**RESEARCH ARTICLE** 

## **Optimizing Respiratory Defense Against Viral Threats**

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## **ABSTRACT**

People of all ages are susceptible to respiratory tract viral infections, placing a significant burden on healthcare systems worldwide. Adenoviruses, coronaviruses, rhinoviruses, influenza, and respiratory syncytial virus (RSV) are among the most prevalent respiratory viruses that cause illness, hospitalization, and mortality worldwide. Their fast spread in communal settings is facilitated by their persistence on contaminated surfaces, in droplets, and in aerosols. While certain infections may lead to more serious problems, such as pneumonia or acute respiratory distress syndrome (ARDS), the majority of cases cause only moderate upper respiratory illness. Dryness, temperature fluctuations, and airborne particles are all threats to the respiratory mucosa. Additionally, ventilatory demand increases during exercise, jogging, and daily activities.

Host protection is a multifaceted effort that encompasses physical barriers, mucociliary clearance, adaptive and innate immunity, and optimal lung function. Methods like nose breathing, vaccination, moderate exercise, better air quality, healthy eating, and rehabilitation all contribute to these defenses. Various diagnostic methods, including radiography, molecular and antigen testing, and enhanced genomic monitoring, are utilized throughout the evaluation process.

The therapy options include various methods, such as targeted antivirals, immunomodulatory medications, supportive oxygen therapies, and prophylactic immunizations. Airway hydration, environmental control, and non-pharmaceutical treatments (NPIs) can all work together to increase viral resistance. Lung fibrosis, post-viral fatigue syndrome, persistent airway hyperresponsiveness, and other long-term virus-related consequences necessitate intervention programs. Many problems persist, including the fact that viruses continue to evolve, not everyone has access to vaccines, and communities are still experiencing the effects.

This comprehensive study encompasses a range of topics, including respiratory pathophysiology, the impact of exercise and environment, epidemiologic trends, diagnosis, treatment, and rehabilitation. Supporting airway defenses and helping hosts remain resilient against both new and current viral infections, it stresses evidence-based, real-world techniques.

## 1. Introduction

Tropism and transmission pathway are two methods for categorizing human-threatening respiratory viruses. 1,2. While a primary upper respiratory tract virus causes rhinitis, tracheobronchitis, and pneumonia are associated with a primary lower respiratory tract virus that infects the tracheobronchial epithelium. Although viruses affecting the lower respiratory tract can cause global pandemics when they propagate through the upper tract, viruses affecting the upper respiratory system seldom spread beyond the nasopharynx. Second, unlike viruses disseminated by huge droplets, aerosol-transmitted viruses are unique.3 Droplet viruses are more likely to exhibit upper respiratory tropism; however, viruses dispersed in aerosols may have either a lower or upper respiratory tropism. Pathogens belonging to the same class often elicit comparable immune responses and require comparable defense mechanisms, which guides the selection of target viruses for particular treatments.4 Respiratory viruses, such as influenza, RSV, coronaviruses, rhinoviruses, and adenoviruses, are the culprits behind seasonal epidemics and infrequent pandemics 1,3. Most often, they spread from person to person through contaminated surfaces, droplets, or aerosols; the severity of their symptoms can vary from a minor infection of the upper respiratory tract to a life-threatening acute respiratory distress syndrome (ARDS). Worldwide, respiratory viruses have a major impact. Annually, up to 650,000 people die from influenza, and RSV is still the leading cause of infant hospitalization 3.

The COVID-19 pandemic has drawn greater attention to viral respiratory infections, heightened awareness of the need for scalable respiratory care systems, and highlighted the lack of preparedness. When it comes to respiratory care, this article covers a comprehensive range of topics, including epidemiology, virology, diagnosis, therapy, rehabilitation, and the systemic implications of viruses. Two criteria, tropism and transmission pathway, are used to categorize the respiratory viruses that are harmful to humans.<sup>2</sup> While a primary upper respiratory tract virus causes rhinitis, tracheobronchitis, and pneumonia are associated with a primary lower respiratory tract virus that infects the tracheobronchial epithelium. Although viruses affecting the lower respiratory tract can cause global pandemics when they propagate through the upper tract, viruses affecting the upper respiratory system seldom spread beyond the nasopharynx. Second, unlike viruses disseminated by huge droplets, aerosol-transmitted viruses are unique. Droplet viruses are more likely to exhibit upper respiratory tropism; however, viruses dispersed in aerosols may have either a lower or upper respiratory tropism. Within a given group of pathogens, similar immunological responses and defensive mechanisms are typically required, which informs the selection of target viruses for specific treatments.4

