

**MINISTRY OF HEALTH OF THE REPUBLIC OF UZBEKISTAN**

**TASHKENT STATE DENTAL INSTITUTE**

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**CLINICAL AND EXPERIMENTAL SUBSTANTIATION OF  
TREATMENT OF ACUTE HERPETIC STOMATITIS IN CHILDREN**

**(MONOGRAPH)**

**Tashkent-2022**

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The monograph is based on the analysis of our own research results, and the clinical and experimental justification for the treatment of acute herpetic stomatitis in children is studied.

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

## chapter 1

### Acute herpetic stomatitis. Treatment problems

#### 1.1. Current data on the etiopathogenesis of AHS

The problem of diseases of the oral mucosa is one of the most important in dentistry. A special place in this problem is occupied by acute herpetic stomatitis, primarily because it accounts for more than 80% of diseases of the oral mucosa in children

(Vinogradova T. F., 1988; Kolomiets A. G. et al., 1997; Lukowicz

A.A.V., 1983, etc.). Also, acute herpetic stomatitis occupies one of the leading places in children's infectious pathology, occurring more often than scarlet fever, measles, and mumps, and is only slightly inferior to chickenpox. (Epishev V. A. et al., 1988; Melnichenko E. M., 1992; Vakhobov Kh. D. et al., 1994; Rennie J.S. et al., 1985; Davis L.E. et al., 1988). The disease is highly contagious, most often observed in young children (Epishev V. V., Khersonskaya F. I., 1974; Kolomiets A. G. et al., 1997; Naylor et al., 1987; Zocroix 1., Masks S., 1995). Adults are also susceptible to AHS (Epishev V. A., Khersonskaya F. I., 1974; Melnichenko E. M., 1992; Yeager, 1986, Main D.M.G., 1989).

Among all dental diseases, AHS accounts for 78.6 to 94.894 % of all disability certificates issued per year (L. S. Airapetov et al., 1985).

Joint studies of dentists and virologists performed in recent years have convincingly shown that a large group of acute and chronic stomatitis has a viral etiology. The causative agent of acute herpetic stomatitis in children is the common herpes virus, which contains DNA. Herpes simplex type (HSV) belongs to the subfamily of alpha herpesviruses (DNA virus). The virus enters the ganglia through the mucous membranes, spreads along the nerve trunks and leads to severe lesions of the mucous membranes of the eye, lips, mouth, nose, and genitals. HSV-1 virus is a weak inducer of interferon, and post-infection immunity is not developed. Making a diagnosis of the disease based on clinical signs is not difficult (Yeager, 1986; Pyatkin K. D., Krivoshein Yu. s., 1981). In the human body, the virus multiplies mainly in epithelial cells and therefore affects the mucous membranes of the eyes, oral mucosa, gastrointestinal tract, genitals, and also has a certain significance in the intrauterine pathology of the fetus (Bikpulatov R. M., 1970; Shublazde A. K., Mayevskaya

T. M., 1971; Barinsky I. F., Shubladze A. K., 1980; Khlyustov SV. et al., 1989; Zuev V. A., 1988; L. T. Sibiryakova, A. B. Alkeeva, L. D. Serova, A.M. Borisova, 1982 L. N. Khakhalin, Abazova F. I., 1996; Kolomiets A. G. et al., 1997 Bolis B..F., Franhi M., 1982, Mapp D..M..A., TunklerTunkler A.M., Yates R. O., 198Z; Meier J..S., Straus S.S.E., 1992; kirchner Holger, 1982; Lukoroicz A..Z., 1983; White Ch. T., 1983).

N. F. Filatov, an outstanding Russian pediatrician, pointed out the possible herpetic nature of acute aphthous stomatitis, which is most common among children, at the end of the last century ” " The similarity, and perhaps the identity of these two diseases, that is, acute-gloating stomatitis and herpes of the lips, is expressed in the fact that N. F. Filatov wrote that aphthuses sometimes fall out on the tongue or other places of the mucous membrane in groups of closely fitting round sores“

Thus, to prove the viral etiology of AHS in 1932, kummer used the method of infecting the rabbit cornea with aft material and in all cases received keratitis, and in some animals encephalitis appeared along with eye damage.

In 1938. Dodd virologically examined AFT scrapings in 12 sick children with acute oral mucosal lesions. When the eyes of the rabbit cornea were infected with material from scrapings from the elements of the lesion in the oral cavity, all animals developed herpetic keratoconjunctivitis.

Then, in 1939, Burnet and Williams studied the immunological changes in the body of children under the influence of AHS diseases. All children were diagnosed with the herpes simplex virus.

Similar results were obtained in virological and serological studies by other authors (Antonova N. M., 1963; Vinogradova T. F., et al., 1972, 1973; Ketiladze E. S.). et al., 1972; Airapetov L. S. et al., 1985; Khlyustov SV. et al., 1989; Durov V. M., 1991 \* White Ch.L., Taxg, Taxg J. V., 198Z).

Cytological studies of the material (Antonova N. I., 1965; Vinogradova TO. et al., 1970; Melnichenko E. M., 1981; Airapetov L. S. et al., 1985; Blank et al., 1951; Stricland R. et al., 1989), taken from the elements of the lesion in the oral cavity in children, giant multinucleated cells were found with different frequency, which indicate the presence of viral infection. infections. At the same time, it is impossible to reliably speak about the

herpetic nature of stomatitis, since such cells are found in measles, chickenpox and other viral diseases of the skin and oral mucosa (Vinogradova T. F. et al., 1983).

A convincing proof of the herpetic nature of acute aphthous stomatitis in children is the detection of herpes virus antigen in epithelial cells obtained from elements of oral lesions in patients with stomatitis using the immunofluorescence method of research (Melnichenko E. M., et al., 1963, 1973; Corly L., 1986).

In the blood of children who have had stomatitis, the appearance or increase in titers of virus-neutralizing antibodies (Burnet, and Williams, 1939; Scott, 1941; Black, 1942; Hella, 1963) or complement-binding (Dugeon, 1950) antibodies to the herpes virus (Melnichenko E. M., Balnokina S. A., 1971; Khlyustov ST. JOHN the BAPTIST et al., 1989). With herpetic infection, the reactivity of the entire body changes, the disease is confirmed by the detection of the virus in the saliva of children with stomatitis (Melnichenko E. M., 1970, 1992).

The use of antiviral drugs and their positive effect in treatment also confirms the etiology of this disease.

Thus, researchers from various countries have proved the etiological role of the common herpes virus in acute herpetic stomatitis in children.

Herpes infection is widespread, has diverse manifestations and its characteristic feature is a tendency to relapse. Every tenth child who has had acute herpetic stomatitis has relapses of the disease with a subsequent transition to a chronically recurrent form (Melnichenko E. M., Mikhailovskaya V. T., 1991; Daris L..E.. et al., 1988). Patients with recurrent herpetic infection have profound changes in the immune system (Khlyustov SV. et al., 1984; Belaya GG. 1990; Zhumatov U. zh., 1996; Rennie J..s. et et al., 1988; Guren O.1988; Landesberg K., et al., 1990; Sibiryakova L. G. et al., 1992).

Acute herpetic stomatitis affects not only children, but also adults. Cases of diseases of patients aged 16 to 35 years are described, in which acute herpetic stomatitis was established not only in clinical, but also in virological, serological, immunofluorescent and

epidemiological studies, as a manifestation of primary herpetic infection (Melnichenko E. M., 1977, 1992; Corly L., 1986; Main D..M..G., 1989). However, most acute herpetic stomatitis occurs in children aged 6 months to 3 years. This is due to the fact that at this age, antibodies obtained from the mother interplacentally disappear in children. The manifestation of herpetic infection in the form of acute stomatitis, and not in any other clinical form, is associated with the peculiarities of the structure of the oral mucosa, insufficiently developed local immunity, as well as frequent natural violations of the integrity of the mucous membrane as a result of teething (Vinogradova T. F., et al., 1975;1979;1983;Belaya GG. et al., 1991; EV. Borovsky, VK. Leontiev, 1991; Kolomiets A. G. et al., 1997; Zhumatov U. Zh., 1996)

It is also necessary to take into account the important role of other factors that create a background for the cause: eating disorders and metabolic disorders, general somatic diseases of the child's body, hot climate, decreased immunity, etc. (Vinogradova T. F., 1971; Epishev V. A., Khersonskaya F. I., 1974, etc.; Melnichenko E. M., 1983; Zhumatov U. Zh., 1996; Safarov T. Kh. et al., 1996; Lukowicz A.V..v, 1983;.) as a rule, acute herpetic stomatitis occurs in a child weakened by a transferred or previous disease, as well as against the background of some pathological process in the body. (Epishev V. A., Khersonskaya F. I., 1974; Negametzyanov G. M. et al., 1987; Taieb A. et al., 1987;Porter S..R.. et al., 1988).

Regarding the seasonality of the disease, the authors ' opinions differ. There is evidence that the disease often occurs in the autumn-winter periods due to hypothermia and changes in the reactivity of the body in children (Antonova N. I., 1963; Vakhobov UD. 1994; Kindiy D. E., 1967; Maksimenko P. T., 1970) , in the summer-autumn time (Safarov T. Kh. et al., 1991)

**Some authors** associate the occurrence of this disease in the spring period in connection with the appearance of the first berries (Kazakova R. V., Smolyar N. I., 1989) and hypovitaminosis (Epishev V. A. et al., 1986). Other authors deny seasonality in acute herpetic stomatitis (Juretic M., 1966; Cezario T..S.. et al., 1969, etc.). Also, the lack of seasonality is indicated by Melnichenko E. M.(1980) and connects this with the

widespread spread of the herpes virus among the population due to latent carriage and periodic relapses. Transmission of the infection occurs by airborne droplets and contact. The disease is contagious. Outbreaks are observed in kindergartens, orphanages, hospital wards and families (Mozgovoy P. I., 1964; Khersonskaya F. S., 1968; Melnichenko E. M., et al., 1974; Antonova I. I., 1981; Vakhobov Kh. D. et al., 1994; Nape VO. et al., 1963; Juretic M., 1966; Perrip D., Nicolas N., 1990.). the source of infection is usually adults (close relatives, service personnel), children with relapses of herpes infection, as well as children with acute forms of stomatitis. The pathogenesis of AHS has not been sufficiently studied, but the immune system undoubtedly plays a leading role.

The mucosal immune system functions primarily at the level of humoral immunity, although cellular factors also play a role. In a healthy body with an intact oral mucosa, the protective factors of saliva prevent excessive reproduction of microorganisms . Violation of the species composition of microflora-dysbacteriosis-most often occurs with the use of long-term and irrational antibiotic therapy leading to a decrease in the overall resistance of the body (Shabanskaya M..A., 1991; Khazanova V. V., 1993; Amir L, Straussberg R., Harel L., Smetana L., Varsano I., 1996.), which leads to to the reproduction of pathogenic microbes.

The common herpes virus is DNA-containing and belongs to the neurotropic group. as a result, its toxic effect on the body manifests itself in the form of symptoms of intoxication of the nervous system:

lethargy, drowsiness, moods, lack of contact, fever, nausea, vomiting, loss of appetite. After initial infection of the skin and mucosa, the virus is introduced into the nuclei of nerve cells, as confirmed by Lange (1975); Zukowicz (1983), and the infected DNA enters the host DNA . According to the available literature data, the further spread of the virus through the organization is poorly studied.

There is an assumption that the herpes virus is spread by hematogenic route. In the acute period of stomatitis, children have viremia (Vinogradova T. F., 1983). Reproduction of the infectious agent occurs in the cells of local tissues and nearby

lymphatic formations. In clinical development, the disease is preceded by lymphadenitis of varying severity, and then elementary lesions appear in the oral cavity in children. Most often, lymphadenitis is observed in severe and moderate stomatitis, accompanying the entire course of the disease and remains for 7-10 days after epithelization of the elements.

The body's immunological defense plays an important role in disease resistance. Both specific and non-specific immune factors play a role in immunological response. The set of mechanisms of immune defense in viral infections is divided into humoral, cellular and mixed, which, in turn, are specific with an unlimited spectrum of action. Studies of non-specific immunological reactivity revealed violations of the body's protective barriers, which reflected the form of severity of the disease and the periods of its development (Maksimovskaya L. HN. et al., 1995; Kirchner Holger, 1982; Lopes Carlos, 1984; Perrin D., Nicolas JC., 1990.).

Patients with recurrent herpes infection experience profound changes in the immune system. These changes are characterized by lymphopenia, a decrease in the number of T-lymphocytes, T-suppressors, and cells with membrane-bound immunoglobulins. Against the background of a decrease in the complement titer in the blood serum of patients, an increase in specific humoral antibodies and immune complexes containing complement is noted (Barinsky I. F., 1988; Shcridan L., 1982; Higa Kapo, 1982; Lukoroicz A. U., 1983; Cunningham A. L., Merigan T. S., 1983; Ferguson Appe, 1990; Wallace DE., 1993).

The authors emphasize the dominant role of cellular immune responses in herpes infection, noting their pronounced suppression during the week of illness. (Khlyustov SV., 1989; Rennie et al., 1985; Guren O., 1988; Landesberg et al., 1990; Mamedova SA. et al., 1991). Yeager (1986) notes that primary immunodeficiencies with an exclusive or predominant defect in the T-link of immunity primarily develop infections caused by the herpes virus.

According to the hemogram and cytogram of lesions and some local indicators of immunity (interferon, lysozyme), an immunosuppressive state was established in children with acute herpetic stomatitis. (Melnichenko E. M., et al., 1983; Jensen J. L. et al., 1987).

Depression of the T-immune system has also been established (Carich et al., 1979; Landesberg R. et al., 1990).

Studies of salivary local immunity factors (lysozyme, interferon) and natural serum immunity factors revealed a correlation between them: the more severe the form of stomatitis, the deeper the changes in homeostasis. Serological studies of blood and determination of the antibody titer in saliva indicate that in the early stages of the disease, the body's protection from infection is carried out due to factors of non-specific immunity (Melnichenko E. M., 1973; Kolomnets A. G. et al., 1984; Khlyustov SV. et al., 1989; Mamedova SA. et al., 1991; kirchner N. et al., 1982•, Guren O., 1988).

The search for ways to resolve some issues of the pathogenesis of stomatitis led researchers to the conclusion that it is necessary to study the morphology and histochemistry of the oral mucosa. (Vinogradova T. F. et al., 1983). The study of morphology and histochemistry of the oral mucosa in children explains the patterns and the highest frequency of the disease in children 1-3 years old. In children of this age, the permeability of histohematic barriers increases and morphological immune responses decrease: there is a thin epithelial cover with a low level of glycogen and ribonucleic acids, low differentiation of the basement membrane and connective tissue fibrous structures, abundant vascularization, a high level of mast cells with their low functional activity (Vinogradova T. F., et al.1983). There is also a low differentiation of connective tissue of the own mucosal layer in children aged 1-3 years. There is a moderate content of mainly mast cells and lymphoid elements with perivascular distribution, mast cells are represented by young immature forms. They are involved in the regulation of vascular permeability (Kaznacheyev V. T., 1966, 1968; Vinogradova V. V., 1968; Epishev V. A., Khersonskaya F. I., 1974; Melnichenko E. M., 1981; Vinogradova T. F. et al., 1983; Riley, 1952; Astoe Hayser, 1959; Selye, 1965, etc.) It should be taken into account that in the specialized and integumentary parts of the oral mucosa, epithelial thinning zones are found, which are probably the most "vulnerable" (Epishev V. A., Yunusov R. A., Yunusova I. F., 1986). Electron microscopic studies of patients revealed atypical cells with shrunken nuclei and cytoplasm, the formation

of vacuoles (Knopte T. et al., 1985; N. M. van Hale, R..S..Rogers, Q..A.. Dogle, A..zZ. Schrorres, 1981).

