

# CHAPTER 21

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## ANOSMIA and COVID-19

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### INTRODUCTION

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In December 2019, the Coronavirus outbreak first occurred in Wuhan of China. Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2), a part of the Coronavirus family, caused a pandemic in all over the world. On February 12, 2020, the World Health Organization (WHO) defined the disease which is caused by a new version of coronavirus as COVID-19.

Coronaviruses are enveloped, single-stranded RNA viruses. They affect humans, bats, cats and rodents in the environment. Alpha ( $\alpha$ ) and beta ( $\beta$ ) coronaviruses are often the cause of respiratory diseases in humans and gastroenteritis in animals. SARS-CoV-2 is a coronavirus belonging to the  $\beta$ -coronavirus subgroup. In one study, it was reported that SARS-CoV-2 is a chimeric virus between bat coronavirus and an unknown coronavirus. Furthermore, snakes were found to be the most likely habitat for SARS-CoV-2.

In the early stages of the epidemics symptoms such as fever, shortness of breath and cough are observed. In addition, headache, nasal congestion, runny nose, tonsil swelling, sore throat, fatigue, conjunctivitis, smell and taste disorders (dysgeusia) are also observed during COVID-19 disease. In the course of

the disease, many organs, especially the lungs, may be affected. In COVID-19 disease, the disease is mild or asymptomatic in 80-90 % of the cases. The mortality rate varies according to studies, but it is in the range of about 2-5 %.

Postinfectious olfactory dysfunction (OD) is a symptom that can be seen after viral and bacterial infections. It is thought that it results from neuroepithelial dysfunction. OD can be seen in different ways such as anosmia, hyposmia, dysgeusia, and phantosmia. It is known that anosmia that occurs after upper respiratory tract infection accounts for 40 % of cases and is generally associated with nasal obstruction and mucosal congestion. It was also accepted that it is occurred due to nasal mucosal swelling and conduction blockage to the olfactory cleft region. Postviral anosmia studies have shown absence of cilia. In addition, it showed that olfactory sensory neurons transform into metaplastic squamous epithelium. Fornazieri et al. have been reported the frequency of anosmia as 13-26 % due to upper respiratory tract infection. Additionally, Suzuki et al. detected coronavirus, rhinovirus, parainfluenza virus and Epstein-Barr virus in the nasal secretion of individuals with different diseases after viral infection. Various animal studies have also shown that viruses can damage central olfactory pathways and other brain regions.

At the onset of COVID-19, anosmia was not among the clinical symptoms. However, on March 26, the American Academy of Otolaryngology – Head and Neck Surgery (AAO-HNS) published a statement highlighting that anosmia with dysgeusia is a symptom associated with COVID-19 patients. The Academy has set up the COVID-19 Anosmia Reporting Tool, an online survey (COVID-19 Anosmia Reporting Tool for Clinicians) for patients to submit data around the World. On April 17 (Centers for Disease Control and Prevention), the CDC summarized and updated the most common symptoms of COVID-19, adding “new taste or smell loss” to the symptom list.

COVID-19 is a neurotropic virus. The virus not only affects the respiratory tract, but also causes neurological symptoms. Neurological symptoms are observed in 1/3 of the patients. Anosmia is also an accepted symptom among neurological symptoms. Anosmia may be an isolated symptom or associated with other general and otolaryngological symptoms. Among covid patients, the incidence varies between 30-88 %. In the study by Mao et al., 36.4 % of COVID-19 patients had central nervous system findings and anosmia was reported in approximately 5 % of these patients. It has been reported that it is more common in women and approximately 70% of the patients have sudden onset. A recent study found that 45% of COVID-19 patients had OD.

Anosmia is one of the most common symptoms seen in COVID-19 patients. In 5% of patients with COVID-19, the first symptom is anosmia. OD starts suddenly in most cases, usually lasts 1-3 weeks and is a temporary condition. One study found that patients generally develop anosmia in 8.96 days, 4.4 days after the SARS-CoV-2 infection, and found that 98 % of patients were able to recover within 28 days. The prevalence of taste and / or smell disorders in COVID-19 proved to be significantly higher than patients with influenza, at a frequency of 12.5 % and 39.2 %, respectively. An artificial intelligence study found that the prevalence of anosmia / taste disturbance was 28.6 times higher in COVID-19 positive patients than in COVID-19 negative patients.

