40$ mg% in the mild form, $13.2+0.5$ mg% in the moderate form, and $11.2+0.21$ mg% in the severe form, when the norm is $19.7+0.70$ mg%.

The phagocytic index before treatment for mild form is $51.5+1.00\%$, for moderate-severe form $44.5+1.3\%$, for severe form $39.0+0.85\%$, and the norm is $58.1+1.50\%$. The Ig A level before treatment for mild form upon admission is $1.71+0.1$ g/l, for moderate-severe form $0.51+0.2$ g/l, for severe form $0.51+0.11$ g/l, and in healthy children this indicator was $1.8+0.30$ g/l.

Among all the studied parameters of the immune system, the indicators for secretory IgA were the most reduced.

All examined children with acute herpetic stomatitis were divided into 2 groups: the first group received traditional treatment, the second group received treatment with the drug "Citeal".

Thus, in children who underwent traditional treatment, we see that traditional therapy has a positive effect on the state of the oral fluid microbiocenosis. The number of anaerobic microbes after traditional therapy in

the mild form was $\lg 6.11+0.32$ CFU/ml, in the moderate form $\lg 5.47+0.37$ CFU/ml, in the severe form $\lg 4.59+0.25$ CFU/ml, which is higher compared to the data in healthy children. The number of anaerobes increased, the indicators of facultative flora, on the contrary, tend to decrease compared to the data upon admission. Thus, in the mild form of acute gastritis, the number of aerobes $\lg 6.17+0.34$ CFU/ml, in the moderate form $\lg 6.49+0.41$ CFU/ml, in the severe form $\lg 6.85+0.37$ CFU/ml. The readings upon admission are higher, and the normal number of aerobes is $\lg 5.30+0.17$ CFU/ml. We see the same tendency in microorganisms related to saprophytic staphylococci, enterococci, Escherichia and fungi.

Based on the obtained microbiological data, we can rightfully assert that the course of traditional therapy conducted in patients with OGS had a positive effect on the state of the oral microflora. However, we cannot speak of a complete microbiological recovery, since the picture of dysbiotic shifts in the oral cavity still persists and requires additional intervention.

In addition, the most significant indicator of oral dysbiosis in these children are the quantitative parameters of Candida fungi, so their quantity upon admission is $\lg 7.89+0.52$ CFU/ml, after treatment $\lg 6.12+0.37$ CFU/ml, and normally $\lg 2.15+0.18$ CFU/ml, which is 4 orders of magnitude higher.

The quantitative and qualitative changes in the autoflora of the oral cavity that we have identified can lead to chronicity of the disease, therefore it is necessary to find more effective methods of treating such patients.

In the main group, 95 patients with acute gastritis were treated with Citeal depending on the severity. Based on the studies conducted, we see a significant difference compared to traditional treatment:

Firstly, the quantitative indicators of anaerobic flora are normalized.

Secondly, a highly positive effect on the quantitative indicators of facultative flora is noted.

Thirdly, the most important thing is the complete elimination of microbes with aggressive properties. The data we obtained fully correlate with the data obtained when testing the sensitivity of microbes to the drug "Citeal". Thus, after treatment with the drug "Citeal" we see that the number of anaerobes in the mild form is - $5.19 + 0.17$ CFU / ml, in the moderate - $5.67 + 0.21$ CFU / ml, and in the severe form $5.87 + 0.17$ CFU / ml. The number of lactobacilli in the mild form is $4.30 + 0.15$ CFU / ml, in the moderate - $3.80 + 0.31$ CFU / ml, in the severe form - $3.60 + 0.13$ CFU / ml. Peptostreptococci in mild form - $3.47+0.12$ CFU/ml, in moderate form - $4.41+0.25$ CFU/ml, in severe form - $3.11+0.15$ CFU/ml. The total number of aerobes in mild form is: $4.89+0.15$ CFU/ml, in moderate form - $5.00+0.31$ CFU/ml, in severe form - $4.90+0.16$ CFU/ml.

The number of Candida fungi is also reduced: in mild form – $1.98+0.12$ CFU/ml, in moderate form – $2.60+0.010$ CFU/ml, and in severe form – $2.60+0.12$ CFU/ml.

From the data obtained, we see complete quantitative restoration, both anaerobic and facultative group of microbes, complete elimination of aggressive microbes, this indicates that the concentration of the drug is chosen correctly to provide therapeutic assistance.

