

Editorial

Post-Viral Olfactory Loss: What We Learned from the SARS-CoV-2 Pandemic

Luigi Angelo Vaira ^{1,2,*}, Giovanna Deiana ^{2,3}, Fabio Maglitto ⁴ and Giovanni Salzano ⁴

¹ Maxillofacial Surgery Operative Unit, Department of Medicine, Surgery and Pharmacy, University of Sassari, 07100 Sassari, Italy

² Biomedical Science Department, PhD School of Biomedical Science, University of Sassari, 07100 Sassari, Italy

³ Direction, Hygiene and Hospital Infection Control Operative Unit, University Hospital of Sassari, 07100 Sassari, Italy

⁴ Maxillofacial Surgery Operative Unit, University Hospital of Naples “Federico II”, 80131 Naples, Italy

* Correspondence: lavaira@uniss.it; Tel.: +39-3401846168

Viral infections have always been one of the most frequent causes of persistent olfactory dysfunctions accounting for 18% to 45% of all cases [1,2]. However, the exact prevalence of olfactory dysfunctions during common flu has never been determined with absolute certainty; the risk factors for the development of persistent disorders are unknown and there are no therapeutic guidelines. The management of patients with olfactory disorders was the prerogative of a few smell specialists and is mostly unknown to the rest of the healthcare community.

The COVID-19 pandemic represented a marked turning point in this field. First, it caused a large number of people to lose their sense of smell. The prevalence of olfactory dysfunctions in the acute phase of the infection was greater than 50% in the first pandemic waves [3–6] and continues to remain significant, even for the Omicron variant [7,8]. Moreover, the great media coverage that olfactory disorders have received in recent years has contributed to raising the awareness of this type of problem among the public. The number of patients requesting assistance for olfactory disorders of various etiology is therefore constantly increasing and it is no longer possible, as often happened in the past, not to offer them solutions or ignore their requests [9,10].

SARS-CoV-2 has demonstrated the ability to induce persistent severe olfactory disturbances in approximately 5% of all those infected [11–13]. A huge number of individuals experience severe long-term morbidity, with devastating effects on quality of life, which can lead to social isolation or exposure to environmental dangers [14,15]. On the other hand, the pandemic has pushed research in this area and uncovered a huge amount of information on post-viral olfactory disorders. In the past, this has not been possible because patients sought assistance at a great distance from the infection, when it was no longer possible to identify the pathogen [2]. Moreover, the psychophysical tests with which the olfactory function is assessed must be administered in person, introducing safety problems for operators who dispute their use to evaluate contagious patients. During the pandemic, many researchers bravely evaluated patients within isolation departments, and for the first time, we were able to estimate the prevalence of olfactory dysfunctions during an infection [16–18] and study the diagnostic [19,20] and prognostic value of these symptoms [21–23].

In the months that followed, it was possible to monitor the recovery of olfactory function over time, confirming that, in most cases, the loss of smell following viral infections recovers within a few weeks. However, reliable studies with follow-up at 6 [24–26], 12 [27–30] and 24 months [31,32] have been conducted, confirming that up to 5% of patients develop long-term disorders with significant effects on quality of life [33]. For the first time, it was possible to identify the risk factors [34–37] for the development of persistent olfactory disorders, including female gender [26,38], younger age [38,39], smokers [40] or non-smokers [38], hypertension [41], diabetes [41], depression [42], symptoms such as



Citation: Vaira, L.A.; Deiana, G.; Maglitto, F.; Salzano, G. Post-Viral Olfactory Loss: What We Learned from the SARS-CoV-2 Pandemic. *Life* **2022**, *12*, 1868. <https://doi.org/10.3390/life12111868>

Received: 10 November 2022

Accepted: 11 November 2022

Published: 12 November 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

fever [38] and nasal obstruction [43], circulating levels of D-dimer during infection [44], and levels of nasal immunoglobulins [45,46].

At the same time, important new advances have been made in studying the pathogenesis of olfactory disorders after viral infections [47–52]. All of these efforts have ultimately led to numerous therapeutic trials to identify effective therapies for the prevention and treatment of persistent olfactory disorders [53–58].

