



## Mechanisms of Local Immunity of The Oral Mucosa in Coronavirus Infection

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**Abstract:** Non-specific immunity of the oral mucosa is provided by cellular elements-neutrophils and macrophages, as well as secretory elements-various chemotaxis factors for inflammatory agents (interleukins, leukotrienes, etc.). Specific immunity is provided by lymphoid tissue contained in a significant amount around the oral cavity — in the form of diffuse infiltration or in the form of nodular clusters devoid of a closed connective tissue case. The cells that provide specific immunity are T-lymphocytes and plasmocytes. In most cases, non-specific and specific immune protective factors neutralize bacteria and viruses. However, often microorganisms overcome these barriers, penetrate into the internal environment of the body and cause disease. This is facilitated by the weakening of local immunity, in particular against the background of coronavirus infection. Moreover, the oral mucosa is very intensively supplied with blood, has a relatively large surface and is a convenient entrance gate for the penetration of infections into the body, and also serves as a place of colonization and infection with potentially pathogenic microorganisms in case of weakening of natural immunity. Inflammatory diseases of the oral mucosa can manifest themselves by various nosological processes of the oral cavity, but sometimes even against the background of pronounced inflammatory processes, stomatitis, gingivitis and many other diseases do not form, often this is due to systemic viral processes, for example, coronavirus infection. At the same time, clinical symptoms can be very diverse, or even absent even against the background of changes in the immune and microbial landscape of the oral cavity. With the progression of the disease, the process may spread to the palate, gums, palatine tonsils, larynx, and digestive tract. It is important to distinguish weakened individuals, individuals with immunodeficiency conditions who were on long-term use of antibacterial agents, corticosteroids and antineoplastic drugs.

### Introduction

The persistence and recurrent nature of such inflammatory lesions requires not only the usual hygienic

measures for the care of the oral cavity and teeth, but also appropriate justified therapy aimed at stimulating the protective forces of the oral mucosa. The oral cavity is anatomically and functionally connected with the pharynx, whose inflammatory diseases are currently in the focus of attention of otolaryngologists due to their wide prevalence, and mainly in people of working age. These diseases are dangerous because they can cause the development of severe complications from the cardiovascular system, kidneys and joints. Most respiratory diseases are accompanied by damage to the pharyngeal mucosa and the lymphopharyngeal ring, which is part of the immune system and plays an important role in the formation of both local and general protective reactions of the body. In response to the introduction of an infectious agent, an inflammatory process develops, which is characterized by a number of protective mechanisms: a change in the permeability of the vascular wall, increased blood flow, increased activity of macrophages and polymorphonuclear cell elements, the release of inflammatory mediators, free oxygen radicals. Macrophages, through the release of cytokines, play a major role in the protective mechanism, causing an increase in the level of T-lymphocytes.