In the pathological link of acute herpetic stomatitis, a certain place is occupied by allergies, which are based on the reaction of the body's interaction with products of bacterial, medicinal or food origin, which, reacting with serum or tissue proteins, acquire the properties of antigens (Lysenko N. V., Volkova A. A., 1966; Reznikova L. S., Grebnyuk V. N., 1975; Khlyustov Sv. et al., 1989; E. M. Melnichenko, V. P. Mikhailovskaya, A. G. Kolomiets, 1984; Turk, 1975) indicate that antiherpetic antibodies are detected in saliva when determining the antibody titer, which indicates the possible significance of allergies.

Also, in acute herpetic stomatitis, a certain pathogenetic role is attached to the bacterial and fungal microflora of the oral cavity (Epishev V. A., Khersonskaya F. I., 1974; Shmagailo Ya. M., 1975; Marikov M. I. et al., 1978; Filipov E. A., 1978; Antonishin BV. et al., 1987; Shabanskaya M. A., 1991; Khazanova V. V., 199Z et al.), hypersensitivity of the body (Maksimenko P. T., 1970, Khlyustov SV. et al., 1989), as well as the functional state of the gastrointestinal tract (Yunusova I. F., 1978; Veselov A. Ya., 1988).

In the pathogenesis of acute herpetic stomatitis, great importance is attached to the concentration of hydrogen ions (PH) in saliva. The available research is contradictory. Some authors believe that the PH shift in saliva is associated with pathological processes in the oral cavity, while others have not found significant PH shifts in adults with stomatitis (Epishev V. N., .1977). According to Melnichenko E. M. (1972), the saliva pH of practically healthy children is slightly alkaline and is 7.07.4 (on average,  $7.36 \pm 0.01$ ). The saliva pH of children with acute herpetic stomatitis is unstable and its indicators vary depending on the period of the disease and the severity of its course, although within small limits. These deviations are most clearly observed in severe stomatitis (from 5.8 to 8.4), i.e. there is a tendency to acidic and neutral indicators, which is not indifferent to the patient's body.

## 1.2. Clinic and diagnosis of AHS.

Acute herpetic stomatitis, like many other childhood infectious diseases, occurs in mild, moderate and severe forms. The development of the disease passes through five periods: incubation, prodromal, the period of disease development, extinction and clinical recovery (Epishev V. A., Khersonskaya F. I., 1974; Lemiy V. V., Bachinsky Yu. S., 1987; Melnichenko E. M., 1992).

In the period of development of the disease, two phases can be distinguished: catarrhal and rash of elements of the lesion. As noted above, after the virus enters the child's body, it multiplies in the cells of local tissues and nearby lymphatic formations. If the body's defenses can not cope with the pathogen, then already in the incubation period, primary viremia is observed, the virus enters the bloodstream. It is assumed that the penetration of the acute herpes virus into organs and tissues through the capillary barrier is carried out by diapedesis. The virus, settling in the liver, spleen and other organs and tissues, quickly multiplies, there are tissue lesions such as foci of necrosis.

Secondary viremia is characterized by the appearance of a large amount of virus in the blood after its increased reproduction in these organs. It is observed in the prodromal period of the disease and in the first days of its height (Vinogradova T. F., Maksimova O. P., Melnichenko E. M., 1983).

During secondary viremia, viruses rush to the skin and mucous membranes, where their intracellular reproduction continues (Shubladze A. K., Mayevskaya T. M., 1971; Bogdanov I. L., 1974; Kirchnes N., 1983, etc.)

In the viremia of acute herpetic stomatitis, the virus is found in white blood cells, red blood cells and platelets. Bocharov A. F. (1965) established a violation of the interaction of the coagulation and anti-coagulation systems of blood, which is consistent with a clearly pronounced symptom of bleeding of the oral mucosa, gums, and sometimes the nose in acute herpetic stomatitis.

These changes in homeostasis can lead to intravascular thrombosis. There are assumptions (to. Neupe, 1974; Corly L., 1986), that necrotic areas in organs and tissues during herpetic infection occur as a result of both direct destruction of cellular elements by

the virus and capillary thrombosis. The pathological process begins in the depth of the connective tissue and is localized around the vessels, as a result of which the phenomena of reticular ballooning degeneration develop in the epithelium-intraepithelial necrosis. This condition in the clinic corresponds to the evolution of a spot, vesicle, plaque, erosion, aphthous, ulcer, spot.

In the cytological study of fingerprint preparations from the elements of the lesion, 4 stages are distinguished: a) the stage of degeneration and typical cellular damage, b) the stage of degeneration and nonspecific inflammation, c) the stage of regeneration, d) the stage of epithelialization (A. I. Evdokimov, T., F. Vinogradova, 1976). The stage of degeneration or typical elements of cell damage is characterized by an abundance of epithelial cells, often layers of epithelium and masses of destroyed cells in the form of single nuclei and protoplasmic remnants, as well as cells with phenomena of degenerative changes and tinctorial properties. Very often you can see symplasts and, so-called, giant multinucleated cells. They are large in size, their shape is rounded or irregular, with two or more large nuclei, the cytoplasm is usually blue, less often purple. Also found in a large number of different types of microflora, there are single white blood cells.

Giant multinucleated cells are pathognomonic for viral diseases of the skin and mucous membranes. They are found in measles, chickenpox, shingles and other viral, including herpetic, lesions (Kimele EK., 1984; Airapetov L. S. et al., 1985; Trank, 1948; Blank N. et al., 1951; Nicolau Sh., 1965; Lightwool K., Nolan K., 1970).

The stage of degeneration and non-specific inflammation are characterized by significant differences in the qualitative composition cells. Epithelial cells are practically absent, because they are in the stage of decay. The field of vision is completely covered with detritus, remnants of cellular elements, an abundance of microorganisms is noted, white blood cells are found in significant numbers, and you can also see the phenomena of incomplete or perverted phagocytosis. The overall picture corresponds to non-specific inflammation with a predominance of tissue breakdown.

The regeneration stage is characterized by the appearance of young epithelial cells and young forms of leukocytes, mononuclears, and polyblasts in the preparations. All cells acquire a full-fledged morphological structure, some are actively functioning. The number of microorganisms is significantly reduced. Epithelialization has a small number of cellular elements (1-3-5 in the field of view): morphologically complete leukocytes, mononuclears, often erythrocytes, single young epithelial cells, individual microorganisms of the coccoid group (V. A. Epishev, F. I. Khersonskaya, 1974; Kimele E., 1984).

Hyperemic areas of the oral mucosa that do not have lesion elements do not remain intact during all periods of the disease. Cytological examination revealed that the preparations from these sites contain many epithelial cells. They are often located in layers, some cells are destroyed, others have insufficiently clearly visible contours that are atypical cells, in these cells there is a wrinkling of the nuclei and the formation of vacuoles (Nopte T., Saito T., Fujioka U., 1985; Correda (E., Castagnola E., 1994).

In the literature devoted to the study of acute aphthous stomatitis, there are different interpretations of the lesion element, "aphta", which gave the name to stomatitis. In translation, this word means "ulcer"; in acute aphthous stomatitis, it is described as erosion (N. I. Antonova, 1962), papules (plaques) (E. K. Klivanskaya-Krol, 1940; V. I. Uvarov, 1957; I. M. Starobinsky, 1965; DE. Kindii, 1967; L. T. Kulchitskaya, 1968), a site of necrosis of the spot epithelium (Weiss, 1965; S. M. Bazarnova, 1968), a vesicle (F. S. Khersonskaya, 1968; kuzushima K., kimura N., kino U., kido S., 1991), simply aphthae, etc.

According to E. M. Melnichenko (1972), the lesion element in patients with acute herpetic stomatitis is not stable, but passes through the stages of its development, as indicated above. Such clinical stages as spot, vesicle and ulcer are not observed in the development of each element. This is due to the fact that the spot and bubble exist most often for a short time.

The dynamics of lesion elements in acute aphthous stomatitis is indicated by D. A. Entin (1954), P. Pophristov (1953), R. Ya. Pekker (1966), who distinguish from two to three stages in their development. In more detail, these stages (6 names or stages) are

given by A. I. Rybakov (1964): vascular injection-vesicle-tubercle-plaque-ulcer-necrosis. Clinical data confirm the unity of acute aphthous and herpetic stomatitis, which is confirmed by virological, serological and immunofluorescent methods (E. M. Melnichenko, 1972, 1992).

Most authors believe that rashes are more often localized in the oral cavity: on the tongue, mucous lips, cheeks (Pekker Ya. S., 1950; Agapova N. I., 1953; Epishev V. A., F. I. Khersonskaya, 1974). They are located on the gums (Antonova N. I., 1963; Khersonskaya F. I., 1968, etc.), on the hard and soft palate, palatine arches (Pekker Ya. S., 1950; Agapova N. I., Khersonskaya F. I., 1968, etc.), as well as in the posterior parts of the mucous membrane oral cavity (V. A. Epishev, F. I. Khersonskaya, 1974, V. A. Epishev et al., 1976; G. G. Belaya et al., 1991; Taieb A., Body S., Astor 1. Dy Pasquier R., Maleville L, 1987). The number of elements varies depending on the severity of the polylezny flow. Very often there are combined forms of acute herpetic stomatitis in children - not only on the oral mucosa, but also on the skin: most often on the chin, wings of the nose, lips, corners of the mouth. With the aggravation of the disease, the number of combinations also increases (VL. Mikhailovskaya, T. V. Bintsarovskaya, 1981; Nayler et al., 1987; Gill M. U., Arlette U., Buchan K. A., 1990; kuzuchima K. Et al., 1991; Ros s.P., vej R. A., Silver U. A., 1991; MsKeppa D., Murphy G., 1995).

The clinical picture of the disease consists of symptoms of general toxicosis and local manifestations on the oral mucosa. The severity of acute herpetic stomatitis is assessed by the severity and nature of these two groups of symptoms

Most researchers note symptoms of general intoxication: malaise, headache, sleep disturbance, vomiting, delirium, and the presence of gastrointestinal disorders (Epishev V. A., Khersonskaya F. I., 1974; Epishev V. A. et al., 1986). In such patients, the temperature often rises (Kulchitskaya L. T., 1964, 1968; Herrman, 1972, etc.). The temperature increase depends on the severity of the disease (Epishev V. A., Khersonskaya F. I., 1974; TO. Vinogradova T. F. et al., 1983; Melnichenko E. M., 1992). Other authors consider. that this disease is characterized by subfebrility. There are also symptoms such as loss of appetite, nausea, vomiting, headaches, adynamia, apathy, agitation, musculocutaneous

hyperesthesia and arthralgia. Often there are symptoms of damage to the cardiovascular system: brady and tachycardia, muffled heart tones, arterial hypotension. Some children have nosebleeds, pronounced lymphadenitis not only of the submandibular but also of the cervical lymph nodes (V. A. Epishev et al., 1986; Melnichenko E. M., 1992; MSKna D., Murphy G., 1995).

More often, acute herpetic stomatitis occurs as an independent disease, but sometimes it can be combined with acute respiratory viral infections, acute intestinal diseases (King D.L., Steinhauer W., Garcia Codoy E, Elkins S. J., 1992). When examining patients with acute herpetic stomatitis against the background of edematous and hyperemic mucosa, small vesicles with clearly defined edges are found; 1-5 mm in size with transparent contents. With a mild form, there are 1-4 of them, with a severe one - up to several dozen, often the phenomena of gingivitis and lymphadenitis are added. More often, bubbles are located in groups in the form of clusters, on the mucous membrane of the lips, cheeks, palate, and less often on the tongue. Vesicles on the oral mucosa are most often not visible, as they open very quickly, and thick-walled vesicles that exist for 3-5 days are less common. After that, they are opened, and in their place there are soft yellow or grayish - white deposits, when removed, an erosive surface is exposed, bleeding and painful. Vesicles can merge with each other, forming large lesions. Crusts form on the lip border after opening the bubbles

A mild form of acute herpetic stomatitis is characterized by an external lack of intoxication of the body. Most often, the disease begins suddenly, with an increase in temperature to 37-37.50 C, sometimes there is no increase in temperature. The child's general condition is satisfactory. Children sometimes have minor catarrh phenomena of the nasal mucosa, respiratory tract. In the oral cavity, the phenomenon of hyperemia, small edema, mainly in the gingival margin (catarrhal gingivitis). The duration of the period is 1-2 days. In some cases, with an atypical course of the disease, hyperemia increases further and bleeding gums appear, bypassing the phase of rash of the affected elements. This is a catarrhal type of acute herpetic stomatitis. Against the background

of increasing hyperemia, single aphthae appear in the oral cavity, their number does not exceed 6; the period of development of the disease is 1-2 days.

The period of extinction of the disease is longer, aphthae acquire a marble color, their edges and center are blurred. After epithelialization of the elements, the phenomena of catarrhal gingivitis persist.

More often, mild forms of acute herpetic stomatitis occur in children in the first year of life. This is due, on the one hand, to less contact with children, and on the other, to the nature of nutrition: semi-liquid, soft, mashed, mainly dairy food eliminates injury to the oral mucosa. The use of breast milk for nutrition, which to some extent has bactericidal properties, the presence of antibodies in breast milk also causes a milder course of stomatitis (St. Zabyshnaya, 1974).

### **1. Z. Modern methods of treating AHS.**

The issue of treatment of acute herpetic stomatitis, despite the availability of a large number of therapeutic agents, can not be considered completely resolved until today. From the first days of the period of development of acute herpetic stomatitis, taking into account the etiology of the disease, much attention is paid to antiviral therapy in local treatment. For this purpose, antiviral ointments are widely used, such as oxoline 0.25%, 0.5% bonafton ointment, 0.5% tebprofen, 1% florenal, interferon 1% adinalic, 5% alpizarin, 1% riodoxol. (L. I. Drobotko, L. A. Lobimova, 1976; A. N. Stepanov, 1985; St. Petersburg, Russia). (Latysheva, 1985). Comparing the effectiveness of 0.5% tebprofen and 1% florenal ointment, it was proved that 1% florenal ointment is effective in the mild form of acute herpetic stomatitis, while 0.5% tebprofen ointment and 1% florenal ointment are most effective in the moderate form. Also, 0.25% oxoline ointment was compared with these ointments (Vinogradova T. F. et al., 1974; Drobotko L. N. et al., 1974; Melnichenko E. M. et al., 1977, Fokina T. V., 1978). When using oxoline ointment in 100 patients, data were slightly worse with respect to the duration of recovery. In the literature, there is evidence that the

antiviral effect of oxoline is well expressed against the influenza virus and weakly expressed against the herpes virus (Pershin G. N., Bogdanova N. S., 1973). With AHS of 0.5%, tebrofen ointment is effective only if you see a doctor early. Drobotko L. N. et al., 1974; Kukalieva Z. Sh. et al., 1990; Bikpulatov et al., 1972 proved the interferonogenic properties of polyvinyl alcohol and polyvinylpyrrolidone in experimental herpetic infection, which was the basis for the use of these drugs in clinical practice (Vinogradova T. F. et al., 1972, Bostajan Jr. et al., 1973). Due to the fact that in early childhood, the body is protected by non-specific immunological reactivity (Askerov VO, 1969; Vologodskaya I. A., 1972, Mikhailova Z. M. and Mikheeva

T. A., 1974), special attention is paid to the maintenance and stimulation of natural immune factors. Some of these drugs are the bacterial polysaccharide and animal-derived antibiotic lysozyme (Drobotko L. I., Murashova N. S., 1975) and prodigiosan in combination with leukocyte interferon, with the use of which the recovery time is reduced in the mild form of AHS to 4.4 days, in the moderate form to 6.3 days and in the severe form to 6.9 days. 394 megasin ointment is also used (Karmelkova A. A., 1990, etc.).

