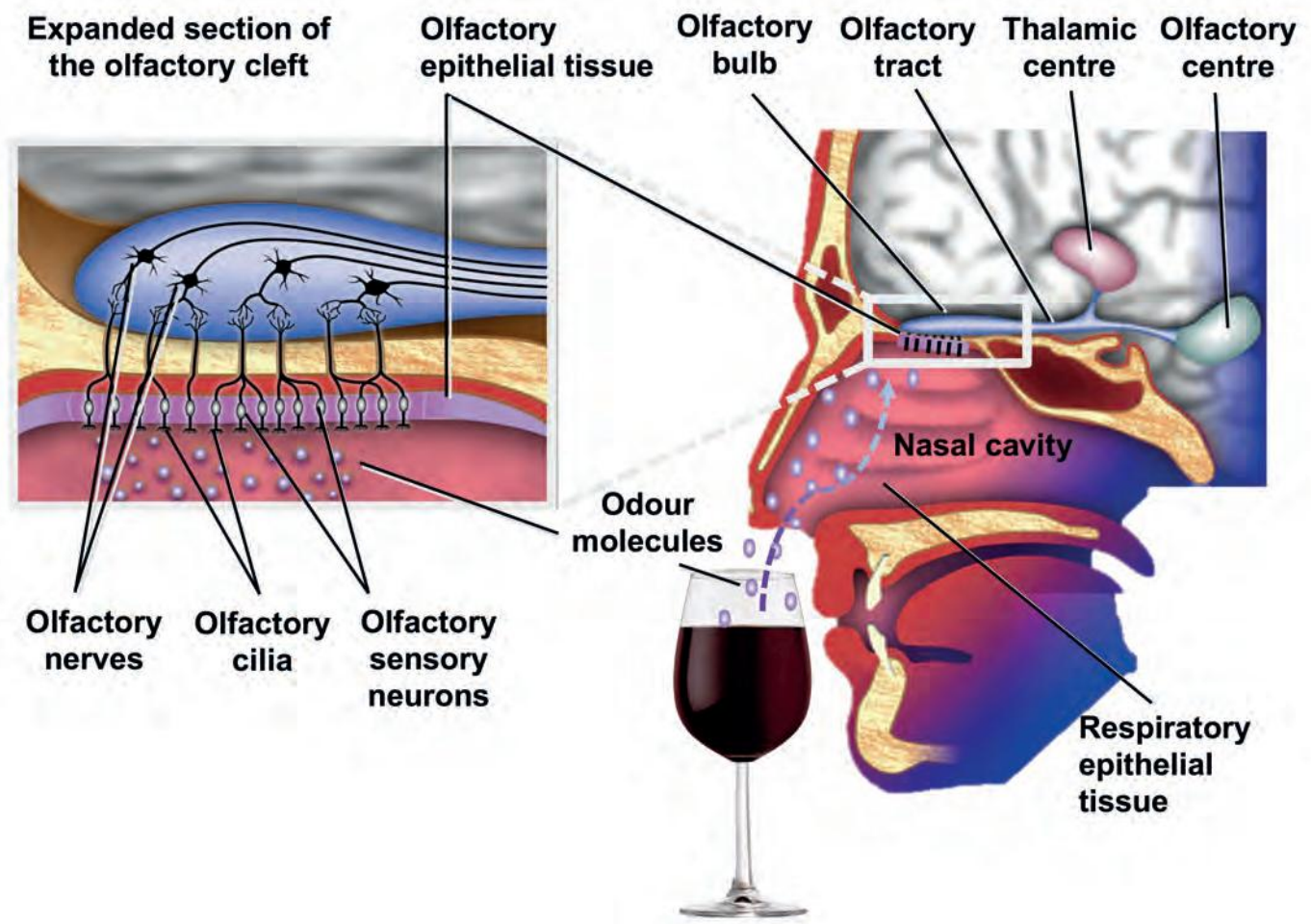




Effects of COVID-19 on sense of smell

Winemakers who have contracted COVID-19 have asked the AWRI helpdesk about one of the common symptoms: loss of or distorted sense of smell. Senior Oenologist, **Geoff Cowey**, has waded through the published clinical research on this topic to answer the most common questions and provide a curated list of references with more detailed information.