The occurrence of non-specific infectious and inflammatory diseases of the pharynx and upper respiratory tract occurs due to an imbalance of local and systemic immunity. The leading role in local immunity is played by cytokines acting on biochemical messengers that regulate the stimulation and inhibition of inflammatory reactions that initiate an immune response. Cytokines are produced by lymphocytes and macrophages embedded in the epithelium of the mucous membrane, the source of cytokines in saliva is serum transudate and salivary glands. Cytokines are also produced by the epithelial cells of the mucous membrane themselves when they come into contact with a microbe. It is important to note that the content of cytokines in saliva does not correlate with their level in the blood, which indicates the autonomy of local immunity. Viral infection can serve as an initiating factor for the attachment of a bacterial pathogen in the future. From the point of view of modern clinical immunology, the state of immunity of the oral cavity is a mirror reflecting the state of systemic, that is, general immunity, which in particular is an indicator primarily of the state of immunity of the gastrointestinal and respiratory tracts. The leading place in the structure of infectious diseases belongs to viral infections. Many respiratory viral infections have manifestations on the oral mucosa, recognizing which, the dentist can be the first to diagnose the disease. As for the coronavirus infection, we still don't know much. Unfortunately, there are more questions than answers. In this regard, we believe that a timely study of local immunity against the background of coronavirus infection during a pandemic will be able to answer many questions not only from dentists and immunologists, but also from doctors of related specialties. All these factors explain the wide interest in the problem of correcting violations of local and systemic immunity. Immunomodulatory drugs include drugs that have immunotropic activity and restore the functions of the immune system in therapeutic doses. It is clear that immunocorrector drugs are needed that have the properties of a local vaccine-it stimulates the defenses of the oral mucosa. Acting through a system of immunological mechanisms, it causes such effects as an increase in the activity of phagocytes with a qualitative improvement in phagocytosis; an increase in the content of lysozyme in saliva, which has bactericidal activity, induction of interferon; stimulation and an increase in the number of immunocompetent cells responsible for the production of antibodies; stimulation and an increase in the content of sIgA, which plays a significant role in the mucosal protection system. The immune reactions of the mucous membranes are based on intermolecular and intercellular interactions. However, it is the mucous membranes, due to their topographical position, that are the first to be attacked by pathogens and interact with antigens (AH). The mucous membranes have a complex of factors of nonspecific and immune protection, which in most cases provide a reliable barrier to the penetration of pathogens. There are cellular and secretory local immunity, each part in turn refers to specific (adaptive) and non-specific (innate, natural). Natural local immunity is carried out by the barrier properties of the integument, their production of antimicrobial substances, normal microflora of an organ or tissue,

phagocytic reaction, as well as mechanical removal or enzymatic cleavage of the damaging agent. Specific (adaptive) local immunity is provided by secretory IgA, sensitized lymphocytes and, probably, by selection of cell populations resistant to the damaging agent. Non-immune non-specific protection factors include: lysozyme; hydrochloric acid of gastric juice; digestive enzymes (proteases); bile; antagonism of the normal intestinal microflora; mucus and glycocalyx; normal intestinal peristalsis; secretory activity of the small intestine (in the crypts of intestinal villi, a liquid is secreted that flushes pathogenic agents into the intestinal lumen).

To study the features of adaptive mechanisms of local immunity of the oral mucosa against the background of coronavirus infection and to justify the principles of immunocorrecting therapy based on the identified changes.

### Research objectives

1. To study the features of the functional state of the oral mucosa and local immunity against the background of coronavirus infection by collecting saliva in adults with an acute form of coronavirus infection and collecting anamnesis of the disease (features of the course of coronavirus infection - from mild to severe forms in comparison with asymptomatic individuals).
2. To investigate the state of cytokines in saliva against the background of coronavirus infection.
3. To investigate the state of the main interferons in saliva against the background of coronavirus infection.
4. To study the level of lysozyme and secretory immunoglobulin A against the background of coronavirus infection.
5. To propose and justify the principles of immunocorrection of local immunity, depending on the features of the course of the viral process. Development of treatment of the oral mucosa in the rehabilitation period.

**Material and methods:** Patients who were taken to the Special Hospital of Zangiota No. 2 of the Republic and who were diagnosed with 68 COVID - 19 were examined by dental examination of the oral cavity.

It was verified that the patients were in contact with those who had COVID-19 disease. Other infectious diseases were also detected. At the time of the examination, the general condition of the patient is very serious. Welcome, without glasses. Answers the questions correctly. To hurt. The skin and visible mucous membranes are pale, without a rash. The nose-lip triangle and the fingers-toes have a slightly bluish hue. Body weight is normal. The tongue is clean, dry. There are no deformities in the musculoskeletal system, but intuition and behavior in both legs of the patient are not fully observed until the chest becomes numb. Breathing through the mouth-nose, with the participation of auxiliary muscles. Against the background of auscultative bubbly breathing, a mixed wheezing is heard. Exhalation and inhalation are observed in hirsuties. Respiratory conduction is not audible on the left side (SpO<sub>2</sub>-84-86%, when it comes to patients with acute respiratory failure and taking into account the severity of the patient's behavior.) the patient begins with oxygen therapy with warm and moistened oxygen through a nasal cannula. After that, the symptoms of respiratory failure in the patient are somewhat improved by reducing the axvols. SpO<sub>2</sub>-increased to 95%. The heart tones are muted, rhythmic. Peripheral vascular stroke has an average fullness and tension. The stomach is soft, painless, intestinal peristalsis is audible. The appearance of constipation was independent, it was not present during the examination. Diuresis is performed through a yellow-colored urethral catheter.

