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## Smell and taste dysfunction in patients with COVID-19

The plural of an anecdote is not evidence, yet anecdotal international reports are accumulating from ear, nose, and throat (ENT) surgeons and other health-care workers on the front lines that anosmia, with or without dysgeusia, are symptoms frequently associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The American Academy of Otolaryngology-Head and Neck Surgery and the British Association of Otorhinolaryngology are now recommending these symptoms be added to the list of primary screening symptoms for COVID-19.

Our understanding of an absent or diminished ability to smell or taste, resulting from a neurotropic or neurovirulent viral infection targeting the olfactory system, remains fragmentary and is largely historically informed. The clinical evaluation of the first cranial nerve (olfactory nerve or CN I) has all but dropped from history taking and physical examination; hence, it is often referred to by ENT professionals as the forgotten cranial nerve. To further complicate matters, immediate self-recognition of olfactory dysfunction is typically only present in the most severe cases, or it is only self-identified after a prolonged latency period.<sup>1,2</sup> A scarcity of acutephase advanced neuroimaging studies, difficulties in obtaining histopathological tissue specimens, and an absence of viral cultures of infected olfactory neuroepithelium compound the difficulties in studying this phenomenon. Moreover, in the context of normal trans-nasal airflow of odorant molecules (ie, no oedema in the nasal vault or olfactory cleft), and in the absence of intranasal disease (eg, infectious rhinosinusitis, allergic or vasomotor rhinitis, or polyposis), until now patients with sensorineural viral anosmia have been seldom seen in general otolaryngology practice on the order of approximately one to two new-onset patients each year. Hence, up until the coronavirus disease 2019 (COVID-19) pandemic, the low prevalence of sensorineural viral anosmia in society as a whole has made clinical research challenging.

Given the urgency and lethality of the current pandemic, knowledge obtained from front-line otolaryngologists who are currently managing and monitoring patients with COVID-19, and those with clinical experience in olfaction and rhinology, would have great value when transferred forward to deployed caregivers. Our multinational group, including one otolaryngologist currently infected with COVID-19 and experiencing anosmia and dysgeusia, suggest that physicians evaluating patients with acute-onset loss of smell or taste, particularly in the context of a patent nasal airway (ie, non-conductive loss), should have a high index of suspicion for concomitant SARS-CoV-2 infection. We have observed that traditional nasal cavity manifestations, as seen in other upper respiratory infections (eq, rhinovirus, influenza, and adenovirus), are commonly absent in patients with COVID-19. We have also observed that SARS-CoV-2 does not appear to generate clinically significant nasal congestion or rhinorrhoea-ie, a red, runny, stuffy, itchy nose. This observation suggests a neurotropic virus that is site-specific for the olfactory system. Although labelled as a respiratory virus, coronaviruses are known to be neurotropic and neuroinvasive.3-6 Finally, we and others7 have observed that anosmia, with or without dysgeusia, manifests either early in the disease process or in patients with mild or no constitutional symptoms.

Nevertheless, it is still too early in our understanding of COVID-19 to definitively establish the incidence, as well as the full-spectrum clinical utility, of these symptoms.

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- Xydakis MS, Mulligan LP, Smith AB, et al. Olfactory impairment and traumatic brain injury in blast-injured combat troops: a cohort study. *Neurology* 2015; 84: 1559–67.
- Xydakis MS, Belluscio L. Detection of neurodegenerative disease using olfaction. Lancet Neurology 2017; 16: 415–16.
- 3 Desforges M, Le Coupanec A, Brison E, et al. Neuroinvasive and neurotropic human respiratory coronaviruses: potential neurovirulent agents in humans. Adv Exp Med Biol 2014; 807: 75–96.
- 4 Li Y, Bai W, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. *J Med Virol* 2020; published online Feb 27. DOI:10.1002/jmv.25728.
- 5 Suzuki M, Saito K, Min WP, et al. Identification of viruses in patients with postviral olfactory dysfunction. *Laryngoscope* 2007; **117**: 272–77.
- 6 Mao L, Wang M, Chen S, et al. Neurological manifestations of hospitalized patients with COVID-19 in Wuhan, China: a retrospective case series study. SSRN 2020; published online Feb 24. https://dx.doi.org/10.2139/ ssrn.3544840 (preprint).
- Giacomelli A, Pezzati L, Conti F, et al. Self-reported olfactory and taste disorders in SARS-CoV-2 patients: a cross-sectional study. *Clin Infect Dis* 2020; published online March 26. DOI:10.1093/cid/ciaa330.



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