This Special Issue represents a good summary of all of these research areas. The study by Haener et al. [59] shows that COVID-19-related olfactory disorders are significantly more frequent and severe than those caused by other cold viruses. The reviews by Scotto et al. [60] and Pang et al. [61] analyze the correlations between taste alterations and SARS-CoV-2 establishing the diagnostic value of this chemosensitive disorder. The diagnostic value of olfactory disorders is instead the subject of studies by Mazzatorta et al. [62,63] and Jungbauer et al. [64].

The two contributions by Schambeck et al. [65] and Albayay et al. [66] analyze the prevalence of long-term olfactory disorders, confirming the important impact of this problem, as underlined by a study of the impact on the quality of life of persistent olfactory disorders by Vaira et al. [67].

Callejon-Leblie et al. [68] and Tipirdamaz et al. [69], in two large studies of 421 and 354 patients with COVID-19, respectively, identified older age, cacosmia and asthma as a risk factor for developing a long-term olfactory disorder. Finally, Hintschich et al. [70] and Tsuchiya [71] analyzed the effects of nasal corticosteroids and zinc in the treatment of COVID-19-related olfactory and gustatory disorders.

In the last few years, we have learned much about post-viral chemosensory disorders. In July 2020, an article by Cooper et al. [72] ran with the title: “COVID-19 and the chemical senses: supporting players take center stage”. The management of chemosensory disorders has always represented a research niche that has suddenly ended up at the center of public attention. Today and in the future, this same public will increasingly demand solutions to their problems, even if not related to COVID-19. Alongside the great efforts made by researchers in recent years, it is necessary for health systems to recognize the importance of chemosensory disorders by providing those who have to deal with these patients adequate organizational and economic tools to cope with increasing demands for assistance.

Author Contributions: Writing—original draft preparation, L.A.V.; writing—review and editing, G.D., F.M., G.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Temmel, A.F.P.; Quind, C.; Schickinger-Fischer, B.; Klimek, L.; Stoller, E.; Hummel, T. Characteristics of olfactory disorders in relation to major causes of olfactory loss. *Arch. Otolaryngol. Head Neck Surg.* **2002**, *128*, 635–641. [[CrossRef](#)] [[PubMed](#)]
2. Suzuki, M.; Saito, K.; Min, W.P.; Cladau, C.; Toida, K.; Itoh, H.; Murakami, S. Identification of viruses in patients with postviral olfactory dysfunction. *Laryngoscope* **2007**, *117*, 272–277. [[CrossRef](#)] [[PubMed](#)]
3. Saniasiaya, J.; Islam, M.A.; Abdullah, B. Prevalence of olfactory dysfunction in coronavirus disease 2019 (COVID-19): A meta-analysis of 27,492 patients. *Laryngoscope* **2021**, *131*, 865–878. [[CrossRef](#)] [[PubMed](#)]
4. Lechien, J.R.; Chiesa-Estomba, C.M.; Vaira, L.A.; Cammaroto, G.; De Riu, G.; Chekkouri-Idrissi, Y.; Circiu, M.; Distinguin, L.; Journe, F.; de Terwagne, C.; et al. Epidemiological, otolaryngological, olfactory and gustatory outcomes according to the severity of COVID-19: A study of 2579 patients. *Eur. Arch. Otorhinolaryngol.* **2021**, *278*, 2851–2859. [[CrossRef](#)]
5. Vaira, L.A.; Lechien, J.R.; Khalife, M.; Petrocelli, M.; Hans, S.; Distinguin, L.; Salzano, G.; Cucurullo, M.; Doneddu, P.; Salzano, F.A.; et al. Psychophysical evaluation of the olfactory function: European multicenter study on 774 COVID-19 patients. *Pathogens* **2021**, *10*, 62. [[CrossRef](#)]
6. Vaira, L.A.; Deiana, G.; Fois, A.G.; Pirina, P.; Madeddu, G.; De Vito, A.; Babudieri, S.; Petrocelli, M.; Serra, A.; Bussu, F.; et al. Objective evaluation of anosmia and ageusia in COVID-19 patients: Single center experience on 72 cases. *Head Neck* **2020**, *42*, 1252–1258. [[CrossRef](#)]

