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# Olfactory Dysfunction in COVID-19
## Diagnosis and Management

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**As of May 1, 2020,** more than 3 000 000 people worldwide have been infected with the novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The CDC has highlighted key symptoms that may suggest coronavirus disease 2019 (COVID-19), including cough, shortness of breath or difficulty breathing, fever, chills, muscle pain, sore throat, and new loss of smell or taste.[1]

The inclusion of loss of smell or taste among these symptoms follows the emergence of evidence that suggests that COVID-19 frequently impairs the sense of smell. For example, in a study from Iran, 59 of 60 patients hospitalized with COVID-19 were found to have an impaired sense of smell according to psychophysical olfactory testing.[2] Olfactory dysfunction (OD), defined as the reduced or distorted ability to smell during sniffing (orthonasal olfaction) or eating (retronasal olfaction), is often reported in mild or even asymptomatic cases; in a study from Italy, 64% of 202 mildly symptomatic patients reported impaired olfaction.[3]

The possibility that OD could act as a marker for disease, particularly among individuals who are otherwise minimally symptomatic or asymptomatic, prompted organizations, such as the American Academy of Otolaryngology–Head and Neck Surgery[4] and ENT UK,[5] to recommend inclusion of sudden-onset loss of smell and/or taste as part of the diagnostic criteria for COVID-19 disease, as has now been done by the CDC. These organizations suggest that new-onset OD is sufficient to justify self-isolation and the use of personal protective equipment (PPE) by medical staff evaluating patients with this clinical problem.

## Olfactory Dysfunction in COVID-19

Reports of COVID-19–related OD describe a sudden onset of olfactory impairment, which may be in the presence or absence of other symptoms. Among hospitalized patients with COVID-19 in Italy, impaired smell/taste was more frequently seen in younger patients and in women.[6] Unpublished data and anecdotal reports support resolution of olfactory symptoms within approximately 2 weeks. However, because of the lack of long-term follow-up, it is unknown what proportion of patients develop persistent postinfectious OD.

Many patients report impairment of smell and taste interchangeably. Although it is possible that SARS-CoV-2 targets both olfactory and gustatory systems, in most cases of dysfunction not related to COVID-19 in which patients describe altered taste, this symptom can be attributed to impaired retronasal olfaction (flavor) rather than impaired gustation (sweet, salty, sour, bitter). For this reason, it is thought that the chemosensory impairment in COVID-19 is likely olfactory.

Coronaviruses are one of many pathogens known to cause postinfectious OD, and nasal epithelial cells show relatively high expression of the angiotensin-converting enzyme 2 receptor, which is required for SARS-CoV-2 entry.[7] Disruption of cells in the olfactory neuroepithelium may result in inflammatory changes that impair olfactory receptor neuron function, cause subsequent olfactory receptor neuron damage, and/or impair subsequent neurogenesis. Such changes may cause temporary or longer-lasting OD. Previous work in transgenic animal models showed intracranial entry of SARS-CoV via the olfactory bulb.[8] This has led to speculation that SARS-CoV-2 may penetrate intracranially with possible downstream effects on olfactory and nonolfactory brain regions, which may adversely affect olfactory function.

## Clinical Assessment

During the current pandemic, patients with recent-onset acute smell and/or taste dysfunction, with or without other symptoms of COVID-19, should undergo a period of self-isolation and, when possible, SARS-CoV-2 testing. In patients with symptoms that require acute hospital admission (eg, respiratory distress), chemosensory assessment of smell and taste should only be considered when the clinical condition allows and appropriate PPE is available. A possible approach to assessment is outlined in the **Figure**.

