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# Respiratory syncytial virus (RSV): prevention and antiviral therapeutic strategies

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**Abstract**

Respiratory syncytial virus (RSV) is a leading cause of acute respiratory infections, particularly among young children and older adults. It specifically targets ciliated epithelial cells, setting off a cascade that includes the release of pro-inflammatory cytokines and the activation of an innate antiviral defense by alveolar macrophages and dendritic cells. Antivirals for the RSV function by preventing the virus from replicating. By interacting with guanosine triphosphate, the nucleoside analog ribavirin prevents the synthesis of viral RNA and causes fatal mutagenesis. Palivizumab, a monoclonal antibody, neutralizes RSV by binding to its F protein, thereby obstructing the virus's ability to fuse with and penetrate host cells. Another monoclonal antibody that neutralizes RSV and prevents cell infection is nisevimab, which offers prolonged protection. Fusing inhibitors, such as the investigative drug presatovir, disrupt the fusing of viral membranes, thereby preventing the virus from entering host cells. Our increasing knowledge of RSV pathophysiology and immunopathology over the past few decades has led to significant advancements in prevention strategies. Although RSV exerts a profound impact on public health, the available clinical interventions are limited to only two approved drugs: ribavirin and palivizumab. It is important to note that palivizumab is used solely as a preventive measure rather than as a treatment option. Currently, numerous research groups are exploring new treatments for RSV, focusing on three main research areas: small molecules, polymeric drugs (proteins and peptides), and plant-derived compounds. Emphasizing the development of therapies designed to disrupt key stages in the virus's life cycle, this article examines the advancements and difficulties in this field. We also give an update on the available treatments for acute RSV disease (both non-specific and RSV-specific), as well as other prevention-oriented strategies.

**Key words** antivirals, RSV, immune responses, prevention, treatment, vaccine

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## Introduction

Globally, RSV remains a leading reason for hospitalizing children, playing a major role in the onset of acute respiratory illnesses in the pediatric population [1]. By the age of two, almost every kid has RSV at least once, and infection rates peak between the ages of two and three months [2]. Because RSV immunity is transient, reinfections occur often throughout life. RSV infections can present with a spectrum of symptoms, ranging from mild, upper respiratory discomfort to severe lower respiratory illnesses that may prove fatal. The most common lower respiratory tract illness is bronchiolitis, which is followed by pneumonia. Serious problems are most likely to occur in older persons and infants. RSV was first identified in infants and children amid a 1961 bronchiolitis outbreak, although its initial isolation dates back to 1956 when it was recovered from a chimpanzee exhibiting cold-like symptoms [3, 4]. This virus features a single-stranded, non-segmented RNA genome of negative polarity and is classified within the Orthopneumovirus genus, a member of the Pneumovirus family [5]. Embedded within the viral envelope are three crucial proteins: the small hydrophobic (SH) transmembrane protein, the attachment (G) glycoprotein, and the Fusion (F) glycoprotein, which facilitates the virus's entry into host cells.

The immune system primarily focuses on RSV's surface glycoproteins—most notably the G and F proteins [6]. To distinguish between RSV groups, serum-neutralizing antibodies, along with mucosal IgA and IgG, target the glycoprotein G, and this recognition varies depending on the strain [7]. On the other hand, RSV groups A and B exhibit cross-reactivity in antibodies against glycoprotein F. IgA is essential for protecting the upper respiratory tract because it supports both long-term immunity during reinfection and the immediate response after a first infection [8]. In the early stages of an infant's initial RSV infection, the IgG antibodies inherited from the mother can obstruct the formation of a localized IgA response in the respiratory tract [9]. While circulating IgG does offer a degree of defense against RSV, its brief duration in the bloodstream, combined with the virus's effective immune evasion tactics, frequently leads to repeated infections [10]. In this review, we examine the current clinically available therapies and prophylactic agents for RSV. We specifically focus on treatments that are tailored for RSV, as well as non-specific agents and approaches that have been explored for RSV management. Additionally, we discuss various strategies aimed at preventing RSV infection.

## Microbiology and structure of RSV

First discovered in 1955 after being isolated from a chimpanzee's upper respiratory tract, human RSV was formerly known as Chimpanzee Coryza Agent [11]. It was identified from humans the next year and connected to pediatric bronchiolitis [12]. RSV was reclassified in 2016 as an orthopneumovirus that belongs to the Mononegavirales order and the Pneumoviridae family [13]. RSV is an enveloped virus whose lipid bilayer originates from the host cell's plasma membrane. Its non-segmented, single-stranded negative-sense RNA genome spans 15.2 kilobases and contains 10 genes that collectively encode 11 proteins. Among these proteins are three transmembrane glycoproteins: the attachment (G) protein, the fusion (F) protein, and the small hydrophobic (SH) protein [14]. RSV features not only a ribonucleocapsid but also an array of regulatory proteins. Among these are the matrix proteins M2.1 and M2.2, the large polymerase (L), nucleoprotein (N), phosphoprotein (P), and the inner envelope matrix protein (M). In addition, the virus produces two nonstructural proteins, NS1 and NS2, which contribute to its ability to circumvent the immune system [15] (**Figure 1**).