7. Vaira, L.A.; Lechien, J.R.; Deiana, G.; Salzano, G.; Maglitto, F.; Piombino, P.; Mazzatorta, A.; Boscolo-Rizzo, P.; Hopkins, C.; De Riu, G. Prevalence of olfactory dysfunction in D614G, alpha, delta and omicron waves: A psychophysical case-control study. *Rhinology* **2022**. [[CrossRef](#)]
8. Boscolo-Rizzo, P.; Tirelli, G.; Meloni, P.; Hopkins, C.; Madeddu, G.; De Vito, A.; Gardenal, N.; Valentini, R.; Tofanelli, M.; Borsetto, D.; et al. Coronavirus disease 2019 (COVID-19)-related smell and taste impairment with widespread diffusion of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) Omicron variant. *Int. Forum Allergy Rhinol.* **2022**, *12*, 1273–1281. [[CrossRef](#)]
9. Boscolo-Rizzo, P.; Polesel, J.; Vaira, L.A. Smell and taste dysfunction after COVID-19. *BMJ* **2022**, *378*, o1653. [[CrossRef](#)]
10. Vaira, L.A.; De Riu, G.; Salzano, G.; Maglitto, F.; Boscolo-Rizzo, P.; Lechien, J.R. COVID-19 related persistent olfactory disorders represent an unprecedented challenge. *Am. J. Otolaryngol.* **2022**, *44*, 103667. [[CrossRef](#)]
11. Tan, B.K.J.; Han, R.; Zhao, J.J.; Tan, N.K.W.; Quah, E.S.H.; Tan, C.J.; Chan, Y.H.; Teo, N.W.Y.; Charn, T.C.; See, A.; et al. Prognosis and persistence of smell and taste dysfunction in patients with COVID-19: Meta-analysis with parametric cure modelling of recovery curves. *BMJ* **2022**, *378*, e069503. [[CrossRef](#)] [[PubMed](#)]
12. Bussiere, N.; Mei, J.; Lévesque-Boissonneault, C.; Blais, M.; Carazo, S.; Gros-Louis, F.; De Serres, G.; Dupré, N.; Frasnelli, J. Chemosensory dysfunctions induced by COVID-19 can persist up to 7 months: A study of over 700 healthcare workers. *Chem. Senses* **2021**, *46*, bjab038. [[CrossRef](#)] [[PubMed](#)]
13. Boscolo-Rizzo, P.; Menegaldo, A.; Fabbris, C.; Spinato, G.; Borsetto, D.; Vaira, L.A.; Calvanese, L.; Pettorelli, A.; Sonego, M.; Frezza, D.; et al. Six-month psychophysical evaluation of olfactory dysfunction in patients with COVID-19. *Chem. Senses* **2021**, *46*, bjab006. [[CrossRef](#)] [[PubMed](#)]
14. Boesveldt, S.; Parma, V. The importance of the olfactory system in human well-being, through nutrition and social behavior. *Cell Tissue Res.* **2021**, *383*, 559–567. [[CrossRef](#)] [[PubMed](#)]
15. Saniasia, J.; Prepageran, N. Impact of olfactory dysfunction on quality of life in coronavirus disease 2019 patients: A systematic review. *J. Laryngol. Otol.* **2021**, *135*, 947–952. [[CrossRef](#)] [[PubMed](#)]
16. Vaira, L.A.; Hopkins, C.; Salzano, G.; Petrocelli, M.; Melis, A.; Cucurullo, M.; Ferrari, M.; Gagliardini, L.; Pipolo, C.; Deiana, G.; et al. Olfactory and gustatory function impairment in COVID-19 patients: Italian objective multicenter-study. *Head Neck* **2020**, *42*, 1560–1569. [[CrossRef](#)]
17. Vaira, L.A.; De Vito, A.; Lechien, J.R.; Chiesa-Estomba, C.M.; Mayo-Yanes, M.; Calvo-Henriquez, C.; Saussez, S.; Madeddu, G.; Babudieri, S.; Boscolo-Rizzo, P.; et al. New onset of smell and taste loss are common findings also in patients with symptomatic COVID-19 after complete vaccination. *Laryngoscope* **2021**, *132*, 419–421. [[CrossRef](#)]
