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Physiology of Immune Responses of Mucous Membranes

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Abstract

Since the SARS-CoV-2 virus primarily affects the upper respiratory tract (VDP), it is possible that the response of the body's defense systems may develop in the nasopharyngeal region, for example, it may be the epithelium of the nasal cavity, tonsils, adenoids. Lymphoid tissue is the site of induction for the protective systems of the mucous membrane. Perhaps the body's response may be caused by inductive sites of the mucous membrane of the lacrimal duct or oral cavity, but the number of such sites in the immune response of the mucous membrane in humans is unclear. Bronchus-associated lymphoid tissue (BALT) is not usually present in adults, but can be found in children and adolescents and can be induced by infections..

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Introduction

This allows us to be interested in questions about whether the responses caused by BALT can contribute to greater resistance of young people to COVID-19, or BALT can be caused by SARS-CoV-2 with consequences for the course of infection. All tissues with such mucosal induction sites produce IgA-producing mucosal B cells, which are home to various remote effector sites of the mucosa, where they differentiate into plasma cells secreting polymeric IgA. In addition, systemic IgG-producing B cells are also induced in the tonsils, and they are home to peripheral lymphoid tissues, where they differentiate and secrete IgG for blood circulation.

In the subepithelial spaces of the mucous membranes and associated glands, plasma cells of the mucous membrane produce pIgA, which is selectively transported to the secretions by polymer receptors of immunoglobulins, being released in the form of sIgA. Both in the nasal passages and as it descends into the trachea and bronchi, the virus encounters a sIgA-dominated environment, which is generated through the immune system of the mucous membrane and maintains an almost non-inflammatory environment. However, once it reaches the terminal airways and alveoli, it enters an environment dominated by IgG derived from the bloodstream. Neutralizing antibodies, especially circulating antibodies, attracted particular attention to the virus. Their effectiveness in preventing infection and disease lies in the fact that they reach the surfaces of the mucous membrane where the virus is present, and do not forget that circulating IgA, even in polymer form, is not effectively transferred to the secret, while plasma IgG is found in URT and especially in the lower respiratory tract (LRT), IgG is inflammatory in its mode of action due to the induction of effector mechanisms such as complement activation and the involvement of phagocytes such as macrophages and neutrophils. as natural killer cells (NK). Serious COVID-19 pathology occurs in the terminal airways of the lungs, where circulating IgG is the dominant immunoglobulin. The resulting intense inflammation involves many molecular factors, including cells recruited by virus-induced chemoattractants.

The cellular arm of the adaptive immune response, including CD4+ and cytotoxic CD8+ cells, is also delivered through the bloodstream and can reach the alveoli. However, cytotoxic cells by their nature cannot prevent infection: they destroy already infected cells and thereby limit the further spread of infection. Almost all efforts to develop a vaccine against COVID-19 are focused on systemic injections, which predominantly induce circulating IgG antibodies and possibly cytotoxic T cells. These pathways are ineffective for generating mucosal immune responses, which can only be triggered by mucosal immunization pathways, including through NALT in URT.

The immune responses of the mucous membrane are partially divided, since the distribution of responses depends on the actual induction pathway. For example, the enteric pathway predominantly elicits responses in the gastrointestinal tract, whereas the nasal pathway predominantly elicits responses in the respiratory tract and salivary glands. The reasons for this differential distribution lie in the imprinting of T and B cells induced in the corresponding inductive sites, lymphoid tissues associated with the intestine (GALT, such as intestinal Peyer plaques) or NALT, with "homing" receptors, including specific integrins. and

chemokine receptors specific to target tissues. When applied in practice, intranasal immunization should be a successful method of generating predominantly sIgA immune responses in URT and LRT, where SARS-CoV-2 can be neutralized and eliminated without inflammatory consequences. If a sample is taken from the nasal or oral cavity for the analysis of IgA antibodies, then this is considered the most informative way to assess effective immune responses against SARS-CoV-2, which can be caused by natural infection or intranasal immunization. The analysis of serum IgA antibodies can be used for diagnosis as an additional method, but this method is not a substitute, since the intake of serum IgA is associated with another source (mainly from bone marrow) and consists mainly of monomeric IgA1. The difference between sIgA of the mucous membrane, which includes various subclasses and is locally synthesized by plasma cells secreting pIgA located in the subepithelial spaces (lamina propria) of mucous tissues and glands [2.4.6.8.10.12].

sIgA antibodies are known to be effective against various pathogens, including viruses, due to mechanisms such as neutralization, inhibition of adhesion and invasion of epithelial cells, agglutination and facilitation of removal in the mucus stream. Intracellular mechanisms of inhibition of virus replication are also described. Moreover, sIgA, by its mechanism of action, has practically no inflammatory or even anti-inflammatory effect. IgA does not activate complement in the classical way, and activation of the alternative IgA pathway is largely an artifact, while the lectin pathway depends on the terminal sugar residues in glycan structures. In addition, IgA antibodies have even been shown to inhibit complement activation mediated by IgM or IgG antibodies. Interestingly, the results of a study on systemic human immunization against HIV suggest that high levels of serum IgA responses compromised the protective function of IgG antibodies with the same antigenic specificity and were associated with a higher risk of HIV infection. Notably, while mucosal sIgA levels rise rapidly in infants and reach adult levels in early childhood, serum IgA levels mature much more slowly and may not reach full adult levels until adolescence. Given the obvious difference in susceptibility to COVID-19 between children and adults, these differences in the maturation of the immune response should be taken into account [1.3.5.7.9.11.13].