In 1987, researchers established that the G protein plays a crucial role as an attachment molecule [16]. About 60% of its structure is composed of carbs, and it is highly glycosylated. There are two forms of this protein: one that is released and one that is membrane-bound, which helps RSV attach to respiratory epithelial cells [17]. The RSV structural element that varies the most is its full-length transmembrane form, which is classified as a type II integral membrane protein. Despite its variability, it contains a conserved central domain of 26 amino acids that plays a critical role in RSV pathophysiology and notably lacks glycosylation. In contrast, while the G protein is less effective in eliciting neutralizing antibodies, the F protein stands out as a highly conserved type I integral membrane glycoprotein that is essential for mediating viral entry. It facilitates membrane fusion between nearby infected cells and the virus as well as between the virus and host cells [18]. The protein exists in two distinct shapes: one is a stable pre-fusion form, and the other is a very stable post-fusion form that appears once the virus attaches to the host cell [19]. The F protein carries six key antigenic sites, designated as Ø and I–V (**see Table 1**). Specifically, epitopes I, II, and IV are present in both the pre- and post-fusion states, whereas epitopes Ø, III, and V are only exposed in the pre-fusion form [20].

## An overview of antivirals

Since idoxuridine was introduced as the pioneering treatment for Herpes simplex ocular infections, the realm of antiviral therapies has undergone remarkable advancements. This medication, which structurally resembles thymidine, disrupts viral replication by integrating into viral DNA in place of thymidine, thereby interfering with its synthesis [21]. Over the past four years, researchers have developed upwards of 90 antiviral medications. Yet, targeted treatments still do not exist for more than 200 viruses, highlighting a persistent challenge for global public health [22]. Viral infections continue to threaten human health, a situation exacerbated by the limited number of approved vaccines and antiviral therapies [23]. Antiviral therapies primarily work to prevent viruses from multiplying inside host cells, and they achieve this by disrupting various phases of the virus's replication process. These include preventing viral protein binding, disrupting maturation, and blocking the exocytosis of newly formed virions (**Figure 2**) [24].

By blocking important functional proteins involved in each stage of the viral replication cycle, antiviral therapies target different stages of the cycle. Some of these treatments target proteins that help the virus connect to receptors on the host cell, blocking fusion and cell entry and others target non-structural proteins of viruses that are essential for replication [25]. To lower the possibility of medication resistance, host-directed therapies, in addition to direct-acting antivirals, work to block cellular elements necessary for the viral life cycle. In order to more successfully remove viruses, these therapies function by inhibiting particular enzymes, stopping viral entry and assembly, and strengthening the host's immune system [26].

Targeting viruses with a protein envelope, viral protease inhibitors are another crucial family of antivirals. These inhibitors work by interfering with the protease enzymes that process viral polyproteins, a critical step for the virus to form both its structural and non-structural proteins. By doing so, they disrupt the assembly of the virus. Moreover, by preventing the production of key structural proteins, they effectively block the formation of new viral particles, thereby halting viral replication [27]. Because they obstruct the enzymes that cause viral DNA or RNA replication, inhibitors of genetic material replication are also essential. By blocking the virus's ability to duplicate its genetic material inside host cells, this method proves effective against both DNA and