Local: right-sided cervical catheter and urethral catheter functional condition is satisfactory, there are no signs of inflammation, treated with antiseptic solutions, fixed with aseptic fixation. Local: the patient has bedsores between the sacrum and the sacrum, the knee joint is located between the sacrum and the sacrum, the hip is located between the palms.

- 1 General analysis of mineral extraction.
- 2 Common stool for urination.

- 3 Biochemical analysis of mining operations.
- 4 Coagulogram.
- 5 C-reactive oxide.
- 6 PCR analysis of COVID-19.
- 7 Mysterious rural scale in Kanda.
- 8 Pralcitonin, ferritin, D-dimer, ELISA (IgMIgG), interleukin-6.
- 9 Examination by an endocrinologist.

Adequate respiratory therapy.

\* Periodic changes in the state of the body + vibration massage. + Breathing Exercises.

- For the purpose of antibacterial treatment – meropenem 1 g. 3 max. i / I.
- For the purpose of treatment of fungi – drink flucanazole 150 mg per day 3 times a day.
- For the purpose of angioprotective therapy - ascorbic acid 5% -10.0 x 2 max. v/V.

\* Anti-inflammatory: continued-dexamethasone 8 mg 1 max. i / V.

\* For the purpose of antiplatelet therapy – Cardiomagnetic drink 75 mg 1 time per day.

- For the purpose of antiremodulation– drink veroshpiron 100 mg 1 time a day.
- For the purpose of gastroprotective therapy – drink omeprazole 20 mg 2 max.
- For the purpose of cardiotropic therapy-meldonium 10% -5.0 1 max. i/ v, thiotriosoline 4.0 1 max. i/V.

Treatment with drugs that affect the virus indirectly, stimulating the human immune system, is always a risk. Treatment is very important for me, because I am a clinical immunologist who deals with the immunology of infectious processes. At the very beginning of the pandemic, a Chinese reference book came into my hands. He was urgently transferred, and I was surprised that "Plakvinil" appeared everywhere there. I knew that it is used not only for malaria, but also rheumatologists prescribe patients in order to suppress the immune response. This drug is an immunosuppressor. It suppresses the immune system. To give it to a person with a hyperergic reaction of the body means not to let him die. But there is also a dualism in this: on the one hand, the person remained alive, on the other-the intervention did not allow the body to form adequate antibodies, and after some time he will be vulnerable again. Therefore, over time, this drug was abandoned. In medicine, this is called "did not show its effectiveness". "Dexamethasone" is another story. It is a systemic corticosteroid hormone. Since the 60s, it has been used for autoimmune rheumatoid processes.

### Conclusion

Corticosteroid hormones have a very wide range of indicators: anti-allergic, decongestant (which is important for COVID-19), anti-inflammatory. Compared with the immunosuppressive "Plakvinil", which belongs to the category of C preparators (very weak), "Dexamethasone" was more successful. Another difference is the duration of immunosuppression, that is, the suppression of the immune response. At "Plakvinil" it is long-lasting, so rheumatologists prescribed it to chronicles. Dexamethasone has a short one. It is done once a day. After this time, the hormone may no longer be in the body — it is easily injected and excreted. At the same time, he can also successfully remove a hyperergic reaction with pulmonary edema. Therefore, sometimes you do not need to invent a bicycle, but just remember what our predecessors did. In medicine, you always work according to the fact. An important point: there are significantly fewer official diagnoses than there are pathological processes that are realized in the human body. The doctor looks at the body, analyzes, and understands how it

reacts. It acts based on the clinic: there is not enough protein — it makes up for it, and so on. The process of learning about a new coronavirus infection has been going on all these months. Temporary protocols appear all the time. Temporary, because as soon as doctors see that the scheme is not successful enough, they change it.

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