

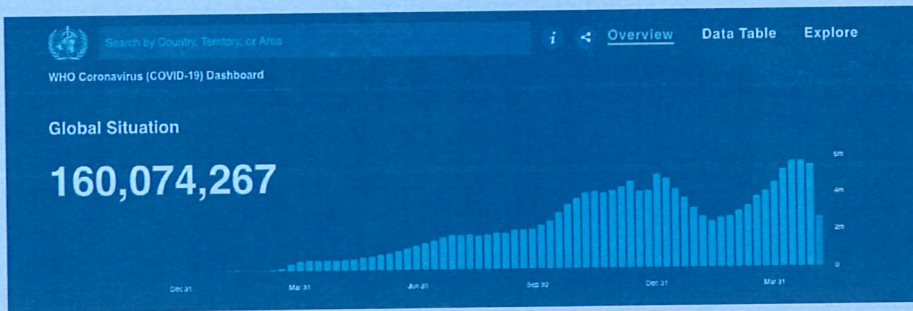


ORAL HEALTH
& SARS-CoV-2

INFORMATION
SHEET



FACTS & FIGURES ABOUT SARS-CoV-2



Oral lesions are evident in about **half of COVID-19** cases

HOW CAN CORONAVIRUS 2 (SARS-CoV-2) AFFECT ORAL HEALTH?

Recently, a global pandemic has emerged triggered by human-to-human transmission of a novel coronavirus (SARS-CoV-2) causing COVID-19 disease. **Since the outbreak in December 2019, COVID-19 has affected >160,000,000 people** (World Health Organization 2021). The most common symptoms are fever and dry cough and in some cases shortness of breath, dysosmia, and dysgeusia (Guan et al. 2020; Lechien et al. 2020). Most cases of COVID-19 are mild (80%) while 20% of infected patients may develop severe disease and 5% may become critically ill and develop pneumonia or acute respiratory distress syndrome, which requires mechanical ventilation and hospitalization in intensive care (Amorim Dos Santos et al. 2021). At the beginning of the COVID-19 pandemic, the lack of oral involvement was thought to be a feature distinguishing COVID-19 exanthema from other viral exanthemas. **Recently, SARS-CoV-2 has been**

detected in the saliva of patients and it has been shown that the reverse transcriptase-polymerase chain reaction test may be more sensitive for saliva samples than for nasopharyngeal samples (Iranmanesh et al. 2021). Oral manifestations, such as taste loss, dry mouth and **oral lesions, are evident in about half of COVID-19 cases** (Amorim Dos Santos et al. 2021). Oral manifestations included ulcer, erosion, bulla, vesicle, pustule, fissured or depapillated tongue, macule, papule, plaque, pigmentation, halitosis, whitish areas, hemorrhagic crust, necrosis, petechiae, swelling, erythema, and spontaneous bleeding. As the diagnoses of the lesions suggest, **aphthous stomatitis**, herpetiform lesions, candidiasis, vasculitis, Kawasaki-like, EM-like, **mucositis, drug eruption, necrotizing periodontal disease**, angina bullosa-like, angular cheilitis, atypical Sweet syndrome, and Melkersson-Rosenthal syndrome, led to the oral lesions (Iranmanesh et al. 2021).

DEFINITION

COVID-19 is an infectious disease caused by a newly discovered coronavirus. Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness (WHO 2021).

GOOD TO KNOW

Recently, SARS-CoV-2 has been detected in the saliva of patients. Oral manifestations, such as taste loss, dry mouth and oral lesions, are evident in about half of COVID-19 cases.

HOW DOES CORONAVIRUS 2 (SARS-CoV-2) FAVOUR THE ONSET OF ORAL LESIONS?

SARS-CoV-2 binds to the [Angiotensin converting enzyme 2 \(ACE2\) receptor](#) for cellular entry and infects epithelial cells of the respiratory tract. Several organs, such as kidneys, lungs, brain, liver and pharynx, can be affected accounting for increased morbidity of the infection. [ACE2 receptors are also present on the epithelial cells of oral mucosa and gingiva, making the oral cavity a potential target for infection](#) (Katz and Yue 2021). Whether oral lesions are directly caused by the virus or associated manifestations resulting from the patient's severely compromised condition remains to be determined. Nevertheless, considering that the distribution of ACE2 receptors may determine the route of SARS-CoV-2 infection, the presence of ACE2 receptors

on the epithelial cells of the tongue and salivary glands, suggests that these cells may be involved in COVID-19 infection and the ensuing dysfunction. This could lead to the development of dysgeusia as well as oral mucosal ulcerations and necrosis. Thus, [the interaction between SARS-CoV-2 and ACE2 might disrupt the function of oral keratinocytes and the epithelial lining of salivary gland ducts, resulting in painful oral ulcers](#) (Brandão et al. 2021). Aphthous-like lesions in COVID-19 patients, described by Iranmanesh et al., appear as multiple shallow ulcers with erythematous halos and yellow-white pseudomembranes on both the keratinized and nonkeratinized mucosae. The authors observed aphthous-like lesions with necrosis and hemorrhagic

crusts more frequently in older, immunosuppressed patients with severe infection, while aphthous-like lesions without necrosis were seen in younger patients with mild infection. Lesions healed after 5 to 15 days and regression of oral lesions was associated with improvement of systemic disease. The authors suggested that [an increased level of tumor necrosis factor \(TNF\)-α in COVID-19 patients could lead to chemotaxis of neutrophils to the oral mucosa and the subsequent development of aphthous like lesions](#). In addition, they hypothesized that [stress and immunosuppression secondary to COVID-19 infection](#) may be other possible reasons for the manifestation of such lesions in COVID-19 patients (Iranmanesh et al. 2021).