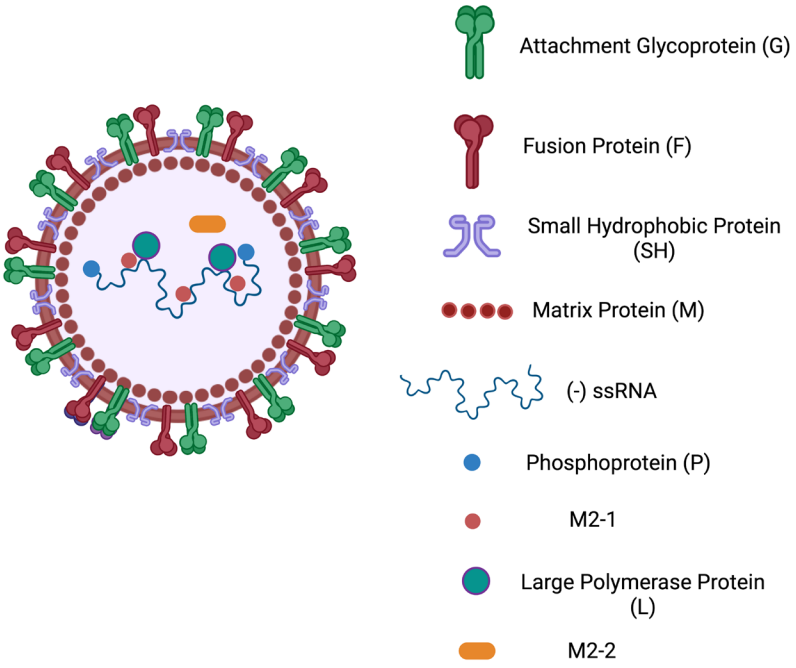


**Figure 1. Schematic representation of the RSV structure. The virus consists of a lipid bilayer embedded with surface glycoproteins, including the Fusion Protein (F), Attachment Glycoprotein (G), and Small Hydrophobic Protein (SH). The Matrix Protein (M) is located beneath the lipid bilayer, providing structural integrity. The viral genome is a negative-sense single-stranded RNA (-ssRNA) that is associated with Nucleoprotein (N), Large Polymerase Protein (L), Phosphoprotein (P), and regulatory proteins such as M2-1 and M2-2, which aid in transcription and replication.**

RNA viruses, showcasing the diverse strategies in antiviral drug development [28] (**Figure 3**).

## Specific RSV therapy

### *Ribavirin*

Ribavirin, a nucleoside analog with broad-spectrum activity, works by preventing the replication of both DNA and RNA viruses. It can be administered in various ways, such as orally, through IV injection, or via aerosol. However, an earlier Cochrane review—which analyzed 12 randomized trials comparing ribavirin to a placebo in infants and young children with RSV-related lower respiratory tract infections—did not find a significant reduction in mortality (OR 0.37; 95% CI, 0.12 to 1.18). No significant differences were observed between the treatment and placebo groups regarding secondary endpoints, disease severity, or oxygenation improvements [29]. The aerosolized form of ribavirin relies on specialized inhalation devices, notably the SPAG-2 small-particle aerosol generator (model-2) [30].

A randomized controlled trial was conducted with bone marrow transplant patients who had tested positive for RSV [31]. Participants who met the eligibility requirements were randomized to receive supportive care alone or aerosolized ribavirin in combination. For ten days, the patient received two grams of ribavirin inhalation solution, which had a 60 mg/mL concentration, three times a day for two hours. According to the study, ribavirin treatment was linked to a decreased risk of pneumonia and viral load. Skin rash, conjunctivitis, chest pain, shortness of breath, and bronchospasm were among the side effects that were reported. Despite using the right delivery techniques, several family members and healthcare professionals reported having additional adverse effects as headaches and vomiting. Urinary concentrations were collected following shifts to evaluate healthcare workers' airborne exposure to ribavirin. In 12% of respiratory therapists' and 62% of nurses' samples, ribavirin was found. Research on animals, notably rats and rabbits, has shown that a ribavirin dose of 1 mg/kg may cause birth defects. In contrast, lower doses—around 0.3 mg/kg (which roughly translates to 0.05 mg/kg when adjusted for an adult's body surface area)—do not appear to have these harmful effects. Despite the absence of teratogenic outcomes in the children of healthcare workers exposed to aerosolized ribavirin, concerns about its potential risks remain [32].

A previous investigation evaluated the application of oral ribavirin in lung transplant recipients suffering from RSV infection [33]. In this study, 52 patients initially received a loading dose of intravenous ribavirin at 33 mg/kg divided into three separate administrations, while two others were given an equivalent dosage orally. Subsequently, 21 patients continued treatment with oral ribavirin at a dosage of 20 mg/kg administered in two doses daily, with the treatment duration ranging from 6 to 31 days (a median of 11 days). The results indicate that using oral ribavirin could serve as a practical alternative to the intravenous form for treating RSV in lung transplant recipients. Furthermore, ribavirin