18. Moein, S.T.; Hahemian, S.M.R.; Mansourafshar, B.; Khorram-Tousi, A.; Tabarsi, P.; Doty, R.L. Smell Dysfunction: A biomarker for COVID-19. *Int. Forum Allergy Rhinol.* **2020**, *10*, 944–950. [[CrossRef](#)]
19. Yan, C.H.; Faraji, F.; Prajapati, D.P.; Boone, C.E.; DeConde, A.S. Association of chemosensory dysfunction and COVID-19 in patients presenting with influenza-like symptoms. *Int. Forum Allergy Rhinol.* **2020**, *10*, 806–813. [[CrossRef](#)]
20. Rocke, J.; Hopkins, C.; Philpott, C.; Kumar, N. Is loss of sense of smell a diagnostic marker in COVID-19: A systematic review and meta-analysis. *Clin. Otolaryngol.* **2020**, *45*, 914–922. [[CrossRef](#)]
21. Yan, C.H.; Faraji, F.; Prajapati, D.P.; Ostrander, B.T.; DeConde, A.S. Self-reported olfactory loss associates with outpatient clinical course in COVID-19. *Int. Forum Allergy Rhinol.* **2020**, *10*, 821–831. [[CrossRef](#)] [[PubMed](#)]
22. Hopkins, C.; Vaira, L.A.; De Riu, G. Self-reported olfactory loss in COVID-19: Is it really a favorable prognostic factor? *Int. Forum Allergy Rhinol.* **2020**, *10*, 926. [[CrossRef](#)] [[PubMed](#)]
23. Vaira, L.A.; Hopkins, C.; Petrocelli, M.; Lechien, J.R.; Soma, D.; Giovanditto, F.; Rizzo, D.; Salzano, G.; Piombino, P.; Saussez, S.; et al. Do olfactory and gustatory psychophysical scores have prognostic value in COVID-19 patients? A prospective study of 106 patients. *J. Otolaryngol. Head Neck Surg.* **2020**, *49*, 56. [[CrossRef](#)] [[PubMed](#)]
24. Riestra-Ayora, J.; Yanes-Díaz, J.; Esteban-Sánchez, J.; Vuduva, C.; Molina-Quiros, C.; Larrañ-Jiménez, A.; Martín-Sanz, E. Long-term follow-up of olfactory and gustatory dysfunction in COVID-19: 6 months case-control study in health workers. *Eur. Arch. Otorhinolaryngol.* **2021**, *278*, 4831–4837. [[CrossRef](#)] [[PubMed](#)]
25. Petrocelli, M.; Cutrupi, S.; Salzano, G.; Maglitto, F.; Salzano, F.A.; Lechien, J.R.; Saussez, S.; Boscolo-Rizzo, P.; De Riu, G.; Vaira, L.A. Six-month smell and taste recovery rates in coronavirus disease 2019 patients: A prospective psychophysical study. *J. Laryngol. Otol.* **2021**, *135*, 436–441. [[CrossRef](#)] [[PubMed](#)]
26. Hopkins, C.; Surda, P.; Vaira, L.A.; Lechien, J.R.; Safarian, M.; Saussez, S.; Kumar, N. Six month follow-up of self-reported loss of smell during the COVID-19 pandemic. *Rhinology* **2021**, *59*, 26–31. [[CrossRef](#)] [[PubMed](#)]
27. Vaira, L.A.; Salzano, G.; Le Bon, S.; Maglio, A.; Petrocelli, M.; Steffens, Y.; Ligas, E.; Maglitto, F.; Lechien, J.R.; Saussez, S.; et al. Prevalence of persistent olfactory disorders in patients with COVID-19: A psychophysical case-control study with 1-year follow-up. *Otolaryngol. Head Neck Surg.* **2021**, *167*, 183–186. [[CrossRef](#)] [[PubMed](#)]
28. Boscolo-Rizzo, P.; Guida, F.; Polesel, J.; Marcuzzo, A.V.; Antonucci, P.; Capriotti, V.; Sacchet, E.; Cragnolini, F.; D'Alessandro, A.; Zanelli, E.; et al. Self-reported smell and taste recovery in coronavirus disease 2019 patients: A one-year prospective study. *Eur. Arch. Otorhinolaryngol.* **2021**, *279*, 515–520. [[CrossRef](#)]