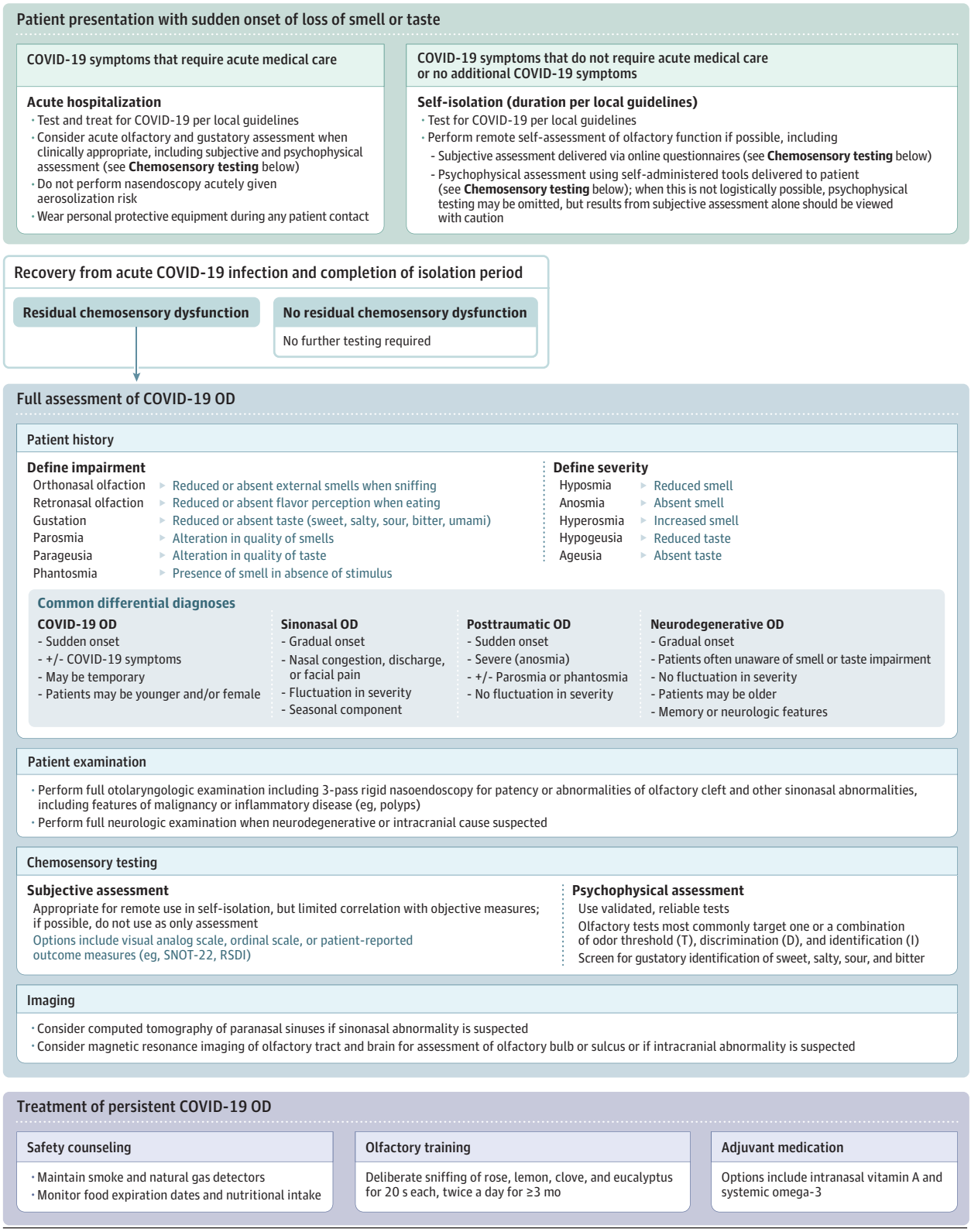
Subjective self-assessment of chemosensory function should not be relied on for diagnosis because of limited correlation with more objective measures.[9] However, remote use of validated tools (eg, visual analog scales, ordinal scales, patient-reported outcome measures) could allow safe, timely capture of data from self-isolating patients. Although such findings should be interpreted with caution, this approach is acceptable in some patients with COVID-19 for whom psychophysical testing is not possible.

