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Review Article

# Anosmia, hyposmia, and dysgeusia as indicators for positive SARS-CoV-2 infection

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## Introduction

As cases of the novel coronavirus, also known as severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) continue to rise, the way in which healthcare is practiced has been markedly impacted. The presence of this new threat has changed the paradigm of society as many self-quarantine, socially distance, and avoid contact to mitigate the rapid spread of the virus. As new evidence regarding SARS-Cov-2 from the World Health O'rganization (WHO) and Central of Disease Control and Prevention (CDC) are reported, medical practice guidelines are in constant flux regarding patient care. In the span of the recent weeks, elective surgeries have been cancelled, non-urgent office visits rescheduled, and even practice of physical exams and diagnostic tests have changed. It is of no surprise that the practice of otolaryngology has been affected, as new guidelines emerge daily from the American Academy of Otolaryngology — Head and Neck Surgery (AAO-HNS), multiple international otolaryngologic societies, and various affiliated university otolaryngologic departments.[1—4] These guidelines have been put in place to curtail the feared development of coronavirus disease 2019 (Covid-19), the disease caused by SARS-Cov-2 in the susceptible patient population.[5] Though practice guidelines have been put in place to mitigate spread among healthcare workers, the identification of infected patients remains at the forefront in reducing transmission within the community. Since PCR testing has been limited, healthcare workers must rely on screening. However, it has been observed that rapid changes in SARS-CoV-2 screening are related to the constant influx of newer evidence as it comes to light.

Among the latest developments, it has come to the attention of many practitioners (not limited to otolaryngologists) that anosmia, hyposmia, and dysgeusia may be strongly correlated with SARS-CoV-2 infection. Otolaryngologists practicing in high incidence locations in Asia, the Middle East, and Europe have attributed these symptoms to be directly linked to the current rise of SARS-Cov-2 infection worldwide.[6—9] The current data about SARS-Cov-2 have been primarily anecdotal, as these reports are communicated with international colleagues within medical community message boards. Peer-reviewed content is extremely limited as we are only at the outset of the pandemic. At present, the pathophysiology of anosmia, hyposmia, and dysgeusia can only be

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deduced from previous studies and models regarding post viral olfactory dysfunction (PVOD).

In this article, we review the current literature on PVOD as it pertains to the current SARS-CoV-2 pandemic. Additionally, we hope to strengthen the recommendations placed by the AAO-HNS and its affiliates for the use of anosmia, hyposmia, and dysgeusia as part of the screening protocol. Lastly, we evaluate the current practice guidelines and recommendations regarding Covid-19.

## Methods

### Literature review and evidence collection

Several questions were raised regarding the recent spike of SARS-CoV-2 cases worldwide and the surge of individuals reporting anosmia, hyposmia, and dysgeusia, and how these symptoms would affect screening, diagnosis, and practice guidance. The proposed mechanism of SARS-CoV-2 induced anosmia is likely what has been previously reported in the literature as PVOD. A literature review was performed by one author searching for all published English-language literature reporting on PVOD. A search strategy was employed with the following search strings: "virus OR corona OR covid" with "anosmia OR olfaction disorder OR hyposmia OR dysgeusia OR olfactory dysfunction" in the last 5 years. An independent search query was also employed with "postviral olfactory". References of individual articles were also utilized. Results were limited to English articles. After the completed search, a total list of records was obtained, and duplicates removed. A final list of full text articles was then compiled, and each article was then screened independently by one author.

## Discussion

Olfactory dysfunction is a well-known phenomenon that has been explored robustly in the literature. Etiologies can be classified into three major categories: conduction, central, and sensorineural disorders, which need not be mutually exclusive.[10–12] Conduction disorders are seen in patients with allergic rhinitis, acute or chronic rhinosinusitis, where inflammation of the nasal mucosa disrupts the mechanical function of olfaction. Central olfactory dysfunction is seen in disorders of the central nervous system, commonly from neurodegenerative diseases or head injury, where olfactory bulb projections to the olfactory mucosa are sheared in the cribriform plate. Lastly, sensorineural olfactory dysfunction is seen in patients where degeneration of the olfactory epithelium and nerves occur secondary to a viral infection or less likely from a drug-induced impairment.[10,11,13] Differences in etiologies obviates distinct treatment approaches and management. For the basis of this article, we will focus on PVOD as it pertains to sensorineural dysfunction caused by a viral illness, correlating it with potential SARS-CoV-2 infectivity status.

Given what is known currently about SARS-CoV-2, evidence seems to point that the rapid spread of the virus is attributed to the long incubation period of up to 14 days, meaning individuals are infectious though they remain asymptomatic. SARS-CoV-2 has been described as a highly diffusible pathogen i.e. the virus has multiple means of spread, with high transmission efficiency. It is suspected that the virus is spread through droplet, direct contact, contact with an infected individual, fecal-oral, and body fluid routes.[14–16] The combination of being highly transmissible and asymptomatic attributes to its rapid spread.

A highly discussed and debated topic is SARS-CoV-2 screening, especially in asymptomatic patients or in individuals that do not meet the current criteria for testing, given that tests are limited and resources scarce. In order to mitigate the rapid spread and to avoid overwhelming the healthcare system, screening is paramount so that appropriate measures can be implemented such as self-isolation and social distancing, actions that reduce the propagation of inadvertent community spread.[5,17,18] One important, symptom that has been rapidly gaining precedence is anosmia. Hyposmia and dysgeusia are also reported at varying degrees.[8] Anecdotal reports have been gaining traction as anosmia has been commonly expressed in positive SARS-CoV-2 patients globally, ranging anywhere from 15% to 66%, often in the absence of any other symptoms.[6,8,9] Strikingly, the majority of these individuals are in their 20s, who otherwise might not feel the need to adopt necessary precautions as they are relatively asymptomatic and otherwise health.[8] However, given the rapidity of SARS-CoV-2 infection and the rise of olfactory dysfunction as being an only symptom in infected patients, it is imperative that these correlations be taken seriously. With the limited evidence, it becomes necessary to review the literature in order to guide current protocols during this time. No peer-reviewed data have been reported relating SARS-CoV-2 and PVOD, largely because symptoms of anosmia have only recently come to the attention of medical practitioners.

