



ORAL MUCOSA, SALIVA AND COVID-19 INFECTION

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Abstract

The SARS-CoV-2 virus has shocked the world with the ongoing COVID-19 pandemic and has presented challenges to every corner of modern healthcare. Coronavirus disease 2019 (COVID-19) is an infectious disease that was first identified in large numbers in Wuhan, China; is caused by a newly discovered coronavirus identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1). On March 1, 2020, the World Health Organization (WHO) declared COVID-19 a global pandemic. As of January 20, 2021, there were 96,866,468 cases worldwide and 20,72,466 deaths. The first cases of COVID-19 were reported in Canada on February 10, 2020, and since then there have been 723,908 cases and 18,421 deaths (90).

Keywords: coronavirus infection, saliva, pathology of the salivary glands, herpes, stomatitis, pathology of the microflora of the oral cavity, candidiasis (thrush) of the oral cavity, gingivitis, periodontitis, coronavirus therapy against the background of pathology of the oral cavity.

Introduction

Coronaviruses are large RNA viruses with betacoronaviruses including SARS-CoV and SARS-CoV-2, which have proven to be the deadliest viruses causing respiratory distress syndrome (2, 3). Coronaviruses are single-stranded RNA viruses 80–120 nm in diameter. There are four types: α -coronavirus, β -coronavirus, δ -coronavirus and γ -coronavirus [4]. SARS-CoV-2, like SARS-CoV and MERSCoV, is a β -coronavirus. The genome sequence homology between SARS-CoV-2 and SARS is approximately 79%; SARS-CoV-2 is closer to SARS-like bat coronaviruses (MG772933) than SARSCoV [5]. Since 1960, six coronaviruses have been found to cause disease in humans. In 2002, SARS-CoV caused a major outbreak known as severe acute respiratory syndrome (SARS), which killed about 10,000 people worldwide (4). It wasn't until a decade later that another pathogenic coronavirus known as the Middle East respiratory syndrome coronavirus (MERS-CoV) became endemic in the Middle East (4, 5). SARS-CoV-2 is the seventh member of the coronavirus family to infect humans (4). Interestingly, the SARS-CoV-2 genome matched the genomes of bat viruses (Bat-CoV and Bat-CoV RaTG13) in *Rhinolophus affinis* species from Yunnan with a similarity of 96%; structural analysis revealed a mutation in the coat protein (Spike protein) and





nucleocapsid protein (6). The coronavirus has a simple structure with few proteins (7). There are 4 main structural proteins: envelope protein (E), spike protein (S), transmembrane protein (M) and nucleoprotein (N). The E, S, and M proteins facilitate virus entry into host cells, virion assembly, and virus pathogenesis. The viral genome is in close association with the N protein and also assists the E protein in virion assembly (7).

Currently, two transmission routes for SARS-CoV-2 have been identified: direct and indirect transmission. Direct transmission involves contact with an infected person's body fluids, droplets from the respiratory tract or saliva, and other body fluids such as feces, urine, semen, and tears (8). Signs and symptoms of COVID-19 can be divided into respiratory and extrapulmonary manifestations. The most common respiratory symptoms are cough, fever, and shortness of breath (9–11). There is a wide range of extrapulmonary signs and symptoms including oral mucosal lesions and neurological dysfunctions such as loss of smell, loss of taste, headache and associated myofascial pain; they are now included in the diagnostic criteria for this disease

Coronaviruses (CoV) are a large family of viruses that cause diseases ranging from the common cold to more severe illnesses such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). A novel coronavirus (nCoV) is a new strain that has not been previously identified in humans. The main task of the virus is to bring its genetic code into the cell and force it to produce its own proteins. If the virus succeeds in this task, then in the end, from just one cell, not one virus, but up to 100,000 virus particles is obtained. In essence, he creates a machine that replicates himself.

At the same time, the virus is not universal; it must be “tuned” for specific organisms and cell types. To do this, he has to evolve. This happens just in the process of copying, by creating inaccurate copies.