29. Boscolo-Rizzo, P.; Hummel, T.; Hopkins, C.; Dibattista, M.; Menini, A.; Spinato, G.; Fabbris, C.; Emanuelli, E.; D’Alessandro, A.; Marzolino, R.; et al. High prevalence of long-term olfactory, gustatory, and chemesthesia dysfunction in post-COVID-19 patients: A matched case-control study with one-year follow-up using a comprehensive psychophysical evaluation. *Rhinology* **2021**, *59*, 517–527. [[CrossRef](#)]
30. Lechien, J.R.; Vaira, L.A.; Saussez, S. Prevalence and 24-month recovery of olfactory dysfunction in COVID-19 patients: A multicentre prospective study. *J. Intern. Med.* **2022**. [[CrossRef](#)]
31. Boscolo-Rizzo, P.; Fabbris, C.; Polesel, J.; Emanuelli, E.; Tirelli, G.; Spinato, G.; Hopkins, C. Two-year prevalence and recovery rate of altered sense of smell and taste in patients with mildly symptomatic COVID-19. *JAMA Otolaryngol. Head Neck Surg.* **2022**, *148*, 889–891. [[CrossRef](#)] [[PubMed](#)]
32. Boscolo-Rizzo, P.; Hokpins, C.; Menini, A.; Dibattista, M.; Cancellieri, E.; Gardenal, N.; Tofanelli, M.; Valentiniotti, R.; Lechien, J.R.; Vaira, L.A.; et al. Parosmia assessment with structured questions and its functional impact in patients with long-term COVID-19-related olfactory dysfunction. *Int. Forum Allergy Rhinol.* **2022**. [[CrossRef](#)] [[PubMed](#)]
33. Vaira, L.A.; Deiana, G.; Lechien, J.R.; De Vito, A.; Cossu, A.; Dettori, M.; Del Rio, A.; Saussez, S.; Madeddu, G.; Babudieri, S.; et al. Correlations between olfactory psychophysical scores and SARS-CoV-2 viral load in COVID-19 patients. *Laryngoscope* **2021**, *131*, 2312–2318. [[CrossRef](#)] [[PubMed](#)]
34. Vaira, L.A.; De Vito, A.; Deiana, G.; Pes, C.; Giovanditto, F.; Fiore, V.; Lechien, J.R.; Saussez, S.; Policicchio, D.; Boccaletti, R.; et al. Systemic inflammatory markers and psychophysical olfactory scores in coronavirus disease 2019 patients: Is there any correlation? *J. Laryngol. Otol.* **2021**, *135*, 723–728. [[CrossRef](#)] [[PubMed](#)]
35. Vaira, L.A.; De Vito, A.; Deiana, G.; Pes, C.; Giovanditto, F.; Fiore, V.; Lechien, J.R.; Le Bon, S.-D.; Saussez, S.; Madeddu, G.; et al. Correlations between IL-6 serum level and olfactory dysfunction severity in COVID-19 patients: A preliminary study. *Eur. Arch. Otorhinolaryngol.* **2022**, *279*, 811–816. [[CrossRef](#)]
36. Amadu, A.M.; Vaira, L.A.; Lechien, J.R.; Scaglione, M.; Saba, L.; Lampus, M.L.; Profili, S.G.; Le Bon, S.-D.; Salzano, G.; Maglitto, F.; et al. Analysis of the correlations between the severity of lung involvement and olfactory and psychophysical scores in coronavirus disease 2019 (COVID-19) patients. *Int. Forum Allergy Rhinol.* **2022**, *12*, 103–107. [[CrossRef](#)] [[PubMed](#)]
37. Paderno, A.; Schreiber, A.; Grammatica, A.; Raffetti, E.; Tomasoni, M.; Gualtieri, T.; Taboni, S.; Zorzi, S.; Lombardi, D.; Deganello, A.; et al. Smell and taste alterations in COVID-19: A cross-sectional analysis of different cohorts. *Int. Forum Allergy Rhinol.* **2020**, *10*, 955–962. [[CrossRef](#)]
38. Speth, M.M.; Singer-Cornelius, T.; Oberle, M.; Gengler, I.; Brockmeier, S.J.; Sedaghat, A.R. Olfactory dysfunction and sinonasal symptomatology in COVID-10: Prevalence, severity, timing, and associated characteristics. *Otolaryngol. Head Neck Surg.* **2020**, *163*, 114–120. [[CrossRef](#)]