How does COVID-19 affect the sense of smell?

Olfactory dysfunction (OD) is defined as the reduced or distorted ability to smell during sniffing (orthonasal olfaction) or eating (retronasal olfaction). Despite the growing body of research showing that COVID-19 can lead to OD, the underlying mechanisms remain uncertain.

Viruses such as the common cold can lead to OD by inflammation of the nasal passage, the majority of which is lined with respiratory epithelial tissue.

Inflammation causes swelling, nasal secretions and congestion which blocks the access of odours reaching the top of the nasal cavity and the olfactory cleft. The olfactory cleft is lined with olfactory epithelium and this is the main sensory tissue responsible for initiation of the sense of smell. As COVID-19-related OD can occur in mild or even asymptomatic cases where no nasal inflammation, congestion or odour restriction occurs, other mechanisms are likely to be at play.

The olfactory epithelium houses mature

olfactory sensory neurons (OSN). Hair-like structures (cilia) extend from the epithelium into the nasal cavity and contain odour receptors, which when activated by odours transmit signals through the OSN to the olfactory bulb in the brain. There are also immature OSN which are produced from basal stem cells that allow continual and life-long self-renewal of OSN.

When SARS-CoV-2 enters the body its glycoprotein spike (S protein) binds to the angiotensin-converting enzyme2

(ACE2) receptor. This receptor is expressed in many organs but is prevalent along the entire respiratory system, which makes it the primary site of viral attachment and attributable for respiratory symptoms. The ACE2 receptor is not present on OSN but is present in abundance in the basal cells of the olfactory epithelium, or the cells that provide the structural and metabolic support to the OSN. Viral infection and local inflammation of these cells have been postulated as causing loss of cilia/cilia receptors, reduced sensitivity of the OSN, or downregulation of receptor and/or signalling genes, which then affect the sense of smell (Mastrangelo et al. 2021, Najafloo et al. 2021, Zazhytska et al. 2022, Douaud et al. 2022). The ACE2 receptor is also present in epithelium of the tongue, taste buds and associated receptors and can thus also lead to taste disorders (ageusia) and loss of taste sensation (chemesthesis) (Oliveira et al. 2022).

Will I lose my sense of smell if I contract COVID-19?

Based on analysis of multiple research projects, an aggregate mean of 47-53% individuals reported some degree of OD during the acute phase of a COVID-19 infection (Borsetto et al. 2020, Boscolo-Rizzo et al. 2021, Karamali et al. 2022,

Tong et al. 2020). This includes both self-reported data and/or psychophysical assessment of loss of chemosensory functions. Individuals self-reporting loss of smell typically underestimate the true prevalence of OD compared to psychophysical testing (Karamali et al. 2022). Olfactory dysfunction is also more often self-reported in those with milder symptoms as those with more severe COVID-19 disease are more likely to overlook OD symptoms while dealing with other more critical symptoms.

Is any group of individuals more likely to experience olfactory dysfunction caused by COVID-19?

Olfactory dysfunction is most common in the 40–50-year-old age bracket, and less reported in the very young or very old, which also correlates with the volume of ACE2 receptor expression in this bracket. Obesity was found to be more prevalent in individuals that experienced OD. Women were also more predisposed to suffer COVID-19-related OD (Najafloo et al. 2021). It should be noted that most of the studies on COVID-19-related OD were conducted relatively early in the pandemic and thus relate to the Alpha strain which was dominant at the time. Further studies are currently investigating the impact of OD from more recent strains, with

indications to date that the Omicron strain results in reduced prevalence and severity of OD.

How will my sense of smell be affected if I contract COVID-19?