We have also studied the effect of the drug in patients with candidal stomatitis. We see that the drug "Citeal" had a positive effect on both quantitative and qualitative indicators of the oral microflora. Quantitative indicators of anaerobic flora were Ig $5.57 + 0.2$ CFU / ml, and normally this indicator is $5.69 + 0.15$ CFU / ml. Expressed positive shifts occurred in the indicators of facultative flora. Thus, the total number of aerobes was $5.12 + 0.31$ CFU / ml, and in healthy children this indicator is $4.30 + 0.17$ CFU / ml. The quantitative indicator of fungi is particularly striking: $2.80 +0.37$ CFU/ml, while after traditional therapy their number was $6.12 +0.37$ CFU/ml, and normally this

indicator was 2.15 ± 0.18 CFU/ml. After treatment with the drug "Citeal", complete elimination of microbes with aggressive properties occurs.

Along with microbiological studies, immunological parameters were studied in children with acute herpetic and candidal stomatitis. Thus, the level of lysozyme in the mild form of AHS after treatment with the drug "Citeal" was 19.1 ± 0.5 mg%, in the moderate form - 18.7 ± 0.5 mg%, and in the severe form - 17.8 ± 0.6 mg%, the normal value is 19.7 ± 0.70 mg%.

The phagocytic index in the mild form was $59.5 \pm 1.4\%$, in the moderate-severe form – $51.1 \pm 1.3\%$, in the severe form – $52.3 \pm 1.1\%$, and the norm is $58.1 \pm 1.50\%$.

The titer of secretory immunoglobulin class A in the mild form is 2.0 ± 0.12 g/l, in the moderate-severe form - 1.60 ± 0.10 g/l, and in the severe form 1.5 ± 0.11 g/l, while in healthy children this figure is 1.8 ± 0.30 g/l.

Thus, based on the dental, microbiological and immunological data we have obtained, we can conclude that the drug "Citeal" has a pronounced antibacterial, antiviral, antifungal effect when used in children with various forms of herpes infection of the oral cavity. It should be noted that the results of the use of various methods of therapy, we came to the conclusion that the use of the drug "Citeal" has a pronounced therapeutic, specific, antimicrobial and anti-inflammatory effect, manifested immediately after treatment and maintaining its effect for a long period. One of the significant aspects of the action of the drug "Citeal" in our patients should be recognized as the fact that it increases the local protective barrier of the oral cavity by increasing the activity of non-specific protective factors, thereby ensuring the prevention of relapses of the disease.

All of the above gives us every right and reason to believe that the drug "Citeal" should be widely used as an independent and additional drug for various infectious diseases of the oral cavity, in particular in children. This drug is especially convenient for children with viral diseases of the oral cavity, which,

as a rule, are difficult to treat and the existing arsenal of antiviral and antifungal drugs is not very accessible from an economic point of view for widespread use.

Chapter V. Corr.relatinal relationship between changes in microflora and immunology of oral fluid during targeted use of the drug "Citeal" in children with herpetic stomatitis.

We studied the correlation links between the indicators of microbiocenosis and the state of non-specific factors protecting the oral cavity in normal and sick children suffering from herpetic stomatitis in the process of traditional and specific treatment.

Analysis of correlation data between the number of microorganisms in normal and sick children with herpetic stomatitis showed (Fig. 17) that the most pronounced relationships are observed in peptostreptococci ($r = 0.66$), epidermal staphylococci ($r = 0.50$), *Staphylococcus aureus* ($r = 0.38$), and *Candida* fungi ($r = 0.37$). At the same time, the number of hemolytic streptococci and lactobacilli have a negative medium-strength correlation ($r = - 0.44$ and $r = - 0.49$, respectively).