**Table 1. RSV F fragments and their main features.**

| RSV F configuration | Position name | Features | Product |
|---|---|---|---|
| pre-F | θ | Contains an α-helical segment from the F1 region (amino acids 196–210) combined with a β-strand from the F2 region (amino acids 62–69). This site is targeted by antibodies such as D25 and AM22. | Nirsevimab, RSM01 (currently in clinical development) |
| post-F | I | Located within the F2 subunit, near residue Pro389, also identified as the 131-2a region. | - |
| pre-F and post-F | II | Features a helix-turn-helix motif from the F1 region (amino acids 253–278) that includes a conserved epitope recognized by a Mota-specific antibody. | Previously targeted by Palivizumab and Motavizumab (now discontinued) |
| pre-F and post-F | III | Comprises two anti-parallel β-strands and is recognized by the MPE8-specific antibody. | - |
| pre-F and post-F | IV | This segment contains a linear epitope (amino acids 422–436) recognized by 101F-targeted antibodies, which, however, do not interfere with viral attachment. | Clesrovimab (currently in clinical development) |
| pre-F | V | Encompassing regions α2–α3 and β3–β4, this portion lies between antigenic sites Ø and III on the pre-fusion RSV F protein and is recognized by AM14-specific antibodies. | Suptavumab (development discontinued) |

treatment significantly decreased mortality among patients with hematological disorders, according to a meta-analysis and comprehensive review [34]. Administering ribavirin by mouth has been demonstrated to be a safe, cost-effective, and user-friendly treatment option. Furthermore, it has proven effective in eliminating the virus.

Nevertheless, because of its overprice and possible adverse effects, ribavirin is not advised for children who are otherwise healthy. It has showed promise in critically immunocompromised populations, which is where its clinical usage is still being studied. Other antiviral drugs that target fusion or replication inhibition as their mechanisms of action, such as RV521 [35] and AK0529 [36], are also being studied in ongoing randomized controlled studies.

*Palivizumab*

In 1998, a breakthrough in RSV prevention was achieved with the approval of palivizumab—a recombinant, humanized monoclonal antibody designed specifically for high-risk patients. This therapeutic agent works by binding to the virus's fusion protein, thereby blocking its ability to infect cells. Researchers have looked into its possible application in treating acute RSV infections because of its demonstrated effectiveness in prevention. Palivizumab (15 mg/kg) or a placebo was given to 420 infants with RSV bronchiolitis who had previously been healthy as part of a double-blinded randomized controlled study (RCT) [37]. The study revealed that the frequency of hospital readmissions and the length of hospital stays were nearly identical for patients treated with palivizumab compared to those given a placebo. Similarly, no statistically significant differences in clinical outcomes were observed between the two groups in another multicenter RCT that randomly allocated palivizumab or placebo to babies with acute bronchiolitis who tested positive for RSV [38].

*Motavizumab*

Motavizumab, a second-generation, humanized monoclonal antibody derived from palivizumab, has been investigated for its potential to treat RSV. In one multicenter randomized controlled trial, pediatric patients with RSV were randomly assigned to receive either 30 mg/kg or 100 mg/kg of motavizumab, or a placebo [39]. Over a follow-up period of 12 months, the trial found no significant differences between the groups in terms of hospitalization duration, illness severity, or the rate of subsequent wheezing episodes.

Research has explored the use of RSV-IVIG as an alternative therapeutic approach for managing acute RSV infections. Intravenous polyclonal immunoglobulin, which is made by separating RSV antibodies from pooled blood, has demonstrated potent anti-RSV properties in vivo. In addition, RSV-IVIG effectively curbs viral multiplication in lung tissue in vivo. This reduction in viral activity translates to a decreased overall viral

