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# Loss of Smell and Taste as Clinical Onset of COVID-19

*Nihal Seden*

## Abstract

Initially, symptoms of COVID-19 associated with Ear-Nose-Throat were thought to be flulike symptoms in the foreground. Such as fever, chills, cough, dyspnoea, myalgia, headache, sore throat. Olfactory and gustatory dysfunction was not a noticeable symptom at first. As the number of cases has risen worldwide, sudden onset hyposmia/anosmia has received increasing attention as a symptom of COVID-19. The reported incidence of anosmia varies internationally: as low as 30% in South Korea, and as high as 88% in Europe. The loss of smell that occurs in COVID-19 infection its general character is sudden onset anosmia. There is currently no specific treatment for COVID-19 related anosmia. Olfactory dysfunction can heal spontaneously. However, not a small number of patients may have permanent impairment.

**Keywords:** olfactory dysfunction, postviral anosmia, COVID-19 related anosmia, ENT

## 1. Introduction

Like all healthcare workers, Ear-Nose-Throat (ENT) specialists did not hesitate to take part in the forefront of the epidemic, and investigated the issues where they could benefit both in terms of their expertise and as primary physicians in combating the pandemic.

Initially, symptoms of COVID-19 associated with ENT were thought to be flulike symptoms in the foreground. Such as fever, chills, cough, dyspnoea, myalgia, headache, sore throat, etc. [1]. Olfactory and gustatory dysfunction was not a noticeable symptom at first. In the first studies reported from China, there were no evidence of patients with symptoms of changes and/or loss of smell and taste [2–4]. As the number of cases has risen worldwide, sudden onset hyposmia/anosmia was received increasing attention as a symptom of COVID-19. Due to the efforts of the American Academy of Otolaryngology-Head and Neck Surgery and the British Association of Otorhinolaryngology-Head and Neck Surgery, sudden onset hyposmia and anosmia were accepted as symptoms of COVID-19 by the Centers for Disease Control and Prevention (CDC) and the World Health Organization on 17 April 2020 and 4 May 2020, respectively [5–7]. The reported incidence of anosmia varies internationally: as low as 30% in South Korea, and as high as 88% in Europe [8]. Various hypotheses are on the agenda as to what might cause this difference. One hypothesis is focused on the ethnicity-host factor. A meta-analysis, reported on nearly 40,000 patients across 104 studies found that anosmia (and ageusia) is more prevalent in Caucasians than Asians (54.8 vs. 17.7%, respectively) [9]. In another hypothesis, spike protein mutations - pathogenic factor - are questioned as the cause of the difference in smell loss [10].

In a multicenter European study, a total of 357 patients (85.6%) had olfactory dysfunction related to COVID-19 infection. Among them, 284 (79.6%) patients were anosmic, and 73 (20.4%) were hyposmic. Phantosmia and parosmia were noted in 12.6% and 32.4% of the patients during the disease course, respectively [11]. As we leave behind a year of the pandemic today, the sudden onset of odor loss and taste disturbance are now among the most important ENT-related symptoms, and olfactory disorder is the best predictor of COVID-19 status of all the associated symptoms [12].

## **2. Pathophysiology**

Coronaviruses are known to cause odor loss from previous studies [13]. However, the pathophysiological mechanism of COVID-19 that causes odor and taste disorders has not been fully clarified yet.

### **2.1 Pathophysiology of gustatory dysfunction**

In humans, the sense of taste is carried by three cranial nerves. Facial nerve (7th cranial nerve), glossopharyngeal nerve (9th cranial nerve) and vagus (10th cranial nerve). When the terminal branches are stimulated, the sense of taste reaches to the nucleus solitarius in the brainstem and then it is carried to the thalamus. Hypogeusia can develop through the involvement of one of these three nerves, the nucleus solitarius or tract, or any of the thalamus nuclei. Angiotensin-Converting Enzyme 2 (ACE2) receptors, which allow SARS-CoV-2 to attach to the tissue, are widely expressed in the mucous membrane of the entire oral cavity, especially in the tongue [14–16]. The role of ACE2 in modulating taste perception has been emphasized in many studies analyzing the chemosensitive side effects of ACE2 inhibitors and angiotensin II blockers [16, 17]. Taste disturbance usually regresses after cessation of treatment. Also, a condition recently identified for SARS-CoV-2 is that it can bind to sialic acid receptors [18]. Sialic acid is an essential component of saliva mucin and protects glycoproteins that transport taste molecules into taste pores from early enzymatic degradation [16]. A decrease in sialic acid in saliva is associated with an increase in the threshold of taste [19]. Although it has been suggested that the deterioration in the perception of smell may also cause the loss of taste function due to the close functional link between these two chemosensory systems, the sense of taste seems to be more affected in recent publications.

### **2.2 Pathophysiology of olfactory dysfunction**

Chen et al. reported that ACE2 immunohistochemical expression was 200 to 700 times greater in the sustentacular cells of the olfactory neuroepithelium than nasal or tracheal epithelia [20]. An animal study, showed increase in macrophages in the olfactory epithelium and lamina propria after SARS-CoV-2 infection [21]. Generally, most data indicate that the main targets of SARS-CoV-2 are sustentacular cells in the olfactory epithelium [20–24].

These results show that hyposmia or anosmia is mainly caused by nasal epithelial infection and not a result of general malaise.