For a number of years, sulfonamides and antibiotics in the form of powders and ointments have been widely used in the treatment of AHS. Various combinations of sulfonamide preparations and antibiotics with the addition of anesthetics were proposed (Antonova N. I., 1963, Reusova E. P., 1966; Khersonskaya F. S., 1968; Postkowska V., Pospich L., Jankowska M., 1993). R. Kadyrov, (1977), suggested using the drug Kanazol "C" for the treatment of all types of diseases. forms of acute herpetic stomatitis in combination with keratoplastic and analgesic substances. But antibiotics and sulfonamide preparations do not have a depressing effect on the viral infection. In 1985, E. M. Melnichenko proposed the use of DNA-aza as an antiviral agent for the treatment of acute herpetic stomatitis. DNA-aza is an antiviral agent that prevents DNA reduplication and stops the reproduction of the herpes virus. Kh. D. Vakhobov and T.

I. Rudenko in 1988 proposed the use of 3 % gossypol liniment in viral diseases of the oral cavity, and in particular, in the treatment of acute herpetic stomatitis for local treatment of the oral cavity and shortening the epithelialization period. Mattheus R..W., Scully SEE, Levers B. Hislop W..S.(1988) have proven the effectiveness of mouthwash with such agents as benzydamine and chlorhexidine. Bernstein D., Shiff 1., Rrince A., Filler M., Briner W.(1991) showed that chlorhexidine-gluconate gives an antiviral effect, affecting the envelope of the herpes virus destructively, and benzinamide also has an analgesic effect, but the epithelialization time when using chlorhexidine is not reduced, it is better to use it for recurrent aphthous stomatitis.

In the literature of recent years, there are data on the use of human immunoglobulin for the prevention and treatment of recurrent herpetic stomatitis. Use of immunoglobulin with a high antibody titer (1 : 640 - 1 • 1280) to the herpes simplex virus, reduces the time of epithelialization. Relapse of the disease occurs in 12-24 months (Melnichenko E. M., Kolomets A. T., 1989; Rukavishnikova I. A. et al., 1991).Kukaliev et al. (1990)proposed interferon ointments for the treatment of acute herpetic stomatitis a and u, which reduced the time of epithelialization. For various manifestations of herpetic infection, concentrated interferon is used for ointment applications (Tarashkevich Z. Sh., 1980; Stepanov A. N., 1985). Human leukocyte interferon with an activity of 20,000 IU per 1 year is also widely used (E. P. Deggyareva et al., 1991).

Interferon can be used with an ultrasonic nebulizer, the effect of the drug is enhanced by deep penetration into the tissue, which reduces the time of epithelialization. After the release of the mucous membrane from necrotic masses and the appearance of hyperemia around the lesion, drugs that promote epithelialization are prescribed. These are oil solutions of vitamin A, rosehip oil, sea buckthorn, solcoseryl ointment and jelly, sodium nucleinate, aloe liniment, kalanchoe juice, basil, linden, the drug "Livian", "Vinizol", fortified mixtures according to V. V. Zhilina on an oil basis. (Luciu Ch. et al., 1988; Henricsson U., Aachen T., 1985). During this

period, the use of antiviral ointments is limited, up to complete withdrawal. N. N. Bazhanov et al. (1977) suggested using "propolis", a propolis drug, and you can also prescribe 10% propolis aerosol with rosehip oil (V. I. Potiyko et al.). From physiotherapy procedures, local administration gives good results UV irradiation, the use of a helium-neon laser, low-intensity radiation with a wavelength of 633 nm, which has a pronounced stimulating effect on the synthesis of ATP in cells (Melnichenko EM. et al., 1991, 1992, 1993; Orda EM. et al., 1992; Horoell R. M. et al., 1988; Woods R., 1993).

As mentioned above, all patients are prescribed antihistamines in doses appropriate to the age of the child. Since moderate-severe and severe forms of acute herpetic stomatitis develop against the background of a decrease in local and general immunity, complex therapy includes drugs that stimulate the body's defenses: methyluracil (0.15 -0.25 g)-pentoxyl (0.05-0.1 g), sodium nucleinate (0.001-0.002 g). They are prescribed 2-3 times a day for 3-5 days in age-appropriate doses. Gamma-globulin is administered 1.5-2 ml once every 3-4 days (1-3 injections), prodigiosan - once every 3-4 days 15-25 mcg (2-3 injections) and lysozyme 75-100 mg daily for 5-7 days. Treatment is carried out in a hospital setting. Levamisole is used to treat recurrent forms of herpetic stomatitis (Abramova E. I., Lyubomirova I. M., 1986, Melnichenko E. M., 1988). When it is used, the remission period increases, aphthae take on an abortive character. Shumsky A., Grebnev E., 1996 suggest the influence of a magnetic field on the blood as a method of treating chronic herpetic stomatitis.

In addition, acyclovir (zovirax) is used in the treatment of acute herpetic and recurrent stomatitis (Latysheva SV. et al., 1987; Khakhalin L. N., Abazova F. I., 1996; Cataldo F. et al., 1993; Amir L. et al., 1997). The use of zovirax with phonophoresis and laser therapy promotes rapid epithelialization and heals the lesion of the lips and skin of the oral region (Latysheva SV. et al., 1988). N. V. Terekhova et al. (1990) proposed an immunomodulator – kenantan for the treatment of patients suffering from severe forms of acute herpetic and recurrent forms of stomatitis. I. A. Kazantseva and

R. M. Bikpulatov (1994) proposed timalin, which is also an immunomodulator and is used for the prevention and treatment of AHS.

For the prevention of AHS, vaccination with the herpes simplex virus vaccine is used (Bos SL., 1988; Schmitt D..L., Johnson D..W., Henderson F..W., 1991). Since the herpes simplex virus is a weak inducer of interferon, the use of interferon inducers for a short time is of great importance in the treatment of AHS with the development of local lesions (Sadykov AS. et al., 1978; Cheshik SG. et al., 1988). Interfron inducers used in the clinic should be highly effective and low-toxic, not have carcinogenic and teratogenic properties, as well as antigenicity. Plant extracts are also used as interferon inducers. There are medicines obtained from domestic raw materials and having an immunostimulating effect. These include medicinal products made from licorice roots (Nurmukhamedova Sh. D., 1981; Azimov M. A., 1989 etc.) But their ability to induce interferon has not been studied.

Thus, AHS occurs and develops against the background of changes in the body's immunological reactivity. At the same time, the virus is constantly persistent, periodically causing relapses of the disease. An analysis of the literature has shown that despite numerous studies devoted to the state of immunity and treatment of children with APS, many issues remain insufficiently studied. These include studies of the oral microflora, indicators of local immunity, their relationship with the clinical manifestations of AHS, changes in the dynamics of treatment, and the development and application of new methods of treatment with products made from local raw materials.

### Chapter 3

## CLINICAL AND STATISTICAL ANALYSIS OF PATIENTS WITH ACUTE HERPETICSTOMATITIS IN 2018-2020 ГГ.

A retrospective clinical and statistical analysis of patients with acute herpetic stomatitis who were treated in the 3rd children's dental clinic, Mirzo-Ulugbek district of Tashkent for the period 2018-2020 revealed a high incidence rate.

In 2018, 986 patients applied to the polyclinic for acute herpetic stomatitis, including 520 boys (52,794), 466 girls (47,394) (Fig.

Children aged from 1 year to 3 years were more common (57,994), the least number of patients were in the group up to 6 months (1,196). Of these, 448 children (45.4%) were organized, and 538 children (54.6%) were not organized (fig. NN<sup>o</sup> 2,3).

According to the clinical course, the division was as follows: 101 patients (10,296) were identified with a mild form of the disease, 880 patients (89.2%) with a moderate severe form, and 5 patients (0.5%) with a severe form of the disease (Fig.

Analysis of concomitant diseases revealed that among all patients, patients with the most frequent diseases of the respiratory organs prevailed - in 868 patients (88%), acute intestinal diseases - in 66 children (6.7%), of the transferred diseases, hepatitis was found in 11 patients (1.1%), in 4.2% of children did not experience concomitant diseases (Fig. 4).

The presence of dental caries was determined in children (523 (53.04%) patients had it). The largest number of carious teeth was observed in children aged 4 to 6 years - 165 (91.2%).

The seasonal morbidity survey in 2018 2018 revealed the following dynamics. Most patients were observed in October - 147 patients (14.9%), in May - 113 (11.4%) and in June - 12 (11.3%) patients, i.e. the main peak occurs in the autumn and spring months (Fig.

The average severe form of the disease was observed in 89.2%. In all patients with an average severe course, the onset of acute herpetic stomatitis was acute, with a temperature rise to 38.20 C (8694), with chills, drooling (8494), moodiness, lethargy (10094), and refusal to eat (10094). Of the clinical symptoms, the most common was an increase in regional lymph nodes (100%).

Gum bleeding was observed in all patients with different duration in days: 1 day-29%, 2 days-58.2%, 3 days-12.8%.

The number of afts up to 3 in children with moderate severity of the disease was observed in 2 patients (10.3%), from 4 to 6 afts - 457 patients (51.9%), 6-10 afts - in 387 patients (43.9%), completely - in 34 patients (3.9%). The temperature in these children was observed to be elevated mainly in the first 1-3 days.

Temperature increase within 1 day was observed in 81 patients (10.7%), 2 days - in 547 (72.4%), 3 days-in 127 patients (16.8%).

The days of aft rash in all children were different: in children under 6 months-6.3 days; from 6 months to 1 year-5.7 days; from 1 year to 3 years-5.1 days; from 4 to 6 years-6.2 days; from 7 to 10 years-5.2 days; 11-14 years - 5.12 days.

In children with a mild degree of damage, a subfebrile temperature was observed in 8594 children. The number of rashes before AFT was observed in 100 patients, and only one patient had 4 afts. Bleeding gums were present in all patients, salivation was not observed in any patient. Moodiness, lethargy with a mild form of the disease were found in 100% of patients, difficult food intake was also observed in all patients. Lymph nodes were enlarged in all patients, pain on palpation was noted in all children.

С тяжелой фIn 2018, 5 children applied to the polyclinic with a severe form of the disease. They were immediately sent to the TDSI Children's Hospital for hospitalization. On external examination of these patients, a large number of rashes were observed on the face: in the area of the wings of the nose, around and on the red border of the lips. The lips are completely closed, caked with blood, covered with crusts. The children couldn't open their mouths by themselves. The chin and regional lymph nodes are enlarged about the size of walnuts, and are very painful on palpation. All children were treated with a temperature of up to 39°C. After medical treatment and opening of the mouth, a large number of erosions and ulcers were noted, the mucous membrane was

edematous, hyperemic. Erosions and ulcers when touched were sharply painful, bleeding, and there was an unpleasant smell from the mouth.

During the year, the polyclinic for acute herpetic stomatitis issued 106 sick leaves lasting 783 days, an average of 7.4 days for each patient.

In 2019, 767 patients applied for acute herpetic stomatitis, including 411 boys (53.6%), 356 girls (46.4%).

Children aged from one year to 3 years were more common (61.1%), and children under 6 months were less common (1.1%). The total number of children examined was 417 (54.4%), and the total number of unorganized children was 350 (45.6%) (Figure 2). According to the clinical course, the division was as follows: 193 patients with mild disease (25.1%), 568 patients with moderate severity (74.8%), and those with severe disease - 6 (0.1%).

Analysis of concomitant diseases revealed that among all patients, patients with the most frequent diseases of the respiratory organs prevailed - 607 cases (79.1%), acute intestinal diseases - 129 cases (16.8%), and hepatitis was noted in 31 patients (4.1%) (Fig.).

The presence of dental caries was determined in children: 375 children with caries were identified (48,894). Children aged 1 to 3 years had the most carious teeth - 203 cases (26.4%).

The study of seasonal morbidity in 2019 revealed the following dynamics: most patients were in September - 126 people (16.4%), in October - 82 people (10.6%), i.e. the main peak occurred in the autumn time (Fig.).

More often there was a moderate-severe form of the disease. In all patients, the onset of the disease was acute, with fever (100%), chills, drooling (89.8%), moodiness, lethargy (100%), refusal to eat or difficulty eating (100%).

Of the clinical symptoms, the most common was an increase in lymph nodes, in particular the chin (100%). Gingival bleeding in children with a moderately severe course of the disease was observed in 100% of children, with a duration in days: 1 day - 64.1%, 2 days - 27.82%, 3 days - 2.9%.

The number of afts up to 3 in children with moderate severity was not observed, from 4 to 6 afts - in 289 patients (50.8%), from 6 to 10 afts - in 279 children (49.1%), completely - 0.1%. The temperature in these children was

observed to be elevated mainly in the first 1-3 days. Elevated temperature during one day was observed in 483 patients (85.2%), the temperature was maintained for two days in 78 (13.7%) patients, 7 patients (1.2%) had a low temperature. The days of aft and erosion eruptions were different for all children.

With a mild degree of damage, a subfebrile temperature was observed in 7394 children, the number of aft rashes up to 3 was observed in 122 patients, from 4 to 6 was observed in 71 patients. Bleeding gums were observed in all patients, salivation was not observed. Moodiness and lethargy in the mild course of the disease were found in 144 patients (74.6%). Difficult food intake was observed in 138 sick children (71.5%). Lymph nodes in all children were enlarged, and palpation showed splotchiness in all children.

С т In 2019, 6 children were admitted with the most severe form of the disease. They were immediately sent to the TDSI Children's Hospital for hospitalization.

In 2020, 642 patients applied for acute herpetic stomatitis, including 352 boys (54%) and 290 girls (46%).

Children aged from 1 year to 2 years were more common - 363 patients (56.5%), in the group up to 6 months. no children were observed. 226 patients (34.7%) were organized, 416 patients (63.9%) were unorganized (fig. According to the clinical course: 61 patients (9.5%) presented with a mild среднетяжелой формой заболевform of the disease, 581 patients (89.3%) with a moderate form of the disease, and 9 patients (1.1%) with a severe course of the disease.