## 2. Respiratory Viral Infections Epidemiology: Overview

Influential factors in the seasonal patterns of respiratory viruses include weather conditions, population density, and host immunity. While mild coronaviruses, such as those causing the common cold, are widespread, more severe

varieties, including SARS-CoV, MERS-CoV, and SARS-CoV-2, can produce devastating epidemics and high mortality rates.  $^{4,5}$ 

- Influenza viruses: A type of virus that causes seasonal epidemics and recurring outbreaks due to its changing antigenic profile
- Respiratory Syncytial Virus: mainly affects newborns and the elderly; causes pneumonia and bronchiolitis.
- Coronaviruses: Although coronaviruses, which cause the common cold, are very contagious, they mostly affect young children and the elderly.
- Rhinoviruses: Although rhinoviruses are most commonly associated with causing colds, they can exacerbate asthma and COPD. 5,6

Genomic sequencing and epidemiological surveillance are crucial for tracking viral evolution and informing vaccine development 5,6

## 2.1. CURRENT STATE OF RESPIRATORY VIRAL INFECTIONS (2025)

Seasonal viruses, such as influenza, RSV, and COVID-19, continue to pose a significant challenge for healthcare systems worldwide and threaten respiratory health. Hospitalization rates for COVID-19 in the United States are lower than at similar times in past seasons, and the virus is currently showing signs of decline.<sup>7,8</sup> The Centers for Disease Control and Prevention (CDC) has estimated that COVID-19 hospitalizations during the 2025–26 respiratory season might reach 3.8 to 5.9 per 100,000 people weekly, assuming no new immune-escape variants emerge. Hospitalization data globally are still being collected, though severity varies by location. Influenza and RSV remain the main respiratory illnesses during winter. By mid-2025, respiratory virus activity in Europe had notably decreased. However, acute respiratory infections have increased in many Northern Hemisphere countries as the weather warmed, and reports of RSV resurgence have matched or exceeded pre-pandemic levels. These seasonal spikes may have worsened due to "immunity debt" caused by the relaxation of laws on nonpharmaceutical interventions (NPIs). Viruses such as rhinoviruses, seasonal coronaviruses, and metapneumoviruses can still infect the elderly and young children, even when influenza and RSV are less prevalent.

The difficulty of distinguishing between the incidence and severity of diseases persists. Vaccine and prior infection immunity, combined with improved treatment procedures, have reduced the severity of clinical outcomes, even though the virus remains widely prevalent.<sup>8,9</sup> The overlapping peaks of COVID-19, influenza, and RSV increase the risk of healthcare services being overwhelmed. Prolonged chronic obstructive pulmonary disease (COPD) and other long-term consequences can show up months or even years after the virus has passed. This raises serious concerns for the public's well-being.<sup>11,12</sup>

The importance of syndromic reporting and wastewater monitoring has grown in response to a decline in diagnostic testing rates; yet, there are still gaps in surveillance. <sup>13,14,15</sup>. This can cause a delay in identifying new variants or surges. Given that SARS-CoV-2,

influenza, and RSV all emerged simultaneously, it is imperative that we move forward with integrated surveillance, vaccination campaigns, and preparedness plans for coinfection.<sup>16-19</sup>

## 3. Pathophysiology of Viral Respiratory Disease

Viral respiratory infections progress through a complex pathophysiology involving interactions between the host and the virus. The innate immune system is activated when viruses infect cells after adhering to receptors on epithelial cells. 18,19

- The innate immune system's defense mechanism:
   Toll-like receptors and other pattern recognition receptors (PRRs) identify viral RNA and trigger the interferon pathways.<sup>20</sup>
- The adaptive immune response, which includes cytotoxic T cells and neutralizing antibodies, plays an essential role in viral clearance but can potentially cause tissue damage in cases of severe illness.<sup>21</sup>
- Inflammatory damage: A "cytokine storm" and acute respiratory distress syndrome (ARDS) are symptoms of illnesses like COVID-19, which are caused by an overproduction of cytokines.<sup>22</sup>