39. Al-Ani, R.M.; Acharya, D. Prevalence of anosmia and ageusia in patients with COVID-19 at a primary heart center, Doha, Qatar. *Indian J. Otolaryngol. Head Neck Surg.* **2020**. [[CrossRef](#)]
40. Lechien, J.R.; Ducarme, M.; Place, S.; Chiesa-Estomba, C.M.; Khalife, M.; De Riu, G.; Vaira, L.A.; de Terwangne, C.; Machayekhi, S.; Marchant, A.; et al. Objective olfactory findings in hospitalized severe COVID-19 patients. *Pathogens* **2020**, *9*, 627. [[CrossRef](#)]
41. Speth, M.M.; Singer-Cornelius, T.; Oberle, M.; Gengler, I.; Brockmeier, S.J.; Sedaghat, A.R. Mood, anxiety and olfactory dysfunction in COVID-19: Evidence of central nervous system involvement? *Laryngoscope* **2020**, *130*, 2520–2525. [[CrossRef](#)] [[PubMed](#)]
42. Biadsee, A.; Biadsee, A.; Kassem, F.; Dagan, O.; Masarwa, S.; Ormianer, Z. Olfactory and oral manifestations of COVID-19: Sex-related symptoms—A potential pathway to early diagnosis. *Otolaryngol. Head Neck Surg.* **2020**, *163*, 722–728. [[CrossRef](#)] [[PubMed](#)]
43. Benkirane, H.; Heikel, J.; Laamiri, F.Z.; Bouziani, A.; Lahmam, H.; Al-Jawaldeh, A.; El Halou, N.; Ennibi, K.; Akhtar-Khan, N.; El Fahime, E.M.; et al. Study of clinical and biological characteristics of Moroccan COVID-19 patients with and without olfactory and/or gustatory dysfunction. *Front. Physiol.* **2020**, *11*, 595005. [[CrossRef](#)] [[PubMed](#)]
44. Saussez, S.; Sharma, S.; Thiriard, A.; Olislagers, V.; Vu Duc, I.; Le Bon, S.D.; Khalife, M.; Hans, S.; De Riu, G.; Hopkins, C.; et al. Predictive factors of smell recovery in a clinical series of 288 coronavirus disease 2019 patients with olfactory dysfunction. *Eur. J. Neurol.* **2021**, *28*, 3702–3711. [[CrossRef](#)] [[PubMed](#)]
45. Vaira, L.A.; Lechien, J.R.; Salzano, G.; Maglitto, F.; Saussez, S.; De Riu, G. The role of nasal immunoglobulins in the recovery of olfactory function in COVID-19 patients. *Am. J. Otolaryngol.* **2021**, *43*, 103301. [[CrossRef](#)] [[PubMed](#)]
46. Vaira, L.A.; Salzano, G.; Fois, A.G.; Piombino, P.; De Riu, G. Potential pathogenesis of ageusia and anosmia in COVID-19 patients. *Int. Forum Allergy Rhinol.* **2020**, *10*, 1103–1104. [[CrossRef](#)]
47. Liang, F.; Wang, D.Y. COVID-19 anosmia: High prevalence, plural neuropathogenic mechanisms, and scarce neurotropism of SARS-CoV-2? *Viruses* **2021**, *13*, 2225. [[CrossRef](#)]
48. Vaira, L.A.; Hopkins, C.; Sandizon, A.; Manca, A.; Machouchas, N.; Turilli, D.; Lechien, J.R.; Barillari, M.R.; Salzano, G.; Cossu, A.; et al. Olfactory epithelium histopathological findings in long-term coronavirus disease 2019 related anosmia. *J. Laryngol. Otol.* **2020**, *134*, 1123–1127. [[CrossRef](#)]
49. Dias De Melo, G.; Lazarini, F.; Levallois, S.; Hautefort, C.; Michel, V.; Larrous, F.; Verillaud, B.; Aparicio, C.; Wagner, S.; Gheusi, G.; et al. COVID-19-related anosmia is associated with viral persistence and inflammation in human olfactory epithelium and brain infection in hamsters. *Sci. Transl. Med.* **2021**, *13*, eabf8396. [[CrossRef](#)]