Analysis of concomitant diseases revealed that among all patients, patients with the most frequent diseases of the respiratory organs prevailed - 462 cases (71.9%), acute intestinal diseases - in 135 patients (21 %), hepatitis was - in 24 patients (3.7%) as a previous disease. The presence of dental caries was determined in children: there were 203 children with caries (H1. 6%). Most of the carious teeth were found in children aged from 1 year to 3 years - 22 cases (55%).

The study of morbidity by season in 2020 revealed the following dynamics. The highest number of patients was registered in April - 83 people (12.9%), in May - 82 people (12.7%), that is, the main peak occurred in spring (Fig.

In the moderate course of the disease, all patients had fever (100%), chills, drooling (90.9%), moodiness, lethargy (100%), and refusal to eat (100%). In all patients, the onset of the disease was acute, with a rise in temperature (100%), with chills, moodiness, lethargy, difficulty eating or refusal to eat.

Of the clinical symptoms, the most common was an increase in the lymph nodes, in particular the chin 100%, to the size of beans in 79 % of children, in 27 % of walnuts.

With a mild course of the disease, the number of afts up to 3 was observed in 58 children, from 4 to 6 afts - in 3 children. Gum bleeding was observed in all patients. Moodiness and lethargy were found in 45 patients. Subfebrile temperature was observed in 8094 children.

The number of afts up to 3 in children with moderate severity of the disease was not observed, from 4 to 6 afts and erosions - in 291 (50.1%) patients, from 6 to 10 afts and erosions - in 280 (48.2%) children, completely - in 10 (1.7%). The temperature in these children was observed to be elevated, mainly for one day in 491 patients, for 2 days the temperature was kept in 90 patients, for 3 days the temperature was kept in 10 patients. The days of aft and erosion eruptions were different for all children.

For acute herpetic stomatitis, 57 433-day sick leaves were issued during the year. An average of 7.6 days for each patient.

Thus, the results presented in this chapter showed that herpetic stomatitis in children occurs every year with almost the same frequency, with a peak in the autumn and spring months. As a rule, these are weakened children who have had diseases of ENT organs, OCD, more than half of the children have carious teeth. The main percentage of children (7594) with a moderately severe course of the disease (fig. With a severe course, an average of 1.1% are registered per year%, and they are all hospitalized. Each year, up to 100 sick leaves are issued for herpetic stomatitis lasting 7-8 days.

As can be seen from the retrospective analysis we conducted over the course of several years, herpetic stomatitis in children is quite common and takes up a lot of time for the working-age population in connection with child care. Therefore, the issues of adequate treatment of herpetic stomatitis are an urgent problem and require

such a solution that allows you to choose affordable, highly effective drugs obtained from local raw materials.

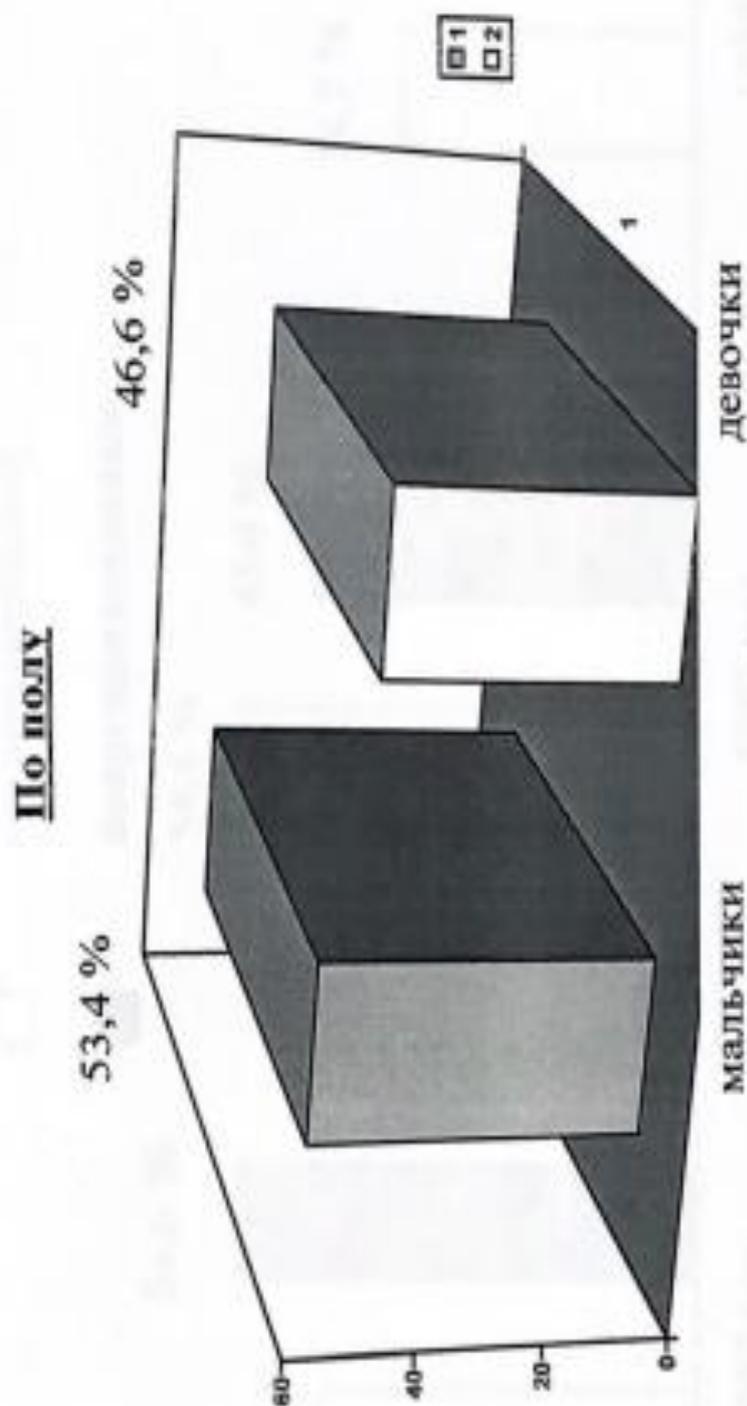


Рис.1. Распределение больных ОГС по полу

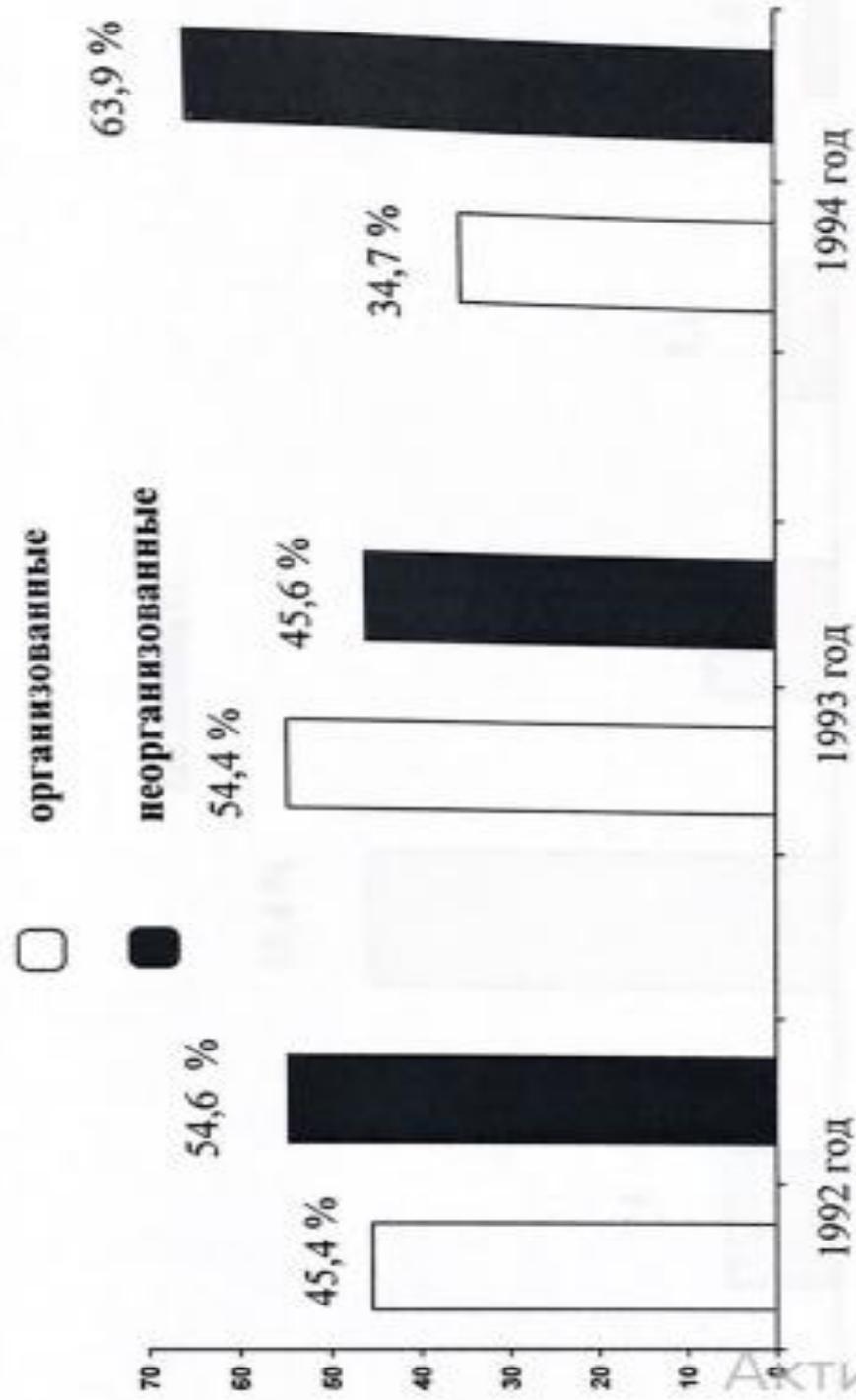


Рис.2. Распределение больных ОГС по организованности

По возрасту

58,4 %

%

60

50

40

30

20

10

0

14

16

7,1

3,8

возраст

до 6 мес.

от 6 мес. до года

от 1 до 3 лет

4 - 6 лет

7 - 10 лет

11-14 лет

Рис.3. Распределение больных ОГС по возрасту

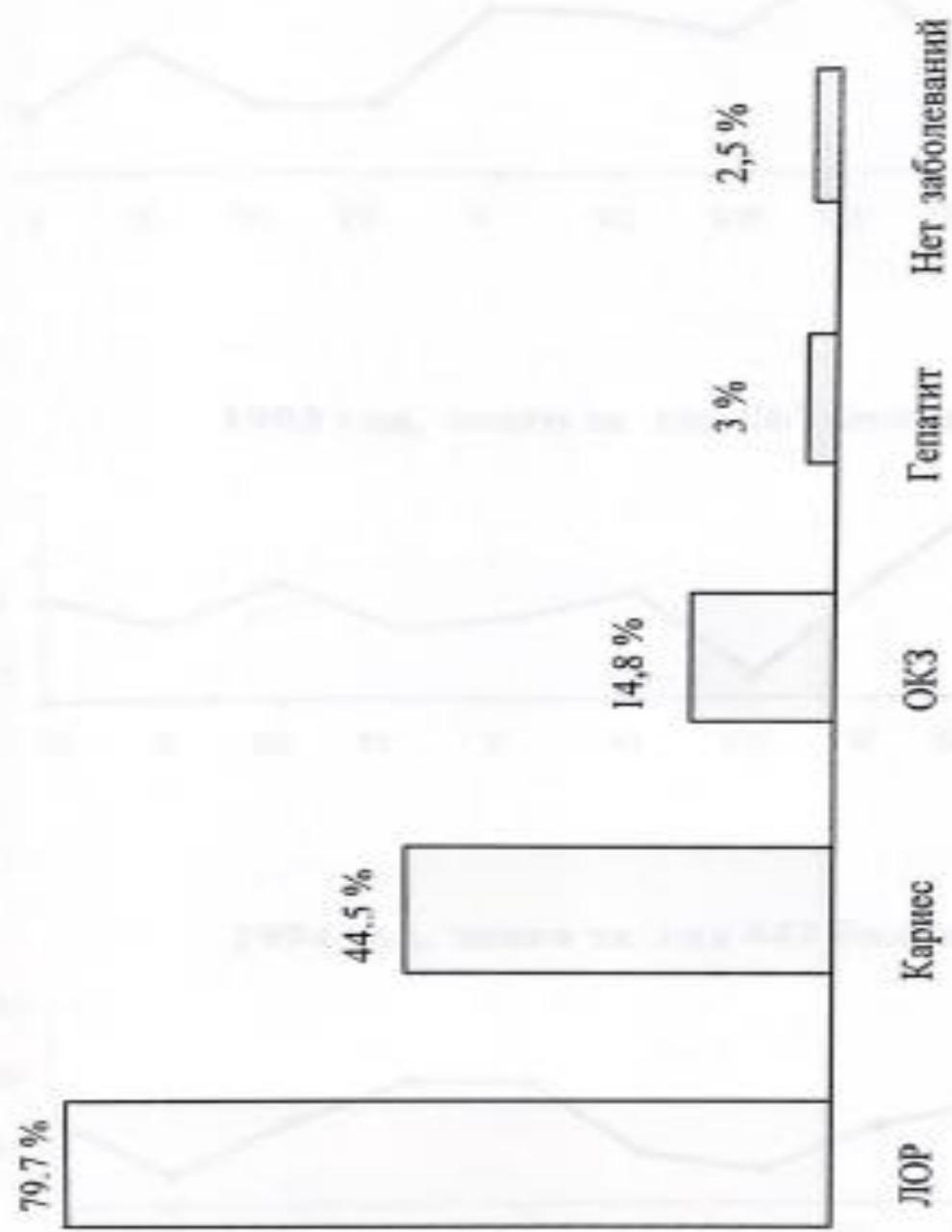
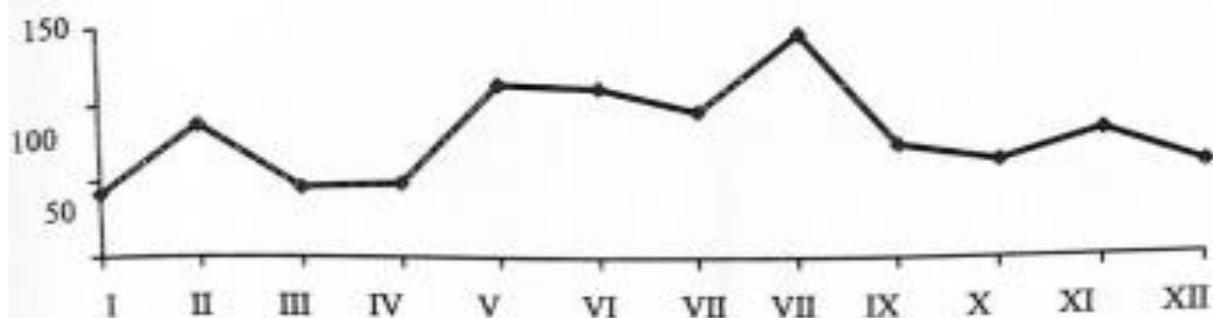
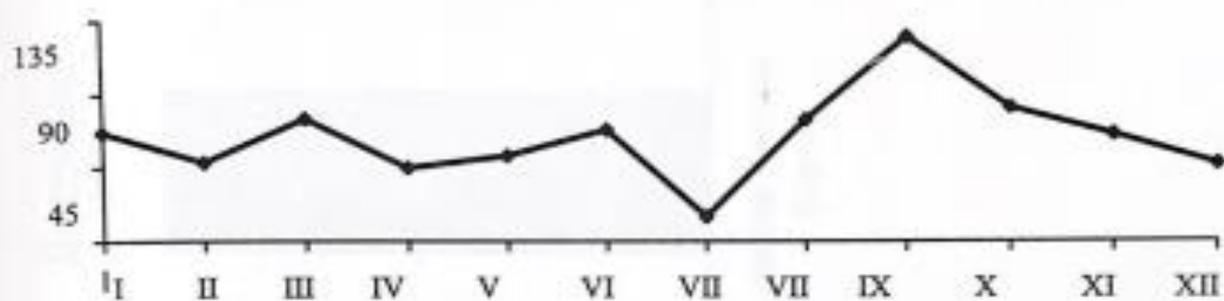