Typically, individuals report hyposmia (a reduced ability to smell and detect odours) during the acute phase of COVID-19, while some report full anosmia (the complete loss of smell). Duration of OD was on average 8-12 days with 70-80% of individuals reporting partial or full recovery 30 days post-infection. Some individuals report parosmia, or a condition where the sense of smell returns but in a distorted fashion. Common smells such as coffee, onion, garlic, meat, citrus and even toothpaste present as an unpleasant burnt, chemical-like aroma. Parosmia has sometimes been reported to occur in individuals two to three months after COVID-19-related anosmia, or sometimes after no reported initial loss of smell. This has been postulated to be a sign of sensory recovery, where the regenerating OSN may be misconnecting with the brain area responsible for smell, or due to a reduced number of functioning OSN, or due to a predominance of immature OSN leading to incomplete aroma characterisation (Karamali et al. 2022).

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Can the effects on sense of smell persist long-term?

SARS-CoV-2 viral persistence in the olfactory epithelium after the acute phase but with continued inflammation could influence the regenerative capacity of the basal stem cells, leading to prolonged symptoms and a delayed recovery. Scar tissue formation from the infection may also be a reason for prolonged OD in some individuals. If direct damage or infection occurred on the OSN themselves or if the virus downregulates olfactory receptor and signalling genes so that the receptors are no longer responsive to odour molecules, this could result in a much longer period of OD, typically weeks to months, longer than that currently being reported for most individuals. The risk of persistent COVID-19-related OD increases from individuals who do not exhibit any OD during the acute phase (lowest risk), to those that experience mild OD and then recover (intermediate risk), to those who report persistent OD throughout and after the disease (highest risk). Concerningly, 46% of individuals who self-reported recovery from OD still had some level of OD by psychophysical assessment and 7% of individuals were found to still have complete loss of smell 13 months after confirmed COVID-19 diagnosis (Boscolo-Rizzo et al. 2021), which could suggest multiple pathways for COVID-19-related OD.

Are there any treatment options?

If loss of smell persists for more than three weeks it is recommended to consult a doctor and consider a referral to an ear, nose and throat (ENT) specialist. Monitoring your senses and performing daily olfactory training of repeated sniffing of a set of strong essential oils (lemon, rose, cloves, eucalyptus) for 20 seconds, twice a day, has been shown to symptomatically improve the dysfunction. Sensonics International offers a Smell Identification Test™, a commercial version of the University of Pennsylvania Smell Identification Test (UPSIT). This is a reliable and accurate olfactory test used clinically, and provides a quantitative measure of smell loss (anosmia or mild, moderate or severe hyposmia). This test can be used to determine if you have recovered from

any OD. The Science Institute of Vine and Wine (ISVV), Bordeaux has produced a training support booklet on Managing taste and smell disorders (Tempere 2021), which may be of assistance. Oral and intranasal corticosteroid treatment has not been recommended due to a lack of evidence of benefit in the trials conducted.

How should I adjust my work while experiencing olfactory dysfunction?

After testing positive for COVID-19 individuals should not have close contact with others until they have recovered from the acute infection and satisfied any requirements to isolate. Post-recovery, winemakers, cellar door staff, sommeliers or other wine professionals who suspect they may still have some degree of OD should not rely fully on their own sensory ability and should conduct tastings with others, to ensure the accuracy of sensory assessments is not impaired. Ideally three tasters should be involved in general tastings to impart some degree of rigour. More information on considerations for performing robust sensory assessment can be found on the AWRI website.

Olfactory dysfunction can also cause a decrease in appetite, weight loss, general distress, depression, and anxiety, particularly for professionals who are reliant on their sensory capabilities. Groups such as Lifeline, Beyond Blue or AbScent.org can provide support and/or olfactory training. It is also important for all of us in the wine community to be supportive of any colleagues who may be experiencing COVID-19-related OD symptoms.

For further information contact the AWRI helpdesk on (08) 8313 6600 or helpdesk@awri.com.au

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