Respiratory diseases, including asthma and chronic obstructive pulmonary disease (COPD), may be made worse by long-term viral infections.<sup>23,24,25</sup>

The pathophysiology of viral respiratory infections is intricate and involves interactions between the host and the virus. Viruses attach to receptors on epithelial cells and infect cells, activating the innate immune system. As a protective measure, the innate immune system uses pattern recognition receptors (PRRs), such as toll-like receptors, to detect viral RNA and trigger the interferon pathways.<sup>20</sup>

- Cytotoxic T cells and neutralizing antibodies are part of the adaptive immune response, which is crucial for viral clearance but, in extreme circumstances of sickness, can damage tissues.<sup>21</sup>
- Inflammatory damage: diseases like COVID-19 are characterized by symptoms such as acute respiratory distress syndrome (ARDS) and a "cytokine storm" due to the overproduction of cytokines. <sup>22</sup> Asthma and COPD are only two of the respiratory disorders that might worsen with time after contracting a virus. <sup>23,24,25</sup>

## 4. Respiratory Viral Infection Diagnosis

A timely and precise diagnosis is essential for guiding management and infection control measures.  $^{24\text{-}27}$ 

When searching for viral RNA, results from RT-PCR testing are considered accurate and reliable. Antigen detection tests are excellent for quick diagnosis at the point of service, although they aren't as sensitive as other procedures. Serology is a valuable tool for epidemiological studies, as it reveals immune responses and indicates previous infections. Chest X-rays and CT scans are important imaging techniques for evaluating outcomes of viral pneumonia. The development of next-generation sequencing and CRISPR-based testing has

significantly enhanced the capacity for surveillance and outbreak detection. <sup>26,27,28</sup>

# 5. Strategies for the Treatment of Respiratory Viral Diseases

There are antivirals designed to target specific viruses. A combination of neuraminidase inhibitors (oseltamivir, zanamivir, and baloxavir) can reduce the impact and spread of influenza if administered early. Several medications have demonstrated therapeutic efficacy in treating COVID-19, including remdesivir, nirmatrelvir/ritonavir, and molnupiravir. <sup>29,30</sup>

People at high risk of contracting RSV are treated with ribavirin and monoclonal antibodies such as palivizumab and nirsevimab.<sup>31</sup>

#### SUPPORTIVE CARE

- Utilizing oxygen for the treatment of hypoxemia
- Mechanical breathing or high-flow nasal oxygen treatment.
- Controlling fluids to minimize pulmonary edema risk while preserving resuscitation efforts. <sup>32</sup>

## TREATMENT WITH IMMUNOMODULATORS

- Corticosteroids: When administered correctly, they can be helpful in cases with COVID-19 ARDS.<sup>33</sup>
- Monoclonal antibodies: They offer passive protection against SARS and influenza. Coronavirus Type 2.34 Virus care approaches must include antipyretics, hydration, and nutritional assistance as adjunctive care.

## 6. Preventive Measures

The primary goal of treating respiratory viruses should always be prevention.

- Immunization: COVID-19 vaccinations considerably lessen serious consequences; influenza vaccines are revised yearly. New RSV vaccines are being developed for use in pregnant women and the elderly.<sup>36,37</sup>
- Non-pharmacological interventions: Social distancing, hand cleanliness, masks, and other nonpharmacological treatments lessen the transmission of viruses. 38
- Prophylaxis: In high-risk populations, antiviral chemoprophylaxis is recommended during influenza outbreaks.

To reduce transmission, it is crucial that the community gets involved and follows preventive measures.

## 7. Care for the Elderly and Rehabilitation

Chronic complications can develop from some viral respiratory infections:

- Dyspnea, exhaustion, and cognitive impairments are some of the long-term symptoms of post-viral tiredness and chronic obstructive pulmonary disease (COPD).<sup>40</sup> In extreme cases of viral pneumonia, pulmonary fibrosis can develop.<sup>41</sup>
- Airway hyperresponsiveness: Asthma flare-ups are prevalent after a viral infection. 42

- One approach to rehabilitation is pulmonary rehabilitation, which includes activities like exercise and breathing exercises.
- Support for mental health issues related to post-viral anxiety and despair.
- Chronic lung illness, pulmonary hypertension, and fibrosis: long-term follow-up.<sup>41</sup>

### A GLOBAL VIEW ON PUBLIC HEALTH

A major concern for public health is the prevalence of viral respiratory infections:

Seasonal influenza surges put a strain on hospital systems, which in turn burdens healthcare.  $^{42}$ 

- Expenditures on healthcare and lost productivity add up to a significant economic burden. 42
- Inequity: Vaccine distribution and access to antivirals are challenges for low- and middle-income nations.

