

# Literature Review of COVID-19-Induced Anosmia

Group Code: #0028

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## Abstract

Anosmia, the complete absence of the sense of smell, is a common symptom of COVID-19, the illness caused by the SARS-CoV-2 virus [1,2,3]. The inflammatory nature of the disease causes damages in the olfactory epithelium and the central olfactory processing pathways, inhibiting the regular functioning of the olfactory sensory neurons (OSNs). [7,8,9] Currently, the frequently-used treatment approaches to this symptom are pharmacological treatments and olfactory training. [2] However, the exact cause of this symptom and a generalized treatment method to treat it are much-debated matters. [7] Here we review the current literature regarding the cause and treatment of this symptom. In our extensive literature review, we found that the two most frequently researched treatment approaches are corticosteroid therapy and olfactory training. [2] While corticosteroid therapy showed promising results in some of the studies reviewed, we also found that it showed no results in some studies. [13,14,15,16,17] However, in our review of olfactory training research we found that it showed promising results in all of the studies reviewed. [16,17] Our results show the lack of consensus in the research community, demonstrating the need for additional literature on both of the treatment approaches.

## Keywords

Anosmia; COVID-19; Olfaction; Olfactory epithelium; Smell.

## Introduction

COVID-19, the illness resulting from contact with the SARS-CoV-2 virus, caused the deadly pandemic that has affected hundreds of millions of people and caused millions of fatalities at the time of writing. With its ever-changing variants threatening public health and its diverse symptoms affecting various systems in the body, COVID-19 has come to be one of the deadliest pandemics in written history. [1] Ergo, the significance of additional research on the virus and its related disease is indisputable.

Anosmia is a condition characterized by the complete loss of the ability to smell. [2] A large number of published studies recognize this disorder as a common symptom of acute COVID-19 infection and post-COVID disorder, and indeed, one that significantly impacts patients' daily lives, having been reported by as many as 60% of people affected by COVID-19. [3] However, exactly how it develops is still not fully understood since numerous

studies have pointed at different causes. Patients with this symptom have not only a decreased quality of life but also a lack of smell-related survival skills. (detecting smoke, gas leaks, etc.) [ ] Also, with the increasing number of post-COVID-19 anosmics has come the increasing number of social media users trying to find “cures” to the widespread symptom. With these worrying statistics and the lack of accessible and accurate information in mind, it can be inferred that COVID-19-induced anosmia and its consequences are understudied causes for concern.

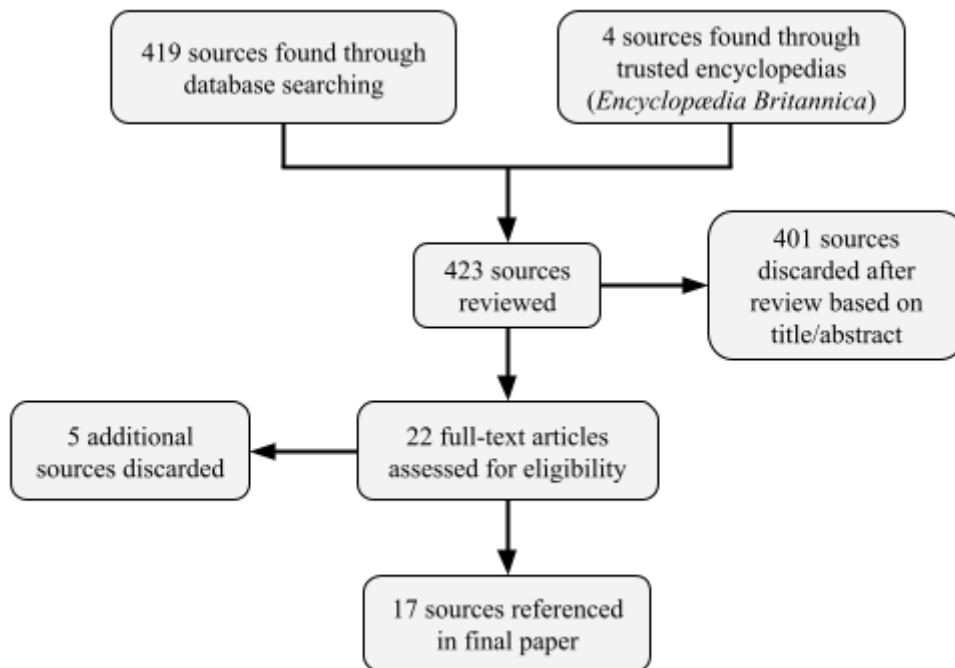
Although studies have recognized this symptom as a common sign of a current or recent COVID-19 infection, research has yet to systematically review the different findings on the causes of anosmia and the current scientific approaches to treating it. [3] The primary aim of this study is to review recent literature attempting to answer the question: “How does COVID-19 cause anosmia, and how can we treat it?” This paper will compare different approaches to the issue and the effectiveness of different treatments currently used. In the pages that follow, it will be argued that COVID-19-induced anosmia can be caused by a range of neurological problems, and that different treatment options are available for the different causes of the symptom. The findings summarize 17 studies written on the topics mentioned earlier. It is hoped that this research will contribute to a deeper understanding of anosmia, the olfactory system, and the COVID-19 pandemic.