## **3. Diagnosis of olfactory and taste disorders in COVID-19**

In many studies on the transmission method of the SARS-CoV-2 virus, it has been shown that this virus is transmitted by droplets. Objective olfactory tests may pose a risk of contamination and therefore require extra precaution.

Commonly used objective olfactory tests are the Connecticut Chemosensory Clinical Research Center (CCCRC) test, University of Pennsylvania Smell Identification test (UPSIT), the Sniffin' Sticks method and the Odor Stick Identification test (OSIT). The UPSIT has four "scratch and sniff" booklets that each contain 10 microcapsule fragrances. After people open the capsule, they smell the page in the booklet [25, 26]. In the CCCRC test, fragrances are offered in bottles that are not transparent [27]. Sniffin' Sticks are felt tip pens impregnated with scents that are handed to the patient to smell [28]. In the OSIT test, the researcher folds a piece of fragrant paraffin paper in half to crush the microcapsule and then offers it to the participant. The participant then opens and smells the paper [29]. For the Sniffin' Sticks and CCCRC tests, the odor threshold is considered along with the ability for odor discrimination, while discrimination alone is assessed in the UPSIT and OSIT.

As for the taste, since taste tests can be performed with disposable strips, they can be used safely in patients with taste disorders.

Many studies have been published on COVID-19 and odor disorders since the beginning of the pandemic, and because of the contamination risk, the vast majority were subjective reports based on questionnaires or self-reports [30–32]. However, in studies that will be done by performing objective odor tests on patients, reports about the importance of obtaining data started to increase; for example Leichen et al. examined 86 patients for anosmia and hyposmia rates by testing with Sniffin' Sticks test, which is a psychophysical odor test. A total of 33 (38%) patients who reported that they had a loss of smell were normosmic according to the Sniffin' Sticks test. In the anosmic group, 78.8% of the patients stated that they had a loss of smell [33]. We had managed to evaluate olfactory objectively, without any risk of contamination, by a method that we described at our study [34].

#### **4. Clinical features**

The general feature of loss of smell in COVID-19 infection is sudden onset anosmia. Gane et al., stated in their case series, the isolated sudden onset anosmia syndrome (ISOA), could be the only finding of COVID-19 without any other symptoms [35]. Usually, olfactory disorder is not accompanied by nasal congestion or rhinorrhea.

Olfactory dysfunction due to COVID-19 infection seems to effect females and young individuals more commonly.

Is this odor dysfunction completely reversible, or how long should a patient wait for full recovery of olfactory function? There have been many studies on the alleviation of the loss of smell in COVID-19 [36–45].

Complete recovery of olfactory dysfunction varies between 11-49% and up to 25% of the patients seems to show no improvement at all.

#### **5. Treatment**

There is currently no specific treatment for COVID-19 related anosmia. Olfactory dysfunction can heal spontaneously. However, not a small number of patients may have permanent impairment. Efficacy of the treatments are unknown due to lack of data; treatments targeting post-infectious olfactory dysfunction could potentially be beneficial for COVID-19. While the use of systemic steroids is not recommended in patients with odor loss, the use of spray form and long applicators has been found appropriate for nasal steroids [46]. Fragrance therapy gives

successful results in postviral odor loss, especially when it is started early and used for at least three months. Therefore, in the loss of smell associated with COVID-19, fragrance therapy, including rose, lemon, clove and eucalyptus fragrances, each scent is sniffed for twenty seconds twice a day [47].

## **6. Other ENT related symptoms of COVID-19**

In patients without pneumonia, the COVID-19 clinic is similar to some diseases frequently encountered by ENT physicians in the outpatient clinic. COVID-19 can be confused with the flu or common cold in terms of initial symptoms, causing patients to apply to the ENT clinic in the foreground. There may be serous nasal discharge, hyperemic oropharynx, watery eyes and tearing. Since hoarseness is not among the symptoms mentioned, it may be thought that there is no cause of laryngitis or findings similar to laryngitis are not found on examination. Sore throat is a common symptom of COVID-19. Most of pharyngitis or sore throat is of viral origin and these pathogens are predominantly rhinovirus, influenza, adenovirus, coronavirus (previously isolated types) and parainfluenza virus [48].

Other human corona viruses are common cause of viral pharyngitis. Considering that, Sars-CoV-2 is likely to cause pharyngitis and/or similar clinical features.

Both possibilities should be kept in mind in a patient presenting with hyperemia in the oropharynx and difficulty swallowing. Unfortunately, in the current situation, definitive diagnosis distinction can only be made by laboratory testing. The rapid progression and sudden onset of the disease should be thought-provoking for COVID-19.

It should be kept in mind that COVID-19 can also cause rhinitis. It may have similar symptoms with allergic rhinitis. Although fatigue and weakness due to sleep disturbance in allergic rhinitis are reported; muscle pain, malaise and sore throat are not expected. Watery and red eyes may occur in both diseases, but itching in the eyes, palate and nose can be a guide for allergic diseases. Likewise, flu and cold are other common diseases that can be confused with COVID-19. While runny nose is more common in colds than other diseases, in influenza and Sars-CoV-2 infection dry cough is in the foreground.

## **7. Conclusions**

In the fight against COVID-19, it would not be wrong to say that the most important and alarming symptoms specifically to ENT are odor and taste disorders. It should be kept in mind that these deficits do not heal completely in all patients.

## **Conflict of interest**

None.

## **Thanks**

I dedicate this book chapter to all healthcare professionals who work devotedly in combating the epidemic, and especially to colleagues who have lost their lives.

With respect and mercy.



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