To mitigate future risks, it is essential to enhance monitoring, foster global collaboration, and improve pandemic preparedness.

## **Challenges**

Problems persist despite advances:

- Rapid evolution of viruses like influenza and SARS-CoV-2 compromises the efficacy of vaccines<sup>38</sup>.
- Inequalities in access to molecular testing continue to contribute to diagnostic discrepancies.
- Heterogeneity of the patient population: treatment becomes more complicated due to comorbidities and immune response variability.

 Long COVID is a prime example of the unpredictability of post-viral disorders, which can last for years. 41,42

Innovative diagnostics, universal immunizations, and fair global health policies are the means by which research must fill these gaps.

## Conclusion

Viruses that cause respiratory infections still cause a lot of harm, including death and economic losses. Prevention, early diagnosis, antiviral and supportive therapies based on research, and long-term rehabilitation are all components of effective respiratory care. While antiviral and immunomodulatory treatments provide specific benefits, the most effective strategies for reducing viral spread are vaccination and non-pharmacological techniques.

Being well-prepared, closely monitored, and receiving care from a variety of medical professionals are all crucial in light of the widespread effects of respiratory viruses, as the COVID-19 pandemic has shown. Although local and systemic illnesses might result from restricted airflow, it is crucial for recovery and long-term health to restore respiratory function through supportive and rehabilitative therapy.

Universal immunizations, rapid diagnostic technologies, personalized immunotherapies, and enhanced public health infrastructure should be the focus of future research and development efforts. It is crucial to prioritize respiratory care for viral diseases as a vital component of global health security and an urgent clinical necessity.

## References

- 1. Jain S, Williams DJ, Arnold SR, et al. Community-acquired pneumonia requiring hospitalization among U.S. children. *N Engl J Med*. 2015;372(9):835-845.
- 2. Killingley B, Nguyen-Van-Tam J. Routes of influenza transmission. *Influenza Other Respir Viruses*. 2013;7(suppl 2):42-51.
- Iuliano AD, Roguski KM, Chang HH, et al. Estimates of global seasonal influenza-associated respiratory mortality. Lancet. 2018;391(10127):1285-1300.
- 4. Shi T, McAllister DA, O'Brien KL, et al. Global burden of RSV in young children. *Lancet*. 2017;390(10098):946-958.
- 5. Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. Nat Rev Microbiol. 2021;19(3):141-154.
- 6. Falsey AR, Walsh EE. Respiratory syncytial virus infection in adults. Clin Microbiol Rev. 2000;13(3):371-384.
- Petrova VN, Russell CA. The evolution of seasonal influenza viruses. Nat Rev Microbiol. 2018;16(1):47-60.
- 8. Jacobs SE, Lamson DM, St George K, Walsh TJ. Human rhinoviruses. Clin Microbiol Rev. 2013;26(1):135-162.
- 9. Bedford T, Riley S, Barr IG, et al. Global circulation patterns of seasonal influenza viruses. *Nature*. 2015;523(7559):217-220.
- CIDRAP. US COVID declining after reaching peak. Published 2025. Available from: https://www.cidrap.umn.edu/covid-19/us-covid-declining-after-reaching-peak
- Centers for Disease Control and Prevention (CDC).
   2025–26 Respiratory Season Outlook. Published
   2025. Available from: https://www.cdc.gov/cfa-qualitative-assessments/php/data-research/season-outlook25-26.html
- 12. World Health Organization (WHO). COVID-19 global hospitalization data dashboard. Published 2025. Available from: https://data.who.int/dashboards/covid19/hospitalizations
- 13. European Centre for Disease Prevention and Control (ECDC). Weekly respiratory virus update, May 2025. Available from: https://www.ecdc.europa.eu/en/publications-data/weekly-respiratory-virus-update-week-19-may-2025
- 14. World Health Organization (WHO). Disease Outbreak News: Respiratory infections, 2025. Available from: https://www.who.int/emergencies/diseaseoutbreak-news/item/2025-DON550
- 15. Agha R, Avner JR. Delayed RSV epidemic in 2021 after relaxation of COVID-19 measures. *Pediatrics*. 2021;148(3):e2021052089.
- 16. Jacobs SE, Lamson DM, St George K, Walsh TJ. Human rhinoviruses. Clin Microbiol Rev. 2013;26(1):135-162.
- 17. Centers for Disease Control and Prevention (CDC). Respiratory virus activity levels. Published 2025. Available from: https://www.cdc.gov/respiratory-viruses/data/activity-levels.html

