

## Parosmia post COVID-19: an unpleasant manifestation of long COVID syndrome

As we begin to slowly unravel the mystery hidden behind the current pandemic, novel clinical manifestations are emerging ceaselessly following SARS-CoV-2. Olfactory dysfunction, which has become one of the sought-after clinical features of COVID-19, has been associated with less severe disease manifestation.<sup>1</sup> Yet, the previously deemed 'fortunate' patients with olfactory dysfunction who successfully recovered from COVID-19 are now being afflicted by another sinister condition known as parosmia, which is found to be more debilitating than loss of smell.

Parosmia or distortion of smell is currently regarded as one of the long COVID-19 syndrome or chronic COVID-19 syndrome. Carfi *et al* found that 87.4% of patients in their study who recovered from COVID-19 had at least one persistent symptom with loss of smell among them.<sup>2</sup> However, recent reports have discovered that a number of patients with loss of smell or anosmia regained their smell, yet surprisingly this time, the smell was distorted. The magical aroma of coffee had turned into a nightmare as coffee began to smell pungent like gasoline and favourite dishes were turning to smell more like rotten food or garbage, which inadvertently affects taste as food becomes almost unpalatable.

The word parosmia is taken from the Greek words: para and osme (smell) which is defined as a distortion of smell with the presence of odorant, whereas phantosmia is a condition when there is a distortion of smell with the absence of odorant. Anosmia, on the other hand, means complete loss of smell.

As of the latest report, three hypotheses exist to explain the pathophysiology of olfactory dysfunction secondary to COVID-19, which include: (1) Mechanical obstruction ensuing the inflammation around the olfactory cleft, which prevents the odorants from binding with the olfactory receptors,<sup>3</sup> (2) infection of the ACE-2 expressing supporting cell, mainly the sustentacular cell of the olfactory epithelium<sup>4</sup> and (3) direct invasion of olfactory neurons by SARS-CoV-2, which impedes the olfaction transmission.<sup>5</sup>

The theory behind parosmia, on the other hand, is attributed to the unique

regenerating capability of the olfactory neurons, whereby the new regenerated olfactory neurons sprouts and re-connects to the brain results in a trial-and-error process. As there are approximately 350 types of receptors to detect odours, human brains interpret smell following a combination of different signals. It is noteworthy that olfactory nerve interruption or damage is followed by regeneration of the olfactory receptor bipolar neurons along with central reattachment of their axons.<sup>6</sup> However, part of the axonal regenerations becomes displaced, leading to this 'misguided' regenerating axons to reach abnormal territories of the brain,<sup>6</sup> which leads to parosmia. Parallel to that, the destruction, as well as regeneration of the olfactory receptors, has been reported previously to occur in a patch, checkerboard manner, thus leading to distortion of smell or parosmia. This information appears to alter Mozell's theory of spatio-temporal pattern of response to magnitude and latency differences across the mucosa to odorants whereby human nose was suggested to separate vapour or odorant in a similar pattern to a gas chromatograph.<sup>7</sup>

Although parosmia following recovery from postviral olfactory loss has long been reported,<sup>8</sup> in patients recovering from COVID-19 it must be a distressing situation. Having said that, the bright side of parosmia is that it denotes gradual recovery of smell function. Parosmia has been reported to be associated with spontaneous olfactory recovery suggesting positive clinical outcome.<sup>9</sup> Although still in infancy, promising reports on the outcome of olfactory retraining therapy for patients with parosmia post COVID-19 are rising. Olfactory retraining therapy aims to strengthen olfactory recovery according to the neuronal plasticity of the olfactory system.<sup>10</sup> In the same vein, olfactory retraining therapy boosts cognitive processing of the incomplete sensory information in patients with parosmia.<sup>10</sup> Olfactory retraining therapy basically allows patients to relearn smell by consciously sniffing at least four different odorants two times per day for several months.

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**Acknowledgements** We would like to acknowledge all involved in writing this manuscript.

**Contributors** JS: Writing, editing, literature review and final approval. PN: Editing, literature review and final approval.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent for publication** Not required.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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**To cite** Saniasiaya J, Narayanan P. *Postgrad Med J* 2022;**98**:e96.

Accepted 25 March 2021

Published Online First 31 March 2021

*Postgrad Med J* 2022;**98**:e96.

doi:10.1136/postgradmedj-2021-139855

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