**Short communication**

# Taste Perception and COVID-19

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## Introduction

COVID-19, the coronavirus disease 2019, an infection of the Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2), needs no introduction. As of 1st March 2022, over 5.9 million individuals have lost their lives to the disease, globally[1]. Although the world population is hurtling to get vaccinated against this dreadful disease, the scientific community is still grappling with the conundrum of finding cures for the persistent, long-term symptoms (over four weeks after infection) in recovered individuals, commonly referred to as the long COVID-19[2]. Factors such as cellular damage due to either the disease or treatment or both, persistent viral shedding, body's response to the immune inflammatory process, and the enhanced tendency for blood clotting induced by the infection, have all been hypothesized as contributing factors to the symptom sequelae[3].

Among the myriad clinical symptoms of COVID-19, an abrupt impairment or loss of the sense of taste (hypogeusia/ageusia/dysgeusia) has been reported frequently[4]. Over a short span of time and numerous case reports later, this symptom has been identified as a significant one, because of its presence, at times, as the only clinical symptom when all other typical symptoms such as such as fever, cough, respiratory failure, are absent during an episode of COVID-19 infection. In many cases, it is accompanied by the impairment or loss of the sense of smell (hyposmia/anosmia). These symptoms are recognized as common symptoms in patients even in their asymptomatic phases. Furthermore, loss of taste or ageusia has been commonly reported as a persistent symptom of long COVID-19, and in many cases with little improvement after two months which could be worrisome especially in patients with co-morbidities[5,6]. Following is a brief note on the physiology of the gustatory mechanism and the etiopathogenesis of its impairment in long COVID-19.

## The Gustatory Mechanism

The sensation of taste occurs when three specialized nerve fibres are activated, namely taste, orosensory, and gastrointestinal fibers[7]. As we are well aware of, the taste buds, are widely distributed in the papillae of the tongue, palate, larynx, and oesophagus, and form the chemosensory units. Each taste bud is made up of about 50 to 100 specialized epithelial cells. These cells are called the taste receptor cells and are of three types, viz. type-I also known as the glial-like cells, type-II cells which express G-protein coupled receptors (GPCR) for sweet,

bitter, or umami tastes, and type-III which are presynaptic cells. Intercellular transfer of information takes place between the gap junctions of these cells that are chemically and electrically charged. The taste buds open on their apical end through a pore filled with microvilli and are innervated by the cranial nerves V, VII, IX and X which transmit information about the chemical nature and quantity of the substances tasted (tastants). Also, these cells are encircled by general sensory thermoreceptors and mechanoreceptors that convey the thermal and physical properties of foods. On the whole, the peripheral gustatory system transmits the sensory information of the tasted foods through neural pathways to the brain resulting in specific taste perception[7].

## The Perception of Taste

The tongue is usually covered by a mucosal film commonly referred to as the "tongue film". Food substances that we eat diffuse through this mucosal film to the apical opening of the taste buds, and the stimulation of the taste receptor cells takes place[8]. Studies have shown that this 'tongue film' harbours unique ecological niche for microbial colonization. The by-products of these microbial metabolism can modulate the threshold for specific taste sensation [9]. The tongue film in healthy individuals is found to be rich in bacterial species of the Fermicutes phylum that metabolizes lactate producing acetate and proprionate by-products[10]. When a high proportion of acetate is present in the vicinity of the taste receptor cells, an increased threshold for sweet perception is noted. On a similar note, a high concentration of organic acids in the tongue film, reduces the sensitivity for fat perception[8]. The turnover rate of taste bud cells is about 8-12 days, as they undergo continuous renewal. Homeostasis of these cells is dependent on the regular supply of properly differentiated taste receptor cells. If the turnover is rapid then an increases in the rate of cell extrusion and apoptosis is seen, to avoid overcrowding and maintain the homeostatic status [11]. Thus, the epithelial cells in healthy tongue films are in different stages of differentiation, such as the basal, parabasal, intermediate, and superficial keratinized cells. The rate of multiplication of epithelial cells, quantity of desmosomes and membrane-coating granules are factors that affect the formation of the tongue film [9]. Solubilizing, diluting, and chemical modification of the food substance can depend on the microbial composition and the saliva in tongue films[10].