Psychophysical assessment involves presentation of odorants/tastants, with test outcome dependent on the patient's response. Such tests are more reliable than a subjective assessment alone and should be performed in patients with COVID-19 when possible.

Olfactory psychophysical assessment tools most commonly test 1 or a combination of odor threshold (minimum strength of an odor that can be perceived), odor discrimination (differentiation between different odors), and odor identification (identification of odors). Ideally, tools targeting odor threshold, discrimination, and identification using a standard multicomponent olfactory testing device should be employed. However, when fast assessment or self-administration is necessary, such as in the assessment of patients with COVID-19, commercially available tools with fewer testing components, self-administered devices, or both may be considered.[9] Any psychophysical test used clinically should be validated for the population being tested, with the diagnoses of impairment and improvement made in relation to age-matched, clinically anchored normative data.

Because the majority of patients who report altered taste are likely experiencing impaired retronasal olfaction, screening of gustatory function should be sufficient as a first-line assessment. For patients in whom abnormalities are identified on screening,

Figure. Possible Approach for the Assessment and Management of Suspected Coronavirus Disease 2019 (COVID-19)–Related Olfactory Dysfunction




RSDI indicates Rhinosinusitis Disability Index; SNOT-22, Sinonasal Outcome Test.

full testing should be performed using a standardized gustatory assessment tool.[9]

Imaging of the paranasal sinuses and brain may be considered to exclude sinonasal or intracranial abnormalities (including

malignancy), but also to delineate the morphology of the olfactory bulb and sulcus, which carries diagnostic and prognostic information for OD. The utility of imaging in COVID-19 has yet to be established, and should be reserved for patients with persistent OD.

## Treatment

When COVID-19–related OD improves spontaneously, specific treatment may not be required. However, when impairment persists beyond 2 weeks, it may be reasonable for treatment to be considered. The efficacy of available treatments for patients with COVID-19–related OD is unknown, although treatments targeting postinfectious OD may potentially be helpful for COVID-19.

Olfactory training involves repeat and deliberate sniffing of a set of odorants (commonly lemon, rose, cloves, and eucalyptus) for 20 seconds each at least twice a day for at least 3 months (or longer if possible). Studies have demonstrated improved olfaction in patients with postinfectious OD after olfactory training.[9] Olfactory training can be considered for patients with persistent COVID-19–related OD because this therapy has low cost and negligible adverse effects.

Oral and intranasal corticosteroids have been used to exclude an inflammatory component in patients with postinfectious OD. However, corticosteroids are not currently recommended for individuals with postinfectious OD because evidence of benefit is lacking and there is a potential risk of harm.[9] Because of safety concerns, the administration of systemic corticosteroids for the routine management of acute COVID-19 is not recommended. In the absence of demonstrable inflammatory disease observed with endoscopy or imaging, it is unlikely that initiation of corticosteroid treatment would benefit post–COVID-19 OD, as is the case for other causes of postinfectious OD. However, for patients who were using intranasal steroids before developing COVID-19 (eg, for allergic rhinitis), such medication should be continued.

Other medications that have shown promise in postinfectious OD include intranasal sodium citrate, which is thought to modulate olfactory receptor transduction cascades, intranasal vitamin A, which may act to promote olfactory neurogenesis, and systemic omega-3, which may act through neuroregenerative or anti-inflammatory means.[9,10] The latter 2 medications may serve as adjuvant therapies in olfactory training. However, to date, there is no evidence that these therapies are effective in patients with OD related to COVID-19.

## Conclusions

COVID-19 is associated with OD in many patients. This symptom should prompt self-isolation and testing for SARS-CoV-2 when possible. Active, collaborative research is required to delineate the natural history and appropriate management of chemosensory impairment in this virulent disease. In the interim, chemosensory assessment and treatments targeting postinfectious OD may be of use in COVID-19–related OD.

### ARTICLE INFORMATION

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