Рис. 4. Сопутствующие и перенесенные заболевания

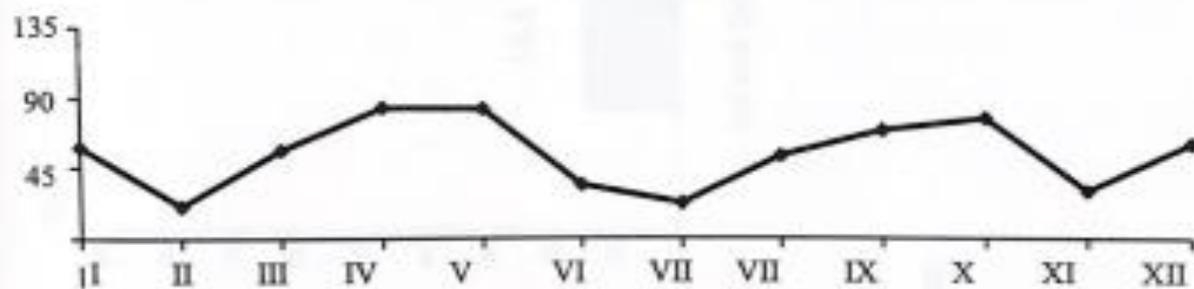
**1992 год, всего за год 986 больных**



**1993 год, всего за год 767 больных**



**1994 год, всего за год 642 больных**



**Рис.5** Распределение больных ОГС детей по сезонам

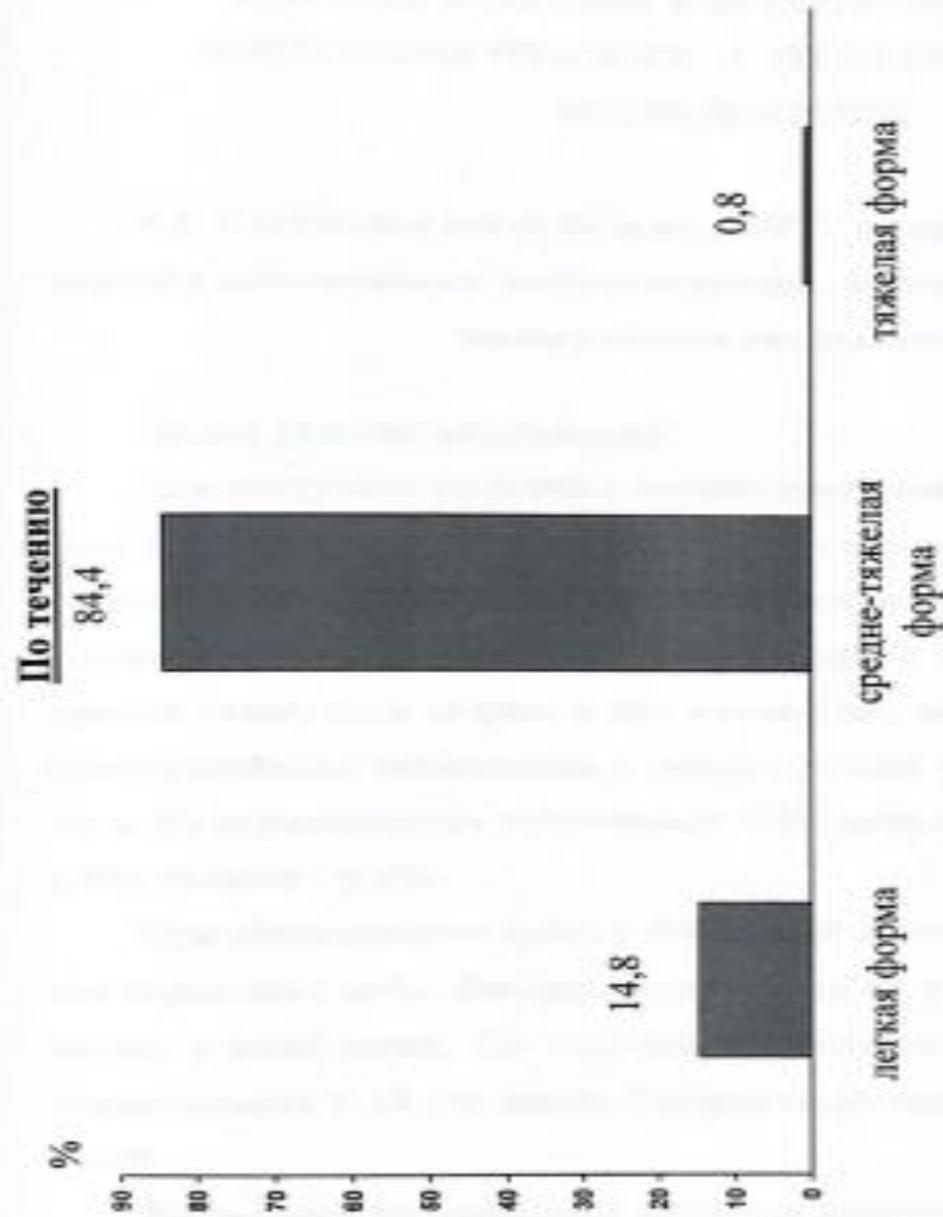


Рис.6. По течению

## Chapter 3

### EVALUATING THE EFFECTIVENESS OF THE APPLICATION GLYDERININ OINTMENT ACCORDING TO CLINICAL, CYTOLOGICAL, BACTERIOLOGICAL AND IMMUNOLOGICAL AND EXPERIMENTAL STUDIES

4.1. The state of children with AHS during the height of the disease according to clinical, cytological, bacteriological and immunological studies

#### Mild course of the disease

At admission of children with a mild course of the disease, an increase in subfebrile temperature was observed in all patients. The general condition of all children was worsened: moodiness, lethargy, headache appeared in 55.5% of children. Young children refused to eat, and children older than 4 years complained of pain when eating. No concomitant diseases were observed in children with mild AHS. Of the previous diseases, ENT was registered in 88%, OCD-in 8%, hepatitis-in 4%.

When examining the teeth, 60% of children had 3 or more carious teeth in the oral cavity. The lymph nodes did not increase, but they are painful in all children. On the part of the oral cavity, increased salivation was observed in 33.3 % of children. Catarrhal gingivitis was observed in all children.

Rashes on the oral mucosa, more often on the mucous membrane of the lips and cheeks, were isolated, sharply painful when touched. There was a wide hyperemic rim around the aphthae, and the aphthae were covered with a grayish-white coating. 66.6% of children had aft up to 3 years of age. 33.4% of children had higher AFT values (up to 5).

During cytological examination, mastocytes and multinucleated cells were found in smears-prints 1-2 in the field of vision *мастоциты*, indicating the viral etiology of this disease. Leukocytes were found in all children, 1-2 in the visual field in 44.4% of children, and more than 3 leukocytes in the visual field in 55.6% of children (Table 5). Red blood cells were found in only one child. Epithelial cells were polygonal, rounded, square, or irregular in shape; the nucleus occupied an insignificant part of the cell, dark with an indistinguishable structure. There were also epithelial cells containing a small nucleus with an indistinguishable structure,

chromatin and nucleoli. A large number of microorganisms were detected, mainly coccoid flora.

Bacteriological examination of saliva in patients with AHS before starting treatment revealed a diverse microflora (Table 6).

In children with mild herpetic stomatitis, *Staf* prevailed. *aureus*, *Str. Salivaris*, and *Enterococci*. The frequency of their occurrence was 86.7%, 60%, and 66.7 %, respectively. The appearance of *Candida* fungi in the oral cavity in hemolytic streptococcus was noted. Dysbiotic changes in the oral cavity composition were multiple in nature, i.e. they affected two or more types of microorganisms. The microbial number increased to  $6.78 \pm 0.5$  lg. CFU/ml of saliva, normally  $4.85 \pm 0.7$  lg CFU/ml.

In all patients in the acute period, serum immunoglobulins of classes A, M, and G, as well as secretory immunoglobulin A, were detected in saliva.

Taking into account that saliva performs many functions in protecting and maintaining the integrity of the oral mucosa, takes part in cleaning the oral cavity from food residues, plaque and bacteria, has antibacterial, antifungal and antiviral properties, we studied the content of serum A, M, (E and secretory immunoglobulin A in saliva during the height of the disease

Analysis of the obtained data on the content of serum immunoglobulins A, M, G and secretory immunoglobulin A in saliva showed that in patients with mild herpetic stomatitis, an increase in immunoglobulin M in saliva was observed by 20 times ( $P < 0.001$ ) and the concentration of immunoglobulins A and G was recorded lower than in the control group ( $P > 0.05$ ). The level of secretory immunoglobulin A in saliva significantly increased 2-fold in the acute period ( $P < 0.05$ ). At the same time, a rather high range of individual values was observed. (Table# 4).

#### Moderate-severe course of the disease

СреднеAccording to our data, the moderate severe form of acute herpetic stomatitis was more common in children than other forms. The disease also started acutely.

In the prodromal period, all children showed a deterioration in their general condition, weakness and decreased appetite. When the disease developed, 88.3% of patients had a fever of 37.2<sup>0-39</sup>-39<sup>0</sup>C. Concomitant diseases were observed in 70 % of children. Most often, these were diseases of ENT organs-62%, OCD-8%. During the dental examination, 83,494 children had 3 or more carious teeth in their mouths. Increased salivation was observed in 74,594 children. Gum bleeding was observed in 74.4% of children. 100 % of the children refused to eat. Older children complained of severe pain during meals. an increase in regional lymphnodes was observed in 100% of children. The lymph nodes were very painful on palpation.

On external examination, some children had rashes on the face, mouth area, and red border of the lips (27.9%).

The number of aft eruptions and erosions in the oral cavity up to 6 was observed in 11.6% of sick children. From 6 to 10 afts and erosions in the oral cavity - in 23.3%. 65.1% had a continuous rash of afts, erosions and the formation of erosive surfaces in the oral cavity. Hyperemia and swelling of the gums were present in 100% of the children.

Cytological examination revealed the following changes in the smear print: mastocytes 1-2 in the field of vision were present in 56% of children. These cells were large in size, their shape was rounded with 2-3 large nuclei. In 44% of children, the number of mastocytes recorded was more than 3 in the visual field. White blood cells in smears-prints were found in all children, 1-2 in the field of vision in 6.3% of children, more than 10 white blood cells in the field of vision in 93.7 % of children. In contrast to smears-prints in children with mild AHS, white blood cells had significantly swollen nuclei or cells were almost completely destroyed.

Red blood cells were often unchanged 20-30% in the field of vision, 65% of patients had a large number of microorganisms, most often coccoid flora (Table 5).

A bacteriological study of the results of seeding in the middle course of AHS revealed Staf in 93.1% of cases Staf. aureus, in 75.8% of the gram-negative cocci, in 72.4% of Str. Salivaris and Candida fungi (Table No. 6). B-hemolytic streptococci appeared in 62.0% of the examined patients. Dysbiotic changes in the composition of the oral microflora were more pronounced than with a mild course.

The total microbial number increased on average  $7.92 \pm 0.71$  g CFU / ml, which significantly exceeded the indicators of healthy children ( $P < 0.001$ ).

It is noteworthy that in the moderate course, both the microbial composition of saliva and the microbial number in 1 ml of saliva differed from the corresponding indicators, which is 14 times higher than in the mild course. ( $P < 0$  for the microbial number).

The study of immunological parameters in moderate course and herpetic stomatitis in the acute period showed an increase in serum immunoglobulin M in the same way as in mild course, by 20 times.  $P < 0$ . Moreover, it is interesting to note that the range of individual values for immunoglobulin M in the moderate course was less than in the mild one. The content of serum immunoglobulins A and G almost did not differ from the control parameters. The content of secretory immunoglobulin A in saliva in patients with a moderate course of the disease was 2.6 times higher than in the control group,  $P < 0.01$ . At the same time, the range of individual values was higher than in patients with mild herpetic stomatitis.

Thus, in cases of mild to moderate severity of herpetic stomatitis, the presence of red blood cells, a large number of white blood cells, multinucleated epithelial cells, and mastocytes were noted in smears-prints. The high frequency of seeding of staphylococci, streptococci and enterococci, changes in immunoglobulins in saliva indicate a weakening of local protective factors.

Table 4

Concentration of serum immunoglobulins and secretory immunoglobulins A in saliva in children during exacerbation in g / l

	immunoglobulins			
	IgA	IgM	IgG	sIgA
duri	$0.0361 \pm$	$0,056 \pm 0$	$0,109 \pm$	$0,0582 \pm$
ng n=18	0,0041	,0066	0,0203	0,0058
Mo	$0,0443 \pm$	$0,0584 \pm$	$0,136 \pm$	$0,0791 \pm$
derate to	0,0032	0,0023	0,0095	0,005

severe course n=43				
Con trol group N=20	0,0416± 0,028	0,0028± 0,0004	0,135± 0,017	0,03±0, 012

Table 5

Results of cytological examination in the acute period(frequency of occurrence)

	red blood cells	Mastoc cytes		Epitheli al cells		white blood cells	
		1 -2	3 i>	1 poison	2 i >	1 -2	3 i>
Mil d	-	7 4%	- 100	1 00%% %	- 4 4, 4	4 4,5	5 5,5 556 555 6
Mo derate to severe degree	65 %	5 5,7 %	4 4,5 53 %	8 ,7%	9 1, 3 %	6 ,3%	9 3,7 %

Control group	Co	-	-	-	1 00%	-		
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Таблица 6

## Результаты посева слюны в остром периоде

№ п/п	Наименование микроба	Контрольная группа n=20		Легкая форма n=18		Средне-тяжелая форма n=43	
		встречаем. в %	микробное число	встречаем. в %	микробное число	встречаем. в %	микробное число
1.	Str. Salivaris	100%	3,68 ±0,25	60%	6,82 ±0,22	72,4%	7,9 ±0,16
2.	Str. Angemaliticus	-	-	46,7%	4,17 ±0,27	62%	5,1 ±0,12
3.	Str. Pyogenis	10%	3,47 ±1,2	40%	5,11 ±0,34	44,8%	5,3 ±0,3
4.	Гр. (-) кокки	100%	4,53 ±0,2	66,7%	3,4 ±0,3	75,8%	4,13 ±0,1
5.	Staf. Aureus	-	-	86,7%	3,82 ±0,2	93,1%	3,85 ±0,23
6.	Staf. Epidermidis	100%	3,58 ±0,1	-	-	-	-
7.	Дифтероиды	100%	2,87 <sup>2</sup> ±0,35	53,3%	4,17 ±0,4	48,3%	4,31 ±0,15
8.	Дрожжеподобные грибы	30%	2,4 ±0,36	33,3%	2,74 ±0,3	34,5%	3,41 ±0,40
9.	Лактобациллы	100%	4,62 ±0,2	60%	4,2 ±0,1	27,6%	3,6 ±0,32
10.	Proteus vulgaris	-	-	-	-	20,7%	4,85 ±0,5
	ИТОГО	-	4,94 ±0,21	-	6,83 ±0,20	-	7,97 ±0,14

The results obtained were the basis for a clinical trial of a new drug obtained from local raw materials, for its antiviral activity and effect on some parts of the immune system. To this end, we conducted an experiment to evaluate the interferoninducing activity of glyderinin.