It is well known that various viruses such as influenza, adenovirus, various coronavirus strains (229E, NL63, OC43), bocavirus, metapneumovirus, parainfluenza virus (serotypes 1–3), and rhinovirus all can cause pneumonia and severe respiratory symptoms.[14,16] However, not all individuals routinely develop pneumonia or severe respiratory symptoms. In the majority of cases, infected individuals only experience mild upper respiratory symptoms; some may experience a variation of anosmia, hyposmia, or dysgeusia. In a study done by Suzuki et al,[19] patients that had an acute onset of PVOD without any prior history of olfactory dysfunction, sinusitis, allergic rhinitis, or neurological dysfunction were identified. Their selected cohort met the criteria of sensorineural olfactory dysfunction. Coronavirus (CoV 229E) was among the viral strains identified to cause anosmia. In a study by Akerlund et al,[20] PVOD developed after healthy human subjects with no previous olfactory deficiencies were inoculated with coronavirus. Interestingly enough, influenza has not been found to be a major contributor to PVOD. In a prospective study by Malhotra et al,[21] clinical features of patients infected with various viral strains were evaluated, of which, altered smell was one of the clinical symptoms investigated. Among the 30% of their study population that reported dysosmia, influenza was not significantly associated with a change in smell because only 10% of upper respiratory infections are caused by influenza. It is

important to note that coronavirus strains (229E, HKU1, NL63, OC43) were not tested and that their study does not identify which viral strains were associated with an altered sense of smell among their study group. It begs the question that coronavirus may have been among those infected that developed PVOD. We suggest that because coronavirus (non SARS-CoV-2 strains) is among the many viruses that collectively account for 70% of the common cold, which in turn can cause PVOD, its presence among their study population must be taken into consideration.[19] Furthermore, given that the SARS-CoV-2 is part of the larger family of coronaviridae, reports of asymptomatic, SARS-CoV-2 positive patients experiencing anosmia can be further evidenced by the aforementioned studies.[16]

The exact pathophysiology of PVOD is not well understood. The leading evidence suggests several mechanisms. Nasal mucosal inflammation and swelling from a viral infection obstructs airflow from adequately delivering odors to the olfactory mucosa.[19,20,22] Viral disruption of the olfactory mucosa may also participate in the severity of dysosmia, such that the severities and time courses observed in patients infected by the same virus may suggest a component of reactivity in the olfactory mucosa to the viral load and viral serotype.[19,20,22]

Anosmia is regularly evaluated by the otolaryngologist. However, in the midst of the current pandemic, practice guidelines have been rapidly changing. As recommended by the AAO-HNS and international societies, certain physical exams and procedures should be limited to urgent cases. Many physical exams and in-office procedures places the otolaryngologist in close proximity with mucosal tissue, blood, and aerosolized particles placing them at high risk.[14–17,23] This presents several problems as patients with anosmia warrant a full history and physical exam, where nasal endoscopy is standard in evaluating a patient with anosmia. Endoscopy provides valuable visualization of the nasal passageway that might reveal the presence of an obstruction, mucosal inflammation, polyps, or even malignancies that may obstruct the olfactory cleft.[10,22] These practice changes place the otolaryngologist and the patient in unique predicament. Without nasal endoscopy, a delay in a proper diagnosis places a patient at risk for delay of treatment, especially in more insidious etiologies such as malignancies.

Currently there is no therapeutic consensus in the treatment management of PVOD, most likely attributed to the majority of symptoms resolving with time.[19] In a guideline study for olfactory dysfunction proposed Miwa et al,[10] medical therapies for PVOD was given a low recommendation. Studies testing the efficacy of therapies for PVOD, including steroids had conflicting evidence. A critical review of possible treatments for PVOD and other olfactory disorders is provided by Doty.[24] Due to the high suspicions of anosmia in SARS-CoV-2 positive individuals, the use of corticosteroids is a direct contraindication to patients presenting with anosmia, notably in the absence of known head trauma or allergic symptoms. Reports have demonstrated that the use of corticosteroids may escalate Covid-19 infection.[6,25] As more evidence is revealed about SARS-CoV-2 and PVOD, more studies are needed to address therapeutic approaches to anosmia, dysosmia, and dysgeusia.

Nonetheless, the AAO-HNS and its affiliates stand by these statements that all non-urgent, non-emergent otolaryngology procedures are to be postponed in order to reduce the risk of SARS-CoV-2 transmission, which are all necessary strategies at this time to lessen the impact of a rapidly spreading and dangerous virus.[1–7,14,17,18]

## Conclusion

### Recommendation

With limited information and what has been reported in the literature, we propose that the current management of patients that present with anosmia, that cannot be evaluated otherwise, should be advised to self-isolate, social distance, or warrant testing of SARS-CoV-2. If for any reason, a patient with anosmia may need evaluation, it is essential that the otolaryngologist employ full personal protective equipment. Additionally, we support the recommendations of the AAO-HNS guidelines that the reported symptoms of anosmia, hyposmia, or dysgeusia are symptoms that should be used for screening of SARS-CoV-2 in asymptomatic patients. As healthcare workers depend on their administration and respective societies for guidance, we are anticipating these recommendations may aid in the action to mitigate the spread of this novel virus.

## Publication statement

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