This paper will be divided into three distinct chapters. The first chapter, titled “Methods,” will summarize the algorithm utilized to determine the literature to be reviewed. The second chapter, titled “Discussion,” will contextualize the research and discuss the significant findings in their respective subsections. The final chapter, titled “Conclusion,” will summarize the findings and explain their relevance to the research question, concluding the paper.

## **Methods**

This investigation utilized existing data published on PubMed, a research database by the United States National Library of Medicine (NLM). After the research question and keywords were finalized, medical studies to be considered were searched on PubMed using those keywords. Other sources were found through *Encyclopedia Britannica School Advanced*. This study is unable to encompass the entire literature investigating the symptom and therefore used an algorithm to determine the literature to be reviewed, during which the relevant articles entered the evaluation process, discarding duplicate articles and articles of questionable relevance. Additional sources were discarded during the writing process. At the end of the process, 17 sources were selected to be referenced in the paper. The paper selection process is summarized in the flowchart below.

*Figure 1, Flowchart of the paper selection process*



## Discussion

### Post-Infectious Anosmia: Causes and Risk Factors

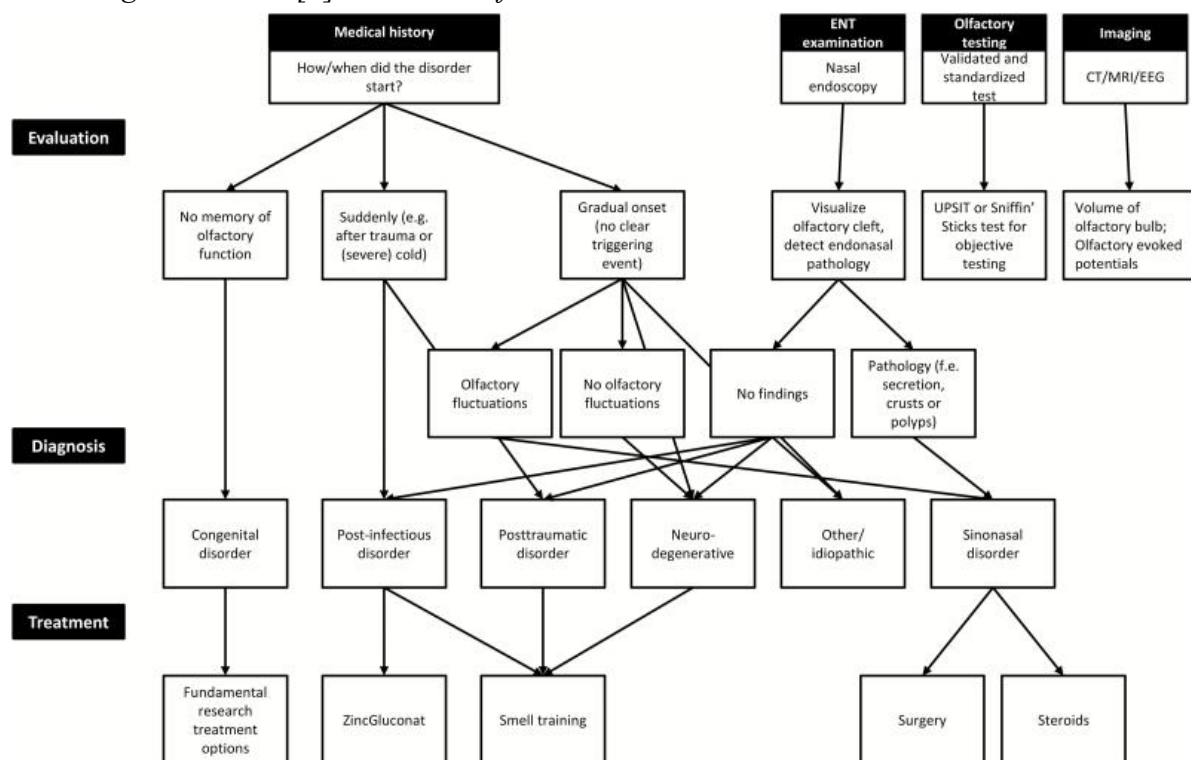
Previous studies mostly categorized COVID-19-induced anosmia as a subtype of post-infectious anosmia. [5,6] However, modern medicine has yet to have reached a consensus on the cause of this disorder. [7] According to a study conducted by Baker H, diseases like COVID-19 cause damage to the olfactory neuroepithelium, the lining on the nasal cavity where olfactory sensory neurons (OSNs) are located. [7,8] However, according to Youngelto S, the damage occurs at the central olfactory processing pathways. [7,9] Another study by Chiu A has identified olfactory bulb atrophy as a potential cause for the symptom. [10] Despite these different approaches, the medical research community agrees that the reported post-infectious anosmia cases usually affect the neuroanatomy of the olfactory system. [7]