#### **4.2. Evaluation of the interferoninducing activity of glyderinin in the experiment**

Since the state of immunological insufficiency plays an important role in the development of acute herpetic stomatitis, which must be corrected with the help of drugs that increase the body's defenses, we tested a drug obtained from local raw materials, such as the plant licorice glabra L., which is common in our region *Glycyrrhiza glabra* L.

We studied the interferoninducing activity of glyderinin from compounds obtained on the basis of glycyrrhetic acid isolated from licorice.

As the results of the study showed, glyderinin at a dose of 100 mg/kg of body weight with intraperitoneal and intramuscular administration stimulates the production of interferon 320-640 u / ml, and at a dose of 200 mg/kg of body weight 40-80 u/ml. When glyderinin is administered orally at a dose of 50 mg / kg of serum weight, 320 u / ml of interferon is determined.

Analysis of the dynamics of endogenous interferon accumulation in the blood serum of mice showed that the interferon response to the administration of the same dose of the studied inducer by intraperitoneal, intramuscular, and oral methods had certain differences (Table 7).

Table 7

	administration Induction time /hours/
--	---------------------------------------

Methods of drug	Interferon titers u / ml						
	6	1	2	4	7	9	0
Ora	4	4	8	1	2	1	0
Intr	4	0	0-	60-	0	0	0
a-	1	8	160	320	3	2	0
Abdomin	0	0-	8	3	20	0	0
al		160	0-	20-	1	3	0
Intr		1	160	640	60	20	0
amuscular		0	2	2	-	-	-
			0	0	32	0	1
							6
							0

Dynamics of interferon accumulation in the blood of mice with different routes of glyderinin administration

Intraperitoneal administration of glidirin induces the production of significant amounts of interferon, the maximum serum levels of which were recorded in mice 48 hours after administration of the drug. By 96 hours, interferon titers were significantly reduced.

With intramuscular administration of glidyrrinin, interferon synthesis begins later than with intra-abdominal administration. Interferon titers reach a maximum by 96 hours after induction.

The dynamics of interferon formation in the oral route of administration coincides with that in the intra-abdominal method of administration of the drug. For preliminary testing of the nature of the resulting interferon, we determined its stability to the action of *отеолитических фермен* proteolytic agents. The data obtained showed that trypsin treatment suppresses antiviral activity in samples induced by intra-abdominal administration of glyderinin, which indicates the protein nature of the viral activity inhibitor.

In parallel, the ability of the test samples to be neutralized by an antiserum to murine interferon type 1 was studied. The results of the neutralization reaction are shown in Table 8.

Полученные результатыThe results obtained showed that antiserum to murine interferon type 1 completely neutralizes the antiviral activity of the sample obtained after glyderinin induction. It follows that interferon synthesized in response to glyderinin induction in the body of experimental animals belongs to type 1.

Table 8

Reaction of neutralization of the antiviral activity of interferon induced by glyderinin in an experiment with antiserum to murine interferon type 1

Interferon	Inducer	Control u / ml	Interferon /u / ml/ in the presence of antiserum
Standard mouse	-	320	10
Serum	Glyderinin	640	10

Note: Serum interferon was obtained 48 hours after intraperitoneal administration of glyderinin to mice at a dose of 100 mg / kg body weight.

Thus, the glyderinin preparation is able to cause the production of highly active interferon in the body of the studied animals with various routes of administration. Since glyderinin is a drug of plant origin and causes the synthesis of highly active interferon by oral administration, this indicates the clinical prospects of the studied drug in viral infections of *официях широкого спектра* wide spectrum.

#### **4.3. Comparative evaluation of the effectiveness of glyderinin and bonophthone ointments in the complex therapy of patients with AHS**

The clinical effectiveness of the treatment was determined using the following indicators: a decrease in body temperature, acceleration of epithelization of elements of the lesion of the mucous membrane of the oral cavity. Changes in the general condition of the sick child, reduction of pain in the oral cavity and free food intake. Based on cytological and bacteriological data. Changes in immunity in patients with AHS were assessed by the dynamics of serum and secretory immunoglobulin levels in saliva.

When applied to the oral mucosa, the ointment was well applied, evenly distributed. At the same time, the crusts on the lips softened and the child opened his mouth freely. Before applying the ointment, children did not touch the mouth, fearing pain, and 10 minutes after oral treatment, they calmed down significantly, older children noted a decrease in pain in the oral cavity. The smell and appearance of the drug did not cause unpleasant sensations. According to the mothers of sick children, after the treatment of the mouth with ointment, the children freely began to eat on the second day. All of the above indicates the analgesic effect of glyderinin ointment.

In the second group, when treated with 0.75% glyderinin ointment, no child had an allergic reaction to the ointment.

#### **4.3.1. Comparative evaluation of the therapy performed in patients with a mild course**

In the first group, with a mild degree and the use of 0.5% bonaphthane sea buckthorn oil, moodiness and lethargy passed on the second day, the children also ate freely from the second day. Epithelialization of the elements began on 2.5-3 days, which consisted in a decrease in the hyperemic rim around the aft, the afts became less painful when touched, and decreased in size. Complete recovery occurred after  $4.3 \pm 0.19$  days. In patients with mild severity after therapy with bonafton ointment, *St. aureus* was seeded in 50% of cases ( $\lg 2.77$  CFU/ml), *Str. Salivaris* in 66.6% ( $\lg 3.84$  CFU/ml). The average microbial number was  $\lg 3.24 \pm 0.3$   $\lg$  CFU / ml, which is 70 times less than the bacterial contamination at admission.

During cytological examination after recovery, red blood cells were not recorded in smears. In no case were mastocytes detected after treatment. The content of epithelial cells changed. All epithelial cells were mononuclear, which indicates the process of regeneration, sanitation from the virus of the oral mucosa. In 83.4% of children, 1-2 white blood cells were found in the visual field. Completely disappeared degenerative forms of white blood cells. A large number of unchanged cells of the multilayered squamous epithelium was noted, which also indicated the process of regeneration of the oral mucosa (Table 9)

Table 9

Results of cytological examination of smears-prints of mild AHS after treatment

	Traditional	glyderinin	Glyderinin Antivir therapy. +glyderinin
red blood cells	-	-	-
Mastocytes i1-2 3 i >	- -	- -	- -
Epithelial cells 1 2 I >	100% -100	% -100	% -
White blood cells 1i2 White blood cells 1 I2 3 I >	83.4%	88.8%	100%

the use of 0.5% bonaphthone ointment therapy caused a decrease in the concentration of serum immunoglobulins A, M, (E) and secretory immunoglobulin A compared to the data at admission.

In the second group of patients with a mild form of AHS, when using 0.75% glyderinin ointment, children opened their mouths freely in the evening and ate without difficulty. Moodiness, lethargy passed on the second day.

Epithelialization of aft also occurred on the second day after treatment. The aphthae were significantly reduced in size, were painless when touched, and the hyperemic rim around the aphthae disappeared completely on the second day. Complete recovery occurred on  $3.7 \pm 0.2$  days compared to traditional therapy).

При цитологическом исследовании после проведенного нами No mastocytes were detected in any case during the cytological examination after our study. The number of leucocytes sharply decreased to 1-2 in the visual field in 88,894 children, and more than 30 in children. Young white blood cells with a full-

fledged structure appeared. in all cases, the epithelial cells were mononuclear (Table 9).

In the bacteriological study, *Staf aureus* was seeded in 33,396 patients (lg 2.48 CFU/ml of microbial bodies), *Str. salivaris* in 88,894 patients (lg CFU/ml of microbial bodies in 1 ml). After treatment, bacterial contamination with NCDs decreased almost 120-fold and amounted to  $3.8 + 0.2$  lg CFU/ml.

The use of 0.75% glycerin ointment in mild cases also caused a decrease in the content of both serum and secretory immunoglobulins, the most pronounced changes in the indicators were found for immunoglobulins A and G..  
Концентрация

Table

Concentration of serum immunoglobulins and secretory immunoglobulin A in the saliva of children after recovery using the traditional method of treatment.

	Immunoglobulins g / l			
	IgA	IgM	IgG	sIgA
Mild course n=6	0.021 $1 \pm 0.0011$	traces	traces	0.023 $6 \pm 0.0113$
Moderate-severe course N=14	0,026 $1 \pm 0,0035$	$0,007 \pm$ 0,0005	0,036 $9 \pm 0,0085$	0,040 $8 \pm 0,0047$
Control group	0,041 $6 \pm 0,0028$	0,0026 $8 \pm 0,0004$	0,135 $\pm 0,017$	$0,03 \pm$ 0,012

immunoglobulin G in saliva decreased to 12.6 mg% (Table 13), which is 9 times less than the data before treatment.

The following changes occurred with the step-by-step method of treatment: moodiness, lethargy passed on the second day; the beginning of epithelialization, as with the traditional method, occurred on the 2.5-3 day, complete recovery occurred on the  $3.7 \pm 0.3$  day ( $P < 0.05$  compared with traditional therapy).

Cytological examination after treatment% revealed 1-2 white blood cells in 100% of children in the field of vision. All white blood cells had a complete cell structure. Mastocytes were not detected *дались* in any case. The epithelial cells were all mononuclear with a complete cell structure.

Immunological studies have shown that step-by-step therapy with glyderinin ointment caused a decrease in IgG concentration by 1.5 times, the most significant decrease was for immunoglobulin M-by 8 times  $P < 0.00$

Thus, the use of glyderinin ointment compared with bonafton ointment therapy caused an earlier improvement in the clinical condition of children, as well as an improvement in cytological, bacteriological and immunological parameters in the mild course of AHS. Recovery occurred earlier by  $3.7 \pm 0.2$  days than with the use of bonafton ointment ( $4.3 \pm 0.19$  days at  $P < 0.01$ ).

#### Table 11

The concentration of serum immunoglobulins and secretory IgA in saliva in children after recovery with the use of 0.5% bonaphthan ointment and 0.7% glyderinin in g/l.

G roups of patient s examin ed	Immun oglobulin IgA	Immun oglobulin IgM	Immun oglobulin IgG	Immun oglobulin IgA
M ild n=3	0,0279 ±0,009	0,007± 0,005	0,0416 ±0,0178	Did not put
a modera te- severe course n=12	0,0197 ±0,0031	0,0187 ±0,006	0,0295 ±0,0066	They didn't put
i t in the Control group	0,0416 ±0,0028	0,0028 ±0,0004	0,135± 0,017	0,03±0 ,012

#### **4.3.2. Comparative evaluation of the current therapy in moderate course of AHS.**

With moderate-тяжелой severe damage and the use of treatment with bonafton ointment, children had a fever for 2 days, did not eat well, were adynamic, salivation continued for 4 days, and the lymph nodes were painful on palpation during the entire treatment period. Reduction of lymph nodes in size occurred 5-6 days after treatment. Bleeding gums disappeared on 3-4 days. Epithelialization occurred 3.5-4 days after the start of treatment. The aphthae epithelized slowly, and the hyperemic corolla around the aphthae decreased within 3-4 days. Aphthae began to decrease in size by 3.5-4 days, and were painful for a long time.

	Traditional	Glyderin in	Antivira l therapy. + glyderinin
red blood cells	-	-	-
Mastocyte s 1-2 3i>	- -	- -	- -
Epithelial cells 1 2i>	100% -94.2	% -100	% -
Whit e blood cells 1-2 3i>	50% 50%	64,7% 35,3%	75% 25%

Recovery occurred on 7+0.2 days.

During cytological examination after recovery, mastocytes were not detected in any case. Red blood cells were also not found. White blood cells were detected in smears in all children, 1-2 in the visual field in 50% of children, and more than 3 also in 50 % of children. The disappearance of degenerative cells, white blood cells and the appearance of young white blood cells were noted. All epithelial cells were mononuclear, which indicated the process of regeneration of the oral mucosa. A large number of unchanged cells of the multilayered squamous epithelium was noted, which also indicated the regeneration process (Table 12).

Table 12

Results of cytological examination in moderate course of AHS after treatment

In a bacteriological study after treatment with bonafton ointment, Staf. auerus was seeded in 40%of children (lg 3.11 CFU/ml of microbial bodies in 1 ml), Str.

Salivaris in 60% of children (lg 3.58 CFU/ml), the average groprobic number was  $3.37 + 0.3$  lg CFU/ml, which is 20 times lower others upon admission.

A decrease in immunoglobulins A, M, G and secretory immunoglobulin A. It should also be noted that the greatest decrease in the concentration was recorded for immunoglobulin M, which is evidence of restoration of the mucous membrane of the T and mouth bands (Table No. 10).

In the second group, when children were treated with 0.75% glyderinin ointment with a moderate-severe course of the disease, a decrease in temperature was

	Immunoglobulins			
	IgA	Ig M	IgG	sIgA
Mild n=9	35, 0±3,3	59, 5±9,3	113,2 ±12,7	71,3 ±11,2
Moderate to severe course n=17	37, 2±6,0	24, 5±7,6	144,5 ±26,8	13,9 ±6,1
Control group	41, 6±2,8	2,8 ±0,4	135± 17	30± 12

observed in the evening. On day 2, the children freely opened their mouths and took food. Also, on the second day after the treatment, salivation sharply decreased. For older children

reduced headaches, decreased bleeding gums. On day 3, epithelialization began in children after the treatment, the lymph nodes decreased in size, the hyperemic rim around the aft disappeared, and the afts

Table 13

they became less painful when touched, there was not a large catarrhal gingivitis.

Complete recovery occurred on  $5.9 \pm 0.18$  days ( $P < 0.001$  compared to traditional therapy).

Cytological examination after treatment did not detect mastocytes in any case. Mastocytes. White blood cells were not detected in all cases: 1-2 in the field of vision in 64.7% of children, more than 3 in 23.5%, in 12.8% of children, no leukocytes were detected. Epithelial cells in 94.2% of children were mononuclear, while 5.8% had two-nuclear epithelial cells (Table 12).

