



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Hypogeusia was reported by 63 patients (24%), hyposmia by 51 patients (20%), both hypogeusia and hyposmia by 43 patients (17%), and ENT disorders by 82 patients (32%). Hypogeusia and hyposmia were strongly associated with COVID-19 diagnosis, separately and combined, in patients with and without a medical history of ENT disorders (appendix p 2). The best performance was obtained with the combination of hypogeusia and hyposmia in patients with no medical history of ENT disorders, with a sensitivity of 42% (95% CI 27–58) and a specificity of 95% (90–98; appendix p 2).

To our knowledge, this is the first report of discriminant clinical features that might be used for the diagnosis of COVID-19 in patients with ILI. Taste and smell disorders have been associated with herpes zoster and HIV.^{3,4} The neuroinvasive potential of SARS-CoV-2 might have a role in the pathophysiology of hypogeusia and hyposmia.⁵ As the olfactory mucosa is located in the upper region of the nasal cavity, a direct or indirect effect of SARS-CoV-2 in situ might be another explanation for these symptoms. The prevalence of taste and smell disorders in patients with COVID-19 was estimated to be 5% in a previous study;⁶ however, the data were retrospectively collected from medical files, which might have led to underestimation of the real prevalence. Indeed, these symptoms might not be spontaneously reported if not searched for.

This study has limitations. First, data were retrospectively collected through a web-based questionnaire, and we collected no data on age, sex, or other symptoms. Second, data were collected anonymously, so we could not check the accuracy of the diagnosis reported by patients. Third, the sample size was small and the response rate suboptimal. Finally, as the diagnosis relied on detection of SARS-CoV-2 by RT-PCR on nasopharyngeal samples, suboptimal

sensitivity of this test (as low as 60% in some reports) might have led to misclassification and diagnostic bias.⁷ However, this preliminary report of an association between hypogeusia or hyposmia and COVID-19 diagnosis in patients with ILI suggests that these symptoms might be a useful tool for initial diagnostic work-up in patients with suspected COVID-19. These symptoms, which are easy to collect, could be used for mass screening, by professionals with limited medical knowledge, and through telemedicine. Larger prospective studies are required to confirm these preliminary findings.

We declare no competing interests.

François Bénézit, Paul Le Turnier, Charles Declerck, Cécile Paillé, Matthieu Revest, Vincent Dubée, *Pierre Tattevin, for the RAN COVID Study Group†

pierre.tattevin@chu-rennes.fr

†Members are listed in the appendix (p 1)

Infectious Diseases and Intensive Care Unit, Pontchaillou University Hospital, Rennes, France (FB, MR, PT); Infectious Diseases and Tropical Medicine, Hotel Dieu, University Hospital of Nantes, France (PLT, CP); and Infectious Diseases and Tropical Medicine, University Hospital of Angers, France (CD, VD)

- 1 Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; published online Feb 28. DOI:10.1056/NEJMoa2002032.
- 2 Hopkins C, Kumar N. Loss of sense of smell as marker of COVID-19 infection. March 21, 2020. <https://www.sforl.org/wp-content/uploads/2020/03/Loss-of-sense-of-smell-as-marker-of-COVID-21-Mar-2020.pdf> (accessed April 4, 2020).
- 3 Heymans F, Lacroix J-S, Terzic A, Landis BN. Gustatory dysfunction after mandibular zoster. *Neuro Sci* 2011; **32**: 461–64.
- 4 Graham CS, Graham BG, Bartlett JA, Heald AE, Schiffman SS. Taste and smell losses in HIV infected patients. *Physiol Behav* 1995; **58**: 287–93.
- 5 Li Y, Bai W, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may be at least partially responsible for the respiratory failure of COVID-19 patients. *J Med Virol* 2020; published online Feb 27. DOI:10.1002/jmv.25728.
- 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. *medRxiv* 2020; published online Feb 25. DOI:10.1101/2020.02.22.20026500 (preprint).
- 7 Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in different types of clinical specimens. *JAMA* 2020; published online March 11. DOI:10.1001/jama.2020.3786.

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.^{1,2} A scarcity of acute-phase 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



Published Online
April 15, 2020
[https://doi.org/10.1016/S1473-3099\(20\)30293-0](https://doi.org/10.1016/S1473-3099(20)30293-0)

See Online for appendix

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 (eg, 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.

We declare no competing interests. The views expressed in this Correspondence do not necessarily reflect the official position of the US Department of Defense or any of the institutions with which the authors are affiliated.

***Michael S Xydakis,
Puya Dehgani-Mobaraki,
Eric H Holbrook, Urban W Geisthoff,
Christian Bauer, Charlotte Hautefort,
Philippe Herman, Geoffrey T Manley,
Dina M Lyon, Claire Hopkins
michael.xydakis@us.af.mil**

Department of Defense, United States Air Force Medical Corp (MSX), and Air Force Research Lab

(DML), Wright-Patterson Air Force Base, OH 45433, USA; Associazione Naso Sano, Umbria Regional Registry of Volunteer Activities, Corciano, Italy (PD-M); Harvard University, Massachusetts Eye and Ear, Boston, MA, USA (EHH); Philipps University Marburg, Marburg, Germany (UWG, CB); Lariboisière Hospital, Assistance Publique—Hôpitaux de Paris, INSERM U1141, Université of Paris, Paris, France (CHa, PH); University of California, San Francisco, CA, USA (GTM); and Guy's and St Thomas' Hospital, London Bridge Hospital, London, UK (CHo)

- 1 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.
- 2 Xydakis MS, Belluscio L. Detection of neurodegenerative disease using olfaction. *Lancet Neurology* 2017; **16**: 415–16.
- 3 Desforges M, Le Coupance 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).
- 7 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.