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interferon γ signalling was prominent. In animal models designed to understand the temporal profiles of the SARS and Middle East respiratory syndrome diseases, the authors showed that interferon α and interferon β action early in the disease was beneficial, but it was damaging in the later stages.⁴

This finding suggests that when hospital care is required for patients with a pathogenic SARS-CoV-2 infection, JAK-STAT pathway inhibition might be a potential strategy. In the current outbreak, we need to understand which patients might benefit from treatment with such cytokine inhibitors and whether more than one pattern of disease progression exists; stratification and prognostic models are required. Additionally, we need to identify the optimum time to administer cytokine inhibitors, which requires identification of appropriate biomarkers.⁵ Anecdotal experience suggests that the short time baricitinib might be used (duration of doses is 7–14 days) will not cause reactivation of any latent infections, such as herpes viruses or tuberculosis.

We and others are awaiting the results of investigator-led and other prospective studies (eg, NCT04320277 and NCT04321993) with numerous treatments, including baricitinib, in individuals with COVID-19. Because of the single-arm nature of such studies, data might be difficult to interpret, and we caution against headlines of a so-called cure when most infected individuals will recover. We also suggest that the systemic administration of interferons α and β to patients being treated in hospital might be harmful and explains why previous studies with interferons have yielded inconsistent results. Although we have ongoing concerns regarding the design of, and the drugs used in, the multicountry WHO SOLIDARITY trial (NCT04321616), which includes use of interferon β , the reality is that

all of these opinions, however valid, only lend credence to the evidence-based view that the optimal data are ultimately best obtained from randomised controlled trials.

PJR is an employee of Benevolent AI. JS is editor-in-chief of *Oncogene*. JS has sat on a number of scientific advisory boards, including Benevolent AI, and consults with Lansdowne partners and Vitruvian; he sits on the Board of Directors for BB Biotech Healthcare Trust and chairs Xerion Healthcare. MC declares no competing interests. Events in relation to the COVID-19 outbreak are evolving rapidly, and we make our initial thoughts available in this Correspondence in good faith and to assist in the global response. Our early investigations and suggestions require further detailed work and analysis and should not be relied on as constituting any kind of medical or other advice or recommendation.

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Utility of hyposmia and hypogeusia for the diagnosis of COVID-19

Early and accurate diagnosis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is key to the management of the coronavirus disease 2019 (COVID-19)

pandemic. Following its emergence in China in December, 2019, SARS-CoV-2 has spread in the northern hemisphere during the winter season, when other respiratory viruses, including influenza, co-circulate. This epidemiological conjunction complicates clinical diagnosis of COVID-19 because patients often present with influenza-like illness (ILI). Consequently, the definite diagnosis of COVID-19 mostly relies on positive RT-PCR on respiratory samples, although discriminant features have been reported on thoracic CT scan.¹ However, access to these diagnostic tests is limited in the context of this large-scale pandemic. Distinctive clinical features would be welcome to better select patients who require investigations. During the early phase of the COVID-19 outbreak in France, we noticed that many patients reported loss of smell (hyposmia) and taste (hypogeusia). We aimed to investigate the diagnostic value of these symptoms.

Rennes, Angers, and Nantes are referral centres for emerging infectious diseases in western France (population catchment area includes 5 million inhabitants). The study was done from March 15–18, 2020, at which time there was no public awareness of the potential link between taste or smell disorders and COVID-19 (the first report² was on March 21). All patients who underwent tests for SARS-CoV-2 by RT-PCR on nasopharyngeal samples since Feb 16 were invited by e-mail or telephone to complete a web-based questionnaire comprised of four questions: Have you been diagnosed with COVID-19 following diagnostic screening? Did you notice a loss of smell during your disease? Did you notice a loss of taste? Do you regularly suffer from ear, nose, and throat (ENT) disorders? The study was approved by the Rennes University Hospital institutional review board. Informed consent was waived.

Of the 452 patients contacted, 259 (57%) replied, of whom 68 (26%) reported a positive test for SARS-CoV-2.



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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.

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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.^{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



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See Online for appendix