50. Lechien, J.R.; Michel, J.; Radulesco, T.; Chiesa-Estomba, C.M.; Vaira, L.A.; De Riu, G.; Sowerby, L.; Hopkins, C.; Saussez, S. Clinical and radiological evaluations of COVID-19 patients with anosmia: Preliminary report. *Laryngoscope* **2020**, *130*, 2526–2531. [[CrossRef](#)]
51. Lechien, J.R.; Radulesco, T.; Calvo-Henriquez, C.; Chiesa-Estomba, C.M.; Hans, S.; Barillari, M.R.; Cammaroto, G.; Descamps, G.; Hsieh, J.; Vaira, L.; et al. ACE2 & TMPRSS2 expressions in head & neck tissues: A systemic review. *Head Neck Pathol.* **2021**, *15*, 225–235. [[PubMed](#)]
52. Hopkins, C.; Alanin, M.; Philpott, C.; Harries, P.; Withcroft, K.; Qureish, A.; Anari, S.; Ramakrishnan, Y.; Sama, A.; Davies, E.; et al. Management of new onset loss of sense of smell during the COVID-19 pandemic-BRS consensus guidelines. *Clin. Otolaryngol.* **2021**, *46*, 16–22. [[CrossRef](#)] [[PubMed](#)]
53. Vaira, L.A.; Hopkins, C.; Petrocelli, M.; Lechien, J.R.; Cutrupi, S.; Salzano, G.; Chiesa-Estomba, C.M.; Saussez, S.; De Riu, G. Efficacy of corticosteroid therapy in the treatment of long-lasting olfactory disorders in COVID-19 patients. *Rhinology* **2021**, *59*, 21–25. [[CrossRef](#)] [[PubMed](#)]
54. Whitcroft, K.L.; Hummel, T. Olfactory dysfunction in COVID-19: Diagnosis and management. *JAMA* **2020**, *323*, 2512–2514. [[CrossRef](#)] [[PubMed](#)]
55. Vaira, L.A.; Lechien, J.R.; Dore, S.; Boccaletti, R.; Saussez, S.; De Riu, G. Specific therapy of olfactory disorders in COVID-19 patients is essential for the prevention of long-term dysfunction. *Indian J. Otolaryngol. Head Neck Surg.* **2021**. [[CrossRef](#)] [[PubMed](#)]
56. Saussez, S.; Vaira, L.A.; Chiesa-Estomba, C.M.; Bon, S.L.; Horoi, M.; Deiana, G.; Petrocelli, M.; Boelpaep, P.; Salzano, G.; Khalife, M.; et al. Short-term efficacy and safety of oral and nasal corticosteroids in COVID-19 patients with olfactory dysfunction: A European multicenter study. *Pathogens* **2021**, *10*, 698. [[CrossRef](#)] [[PubMed](#)]
57. Lechien, J.R.; Hoch, C.C.; Vaira, L.A.; Saussez, S. The interest of fluticasone nasal spray in COVID-19 related anosmia is still not demonstrated. *Am. J. Otolaryngol.* **2021**, *42*, 103008. [[CrossRef](#)]
58. Lechien, J.R.; Vaira, L.A.; Saussez, S. Effectiveness of olfactory training in COVID-19 patients with olfactory dysfunction: A prospective study. *Eur. Arch. Otolaryngol.* **2022**. [[CrossRef](#)]
59. Haehner, A.; Marquardt, B.; Kardashi, R.; de With, K.; Robler, S.; Landis, B.N.; Welge-Luessen, A.; Hummel, T. SARS-CoV-2 leads to significantly more severe olfactory loss than other seasonal cold viruses. *Life* **2022**, *12*, 461. [[CrossRef](#)]
60. Scotto, C.; Fazio, F.; Lo Muzio, E.; Lo Muzio, L.; Spirito, F. SARS-CoV-2 infection and taste alteration: An overview. *Life* **2022**, *12*, 690. [[CrossRef](#)]