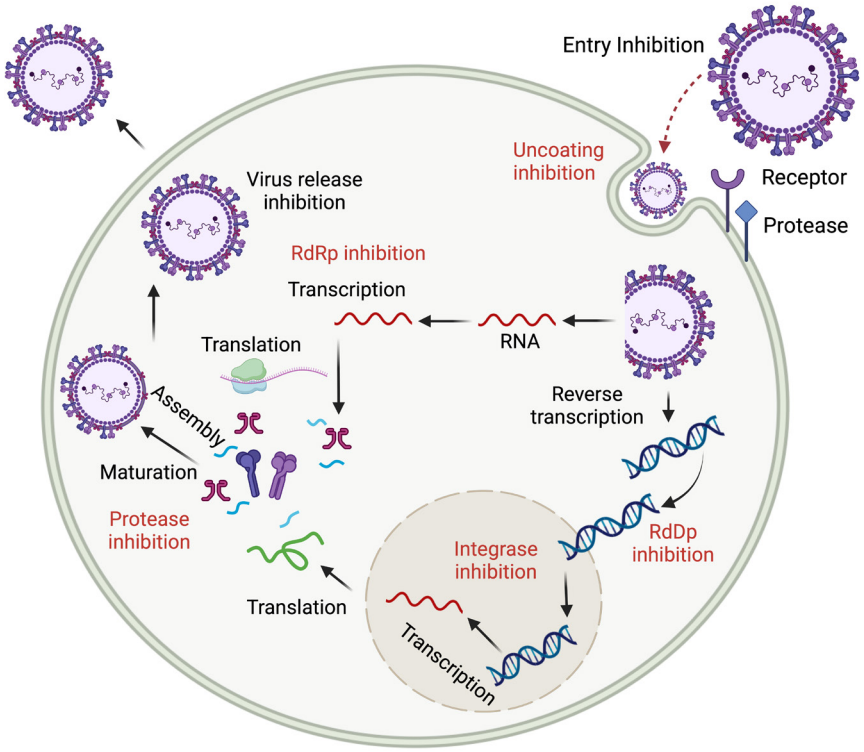


**Figure 2. Viral Replication Cycle and Antiviral Targets in Respiratory Viruses. The respiratory virus replication cycle involves key stages: viral attachment to receptors, entry via fusion or endocytosis, replication and transcription of genetic material, assembly of new virions, and their release. Each stage serves as a target for antivirals—entry inhibitors block attachment and fusion, replication inhibitors limit viral RNA/DNA synthesis, and assembly/release inhibitors prevent new virion formation and spread. Additionally, targeting host cell components offers an alternative strategy to disrupt the viral cycle and reduce resistance.**

burden, which may, in turn, prevent the emergence of respiratory illnesses [40]. In a double-blinded randomized controlled trial, 107 high-risk children under two years old, suffering from conditions such as prematurity, congenital heart disease, or chronic lung disorders, were evaluated for their response to RSV-IGIV treatment for RSV infection. One group received a single intravenous infusion of RSV-IGIV at a dosage of 1500 mg/kg, while the comparison group was administered a matching placebo. The study ultimately found that the duration of hospital stays and the overall severity of the illness did not differ significantly between the two groups [38]. Concerns regarding probable blood-borne product transfer and potential interference with routine live vaccination delivery are raised by the massive intravenous dose of RSV-IGIV. A 2019 Cochrane review that analyzed seven studies involving 486 infants with RSV bronchiolitis concluded that there wasn't sufficient evidence to show that immunoglobulin treatment led to different outcomes compared to a placebo [41]. Later, as more effective alternatives emerged, RSV-IGIV was voluntarily withdrawn from the market in 2003 [42].

*Non-specific RSV treatments*

It is essential to comprehend the biology of acute infection when researching non-specific treatments for RSV bronchiolitis or infection. RSV begins its journey by infecting and multiplying along the mucosal surfaces of the respiratory tract, from the nasopharynx all the way to the smallest alveoli. In adults and older children, this often results in symptoms typical of the common cold, such as a runny nose and nasal congestion. However, the illness primarily affects the lower respiratory tract in younger children, especially newborns and preschool-aged children, which can result in more serious and sometimes fatal consequences including bronchiolitis. This variation in intensity is thought to be caused by a number of causes. One important consideration is the size of the airways: an adult's respiratory bronchiole has an average diameter of about 250 μm, but a 4-month-old infant's only has 120 μm [43]. During viral infections, this much smaller bronchiolar lumen is more prone to blockage [44]. In newborns, the risk of obstruction is heightened because their collateral ventilation pathways, specifically the pores of Kohn and the canals of Lambert, have not yet reached full maturity, unlike those found in older children and adults [45]. Due to these structural variations and their developing immune systems, newborns are more susceptible to bronchiolitis episodes that are clinically significant.

Studies conducted on lung tissue from infants who succumbed to severe RSV infections have shed light on the underlying processes of RSV bronchiolitis. Histological studies reveal that the most significant changes occur within the medium and small bronchioles (those with diameters of 150 μm or less). These alterations include airway swelling, damage to the epithelial cells accompanied by a buildup of inflammatory cells and cellular debris, as well as an increase in mucus production—all of which contribute to the obstruction of the airways [46]. Higher airway resistance brought on by this obstruction causes hyperinflation,

