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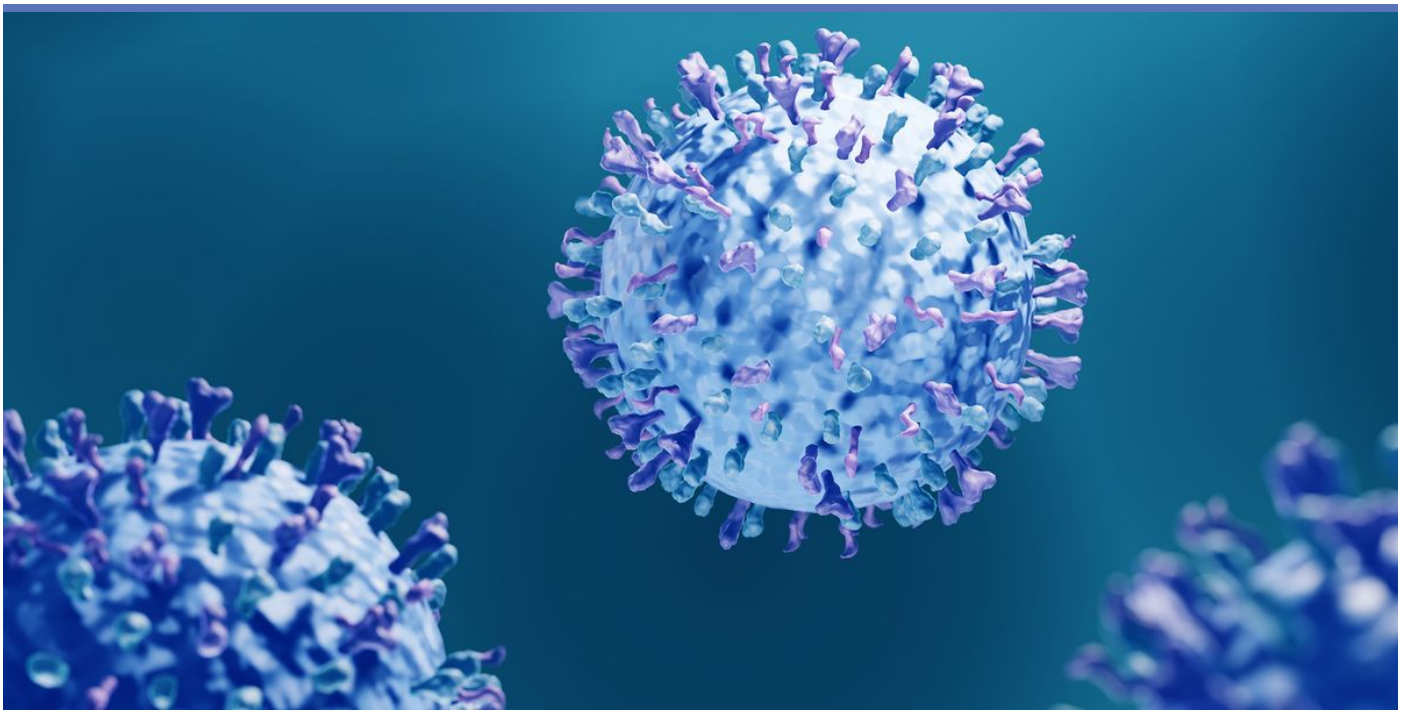

# Everything You Need to Know about RSV

## Updates on respiratory syncytial virus (RSV), including diagnostic tools and treatment options

Feb 27, 2023 PALLAVI UPADHYAY, PHD

Respiratory syncytial virus, or RSV, is universally recognized as one of the most crucial and common causes of childhood illness. Its impact on the elderly is equally harmful. Prior to the COVID-19 pandemic, RSV infections in the US displayed predictable seasonality for the winter months, and outbreaks were mostly concentrated from December through February. During the winter of 2020 and 2021, at the height of the COVID- 19 pandemic and associated public health measures, RSV infection levels plummeted.

However, at the tail end of 2022, when COVID-19 restrictions were eased, we found ourselves amid a new RSV outbreak, which quickly overwhelmed our health care system with increased hospitalizations and outpatient admissions. According to an alert issued by the CDC on November 4, 2022, RSV levels in the population were much higher and the occurrence of outbreaks much earlier than what had been noted in previous years.[1]

The long-term impact of the COVID-19 pandemic on the occurrence and severity of other

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respiratory viruses including RSV remains unknown, but preparedness is the key to handling increases in disease burden. Disease awareness and advancements in therapeutics, diagnostics, and prophylactics— especially vaccines—are all crucial to combating these viruses.

## What is RSV?

Respiratory syncytial virus, or RSV, is a single- stranded RNA virus discovered in 1956 that belongs to the Paramyxoviridae family and causes respiratory tract infections (RTIs).[2] To date, the only known hosts for RSV are humans and chimpanzees. The two antigenic subtypes of RSV are A and B,[3] and the predominant RSV strain in circulation varies from year to year and differs with respect to populations, making it difficult for researchers to conduct epidemiological studies of the virus, as well as to predict outbreaks.

## How does RSV spread?

RSV spreads through contact with respiratory droplets from an infected individual or through being in direct contact with objects contaminated with the virus. Due to its genetic makeup and replication mechanisms, RSV evades host immune responses and easily avoids any potential vaccine and/or antiviral agents.[4] This can lead to frequent reinfections (sometimes more than twice during the same season).[5]

## How does RSV affect children?

RSV is a highly contagious respiratory virus. According to the CDC, almost every child will have acquired an RSV infection by their second birthday. While RSV can infect any age group, young children and older adults (mainly adults aged 65 years and above) make up the majority of RSV-associated hospitalizations and ER visits.[6] RSV is one of the most frequent causes of bronchiolitis (inflammation of the small airways in the lung) and pneumonia (lung inflammation) in people aged 0–1 years old. Children and the elderly with preexisting and/or chronic health conditions are considered high-risk for severe RSV infections.