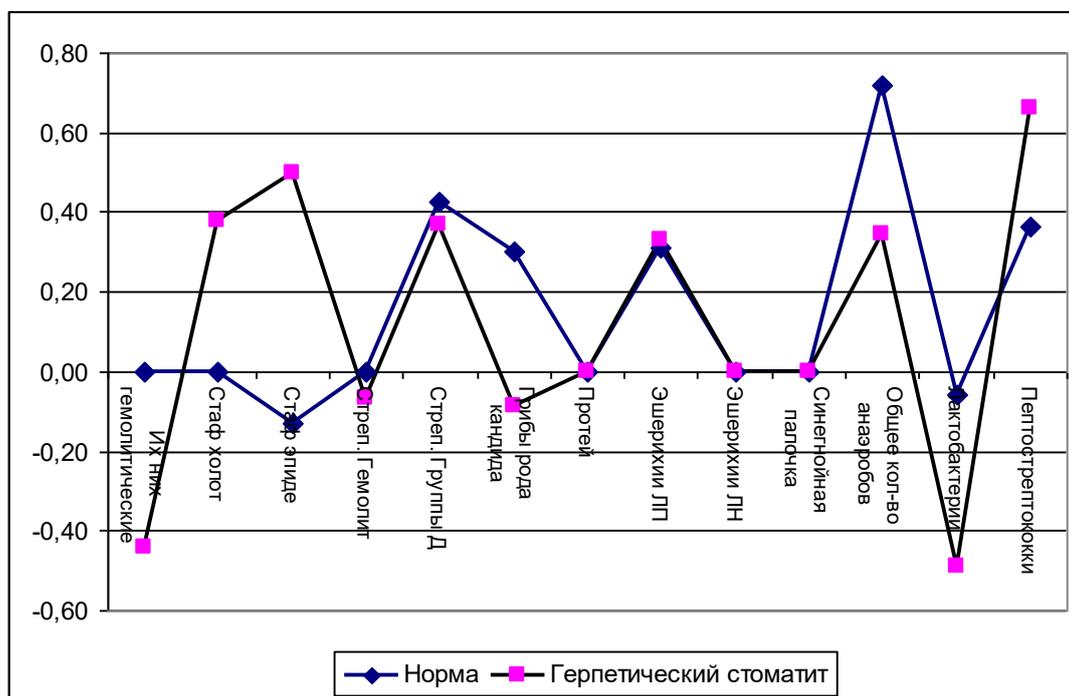


Fig. 17. Correlation relationship between microbes of the oral cavity in normal children and in children with herpetic stomatitis.

Comparing the same data after the treatment, we obtained data characterizing a sharp change in the microbial landscape (Fig. 18). Thus, if

normally lactobacilli had a very weak negative relationship ($r = +0.79$). Candida fungi also changed the relationship. From a positive average relationship in untreated herpetic stomatitis, they acquired a correlation coefficient characterizing a strong inverse relationship ($r = +0.33$ before treatment and $r = -0.68$ after treatment).

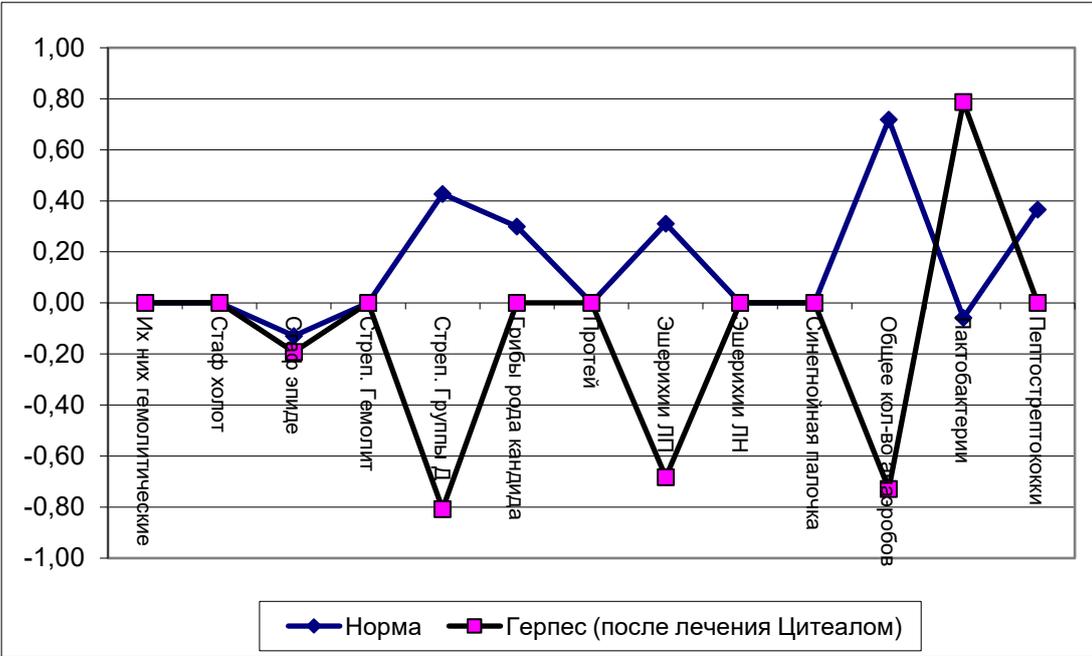


Fig. 18. Correlation between microbes in the oral cavity of children in the norm and after special treatment of patients with herpetic stomatitis.