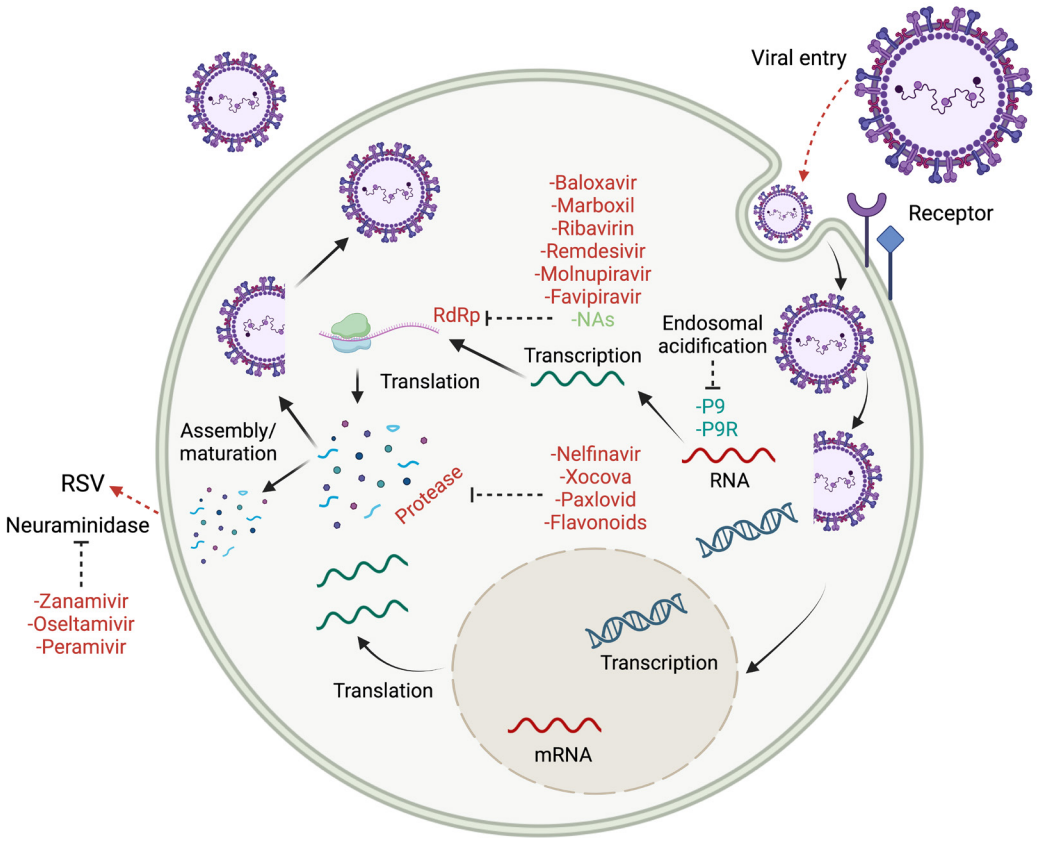


**Figure 3. Mechanism of Antiviral Action Against RSV. The replication cycle of RSV is depicted in a simplified form, highlighting key antiviral targets. Inhibitory actions include blocking viral entry, endosome acidification, RdRp activity, protease function, and viral release via neuraminidase. The figure presents FDA-approved antivirals and potential future treatments currently under in vitro or clinical evaluation.**

hypoxemia, crackles, wheezing, and an increase in respiratory effort.

Normally, mucus lines the airways as a protective substance that traps particulates that are inhaled. Cilia, enveloped in periciliary fluid, beat in unison to drive mucus upward toward the upper respiratory tract. This coordinated action, coupled with an effective cough, forms the body's primary defense against airborne pathogens and particulate matter. This mechanism is compromised in bronchiolitis, in part because of the overproduction of mucus and in part because of viral damage to the cilia. Multiple studies have identified genes connected to inflammatory pathways that appear to play a role in the severe manifestations of RSV infection in infants [47]. Furthermore, the complex interaction between the virus's genetic material and the host's immune response may contribute to an increase in airway obstruction. [48]. Understanding these processes has influenced the creation of several treatment strategies meant to reverse airway blockage, such as bronchodilators, anti-inflammatory drugs and mucolytics [49], which are included in **Table 2**. Even with these molecular connections, the evidence does not always support the effectiveness of these drugs in treating RSV infections.

*Dornase alfa*

In cases of RSV bronchiolitis, mucus plugs are found to contain high concentrations of extracellular DNA, a substance released during the influx and subsequent disintegration of leukocytes [50]. This extracellular DNA is broken down by the enzyme human recombinant DNase (hrDNase), which lowers mucus viscosity. Because of this activity, hrDNase has been proposed as a possible bronchiolitis therapy. In the most extensive randomized, double-blind controlled trial to date, encompassing 225 infants hospitalized with bronchiolitis, researchers observed no notable reduction in either the duration of hospitalization or the period requiring supplemental oxygen. This outcome contrasts with earlier, smaller-scale studies and case reports that suggested improvements in radiographic signs of atelectasis among severely affected infants [51, 52]. A 2012 Cochrane review examined three studies, including the one where infants with viral bronchiolitis received hrDNase, involving a total of 333 children under 24 months. The review concluded that the treatment did not yield any significant benefits [53]. Therefore, although nebulized hrDNase is not usually advised for the treatment of RSV infection, it may be taken into consideration in cases of severe atelectasis linked to bronchiolitis when traditional treatments have failed.