> “Predicting the future spread and epidemiology of RSV will be key to public health.”

The CDC estimates that in the US, approximately 58,000–80,000 hospitalizations due to RSV infection are recorded each year in children aged less than five years old. Globally, this burden equates to more than 3 million hospitalizations per year. Worldwide, RSV remains the second most prevalent cause of mortality in children less than one year of age.[7]

## How does RSV affect older adults?

The burden of RSV is not as elaborately studied in the elderly population as it is in children; however, within the past decade, RSV has been identified as one of the major causes of morbidity and mortality in older adults. According to a 2003 study published in the *JAMA*, while the highest RSV infection rates are noted in children, the RSV-associated death rate is the highest in elderly populations.[8] The CDC estimates that 60,000–120,000 hospitalizations and approximately 10,000 deaths occur annually due to RSV infection in older adults.

## RSV testing methods

There are currently four major diagnostic testing options to detect RSV from patient samples:[9]

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| **Viral culture** | Formerly considered the gold standard for detecting viral species in clinical specimens, viral cultures have some drawbacks—assessing and reading viral cultures not only requires specialized expertise, but it is also time and resource intensive, with a turnaround time from anywhere between three and seven days. |
| **Immunofluorescence testing** | Though immunofluorescence testing can quickly detect RSV in only three to four hours, the technique requires specialists and is comparatively less sensitive than nucleic acid amplification (NAAT)-based tests. |
| **Rapid antigen diagnostic tests (RADTs)** | There are many commercially available RADTs that are easy to perform with a quick turnaround time of 30 minutes or less. However, RADTs suffer from low sensitivity, leading to high rates of false negative detections. |
| **Nucleic acid** | RT-PCR is currently considered the standard reference diagnostic method for respiratory virus testing, including for RSV, due to its specificity and sensitivity and rapid turnaround time. |

**amplification tests (NAATs)**

## The impact of COVID-19 on RSV seasonality

In the US, the regular seasonality of RSV infections begins in November and peaks from December through February before quickly dissipating in March. In the Southern Hemisphere, RSV circulates from June to September. However, in both cases, the virus does not lie dormant during the "off season"—low levels of RSV can be detected in both asymptomatic and symptomatic patients (e.g., immunodeficient children and adults and patients with COPD) throughout the year.

> **"The long-term impact of the COVID-19 pandemic on the occurrence and severity of other respiratory viruses including RSV remains unknown."**

Before the COVID-19 pandemic, RSV seasonality and circulation was quite predictable. In the past two years, influenza-like illness (ILI) was dominated by SARS-CoV-2. In 2020 and 2021, the CDC reported drastically low levels of RSV (averaging at 1 percent per week as opposed to 12 percent–16 percent per week pre-COVID-19).[10] These low levels overlapped with strict public health measures (including non-pharmaceutical interventions, or NPIs, such as social distancing, lockdowns, restricted international travel, etc.) to slow the COVID-19 pandemic.

More specifically, recent epidemiological studies of infections in 2020 showed that international travel restrictions coincided with the decrease of RSV.[11] One explanation for this was that NPI measures implemented for COVID-19 were actually more effective for reducing RSV infections, reducing the spread of RSV from one country to another. Another hypothesis suggested "viral–viral interference," where one virus prohibits the spread and proliferation of another, as the reason for fewer cases of RSV. In this scenario, SARS-CoV-2 was thought to have interfered in the transmission of RSV. The very low incidence of SARS-CoV-2 coinfections with other respiratory viruses seems to support this hypothesis.[12]

Due to the clinical importance of RSV and the noted co-circulation pattern of winter viruses (RSV, influenza, and COVID-19), predicting the future spread and epidemiology of RSV will be

key to public health. As the CDC announced last November, this winter saw a significantly higher uptick in respiratory viruses compared to last year—often referred to as a "tripledemic." The term tripledemic does not refer to coinfections but to "co-circulation" of the three prominent respiratory viruses within a population. The drastic increase in the detection and spread of these respiratory viruses has been attributed to an "immunity gap" or "immunity debt," which refers to diminished immunity due to low or zero exposure to a specific pathogen for an extended period of time, making a community or population prone to the infection.

## Advances in RSV diagnostics, treatment, and prevention

The COVID-19 pandemic has taught us how important it is to also follow public health measures for curtailing the spread of other respiratory viruses, including RSV.

In its alert, the CDC highlighted the importance of timely testing and vaccination (influenza and COVID-19) to minimize the health care burden of respiratory illness during a "tripledemic." For RSV infections, it is recommended that at-risk populations (infants, children, and the elderly) be administered palivizumab, an FDA-approved antiviral against RSV.

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Vaccines remain one of the prime strategies to prevent RTIs and associated morbidities. At present, there are multiple vaccine candidates under review/investigation. In fact, Pfizer recently released their data from a Phase 3 trial of its bivalent RSV vaccine candidate, which promises 81 percent efficacy against RTIs due to RSV in infants during the initial 90 days of life.[13] Review of the trial has been fast-tracked by the FDA.

While prevention is better than treatment, accurate and timely diagnostic testing remains the vanguard against the spread of infectious disease. All respiratory viruses depict similar ILI symptoms, making it cumbersome to distinguish between them, which is crucial to effective patient management and care. Therefore, in its alert, the CDC recommended using multiplex PCR-based molecular diagnostic tests for patients (especially inpatients and patients that present comorbidities like risk factors) suspected of viral respiratory infections.

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