Concentration of serum immunoglobulins and secretory immunoglobulin A in the saliva of children after their recovery with the use of 0.7% glyderinin ointment

A bacteriological study after treatment with glyderinin ointment revealed a decrease in bacterial contamination by almost 100 times. *Staf. aureus* was seeded in 33.3% of patients (lg 3.16 CFU/ml), *Str. salivaris* in 53.394 (lg 4.09 CFU/ml of microbial bodies in 1 ml). The total microbial number decreased to  $3.34 + 0.4$  lg CFU / ml. The nature of the microflora after treatment with bonafton and gliderenin ointments underwent significant changes, and терапия только глидериновой мазью a more pronounced decrease in microorganisms was revealed during therapy with gliderinic ointment alone.

When treated with glyderinin ointment, serum immunoglobulins in saliva were detected with a reduced frequency of IgA and IgG in 47% of patients and immunoglobulin M in 23% of patients (Table 14).

In the third group, the following changes occurred with a step-by-step treatment method (0.5% bonafton ointment and 0.75% glyderinin ointment): the temperature decreased on the second day, children did not eat well, remained adynamic and sluggish for 3 days, and did not sleep well for 2 days. The lymph nodes remained enlarged and painful for 5 days. Bleeding gums decreased by 3 days after the start of treatment, and salivation continued for 4 days.

Epithelialization occurred on 3.5-4 days. At the time of epithelialization, 0.75% glyderinin ointment was used as a keratoplastic preparation. The aphthae began to

rapidly epithelize, the hyperemic corolla decreased, and the aphthae became painless when touched. Final recovery occurred on day  $6.2 \pm 0.4$  ( $P > 0.05$ ).

Table 14

Frequency of detection of serum and secretory immunoglobulin depending on the type of therapy performed for moderate severity of the disease (%)

	Prior to treatment	with Glyderinin	Bonafta. + glyderin.	Traditional
IgA	79.1	47.0	75.0	92.8
IgM	39.5	23.0	41.7	35.7
IgG	74.4	47.0	41.7	75.0
sIgA	42.6	23.5	Non-oda	78.6

Microscopic examination revealed no mastocytes in any of the cases. White blood cells were found in all children, 1-2 in the visual field in 75% of children, in 25% - 3 or more in the visual field. The epithelial cells were all mononuclear. Red blood cells were not detected in any case (Table 12).

With a step - by-step method of treatment in moderate cases, the concentration of immunoglobulins in saliva also decreased IgA by 2.2 times, M-by 3.1 times and 4.6 times for IgG (Table 11).

Thus, the use of glyderinin in the moderate course of AH caused an earlier improvement in the clinical condition of patients, earlier epithelialization and recovery periods in comparison with the traditional method of therapy. Our studies have shown that glyderinin is not only a keratoplastic drug, but also has antipyretic, analgesic properties and interferoninducing activity.

As an example, here are extracts from the medical history:

Sabina Kilmetova, born in 1991, no. ist.diseases of BZ877. She came to the reception on October 3, 2018 with her mother's complaints: the presence of rashes in the oral cavity, temperature 38.2<sup>0</sup>, malaise, drooling, refusal to eat. External examination shows pallor of the skin, salivation from the mouth, regional lymph nodes are enlarged to the size of beans, painful on palpation. On objective examination: on the mucous membrane of the oral cavity there are multiple rashes: on the mucous membrane of the lips, cheeks, tongue, aphthae with a size of 2x2 and covered with a grayish-white coating, there is hyperemia around the aphthus, the gums are hyperemic, swollen, and bleed when touched.

The following diagnosis was made:

Acute herpetic stomatitis of moderate severity.

On the first day, a smear print was made, saliva was collected for immunoglobulins and bacteriological culture. Analysis data: multicore epithelial cells in large numbers, 8-10 white blood cells in the field of vision, no red blood cells detected, mastocytes-2, twoъ-nuclear cells-3, threeъ-nuclear cells-4, immunoglobulin G-0.1665 g / l, IgA-0.05 g/l, IgM-0.123 g/l, sIgA 0,2GЉ1. In 1 ml of saliva inoculated with Streptococcus Salivaris lg 4.60 CFU /ml, Streptococcus pyogenis lg 3.30 CFU/ml, Gram negative cocci lg 2.00, Staf. aureus -102, proteus vulgaris 2,47.

On the first day, the oral cavity was treated with 0.002% furacilin solution and applied with 0.75 % glyderinin ointment. The ointment was given to the mother's hands to treat the oral cavity at home. The temperature dropped to normal that evening. The next day, the child began to eat, salivation decreased, and the lymph nodes were painless on palpation. On day 3, when examining the child's oral cavity, the beginning of epithelialization was noted, the aphthae slightly decreased in size, when touched, they are painless, do not bleed. Gums are pale pink in color, Recovery occurred in 6 days. On the seventh day, the following tests were taken:

Epithelial cells were detected, 1 leukocyte in the visual field, IgG-0.1033 hl, IgA -0.05 g / l, IgM-0.083 g / l, sIgA -0.1 g/l. In one ml of saliva during seeding: Streptococcus Salivaris lg 3.47, Streptococcus pyogenis lg 3.00.

Khalikova Rakhilya - born in 1992, questionnaire no. B2472.

She went to the ZDSP polyclinic with complaints from her mother about malaise, the presence of rashes in the oral cavity, fever up to 38.2<sup>0</sup>, salivation, refusal to eat.

On objective examination: paleness of the skin is noted, on palpation, the lymph nodes are enlarged the size of beans.

On examination of the mouth: on the mucous membrane of the lips, cheeks of the tongue there are multiple rashes in the form of aft 2x2 mm in size, covered with gray fibrinous plaques, sharply painful when touched, bleed. The mucous membranes of the gums are hyperemic, swollen, and bleed when touched.

The patient was diagnosed with moderate acute herpetic stomatitis. On the first day, a smear print was made, saliva was collected for the determination of immunoglobulins and bacteriological culture.

Analysis data: multicore epithelial cells in large numbers, leukocytes 6-8 in the field of vision, red blood cells were not detected, mastocytes-3, binuclear-2, trinuclear-3, IgG -0.297 g/l, IgA - 0.096 g/l, IgM-0.022 g/l, sIgA -0.096 g/l. When seeding 1 ml of saliva: Streptococcus Salivaris 3\*10<sup>4</sup>; Streptococcus angemaliticus lg 3.30; Gram negative cocci lg 2.60; diphtheroids lg 3.84.

On the first day, the oral cavity was treated with 0.00294 furacilin solution and applied with 0.5 % bonafon ointment. Bonaphthon ointment was given to the mother's hands to treat the oral cavity at home. The child's temperature dropped only the next day. On the third day, the child began to eat, salivation also decreased on the third day, and lymph nodes decreased to normal on day 6. On day 4, epithelialization began. From that day on, they began to carry out treatment with sea buckthorn oil. Recovery came in 7 days.

On day 8, the following tests were taken:

IgG -0.145 g / l, IgA-0.059 g/l, no. M-traces, sIgA -0.059 g/l.

Epithelial markers are mononuclear, with a large number of 1-2 white blood cells in the field of view. When seeding in ml of saliva: Streptococcus Salivaris lg 2.30, Streptococcus angemaliticus lg 2.30, Staf. aureus lg 2.00, diphtheroids lg 2.77.

Currant Julia-1993 gr. G-1048

She came to the reception on May 6 2020, 2020 with complaints from her mother: fever up to 38.2 C, the presence of rashes on the skin of the chin, in the mouth, drooling and refusal to eat.

External examination shows pale skin, salivation from the mouth, submandibular lymph nodes are enlarged, the size of a walnut. On the chin there are multiple rashes covered with a crust. On objective examination: on the mucous membrane of the lips, cheeks, tongue there are multiple aphthae, sharply painful when touched, the aphthae are covered with a fibrinous white coating, there is a wide hyperemic rim around the aphthae, the aphthae are not fused, 3.5 x 3.5 mm in size. The gums are hyperemic, swollen, and bleed when touched.

The patient was diagnosed with moderate acute herpetic stomatitis.

On the first day, a smear-print was made, saliva was collected to determine immunoglobulins.

Analysis data: epithelial cells: multinucleated, twoъ-nuclear 1, mastocytes-Z in the field of vision, no red blood cells, coccoid flora. IgA 0.011 g / l, IgM-0.093 hl, IgG-0.075 hl

On the first day, the oral cavity was treated with 0.002% furacilin solution and applied with 0.5 % bonafon ointment. Bonaphthon ointment was given to the mother's hands for treatment and oral cavity at home.

The child's temperature dropped on the second day. On the third day, the child began to eat, salivation decreased. On the 4th day, epithelialization began, after treatment with 0.002% furacillin solution and dmelana application of 0.75 % glyderi with anew ointment. The ointment was given to the hands for oral treatment at home.

On the fifth day, the child began to eat freely, and the rash on his chin disappeared. The general condition has improved, the aphthae have sharply decreased in size, the gums are slightly hyperemic, and there is no edema.

Full recovery occurred in 6 days. On day 7, ANAJ1 samples were taken. epithelial cells are mononuclear, white blood cells 1-2 in the field of vision. IgA - 0.019 g / l, IgM-0.068 g/l, IgG-traces.

## Chapter 5

### DISCUSSION OF THE RESULTS OF YOUR OWN RESEARCH RESEARCH PROJECTS

When analyzing AHS in children who were treated in the 3rd children's dental polyclinic for the period 2018-2020, we established the corresponding referral rate: 986 (49%) patients in 2018, 767 (43.7%) in 1993, and 642 (38.3%) in 1994. Among them, 53.4% of boys and 46.6% of girls were registered at the age of 6 months to 16 years, with the highest frequency in the age of 1 to 3 years (58.5%).

С легкой степенью поражения регистриро14.8% of children were registered with a mild lesion% детей, со средне, 84.4% with a moderate severe course, and 0.8% with a severe course. Moreover, in the last year (2020), 63.9% of unorganized children were more ill, and in 2019 - 45.6%, which differs from the data of other authors (Epishev V. A., Khersonskaya F. I., 1974; Zhumatov U. Zh., 1996, etc.).

Analysis of the impact of previous and concomitant diseases revealed the highest incidence of ENT diseases - 79.7%, followed by OCD-14.8% and hepatitis in 3% of children. In 2.5% of children, no previous diseases were detected. Caries was detected in 44.5% of the examined children, with the greatest frequency at the age of 4 to 6 years.

It should be noted that past illnesses weaken the immune system and contribute to the development of AHS in children. Our data confirm the observations of other authors (Vinogradova T. F., 1971, Epishev V. A., Khersonskaya F. I., 1974, Vinogradova T. F., Maksimova E. M., Melnichenko, 1983, Safarov T. Kh. et al., 1991, Zhumatov U. Zh., 1996).

The study of morbidity by seasons of the year revealed its highest frequency in spring and autumn, which is consistent with the literature data of V. A. Epishev et al. (1986) and differs somewhat from the data of E. M. Melnichenko et al. (1980).

Apparently, this dynamic is explained by hypovitaminosis in the spring, and high contagiousness in organized groups of children in the fall after summer vacations and vacations.

the clinical manifestations of AHS in children noted by us did not differ from the observations of other authors: in all patients, the onset of the disease with a moderate course was acute with a rise in temperature (95,394), with chills, salivation (88.7%), moodiness and lethargy (10094), refusal of food (100%). bleeding gums (100%), enlarged chin lymphnodes the size of beans (100%).

The number of afts with moderate severity upto H was recorded in 0.3% of children, 4-6 afts - in 50.9%, 6-10 afts and erosions - in 47.1%, all rashes - in 1.7%

The rash days differed by age group: in children under 6 months - 6.3 days, 6 months - 1 year - 5.7 days, from 1 year to 3 years - 5.1 days, from 4-6 years - 6.2 days, 7-10 years - 5.2 days, 11-14 years - 5.1 days, which is probably the main reason for the development of the disease. It is explained by the peculiarities of the formation of immunity in children (Vinogradova T. F. et al., 1975, 1979; Belaya et al., 1991; Zhumatov U. zh., 1996).

Each year, up to 100 sick leaves are issued for AHS with a duration of 7-8 days.

Thus, the analysis showed that acute herpetic stomatitis in children occurs with a peak in the autumn and spring months and with a tendency to increase among unorganized children.

The study of clinical, cytological, bacteriological, and immunological parameters in children with AHS at the height of tuberculosis with varying severity of the disease was performed in 61 sick children.

A mild form of herpetic stomatitis was characterized by an external absence of intoxication. An increase in subfebrile temperature was observed in all children. The number of aft before Z was recorded in 66.77 % of children, from Z to 5-in 33.5 %. No concomitant diseases were observed. Of the acquired diseases, ENT diseases occurred in 88.9%, OCD - in 89.4,4%, hepatitis-in 40

%. Moodiness and lethargy appeared in 55.6 % of children, drooling in 33.4 %. Bleeding gums were observed in all children. Regional lymph nodes are not enlarged, but they are painful on palpation. All patients refused to eat.

Cytological examination showed that in children with a mild course of the disease, mastocytes were found 1-2 in the field of vision in 74% of cases, which is characteristic of acute herpetic infection. In 45.6% of 5 cases, from 10 to 25-30 leukocytes were recorded in the visual field. Leukocytes are altered, with swollen nuclei, with an indistinct structure of the cytoplasm. Red blood cells were detected in 5.5 % of children. A large number of microorganisms were detected in smears (cocci flora).

When saliva was seeded for microbes, the number of staphylococci and gram-negative cocci significantly increased (86.8 % and 66.7%, respectively). The appearance of hemolytic streptococcus and *Candida* fungi in the oral cavity was noted. Dysbiotic changes in the composition of the oral microflora were more often multiple in nature, i.e. they affected two or more types of microorganisms. The microbial number increased to  $6.78 \pm 0.5$  lg CFU in 1 ml of saliva in the norm  $4.85 \pm 0.7$  lg CFU/ml.

ТакимThus, despite the mild severity of AHS, changes in the oral cavity were observed in all patients. The presence of red blood cells, white blood cells, multinucleated epithelial cells, mastocytes in smears, as well as an increase in the aggressiveness of the autoflora of the oral cavity indicates a sharp decrease in the natural factors of protective and adaptive reactions of the body.

Analysis of serum IgA, IgM, IgG, and sIgA concentrations in saliva in patients with mild AHS revealed a 20-fold increase in IgM ( $P > 0.001$ ), a decrease in IgA and IgG content, and an increase in secretory IgA. The growth of serum levels in saliva indicates an increase in the permeability of proteins through the oral mucosa of patients, which characterizes an acute inflammatory process in the oral cavity.

The moderate-severe form of AHS was characterized by intoxication phenomena. In the prodromal period, all children showed a deterioration in their general condition. The disease began acutely. With the development of the disease, 88.4% of children had a fever of up to  $37.2^{\circ}$  -  $39^{\circ}$ . With 11.7% of patients

did not have fever and had a reactive course of the disease. Concomitant diseases were observed in 70 % of children. Most often, these were diseases of ENT organs-62.9%, OCD-89.4,4 %.