*N-acetylcysteine (NAC)*

A substance called NAC has antioxidant qualities and dissolves the disulfide bonds in mucins, both of which may help treat bronchiolitis [54]. In an in vitro model using alveolar type-II epithelial cells infected with RSV, NAC significantly reduced both mucin production and the synthesis of pro-inflammatory mediators [55]. A randomized controlled study compared nebulized NAC with nebulized salbutamol in 100 infants. However, the trial, which may have been underpowered, failed to show significant differences in hospitalization duration or symptom severity [56]. Consequently, further research is needed before NAC can be

**Table 2. Methods for treating non-specific acute RSV bronchiolitis**.

| Product | Mechanism of action | Feedback | Ref. |
|---|---|---|---|
| *Bronchodilators* | | | |
| Salbutamol, albuterol, etc. | Nebulized solution;<br>β-2 adrenergic receptor agonist, which opens airways and relaxes smooth muscle. | Not recommended. | [49] |
| Epinephrine | Nebulized solution;<br>A few consequences of β-2 adrenergic airway edema is also reduced by vasoconstriction brought on the α-1 adrenergic receptor actions. | Not recommended;<br>May reduce risk of hospitalization in the ED setting. | [75, 66] |
| *Mucus therapies* | | | |
| 3% hypertonic saline | Nebulized solution;<br>Enhances ciliary action by generating an osmotic gradient and drawing water into the mucus layer, cough stimulation. | Not recommended for inpatient management;<br>May reduce the risk of hospitalization in the ED setting. | [41] |
| N-acetylcysteine | Nebulized solution;<br>Mucolytic substance, hydrolyzes mucus protein disulfide bonds. | Insufficient data - Not recommended. | [76] |
| Deoxyribonuclease (hrDNase) | Mucolytic substance with nebulized solution;<br>Breaks down extracellular DNA. | Not recommended;<br>In severe circumstances, when traditional therapy fails, it could be taken into consideration as a treatment option for atelectasis. | [54, 51] |
| *Therapies targeting inflammation* | | | |
| Leukotriene inhibitors | Oral solution | Poor evidence, not recommended. | [71] |
| Glucocorticoids | Oral solution, inhaled or nebulized preparations;<br>Anti-inflammatory with a broad spectrum, inhibit the production of cytokines that promote inflammation. | Not recommended;<br>When reactive airway disease is highly suspected, it might be taken into consideration. | [69, 68] |
| *Manual therapies* | | | |
| Chest physiotherapy | Chest percussion, suction;<br>Facilitates the removal of secretions believed to lessen the ventilatory effort required for babies with the most severe illnesses. | Not routinely recommended;<br>When pertinent comorbidities exist, it may be taken into consideration. | [77, 74] |

considered a promising treatment option for RSV infection.

*Nebulized hypertonic saline*

Research indicates that administering nebulized hypertonic saline can significantly enhance mucociliary clearance in both healthy individuals and patients with respiratory conditions such as cystic fibrosis, bronchiectasis, and asthma. It may also lessen airway edema by generating an osmotic gradient that pulls water from the mucosa and submucosa into the mucus layer [57]. When paired with a productive cough, this hydration of the mucus layer aids in secretion mobilization and is believed to reduce airway blockage [58]. Despite these theoretical explanations, clinical evaluations and computed acoustic airflow techniques have not demonstrated that using 3% hypertonic saline improves wheeze or airflow [59]. Multiple clinical studies examining hypertonic saline as a treatment for viral bronchiolitis have not produced the anticipated positive outcomes. Although some research suggested that 3% hypertonic saline had a slight impact on hospital stay duration and symptom scores [60], a Cochrane meta-analysis in 2017, reviewing 28 trials involving 4,195 infants with acute bronchiolitis, concluded that the available evidence does not sufficiently support its use. The length of stay was somewhat shortened, nevertheless, and there were very few mild adverse events, according to the authors [60]. Subsequent randomized trials failed to show any improvement when 3% hypertonic saline was used instead of the standard supportive care [61]. Therefore, hypertonic saline is not part of the current standard of therapy for RSV bronchiolitis.

*Bronchodilators*

Infants with bronchiolitis often present with symptoms such as wheezing, a prolonged phase of exhalation, and distinct crackling sounds during chest examinations. Medications like salbutamol and albuterol, which are β-2 adrenergic agonists, work by relaxing the airway's smooth muscles to relieve constriction [62]. While initial meta-analyses suggested that these drugs might offer moderate short-term benefits in mild to moderate cases, a 2014 Cochrane review of 30 studies involving 1,992 infants found no significant improvements in oxygen saturation, hospitalization

frequency, or length of hospital stay. Moreover, the use of these agents is associated with side effects including rapid heart rate, decreased oxygen levels, tremors, and electrolyte disturbances, leading to the general recommendation against their routine use in treating bronchiolitis, however they can be tested on infants whose primary symptom is wheezing in order to gauge the response. Notwithstanding the paucity of information, the many manifestations and symptoms of RSV infection are widely known, and future randomized clinical trials should benefit from focusing bronchodilator use on the clinical phenotype [63].