Given that SARS-CoV-2 is first infected mainly through the nasal passages, possibly through the eyes, followed by drainage into the URT, as well as through the mouth, we could predict that the first immune responses should manifest themselves through the immune system of the mucous membrane, with the appearance of sIgA antibodies in the secretions of the VDP, as well as in saliva and tear fluid. Concomitant production of IgG and IgA serum antibodies may also occur. Before producing sIgA antibodies, there should be a wave of cells secreting IgA antibodies in the bloodstream. This usually occurs with a peak about 6-10 days after discrete mucosal immunization, as B cells induced in mucosal immune induction sites (such as NALT) express mucosal homing receptors such as integrin α4β7 and migrate to effector sites, where they finally differentiate into plasma cells secreting pIgA. Circulating cells secreting IgG antibodies are also induced by antigens that stimulate responses in the tonsils, and they usually express peripheral homing receptors such as L-selectin. The period during which these cells can be detected is limited because this wave of B cell migration is temporary after an inducing event, which in the case of SARS-CoV-2 infection can last up to 4-5 days (or longer) before symptoms first occur. If this is the case, peak cell migration may

be 4-5 days after the onset of symptoms. However, in the presence of ongoing infection and ongoing immunostimulation, it is possible that antibody-secreting cells will continue to circulate as repeated waves of induced B cells are released from the inductive sites.

Due to uncertainties in the kinetics of IgM, IgG and IgA antibody development in infected people, a detailed analysis of antibody-secreting cells and their expression of homing receptors, as well as their resistance in lymphoid tissues, will provide important additional and more complete information about the immune response to SARS-CoV-2. Such an analysis may shed light on differences in the clinical outcomes of infection in children compared to adults with symptoms or asymptomatic. It can be expected that the determination of these antibodies and cellular responses of the mucosal immune system will provide valuable information that differs from and complements the determination of serum IgG antibody responses. In addition, it is reasonable to expect that this information will provide valuable information about the progress of COVID-19 disease. However, a key requirement for obtaining reliable results is that the procedures used for collecting samples, as well as analysis methods, should be developed taking into account the characteristics of the immune responses of the mucous membranes and the distinctive features of the secretions compared to serum. Thus, based on the pathway of SARS-CoV-2 infection and the independence of the mucous membranes and systemic responses, there should be an immune aspect of the mucosa to COVID-19. Whether it makes a significant contribution to the outcome of SARS-CoV-2 infection or whether it can be used with good effect for diagnostic purposes or for therapy and prevention can only be determined by conducting appropriate studies. WHO has announced that outbreaks of the new coronavirus represent a public health emergency of international importance. Infection control measures are needed to prevent further spread of the virus and help control the epidemic situation.

Due to the nature of the dental environment, the risk of cross-infection between patients and dental practitioners may be high. Strict and effective infection control protocols are urgently needed for dental offices and hospitals in areas that are (potentially) affected by COVID-19. Dental patients who cough, sneeze, or undergo dental treatment, including the use of a high-speed handpiece or ultrasound instruments, cause their secretions, saliva, or blood to be aerosolized into the environment. The dental device may be infected with various pathogenic microorganisms after use or be exposed to the contaminated environment of the clinic. After that, infections can occur as a result of puncturing sharp instruments or direct contact between mucous membranes and contaminated hands [14.16.18.20].

Due to the unique characteristics of dental procedures, which can produce large amounts of droplets and aerosols, standard protective measures in daily clinical work are not effective enough to prevent the spread of COVID-19, especially when patients are in the incubation period. they do not know that they are infected, or they prefer to hide their infection. If COVID-19 infection is suspected, interim guidance on infection prevention and control during medical care is recommended. Until now, there has been no consensus on the provision of dental services during the COVID-19 epidemic. Based on our experience, relevant recommendations and research, dentists should take strict personal protective measures and avoid or minimize operations that may result in droplets or aerosols. The 4-handed technique is useful for fighting infection. The use of small or large volume salivary pumps can reduce the formation of droplets and aerosols [13.15.17.19.21].

Conclusion. During the COVID-19 outbreak, dental clinics are advised to carry out preliminary checks to measure and record the temperature of each staff and patient as a routine procedure. Pre-screening staff should ask patients questions about their health status and contact or travel history. Patients and their accompanying persons receive medical masks and temperature measuring equipment at the entrance to our hospital. Patients with fever should be registered and referred to designated hospitals. If the patient has visited the epidemic regions within the last 14 days, quarantine for at least 14 days is recommended. In regions where COVID-19 is spreading, non-emergency dental practice should be postponed.