Thankfully, determining the groups facing the biggest risk of being affected by COVID-19-induced anosmia is a less controversial matter in the world of otolaryngological research. [7] When it comes to the age and sex of people at risk, research has shown that the risk of experiencing COVID-19-induced anosmia gets higher with age and exposure to infectious organisms, and is also higher in females. [11] The reason for this phenomenon is thought to be that the people of those risk groups have less regeneration in their olfactory tissues. Recent studies have also discovered that patients with higher-volume olfactory bulbs are more likely to experience post-COVID anosmia. [12] This means that people who have an exceptional ability to smell are at an increased risk of losing this sense.

## Pharmaceutical Treatments vs. Olfactory Training

When it comes to the treatments of COVID-19-induced anosmia, otolaryngologists consider two treatment options: pharmaceutical treatments and olfactory training. [2] This section of the discussion chapter will compare the two treatment approaches, summarizing the findings in those studies. Below is a flowchart summarizing some of the causes of olfactory dysfunction and their treatment methods.

Figure 2, From [2], Guidelines for clinical evaluation and outcomes



## The Pharmaceutical Approach

The pharmaceutical approach, as the name suggests, is the wide range of treatment options utilizing different pharmaceuticals. This subsection will review the different pharmaceuticals used to treat COVID-19-induced anosmia and their effectiveness. Some substances used include corticosteroids, reducing inflammation in the olfactory bulb and epithelium. [13,14,15,16]

Table 1, Summary of research on corticosteroid therapy

Authors	Title	Participants	Results
Huart et al.	Systemic corticosteroids in coronavirus disease	71 patients treated with topical corticosteroids,	No recovery

	2019 (COVID-19)-related smell dysfunction: an international view	58 patients treated with systemic corticosteroids	
Le Bon et al.	Efficacy and safety of oral corticosteroids and olfactory training in the management of COVID-19-related loss of smell	72 non-hospitalized patients with loss of smell due to COVID-19	No significant improvement
Holbrook et al.	Anosmia: diagnosis and management	60 patients	83% success rate
Vaira et al.	Efficacy of corticosteroid therapy in the treatment of longstanding olfactory disorders in COVID-19 patients	nine patients treated with prednisone, nine control group patients	“the mix of drugs including steroids could represent a useful specific therapy to reduce the prevalence of this long-term morbidity” [15]

As seen in the table above, previous research on corticosteroid treatment gave mixed results.

## Olfactory Training

Olfactory training is a technique used by otolaryngologists worldwide to start the regeneration of the OSNs and olfactory neuroepithelium by stimulating the olfactory system with strong odors training patients to distinguish between them. [16,17] Below is a summary of studies investigating the efficacy of olfactory training.

*Table 2, Summary of research on olfactory training*

Authors	Title	Participants	Results
Liu et al.	Factors associated with relevant olfactory recovery after olfactory training: a retrospective study including 601 participants	601 participants using retrospective research techniques	Olfactory training showed promising improvement in both patients and the control group

Le Bon et al.	Efficacy and safety of oral corticosteroids and olfactory training in the management of COVID-19-related loss of smell	27 participants	Significant improvement
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As seen in the table above, olfactory training resulted in a significant improvement in olfactory function in both studies, showing promising results.

## Conclusion

This study set out to explore the current scientific understanding of COVID-19-induced anosmia, and the efficacies of the novel treatment approaches used. Initially, the paper therefore aimed to test the following hypothesis: “COVID-19-induced anosmia requires different treatments for its different causes.” The findings contribute in several ways to our understanding of post-COVID anosmia and provide a basis for developing a standardized course of treatment for all COVID-19 anosmics. These findings clearly indicate that studies using olfactory training have shown more promising results than studies utilizing corticosteroids. [13,14,15,16,17] However, this does not necessarily mean that olfactory training will always work better than corticosteroids when treating this symptom. This study would have been more generative if the researchers referenced had specified the cause of their patients’ symptoms. One question raised by this study, therefore, is whether these results could be replicated in all those affected by COVID-19-induced anosmia. Further studies should consider including more patients and patients from more diverse backgrounds. This would be a fruitful area for additional research.

As COVID-19 continues to take lives from all around the world, it’s of utmost importance to acknowledge that almost every person on Earth is at risk. With its gruesome respiratory symptoms and notoriously contagious nature, the only tried-and-true way of fighting this novel pandemic is to make accurate information more accessible to the general public through academic research. Anosmia, a common symptom of COVID-19, is a shared experience between most of the people affected by the illness. It is our responsibility, as medical researchers, to ensure the successful recovery of future patients with this symptom. Hopefully, in the future, everyone will be able to smell the blooming honeysuckles in their gardens, the fresh pine leaves at the local park, the salty water at the seashore, and the overwhelming smells at the spice market.

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