## Etiopathogenesis of the Gustatory impairment in COVID-19

The infectivity of an invading virus is dependent on the local commensal microbiota. In most instances, the invading viral organisms increase the prevalence or survival of the pathogenic/opportunistic organisms, thus disrupting the normal host-microbiota homeostasis and causing dysbiosis and upregulates the inflammatory response. This in turn determines the immune modulation and response, and the extent of the viral infection in the host [12]. Virally attacked epithelial cells display biochemical changes due to the degradation of host proteins and synthesis of viral proteins. For instance, in influenza virus infection, there is a reduced secretion of growth factors which retard stem cell activity, upregulate inflammation and apoptosis of taste bud cell apoptosis. These events have been hypothesized as mechanisms for the chronic taste and smell loss in influenza virus infection[13]. In SARS-CoV-1 infection,

patients have been shown to present pale red tongue suggestive of exfoliation of less differentiated cells [14].

It is now known that the taste bud cells, and other oral epithelial cells express angiotensin-receptor-2 (ACE2), the entry receptor for viruses of the Coronaviridae family including the SARS-COV-2. Besides this, we know that the taste bud cells also express TLRs, especially TLR 2.3 and 4 are highly expressed in the gustducin-expressing type II taste bud cells[15]. CoV-2 replication and infection has been to occur within the taste bud cells. This causes a breakdown of the gustatory mechanism by direct invasion and inflammation of the taste bud cells[16]. CoV-2 is capable of using multiple entry receptors such as the salivary sialic acid receptors and the toll like receptors (TLR) to enter the host. Sialic acid is a component of saliva that protects the glycoproteins responsible for the transport of molecules stimulating taste in the taste pores. When SARS-COV-2 binds to salivary sialic acid receptor, the transport of the food substance through the glycoprotein is affected. This eventually leads to an impaired taste perception[15]. Similarly, the binding of the CoV-2 to TLRs could impair taste sensation[16]. It has been established that with a high serum level of the pro-inflammatory cytokine interleukin 6 (IL-6), there has been disturbances in gustatory response. IL-6 has been found to be persistently high in he serum of COVID-19 patients[17]. Furthermore, persistent inflammation increases the incidence of epithelial cell exfoliation. These exfoliated cells harbour the viral particles and could be a reservoir for viral RNA in saliva of patients with persistent long COVID-19, thus impairing gustation for longer duration[18]. The predominance of Prevotella salivae and Veillonella infantium in COVID-19 patients' oropharyngeal swabs has been found to correlate with an increase in inflammatory cytokines[19].

## Summary

Prolonged impairment of the gustatory mechanism and the shedding of viral RNA particles are suggestive that reservoirs for SARS-CoV2 within the taste receptor cells and epithelial cells exist, acting as a source for active or latent taste dysfunction in long COVID-19. Due to the presence of the viral particles in saliva, there is an imbalance in the normal ecological balance of the oral environment, causing dysbiosis and altered epithelial homeostasis. This further causes an upregulation of the surge of pathogenic microbes and prolonged inflammation, resulting in the persistent release of pro-inflammatory cytokines. With persistent inflammation, an increase in the exfoliation of epithelial cells is seen, thus increasing the viral load in saliva. The failure to replenish the lost epithelial cells swiftly due to altered cell turnover could result in fewer taste receptor cells concomitantly leading to persistent taste disturbance.

## Conclusion

Impairment in the gustatory mechanism seems to be a significant and sometimes early symptom in COVID-19, and could present as ageusia, hypogeusia or dysgeusia. Due to this symptom, patients could experience lack of appetite and interest in eating which may result in reduced food intake that can translate to lower energy levels and malnutrition. This could be very crucial for patients with co-morbidities. For this reason, basic knowledge of the gustatory mechanism and awareness of this important symptom is pivotal for dentists and dental students, to help in the early detection and diagnosis of COVID-19 cases in future.

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