The most interesting data we obtained when analyzing the relationship between immunological indices of the oral cavity in children in normal conditions and in patients with herpetic stomatitis, before and after treatment

with the drug "Citeal" (Fig. 21, 22). As can be seen from the figures, in normal conditions they have an inverse correlation of medium strength.

We noted the same relationship in the indicators of non-specific factors of oral cavity protection in patients with herpetic stomatitis before treatment (Fig. 21)

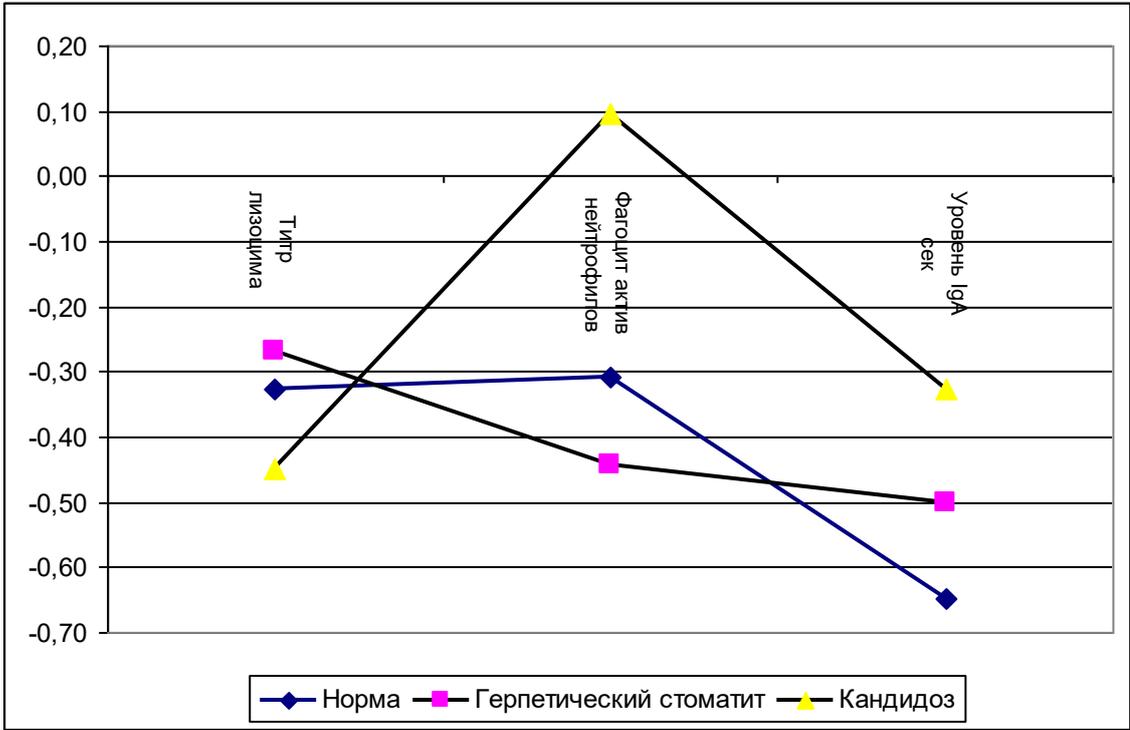


Fig. 21. The relationship between immunological parameters of the oral cavity in children with herpetic stomatitis.

At the same time, after the special treatment using the drug "Citeal", the picture changed completely. At the same time, all the studied immunological indicators in patients suffering from herpetic stomatitis after the treatment acquired a pronounced strong, still inverse relationship (Fig. 22).