No two viruses are the same inside a cell, they are constantly changing. RNA viruses literally make one mistake for every successive genome. Therefore, it should not be surprising that unknown strains constantly appear. This is what happened with the 2019 coronavirus, officially named 2019-nCoV.





SARS-CoV-2 causes acute viral infection in humans with an average incubation period of 3 days [8]. The most common symptoms of COVID-19 are fever (87.9%), cough (67.7%), and fatigue (38.1%) [9,10]. The most common abnormalities in laboratory results include a decrease in lymphocytes [11] and an increase in ALT and AST [12,13], an increase in pro-inflammatory cytokines such as IL-1 β , IL-6 and an increase in TNF- α , D-dimer, C-reactive protein [fourteen]. Also, levels of fibrin breakdown products and prolonged prothrombin time have been associated with poor prognosis in patients affected by SARS-CoV-2 [15].

The oral barrier is the gateway to the human body

The oral mucosa and saliva are high risk sites for higher viral loads and dentists are considered a high risk group. COVID-19-induced oral lesions and loss of taste and smell are common clinical complaints in dental settings. The SARS-CoV-2 virus has been found to cause a wide range of non-specific oral mucosal lesions, but the specific diagnosis of these mucocutaneous lesions as COVID-19 lesions would facilitate the prevention of SARS-CoV-2 in dental care. settings and assistance in the correct management of the patient.

The oral mucosa is the site of the first meeting. Commensal microbes, airborne antigens/allergens, and foods are initially encountered here before entering the gastrointestinal (GI) and often respiratory tracts. As with other barrier sites, the local immune system strikes a delicate balance in that it performs effective immune surveillance without excessive inflammatory reactions, while being tolerant of commensals and harmless antigens [1].



The nasal cavity, nasopharynx, oropharynx, and oral cavity have been identified as potential sites for replication of the SARS-CoV-2 virus (10, 11). Rich in saliva and oral microbiome, the oral cavity is a well-known site for various types of respiratory viruses (12, 13). Oral saliva has been found to contain high levels of viruses, suggesting that the salivary glands are active sites for the proliferation of this virus (14, 15). Moreover, xerostomia and loss of taste may be associated with salivary gland dysfunction associated with COVID-19 (16, 17). However, these signs are often masked by more life-threatening respiratory signs and symptoms, which in most cases are a medical emergency. This review aimed to provide the histological characteristics of the oral mucosa and its functional significance in SARS-CoV-2 infection, focusing on orofacial manifestations and their impact on the dental profession.

Clinical changes in the oral cavity

Dentists warn: coronavirus can cause a number of inflammatory processes in the oral cavity of patients. In particular, the occurrence of ulcers and plaques, as well as cracks in the tongue, has been noted in an elderly patient hospitalized with COVID-19.

In addition, infected people may develop dysgeusia - that is, (taste disorder), fungus, candidiasis and other pathological conditions in the mouth, petechiae (pinpoint hemorrhages in the form of red bumps), candidiasis, traumatic ulcers and various other lesions of the tongue and mucous membranes. In addition to loss of taste on the 24th day of hospitalization, yellow ulcers in the mouth similar to herpetic ones developed, as well as deep cracks and a specific white plaque on the back of the tongue, petechiae (pinpoint hemorrhages in the form of red tubercles), candidiasis, traumatic ulcers and various other lesions of the tongue and mucous membranes. Patients characterize food intake as "chewing soap, cotton wool." This is due to a decrease in immunity. Diseases that increase the risk of infection include various types of stomatitis, gingivitis and periodontitis. As for caries, in itself it is not a "gateway" for infection, but immunity in any case will be "distracted" by such lesions. And this greatly weakens the body's defenses. It was found that the cells of the oral cavity have a high expression of ACE-2, comparable to the cells of the lung tissue. SARS-CoV-2 is able to bind to the ACE-2 molecule (angiotensin-converting enzyme 2 is a membrane protein, the entry gate for the virus into cells and is expressed (multiply) on the cells of the epithelium of the oral mucosa.