61. Pang, W.P.; Tham, S.L.; Ng, L.S. Exploring the clinical utility of gustatory dysfunction (GD) as a triage symptom prior to reverse transcription polymerase chain reaction (RT-PCR) in the diagnosis of COVID-19: A meta-analysis and systematic review. *Life* **2021**, *11*, 1315. [[CrossRef](#)] [[PubMed](#)]
62. Mazzatorta, A.; Berardi, A.; Novarria, G.A.; Neri, G. Unmasking the “asymptomatic” COVID-19: A nose question. *Life* **2022**, *12*, 1248. [[CrossRef](#)] [[PubMed](#)]
63. Mazzatorta, A.; Maffei, M.; Di Giulio, C.; Neri, G. COVID-19 smell impairment and crosstalk with hypoxia physiology. *Life* **2022**, *12*, 1408. [[CrossRef](#)] [[PubMed](#)]
64. Jungbauer, F.; Gerhards, C.; Thiaucourt, M.; Behnes, M.; Rotter, N.; Schell, A.; Haselmann, V.; Neumaier, M.; Kittel, M. Anosmia testing as early detection of SARS-CoV-2 positivity; a prospective study under screening conditions. *Life* **2022**, *12*, 968. [[CrossRef](#)] [[PubMed](#)]
65. Schambeck, S.E.; Mateyka, L.M.; Burrell, T.; Graf, N.; Brill, I.; Stark, T.; Protzer, U.; Busch, D.H.; Gerhard, M.; Riehl, H.; et al. Two-year follow-up on chemosensory dysfunction and adaptive immune response after infection with SARS-CoV-2 in a cohort of 44 healthcare workers. *Life* **2022**, *12*, 1556. [[CrossRef](#)]
66. Albayay, J.; Fontana, L.; Parma, V.; Zampini, M. Chemosensory dysfunction in long-term COVID-19 assessed by self-reported and direct psychophysical methods. *Life* **2022**, *12*, 1487. [[CrossRef](#)]
67. Vaira, L.A.; Gessa, C.; Deiana, G.; Salzano, G.; Maglitto, F.; Lechien, J.R.; Saussez, S.; Piombino, P.; Biglio, A.; Biglioli, F.; et al. The effects of persistent olfactory and gustatory dysfunctions on quality of life in long-COVID-19 patients. *Life* **2022**, *12*, 141. [[CrossRef](#)]
68. Callejon-Leblie, M.A.; Martin-Jimenez, D.I.; Moreno-Luna, R.; Palacios-Garcia, J.M.; Alvarez-Cendrero, M.; Vizcarra-Melgar, J.A.; Fernandez-Velez, C.; Reyes-Tejero, I.M.; Maza-Solano, J.; Gonzalez-Garcia, J.; et al. Analysis of prevalence and predictive factors of long-lasting olfactory and gustatory dysfunction in COVID-19 patients. *Life* **2022**, *12*, 1256. [[CrossRef](#)]
69. Tipirdamaz, C.; Zayet, S.; Osman, M.; Mercier, J.; Bouvier, E.; Gendrin, V.; Bouiller, K.; Lepiller, Q.; Toko, L.; Pierron, A.; et al. Asthma and cacosmia could be predictive factors of olfactory dysfunction persistence 9 months after SARS-CoV-2 infection: The ANOSVID study. *Life* **2022**, *12*, 929. [[CrossRef](#)]
70. Hintschich, C.A.; Dietz, M.; Haehner, A.; Hummel, T. Topical administration of mometasone is no helpful in post-COVID-19 olfactory dysfunction. *Life* **2022**, *12*, 1483. [[CrossRef](#)]
71. Tsuchiya, H. Gustatory and saliva secretory dysfunctions in COVID-19 patients with zinc deficiency. *Life* **2022**, *12*, 353. [[CrossRef](#)] [[PubMed](#)]
72. Cooper, K.W.; Brann, D.H.; Farruggia, M.C.; Bhutani, S.; Pellegrino, R.; Tsukahara, T.; Weinreb, C.; Joseph, P.V.; Larson, E.D.; Parma, V.; et al. COVID-19 and the chemical senses: Supporting players take center stage. *Neuron* **2020**, *107*, 219–233. [[CrossRef](#)] [[PubMed](#)]