## **PATHOGENESIS**

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Although the pathogenesis of COVID-19 anosmia is not completely described, it has been suggested that there may be obstruction, inflammation, and damage of the olfactory region. On the other hand, no significant association was found with symptoms such as nasal congestion and mucosal inflammation in COVID-19 anosmia. This result suggests that mechanisms other than sinusal obstruction may play a role in COVID-19 anosmia. Another potential mechanism is direct damage to the olfactory nerves and retrograde invasion of the olfactory pathways. Anosmia is more widely accepted that the virus does not affect the olfactory neurons directly, but may be due to damage to the other cells of the olfactory epithelium.

SARS-CoV-2 can affect OD in several ways; such as parosmia, phantosmia, hyposmia or anosmia. In addition, taste disturbances may accompany OD. The pathophysiology of the effect of this disease on OD has not been fully established. However, it is reported that the virus reaches the olfactory bulb via the angiotensin converting enzyme 2 (ACE2) receptor located in the basal surface of the nasal mucosa.

The ACE2 receptor is intensely expressed in the nucleus tract solitarius and ventrolateral medulla, which are involved in the organizing of the respiratory period in the brain. Additional, ACE2 receptor and transmembrane protease serine 2 (TMPRSS2) are very abundant in the olfactory bulb. In recent studies, ACE2 release was found to be higher in the olfactory mucosa. The high incidence of these receptors in the olfactory bulb may explain the high affinity of the SARSCoV-2 virus using the same receptor. Therefore, it has been accepted that the way the virus enters the human cell is through the ACE2 receptor.

## DIAGNOSIS METHODS

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Studies have found that patients with mild cases of COVID-19 are much more likely to develop anosmia than patients with moderate to critical cases. Studies have found the rates of anosmia up to 70 % of patients with the mild form of COVID-19.

Magnetic resonance imaging (MRI) of the olfactory pathway is an useful anatomical imaging method for evaluating olfactory function disorders associated with postviral infection, neurodegenerative diseases and trauma. Studies have shown that the width and volume of the olfactory cleft increase in patients with postviral anosmia. In studies conducted with Covid-19, various radiological results were obtained. Galougahi and Eliezer, reported normal olfactory bulb volume with normal signal intensity in COVID-19 patients. Aragao et al. showed an abnormality of the olfactory bulb as micro bleeding or an abnormal increase at MRI. Laurendon showed severe enlargement of olfactory bulb with abnormally high signal intensity in T2, consistent with bulb edema in a COVID-19 patient with anosmia. In the COVID-19 case with anosmia report by Li, MRI of the bilateral olfactory bulb showed a decrease in the right olfactory bulb volume and an increase in linear hyperintensities. In one case report of COVID-19 patient with anosmia by Politi at the MRI of the bilateral olfactory bulb, it was accompanied by right gyrus and mild rectus hyperintensity was seen. The width and volume of the olfactory crest were found to be significantly higher in patients with anosmia caused by SARS-CoV-2.

Smell tests are used to determine OD. Smell tests are generally of two types, psychophysiological and electrophysiological. Psychophysiological tests can be grouped into 3 groups: smell detection, smell discrimination and identification. For identification, CCCRC (Connecticut Chemosensory Clinical Research Center Test), UPSIT (University Of Pennsylvania Smell Identification Test), B-SIT (The Brief Smell Identification Test), OSIT (Odor Stick Identification Test), Sniffin Sticks (SS) test are used. Electrophysiological tests are of two types: electro-electrography and evoked olfactory potentials. The most common SS test is used in Europe. Using the SS test, smell discrimination, smell threshold and smell identification tests can be performed. These tests can also be used in anosmia due to COVID-19.

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## TREATMENT

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It is possible to treat anosmia due to organic causes such as tumor obstructing the nasal passage, polyps, infectious and mechanical reasons. When these reasons are absent, the results of the treatment are not satisfactory. Vitamin A and B treatments have been tried in the problem of smell. It is known that vitamin A provides epithelial regeneration. However, these vitamins have not been found to have a healing effect on smell. In addition, considering its positive effect on wound healing, zinc treatment was tried, but there was no clear clinical response on smell. Sharp smells and smell exercises are applied in the current treatment of anosmia due to COVID-19.

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## CONCLUSION

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In the case of anosmia and hyposmia without any upper respiratory tract infection, it should be taken a symptom that requires caution in terms of Covid 19. In addition, a person presenting anosmia and hyposmia complaints may need an evaluation of the central nervous system involvement. However, it is obvious that larger studies are needed in this respect.

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