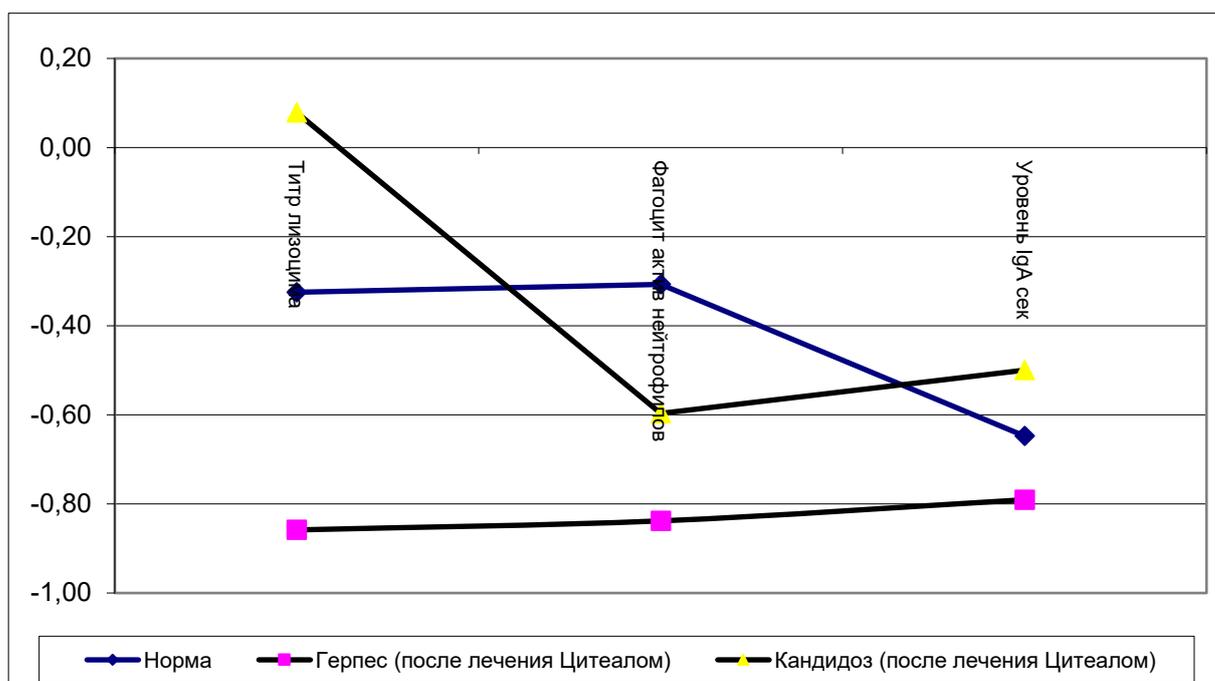


Fig. 22. Relationships between immunological parameters in children with herpetic and candidal stomatitis after special treatment.

The obtained results indicate the existence of direct and inverse relationships between the quantitative parameters of the microbiocenosis and immunological indices of the oral cavity in children suffering from herpetic stomatitis before and after special treatment.

Based on the data obtained, it can be concluded that conventional treatment does not have a significant effect on the correlation links in children suffering from herpetic stomatitis. On the contrary, there is a decrease and weakening of the relationship between the indicators of microbiocenosis and non-specific protective factors.

Thus, judging by the correlation analysis, more pronounced positive changes in the microbiocenosis and immunological indices of the oral cavity occur when using the drug "Citeal" for treatment. Based on this, it becomes quite obvious that the dental, microbiological and immunological studies we conducted and their interrelations provide a full basis for recommending the drug "Citeal" for the treatment of herpetic stomatitis in children.

Thus, based on the results of our research, we can say that:

1. In children with OGS stomatitis, against the background of a violation of the integrity of the oral mucosa and the development of inflammatory phenomena, a sharp deterioration in the RMA and GI indices is observed, which together contributes to the predominance of pathogenic flora and suppression of local immunity.

2. In case of OGS, traditional therapy helps to improve the clinical picture of patients, but does not completely eliminate the development of dysbiosis and immunodeficiency in the oral cavity in children.

3. The action of the drug "Citeal" is aimed at eliminating the aggression of opportunistic and pathogenic strains, promoting the restoration of oral immunity and the elimination of conditions for the chronicity of the disease.

4. It has been established that in diseases of the oral mucosa, the microflora is a highly sensitive indicator system that reacts with qualitative and quantitative shifts. "Citeal" is currently a drug that helps restore biological balance in the microflora system and non-specific factors of oral cavity protection.

5. A direct correlation has been found between the degree of disturbance of the biological balance of the oral microflora and both the severity and the stage of acute herpetic and candidal stomatitis. The more severe the disease, the more pronounced the clinical picture and the deeper the shifts in the local immunity system of the oral cavity.

Based on the work carried out, we can give the following recommendations for the treatment of acute herpetic stomatitis

1. The drug "Citeal" has antiseptic, antibacterial, antiviral and fungicidal effects and is recommended for wide use in the treatment of acute gastritis and stomatitis in children.
2. It is recommended to use the drug "Citeal" in a dilution of 1:10, not only for acute gastritis and stomatitis in children, but also for other viral and fungal diseases of the oral mucosa.
3. Considering the gentle effect of the drug "Citeal" on the microflora of the oral cavity in children, it is recommended to use it both in monotherapy and as an additional remedy in the treatment of all diseases of the oral mucosa, as well as in various dysbiotic conditions.

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