In patients, cyanosis of the lips was expressed, a pronounced vascular pattern was noted on the mucous membrane of the inner surface of the lips, the color of the oral mucosa, with the usual pale pink tint, varied to cyanotic. There were also petechial hemorrhages on the mucous membrane of the lips and cheeks. Also, pronounced





xeroderma of the facial area and angular cheilitis attracted attention. When examining the mucous membrane of the tongue, there was a plaque from white, light yellow to brown, which was easily removed when scraping, the papillae were expressed evenly over the entire surface, without signs of hyperkeratosis. During the observation period, after 5-7 days, complaints were found about perverted perception of taste and smell, which indicated violations of smell and taste sensitivity such as "R43.1 Parosmia" and "R43. Anosmia". and "R43.2 Parageusia".

The role of saliva in the pathogenesis of COVID-19 and the diagnosis of diseases

Human saliva is a unique body fluid of the oral cavity. It is a hypotonic solution of salivary acini, gingival sulcus fluid, and oral mucosal exudate (15). Approximately 90% of saliva is secreted by the salivary glands; major glands include the parotid glands, submandibular glands, and sublingual glands (66). The salivary glands are highly vascular formations where a constant metabolism takes place. A normal person produces 600 ml of saliva per day. It is primarily composed of water (94–99%), with organic molecules accounting for ~0.5% and inorganic molecules accounting for 0.2% (16). It performs the functions of lubricating the oral mucosa, digesting food, cleaning and protecting the oral cavity, and is one of the most important factors affecting oral homeostasis.

Saliva-based diagnostics of COVID-19 is receiving increased attention for several important reasons. First, saliva samples can be easily obtained by asking patients to spit into a container, which is a non-invasive procedure and minimizes the chance of healthcare workers being exposed to the highly infectious SARS-CoV-2 virus; it is also ideal for testing elderly vulnerable populations, pediatric patients, and communities where large sample collections are required (17). SARS-CoV-2 positive levels in saliva are 92% compared with nasopharyngeal aspirate, and live virus can be cultured successfully in saliva samples, highlighting the value of saliva in the diagnosis of COVID-19 (18). As discussed earlier, early detection of SARS-CoV-2 in saliva may be vital in diagnosing COVID-19 patients before respiratory symptoms appear, which greatly helps control public health measures such as the quarantine process .

In COVID-19, impaired salivary secretion is often associated with xerostomia and loss of taste . Xerostomia is a subjective complaint of dry mouth, while salivary gland hypofunction is objectively characterized by reduced salivation (17, 18). In SARS-CoV infections, xerostomia can be exacerbated by impaired nasal breathing due to nasal congestion and rhinorrhea, where mouth breathing becomes more frequent and salivary gland function may be impaired, and xerostomia is secondary (18). Similar to





oral mucosal lesions caused by COVID-19, pandemic-induced psychosocial factors have a greater impact on normal salivary gland function and quantitative secretion. Given the higher viral load in the oral cavity, personal protective equipment (PPE) must be used. Safety goggles or face shields, masks, gloves and caps should be worn regularly, discarded or properly disinfected between each patient. Protect from saliva and blood aerosols to reduce the risk of exposure to COVID-19. The use of rubber dams can significantly minimize saliva-contaminated splashes, droplets, and aerosols, especially when using high-speed dental handpieces and ultrasonic devices. The use of a rubber dam can significantly reduce the amount of airborne particles in an operating field with a diameter of ~3 feet by 70% (19). High speed dental handpieces without anti-retraction valves can aspirate and expel debris and fluids during dental procedures; in addition, hand instruments used during general dental procedures produce significant amounts of aerosol (20). Good ventilation, regular and thorough disinfection of surfaces before and after procedures with alcohol or chlorine, and proper handling of saliva-containing waste are critical to preventing the spread of COVID-19 (20). Recent studies suggest that mouthwashes may reduce the viral load of SARS-CoV-2 (21). Marui et al. have shown that pre-procedural rinsing of the mouth can significantly reduce the microbial load in dental aerosols (21). In addition, the use of mouthwashes before dental treatment may be beneficial during a pandemic (22).

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