Increased salivation was observed in 74.5 % of children. All the children refused to eat. An increase in submandibular lymph nodes was observed in 100 % of children. The lymph nodes were very painful on palpation.

On external examination, 27.9 % of the children had rashes on the face, mouth area, and red border of the lips.

The number of afs in the oral cavity up to 6 was observed in 11.6% of children, from 6 to 10 - in 23.3%, in 65.1% - a solid rash of afs in the oral cavity. Hyperemia and swelling of the gums were observed in 100 % of children.

Cytological examination revealed mastocytes 1-2 in the field of vision in 56% and more than 3 in the field of vision in 44%, which indicates an increase in the number of cells and a severe course of the disease. The number of 1-2 leukocytes also increased in 3.2% of children, from 25-30 leukocytes in 96.1% compared to the mild form (45.6%).

Red blood cells were observed in 45.3% of patients. A large number of microorganisms, mainly coccoid flora, were found.

Saliva culture revealed a significant decrease in the number of lactobacilli and an increase in *Staf. aureus*, gram-negative cocci, and *Candida* fungi. 5-hemolytic streptococci appeared in 62.0% of the examined patients. Dysbiotic changes in the composition of the oral microflora were more pronounced in the moderate-severe course of AHS than in the mild one. The total microbial number in 1 ml of saliva increased on average to  $\lg 7.92 + 0.7$  CFU / ml, which is 14 times higher than normal.

The study of immunological parameters in the moderate-severe course of acute AHS revealed a 20-fold increase in the concentration of serum IgM in the same way as in the mild course ( $P < 0.001$ ). The content of serum IgA and IgG almost did not differ from the control parameters. The content of sIgA in saliva in patients with a moderately severe course of the disease was 2.6 times higher than in the control group ( $P < 0.01$ ).

The data obtained by us indicate that in acute AHS, not only in moderate-severe, but also in mild cases of the disease, there are pronounced changes in the general state of the body of sick children, violations of the integrity of the oral mucosa and its species composition of microflora, which affects the indicators of local immunity, an increase in the concentration of IgM in the saliva. Our data on the clinical condition of sick children,

Cytological and bacteriological characteristics in the acute period of AHS are supplemented by literature data (Epishev V. A. et al., 1974, Vinogradova T. F. et al., 1983, Epishev V. A., Yunusov R. A., Yunusova I. F., 1986, Melnichenko E. M., 1992; Kolomnets A. G. S. et al., 1997).

The conducted studies raise the question of the need for the use of new antiviral agents, affordable, highly effective, obtained from local raw materials.

One of these drugs is glyderinin, obtained from the common licorice plant in our region (*Glycyrrhiza glabra* L). Naked licorice has an anti-inflammatory, stimulating effect on the adrenal cortex, is an immunotropic drug (Mashkovsky M. D., 1987, Nurmukhamedova Zh.D., 1981, Azimov M. M., 1989, Abdullaev A. Kh., 1974, 1995).

It is known that in herpetic infections, the ability to produce interferon, which has antiviral activity, is reduced, and one of the requirements for the use of drugs in the treatment of AHS is their interferon-inducing activity. In this regard, we tested glyderinin for its interferoninducing activity in an animal experiment.

Tests were performed with oral and parenteral administration of the drug in response to a single administration of different doses of the drug - 50100-200 mg/kg of glyderinin.

Intraperitoneal, intramuscular, and oral administration of even 50 mg / kg induced interferon production in fairly high titers after 24-48 hours. The interferon titer increased 8-fold. Then, a decrease in the interferon titer was observed. The dynamics of interferon formation in the oral route of glyderinin administration revealed a more rapid appearance of interferon than in the case of intramuscular administration of lekar

It's a good idea. Rapid formation of interferon is of great importance in the treatment of AHS, as it blocks the spread of infection and prevents viremia (Sadykov A. S. et al., 1978)

Thus, the drug glyderinin obtained from the plant licorice glabra is able to cause rapid formation of highly active interferon within a short time in the body of experimental mice with different routes of administration and in-different doses.

The results obtained were the basis for studying the possibility of using glyderinin as an antiviral, interferoninducing agent in AHS.

0.75% glyderinin ointment prepared at the Department of Pharmacology 2-TDSI (under the supervision of Professor M. M. Asimov) was used.

With additional research, we found that 2% of the ointment produced by the industry causes burns, 1% - burning, and 0.75% does not cause any side effects. In addition, it was found that glyderinin has an analgesic effect, which manifests itself quite quickly after application, after 15 minutes. It also has antipyretic properties, reduces the temperature on the same day after application. Our results were confirmed by the literature data (Nurmukhamedova, 1977, Azimov M. M., 1988, Abdullaev A. Kh., Zakirov N. U., 1996).

Comparative evaluation of the effectiveness of the therapeutic effect of glyderinin ointment (I) was carried out with bonafton ointment (I) and with a step - by-step method of treatment (III) - at the beginning of bonafton ointment, then at the beginning of epithelialization, treatment with glyderinin ointment was started (Table 15).

Table 15

Terms of recovery of patients with acute herpetic stomatitis depending on the treatment methods

	<b>Traditional therapy</b>	<b>Glyderinin ointment</b>	<b>0.5% bonafton ointment with</b>
<b>Mild course</b>	<b>4.3±0.19</b>	<b>3.7±0.2</b>	<b>3.7±0.3</b>
<b>R</b>		<i>h</i> <b>&lt;0.01</b>	<b>&lt;0.05</b>
<b>Moderate severe</b>	<b>7.0±0.2</b>	<b>5.9±0.18</b>	<b>6.2±0.4</b>
<b>P</b>		<b>&lt;0.001</b>	<b>&gt;0.05</b>

During the treatment with 0.5% bonaphthone ointment and sea buckthorn oil, the following results were obtained for a mild course of the disease: moodiness, lethargy, headache disappeared on the second day after the treatment, children also began to eat on the second day. Epithelialization of aft began on days 2.5-3. Complete recovery occurred in 4.3±0.19 days. Bacteriological examination revealed a decrease in the number and frequency of pathogenic staphylococci, gram-negative cocci, and fungi. The microbial number decreased to lg 3.24 + 0.3 lg CFU/ml of microbial bodies in 1 ml of saliva.

During cytological examination, red blood cells were not observed.

In no case were mastocytes detected after treatment. All epithelial cells after our treatment were mononuclear. In 83.4% of children, 1-2 leukocytes were found in the visual field. Degenerative white blood cells completely disappeared. Application

The use of traditional therapy resulted in a decrease in the concentration of serum immunoglobulins A, G, M and secretory immunoglobulin A compared to the data at admission.

In the second group, when using 0.75% glyderinin ointment, moodiness and lethargy also passed on the second day, and children began to eat and open their mouths freely in the evening of the same day, since glyderinin ointment has an analgesic effect. The analgesic effect was evaluated taking into account the child's medical history and behavior in the doctor's office. The onset of epithelialization was observed on the second day after treatment. Complete recovery occurred on day  $3.7 \pm 0.2$  ( $P < 0.01$  compared to conventional therapy).

No mastocytes were detected during cytological examination after the treatment. The number of white blood cells decreased sharply-1-2 in the field of vision in 88.8% of children, which is 5.4% less than with traditional treatment. In all cases, the epithelial cells are mononuclear (Table 9).

A bacteriological study revealed a decrease in the frequency of *Staf seeding. aureus* and gram-negative cocci, fungi of the genus *Candida*. The number of microbial bodies in 1 ml of saliva decreased to  $3.8 \pm 0.2$  lg CFU / ml .

Just as with the traditional method of treatment, the concentration of serum and secretory immunoglobulin A decreased. The concentration of IgG in saliva decreased to 12.6 mg%, which is 9 times less than the data before treatment.

In the third group, with a step-by-step method of treatment, moodiness and lethargy also passed on the second day. The child started eating on the second day. The beginning of epithelialization, as with the traditional method of treatment, occurred on 2.5-3 days, after which

we switched to glyderinin ointment. Complete recovery occurred on day  $3.7 \pm 0.3$  ( $P < 0.05$  compared to conventional therapy). Cytological examination revealed 1-2 white blood cells in the visual field in 100% of the children, while more than 3 in the visual field were not observed in any child. Mastocytes were not detected in any case. The epithelial cells were all mononuclear with a complete cell structure. Immunological studies showed that complex therapy with glyderinin ointment caused a decrease in IgG content by 1.5 times, the most significant decrease was for immunoglobulin M-by 8 times ( $P < 0.001$ ).

Thus, despite the fact that glyderinin ointment was prescribed for 2-3 days of treatment, the effect was still more pronounced than with the traditional method of treatment.

With moderate-severe damage and the use of treatment with bonafton ointment, children were kept at a temperature of 2 days, salivation continued for 4 days. Submandibular lymph nodes were enlarged and painful on palpation throughout the treatment. Their decrease was observed on 5-6 days after treatment. Gum bleeding decreased by 3 days. Epithelialization occurred 3.5-4 days after the start of treatment.

Recovery occurred in  $7.0 \pm 0.2$  days (Table 15).

During cytological examination, mastocytes were not detected in any case. Red blood cells were also not found. White blood cells were detected in all children, including more than 3 in 50% of children. All epithelial cells were mononuclear.

A bacteriological study revealed a decrease in the total number of microbial bodies in 1 ml of saliva to  $3.37 + 0.3$  lg CFU/ml . The seeding rate of *St. aureus* decreased by up to 40%.

A decrease in the concentration of IgA, IgM, IgG and secretory IgA was detected. The greatest decrease was recorded for IgM, which is evidence of restoring the integrity of the oral mucosa.

When treated with 0.75% glyderinin ointment, the temperature decreased by the evening. On day 2, the children freely opened their mouths and took food. Also on the second day, " salivation decreased, bleeding gums disappeared. On the 3rd day after the treatment, epithelizapia began. Complete recovery occurred on  $5.9 \pm 0.18$  days ( $P < 0.001$  compared to conventional therapy).

Cytological examination did not detect mastocytes in any case, and white blood cells were not detected in all cases (12.8% of children had no white blood cells), in contrast to the traditional method of treatment. 5.8% of children had binucleated epithelial cells.

The bacteriological study reduced the frequency of *Staf seeding. aureus* up to 33.3%, the total microbial number decreased to  $3.34 + 0.4$  lg CFU in 1 ml of saliva. When treated with glyderinin ointment, serum immunoglobulins in saliva were detected with a reduced frequency of IgA and IgG in 47% of patients, and immunoglobulin M in 23% of patients.

With the step-by-step method of treatment, the temperature decreased by 2 days, as well as with the traditional method of treatment, poor sleep was noted for 2 days, children remained adynamic, sluggish for 3 days. Submandibular lymph nodes remained enlarged and painful for 5 days. Gum bleeding decreased by 3 days after the start of treatment, and salivation continued for 4 days. Epithelialization occurred on 3.5-4 days

after starting treatment. Final recovery occurred on average within  $6.2 \pm 0.4$  days ( $P > 0.05$ ).

During cytological examination, mastocytes were not detected in any case. White blood cells were found in all children, 1-2 in the visual field in 75% of children, in 25% - 3 or more in the visual field. The epithelial cells were all mononuclear. Red blood cells were not detected in any case..

The concentration of immunoglobulins in saliva decreased - IgA by 2.2 times, IgM by 3.1 times and IgG by 4.6 times.

The results obtained for the traditional treatment of patients with the use of bonafton ointment coincide with the observations of other authors (Bogdanova N. S., 1983; Epishev V. A. et al., 1986).

Thus, the use of glyderinin ointment and step-by-step therapy revealed a similar positive clinical effect. The best results were observed when applying glyderinin ointment in the early stages of the height of the disease. In both mild and moderate cases, the children's recovery time decreased. The best restoration of the integrity of the oral mucosa was also observed with the use of glyderinin ointment, since the frequency of IgM detection decreased, which characterizes the process of regeneration of the oral mucosa. In bacteriological studies, the frequency of seeding of *Staf aureus* and gram-negative cocs sharply decreased, and the number of microbes in 1 ml of saliva decreased. The best effect was observed when applying glyderinine ointment with a step-by-step application. Early administration of glyderinin exerted an analgesic effect for 15-20 minutes, reduced the temperature on the same day, and caused an increase in specific reactions of antiviral immunity (interferon induction), which contributed to more active rehabilitation and led to early treatment.

recovery. Based on the conducted studies, 0.75% glyderinin ointment can be recognized as a valuable drug for the treatment of AHS in children. The proposed ointment is obtained from domestic raw materials, easy to make.

## CONCLUSIONS :

1. Acute herpetic stomatitis is the most common disease in children, with a peak in autumn and spring, with the highest frequency at the age of 1 to 3 years (58.5%), with a tendency to increase in recent years among unorganized children (63.9%). Mild course is registered in 14.8%, Moderate-severe in 84.4% and severe in 0.8% of patients.

2. Significant violations of various components of the protective function and integrity of the oral mucosa were revealed in children with AHS: the appearance of multinucleated epithelial cells, mastocytes, leukocytes and red blood cells in the cell structure, pathogenesis of autoflora and an imbalance of serum IgA, IgG, IgM and secretory IgA in saliva, an increase in IgM by 20 times and IgA by 2.0-2.6 times in the presence of mild and moderate-severe course.

3. In an experiment on mice, oral and parenteral administration of glyderinin, a drug derived from the roots of licorice bare, showed its antiviral effect; which was manifested in the rapid formation of highly active interferon in the blood serum. The oral route of administration was more effective.

4. AHS therapy with the use of bonafton ointment leads to a significant improvement in the condition of the oral mucosa, normalization of the cellular structure and improvement of the species composition of microflora, a decrease in serum and secretory immunoglobulins. Recovery occurs in  $4.3 \pm 0.2$  days and  $7.0 \pm 0.2$  days in mild and moderate-severe cases, respectively.

5. The use of glyderinin ointment in the treatment of AHS has an analgesic effect, improves the condition of the oral mucosa, restores the cellular structure of the mucosa, causes improvement

specific composition of microflora, reduction of serum and secretory immunoglobulins. Recovery occurs in  $3.7\pm 0.2$  days in mild and  $5.9\pm 0.18$  in moderate-severe cases, respectively.

b. Step-by-step therapy with the initial application of bonafton ointment, and then glyderinin, improves the condition of the oral mucosa, restores the cellular structure, improves the species composition of microflora, and causes a decrease in serum and secretory immunoglobulins. Epithelialization time was reduced to  $3.7\pm 0.3$  days in mild and  $6.2\pm 0.4$  days in moderate-severe cases.

## PRACTICAL RECOMMENDATIONS

For the treatment of acute herpetic stomatitis, it is most effective to use 0.75% glyderinin ointment, which has analgesic, anti-inflammatory, antipyretic, antiviral, keratoplastic properties. It should be applied in the form of an application, after pretreatment of the oral cavity with antiseptics 1 hour after eating. In the first days of the disease, the ointment should be applied 5-6 times a day during the day, after improving the general condition and the beginning of epithelialization, the oral cavity treatment is reduced to 3-4 times a day.

Glyderinin ointment (0.75%) significantly improves the clinical condition of patients during the first hours from the moment of application of the drug in the mild course of the disease and from the second day in the moderate-severe course of acute herpetic stomatitis.

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