- Nalbandian A, Sehgal K, Gupta A, et al. Post-acute COVID-19 syndrome. Nat Med. 2021;27(4):601-615.
- 19. Mina MJ, Parker R, Larremore DB. Rethinking COVID-19 test sensitivity. N Engl J Med. 2020;383(22):e120.
- 20. Kawai T, Akira S. Innate immune recognition of viral infection. *Nat Immunol*. 2006;7(2):131-137.
- 21. Altmann DM, Boyton RJ. SARS-CoV-2 T-cell immunity. Nat Rev Immunol. 2020;20(10):587-588.
- 22. Mehta P, McAuley DF, Brown M, et al. COVID-19: cytokine storm. *Lancet*. 2020;395(10229):1033-1034.
- 23. Johnston SL. Viruses and asthma exacerbations. *Proc Am Thorac* Soc. 2005;2(2):150-156.
- 24. Corman VM, Landt O, Kaiser M, et al. Detection of 2019 novel coronavirus by real-time RT-PCR. *Euro Surveill*. 2020;25(3):2000045.
- 25. Scohy A, Anantharajah A, Bodeus M, et al. Low performance of rapid antigen tests for SARS-CoV-2. *Int J Infect Dis.* 2020;97:244-246.
- 26. Long QX, Liu BZ, Deng HJ, et al. Antibody responses to SARS-CoV-2. Nat Med. 2020;26(6):845-848.
- 27. Kanne JP, Little BP, Chung JH, et al. Essentials for radiologists on COVID-19. *Radiology*. 2020;296(2):E113-E114.
- 28. Kellner MJ, Koob JG, Gootenberg JS, et al. CRISPR-based diagnostics. *Science*. 2019;364(6446):1464-1468.
- 29. Dobson J, Whitley RJ, Pocock S, Monto AS. Oseltamivir treatment for influenza in adults. *Lancet*. 2015;385(9979):1729-1737.
- Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for COVID-19. N Engl J Med. 2020;383(19):1813-1826.
- 31. Griffin MP, Yuan Y, Takas T, et al. Nirsevimab for prevention of RSV. N Engl J Med. 2020;383(5):415-425.
- 32. Fan E, Beitler JR, Brochard L, et al. Ventilatory support for COVID-19 patients. *JAMA*. 2020;323(22):2329-2336.
- 33. RECOVERY Collaborative Group. Dexamethasone in hospitalized COVID-19 patients. *N Engl J Med*. 2021;384(8):693-704.
- 34. Weinreich DM, Sivapalasingam S, Norton T, et al. REGN-COV2 antibody cocktail in COVID-19. *N Engl J Med*. 2021;384(3):238-251.
- 35. Grohskopf LA, Alyanak E, Ferdinands JM, et al. Influenza vaccination recommendations. MMWR Recomm Rep. 2021;70(5):1-24.
- 36. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. *N Engl J Med.* 2020;383(27):2603-2615.
- 37. Hammitt LL, Dagan R, Yuan Y, et al. RSV vaccine in pregnancy. *N Engl J Med*. 2022;386(19):1735-1746.
- 38. Chu DK, Akl EA, Duda S, et al. Physical distancing, masks, and eye protection. *Lancet*. 2020;395(10242):1973-1987.
- 39. Hayden FG, Belshe R, Villanueva C, et al. Antiviral prophylaxis in influenza. *N Engl J Med*. 2004;351(10):997-1007.
- 40. Nalbandian A, Sehgal K, Gupta A, et al. Post-acute COVID-19 syndrome. *Nat Med.* 2021;27(4):601-615.

- 41. George PM, Wells AU, Jenkins RG. Pulmonary fibrosis after COVID-19. Lancet Respir Med. 2020;8(8):807-815
- 42. Gallo O, Locatello LG, Mazzoni A, Novelli L, Annunziato F. The central role of the host immune response in COVID-19. Front Immunol. 2021;12:652383.