WHY RESORTING TO NON-DRUG TREATMENTS?

Ulcerations of the oral mucosa are treated mainly by anti-inflammatory, pain-relieving and healing promotion approaches. Anti-inflammatory responses may be achieved using mouthwash (i.e., chlorhexidine solution, povidone-iodine, borax) and chamomile-based solutions as well as by applying lidocaine hydrochloride gels to the ulcer area to achieve pain relief; [anti-ulcer powders, ointments, films, patches, pastes, gels and so on can be used topically to promote healing](#) (Guo et al. 2020). Lack of oral hygiene, opportunistic infections, stress, underlying diseases (diabetes mellitus, immunosuppression), trauma (secondary to intubation), vascular compromise, and hyper-inflammatory response secondary to COVID-19 might be the most important predisposing factors for the development of oral lesions in COVID-19 patients (Iranmanesh et al. 2021).



Indeed, [some authors speculated that an increase in periodontopathic bacteria due to poor oral hygiene aggravates COVID-19](#). The reduced likelihood of professional oral care associated with the long-term hospitalization of COVID-19 patients may increase the risk of inflammation in the lower respiratory tract. Therefore, [good oral hygiene can potentially prevent COVID-19 exacerbation by reducing the amount of aspirated oral bacteria](#) (Takahashi et al. 2021). For example, [some case reports suggested the use of mouthwash containing hyaluronic acid and chlorhexidine](#) (Martín Carreras-Presas et al. 2021) or corticosteroids and palliative drugs to treat mucosal symptoms. Antifungal or antibacterial therapy was also prescribed, where the etiology was relevant (Eghbali Zarch and Hosseinzadeh 2021).

WHY HIGH MOLECULAR WEIGHT HYALURONIC ACID?

Hyaluronic acid (HA), or hyaluronan, is a naturally occurring non-sulphated, linear polymer composed of repeating units of glucuronic acid and N-acetylglucosamine (Chen and Abatangelo 1999; Kavasi et al. 2017). HA levels are particularly high in the extracellular matrix of tissues, such as the oral mucosa, undergoing rapid turnover and where regeneration and repair occur (Valachová et al. 2016). HA has many different functions, including maintenance of tissue homeostasis and cell surface protection, but is also involved in many physiological processes, such as cell attachment, migration and proliferation, embryogenesis, wound healing, and regulation of immune response and inflammation (Kavasi et al. 2017). High molecular weight hyaluronic acid (HMWHA) is deposited in normal tissues and interacts with other components of the ECM to



control the ECM structural organization and signaling. Endogenous HMWHA has a highly complex secondary and tertiary structure in aqueous solution and possesses enhanced anti-angiogenic, anti-inflammatory and immunosuppressive properties (Kavasi et al. 2017). The amphophilic nature of HMWHA allows this molecule to trap large amounts of water while binding to hydrophobic molecules such as cell membrane lipids. This property is relevant to the control of hydration and helps to delay the passage of viruses and bacteria through the hyaluronan-rich pericellular zone, as well as during inflammatory processes (Chen and Abatangelo 1999). Clinical studies have shown that HA accelerates the healing of various types of wounds, including burns, epithelial surgical wounds, and chronic wounds (Shaharudin and Aziz 2016).

Why Aftamed®?

Aftamed® is a specific and innovative treatment for mouth ulcers that relies on the action of its main component, high molecular weight hyaluronic acid (HMWHA) to make the product strongly bioadhesive, an effect that can be enhanced by using a calibrated mixture of additional glycopolymers. Because of its adhesive properties, Aftamed® sticks to the oral mucosa long enough to promote the activation of physiological tissue repair processes which improve the healing response and reduce healing time. In addition, the presence of high molecular weight hyaluronic acid helps Aftamed® maintain the balance of extracellular fluids and promotes the resorption of oedema in inflammatory conditions, rapidly reducing the associated pain. Last but not least, it protects the oral mucosa by preserving the micro-environment of the mucosal surface

and by regularizing the growth of bacterial flora. The evidence on Aftamed® includes clinical data from prospective, comparative studies and can thus be considered of high quality (Nolan, 2006; Nolan, 2009; Koray, 2016). The studies covered various Aftamed® indications, including treatment and pain control of recurrent aphthous stomatitis or recurrent aphthous ulceration and the management of oral lichen planus. In all cases, patients were treated with multiple applications of the gel formulation and, depending on the study, the follow-up period varied between 7 and 29 days. Together, the available studies provide sound clinical data on the efficacy and safety of topical treatment with Aftamed®.



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