

Sniffing out the evidence – COVID-19 and loss of sense of smell and taste

BY CLAIRE HOPKINS

Louis Pasteur once observed: “In the fields of observation chance favors only the prepared mind.” **Professor Hopkins** was certainly prepared when a few anecdotes of smell problems started to accumulate early in the pandemic’s course.

Post-viral olfactory loss is nothing new – depending on the setting, in some series it is reported to account for up to 40% of cases of olfactory dysfunction. It is more common in females and has encouraging spontaneous recovery rates, although as many as 50% also develop parosmia. Prior to COVID-19 it was estimated to complicate roughly 1% of upper respiratory tract viral infections, caused by previously described rhinoviruses and coronaviruses, with a peak incidence in March. It was perhaps therefore no great surprise to see a number of patients with sudden onset smell loss back-to-back in one of my clinics mid-March, at a time when we still thought COVID was largely restricted to travellers from Northern Italy and China. However, I developed a growing sense of unease as I spoke with colleagues around the world who were seeing similar increases in patients with anosmia. News from Italian colleagues that frontline workers on COVID wards were also losing their sense of smell prompted action, with a letter written on behalf of the British Rhinological Society and ENT UK sent to Public Health England (PHE) and put out as a press release in hope that a few ENT surgeons might read it and be better protected.

The response was somewhat unexpected and the press release travelled faster round the world than the virus itself – I found myself on the front pages of newspapers, from the *New York Times* to the *South China*

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Image by Engin Akyurt from Pixabay.

Post, and messages spread rapidly across social media, in part fuelled by a number of high-profile celebrities who had developed anosmia due to COVID-19 and by the many thousands of patients with otherwise mild symptoms who had lost their sense of smell but were unable to access testing. My inbox was soon deluged with requests for help and advice – it was clear that there was much to be done; in terms of establishing the prevalence and diagnostic value of loss of smell and also providing medical advice and support to patients in the midst of a global shut-down of medical services.

Initial attempts to establish the prevalence were thwarted in the UK due to lack of access to testing, although novel approaches using google to analyse trends in internet searches and looking at membership of patient support groups suggested this was a widespread and common issue. Working with teams across Europe, we were soon able to establish that sudden loss of smell was one of the most common symptoms of COVID-19, appearing

in isolation or before other symptoms in some patients. It is the best predictor of a positive test result – making it invaluable as a marker of infection and a trigger for self-isolation and testing. Work to convince PHE of this, however, was protracted and at times frustrating; reliance on UK data where only hospitalised patients with cough or fever were tested for SARS-CoV-2 obviously

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underestimated the added sensitivity of adding loss of the smell to the diagnostic criteria. Perhaps a lack of infrastructure to provide widespread testing also contributed to a deliberate delay, and the National Health Service (NHS) did not adopt loss of smell into the diagnostic criteria until mid-May, a month after the World Health Organization (WHO) and much of the rest of the world.

International collaboration has allowed an accumulation of evidence at an unprecedented rate, with research addressing all aspects of COVID-19 related olfactory dysfunction from the prognostic value, underlying mechanism, recovery rates and potential treatments. Many of those involved have not previously been working within the field of olfaction and rhinology, demonstrating the huge effort to combat the global pandemic from all subspecialties. We have shown widespread epithelial injury occurs in COVID-19, suggesting a peripheral mechanism is most likely, consistent with the finding that ACE2 receptors which mediate viral entry are expressed by the supporting cells of the olfactory epithelium. There is some evidence suggesting the development of olfactory loss to be a positive prognostic factor, with a higher apparent prevalence in mild disease. Could the sacrifice of olfaction be a remarkable defence mechanism against a neurotropic virus? This remains a controversial area, and more prospective studies are required to address this.

Although a significant proportion recover within the first four weeks, at least 10% self-report severe persistent deficits, lasting at least six months. When using psychophysical olfactory tests, as many as 50% have persistent olfactory deficits at six months, many of whom also report parosmia. A number of trials are underway globally, the results of which are eagerly awaited, as there is a paucity of effective therapeutic options at present. Smell training should be recommended to all those where loss persists beyond the first few weeks. We have undertaken a small trial that shows short-term benefit from oral and topical steroids combined, but more work is required to assess the optimal timing or use and to determine if this is associated with better long-term outcomes. We need to explore the role of early treatment to prevent long-term loss, and develop novel therapies for those where this cannot be prevented.

For those with ongoing anosmia, the impact on quality of life and mental health is significant. A colleague who contracted COVID-19 at work reports: "Anosmia is like experiencing the world in two dimensions. There are no smells to evoke good memories

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and I have lost an important coping mechanism. I feel constantly insecure of missing unhealthy fumes or rotten food. Friends trivialise this condition and show no empathy." Support may not be forthcoming from friends and family and will need to be provided by healthcare systems. Data shows that anosmics are at higher risk of food poisoning and exposure to household fire. A family in Texas, in which three members lost their sense of smell after COVID-19, were saved from severe injury when their house burnt to the ground only by the remaining member who had not developed anosmia.

It became clear early in the pandemic that patients were struggling with access to primary care and ENT and, in turn, were often unfamiliar with olfactory dysfunction and at a loss as to how to help. Patients initially reported disappointment with the response from healthcare workers: 'waste of time'; 'didn't know anything'; and 'put myself through appointment and got driven in return' were amongst early reports. To counter this, the British Rhinological Society developed some consensus guidelines which were available by early May, and worked with AbScent and Fifth Sense to provide support and information to those affected. An information page with advice and instructions on smell training, (www.Abscent.org/Nosewell) has been viewed by more than 330,000 unique users since its launch, and the membership of an AbScent Facebook group dedicated to those with COVID-19-related smell loss has swelled to more than 20,000 members. A '10-minute consultation' in the *BMJ* has had over 125,000 full text reads, highlighting the interest in better managing the condition in primary care.

With over 114 million COVID-19 cases confirmed worldwide, and a greater than 50% prevalence of associated smell loss, the number affected by olfactory dysfunction, even temporarily, is staggering. More than five million people worldwide will have long-lasting deficits. As a specialty, we must seize

COVID-19's silver lining and harness the greater awareness of the impact of smell loss to help to develop novel treatments and to provide more empathic care for those affected. In little over a year, the progress we have already made will bring little comfort to those who continue to live it. For those of us who remain fortunate enough to be able to wake up and smell the coffee, we should learn to cherish our most undervalued sense.

Further Reading

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