*Epinephrine*

Epinephrine exerts its effect by binding to β-2 adrenergic receptors, which in turn triggers the relaxation of the smooth muscles lining the air passages. Hence, it may be useful in treating acute bronchiolitis. Furthermore, its potent α-adrenergic actions result in decreased airway edema and vasoconstriction. According to a short trial, racemic epinephrine improved clinical ratings and decreased airway resistance in infants with bronchiolitis more effectively than salbutamol [64]. Nine studies (including 1354 infants) comparing nebulized epinephrine to a placebo were included in a 2011 Cochrane Review, which found that outpatients experienced a little short-term improvement. By day 7, however, the treatment had no effect on the illness's course, and neither shorter hospital stays nor better symptom scores for inpatients were the outcomes [65]. Crucially, the studies showed few side effects and acceptable tolerance. Therefore, epinephrine is not advised as a regular treatment for RSV infections, even though it can be administered in the acute phase.

*Glucocorticoids*

According to a number of studies, glucocorticoids have little anti-inflammatory effect when RSV infection is present, especially when it comes to viral load and cytokine production [66]. Clinical trials have not demonstrated a meaningful impact of glucocorticoids on improving clinical scores, reducing hospitalization rates, or shortening hospital stays. This ineffectiveness may be attributed to the dominant neutrophilic inflammation in RSV infections, which is known to respond poorly to glucocorticoid treatment [67, 68]. Additionally, a six-year follow-up study conducted in the Netherlands involving 185 infants found no evidence to support the claim that inhaled glucocorticoids decrease the likelihood of developing asthma later in life among newborns affected by RSV [69]. Steroids may be helpful for infants with RSV in certain situations, though, such as those who have underlying medical disorders like asthma or bronchopulmonary dysplasia. In comparison to other children infected with RSV, these groups might exhibit a greater level of steroid-responsive inflammation.

*Leukotriene receptor antagonists*

Leukotrienes, which interact with bronchial smooth muscle to induce bronchoconstriction, are thought to play a role in the bronchial hyperresponsiveness and mucus hypersecretion brought on by RSV [70]. A Cochrane review evaluated the impact of leukotriene receptor antagonists using data from five randomized, placebo-controlled studies involving 1,296 hospitalized infants under the age of two with bronchiolitis. The analysis determined that the current high-quality evidence is insufficient to definitively conclude whether these medications affect clinical severity scores or the duration of hospital stays [71]. It is not possible to prescribe this class of drugs for the treatment of RSV infections until more research is done.

**Other therapies**

Researchers have explored a wide range of non-specific treatment options for acute RSV infection. Among these, antibiotics and various mixtures of the previously mentioned drugs have undergone significant investigation [72]. As early as day 3 of treatment, for instance, nebulized epinephrine and 3% hypertonic saline have demonstrated encouraging outcomes in enhancing clinical severity scores [73]. Before this treatment is suggested, more research is required to validate these results. Clinical studies have not demonstrated significant benefits from suctioning or chest physical therapy. As a result, these interventions are usually reserved for cases in which neuromuscular conditions hinder the ability to cough effectively [74].

**Conclusion**

RSV, a major cause of respiratory illnesses globally, was discovered more than 60 years ago. The methods by which RSV infects its host and the roles played by its many components are being increasingly revealed by ongoing research. It is anticipated that research on receptors conducted in recent decades will inform the creation of vaccinations and antiviral medications. The ultimate objective is to develop anti-RSV drugs that are more accessible and reasonably priced in order to meet patient needs worldwide. There is hope for the creation of more potent medicines based on current research, which includes roughly 30 clinical interventions and a large number of preclinical candidates. Antiviral natural compounds may be useful building blocks for the creation of novel medications. It is advised to investigate several targets and multi-site inhibitors that cooperate to lower the danger of drug-resistant RSV mutants in order to improve antiviral efficacy. To increase the effectiveness and specificity of antiviral treatments, future studies should focus on integrating these cutting-edge tactics with a multidisciplinary approach. There are encouraging prospects for creating sustainable and efficient medicines through the combination of drug repurposing, bioinformatics, and the investigation of natural and peptide-based molecules.

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**Ethics approval**

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**Data availability**

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**Authors' contribution**

Shahnaz Parveen contributed to draft, critical revision of the article, table making, and figure production; Shaikh Salam revised the manuscript and approved the final submission.

**Competing interests**

The authors declare no competing interests.

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