LITERATURE USED

1. Жабборова Ф.У. Способ диагностики степени тяжести инфекции, вызванной covid-19 (ротовая жидкость). FAP 01938. 2021 год.
2. Жабборова Ф.У. Способ диагностики степени тяжести инфекции, вызванной covid-19 (периферическая кровь). FAP 01939. 2021 год.
3. Жабборова Ф.У., Исмаилова А.А., Иноятов А.Ш. Features of local mucosal immunity of the oral cavity and sysmic immunity in persons with severe covid-19. Europe’s journal of Psychology (EJOP), in the forthcoming issue 06-11-2021.
4. Жабборова Ф.У. Специфика местного иммунитета слизистой оболочки полости рта и системного иммунитета у лиц с тяжелой формой covid-19. Тиббиётда янги кун. 4(36) 2021
5. Жабборова Ф.У., Исмаилова А.А. Современные методы диагностики местного иммунитета ротовой полости у больных с covid-19 Журнал теоретической и клинической медицины. № 2 2022.
6. Жабборова Ф.У., Иноятов А.Ш., Казакова Н.Н. Особенности изменение ротовой полости у лиц с разным течением covid-19. Журнал стоматологии и краниофациальных исследований. № 2 2022 Самарканд
7. Жабборова Ф.У., Исмаилова А.А. Цитокиновый статус слюнной жидкости у пациентов с коронавирусной инфекцией. Проблемы биологии и медицины. Журнал.
8. Jabborova F.U. Features of local mucosal immunity of the oral cavity and sysmic immunity in persons with severe covid-19. Europe’s journal of Psychology (EJOP), in the forthcoming issue 06-11-2021
9. Jabborova F.U. Adaptation mechanisms of local immunity of the mucous membrane of the oral cavity during coronavirus infection. Journal NX ISSN No-2581-4230 Impacp Factor 7.223 October 11th, 2020.
10. Jabborova F.U. Modern diagnostics of the immune status in patients with coronavirus infection. Инновационные методы лечения заболеваний пародонта в детском возрасте. Сборник тезисов конференции посвящённой Актуальным вопросам детской стоматологии. 4 февраля 2022г. Ташкент.
11. Jabborova F.U. Local immunity of the mucosa coronavirus infection. International Consortium on Academic, Trends on Education and Science Hosted from London Ehgland April 3-4 2021
12. Jabborova F.U. Adaptive mechanisms of the mucosa in coronavirus infection. Procceding of International Conference on Scientific Endeavors and opportunies Hosted

from Tevari, Georgiya on 17-18 march 2021
13. Jabborova F.U., Inoyatov A.Sh. Oral mucosa in coronavirus infection. Middle european scientific bulletin. volume 13, jun 2021. ISSN 2694-9970
14. Жабборова Ф.У., Исмаилова А.А. Методика анализа лабораторных параметров местного мукозального иммунитета ротовой полости иммунного статуса у лиц с разным течением covid-19. Ташкент-2022
15. Жабборова Ф.У., Иноятов А.Ш. Способ оценки состояния ротовой полости у лиц с разным течением covid-19. Ташкент-2022
16. Rajabov O.A. Clinical and immunological Evalution of Orthopedic Treatment of Patients with Inflammatory Periodoal Diseases of Various Orthopedik Constructions. // International journal of Health Systems and Medical Sciences Vol. 2/No 2/ February-2023 ISSN: 2833-7433.-P.-21-24
17. Rajabov O.A., Bekmuradova G. Parameters of Humoral of the Oral Cavity in Patients Before the Start of Orthopedic Treatment // Central asian journal of medical and natural sciences . – Испания - 2023.Vol.04 Issue:02 ISSN: 2660-4159 P.-28-32.
18. Rajabov O.A. Structural and functional changes in periodontal tissues during trostnetics winh metal-ceramic and zirconium dentures Valeology: International journal of Medical Anthropology and Dioethics Voy ume 01 ISSUE 01, 2023
19. Rajabov O.A. The Optimal Ture of Prosthesis Based on a Comparative Assessment of the impact of Cermtt and Zircon Prostheses Vol. 2 Issue: 5/ May-2023 ISSN: 2720-6866.-P.-189-195
20. Kazakova N.N., Rajabov O.A. Pathogenetic treatment and prevention destructive inflammation in women’s oral cavity tissues due to osteoporosis during the period of menopause // journal of Survey in Fisheries Sciences 10(2s) P.-3941-3948
21. Ражабов О.А. Металлокерамик протези бўлган беморлар гурухида даволашдан олдинги ва кейинги иммунологик тадқиқотлар тахлилий натижалари.// journal of oral medicine and craniofacial research impact factor:4.917 VOL. 4 issue 2. 2023 ISSN: 2181-0966 Б.-64-66