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FROM THE FIRST BREATH TO THE GOLDEN YEARS: RESPIRATORY SYNCYTIAL VIRUS PREVENTION IN INFANTS AND OLDER ADULTS

Introduction

Respiratory syncytial virus (RSV) is one of the most common respiratory infections observed in primary care. Although many think of RSV as a 'common cold', it is a serious health threat to certain populations, including children, particularly infants who are 6 months of age or younger, those with comorbidities, and older adults.¹ With the increasing number of options to reduce the impact of RSV infections, including morbidity and mortality, it is important to recognize that primary care clinicians must be able to identify people at risk for RSV infection, effectively educate them on the potential impact of the condition, and identify strategies to lower the risk.

Respiratory Syncytial Virus

RSV is a single stranded RNA virus that is classified into two subgroups: type A (RSVA) and type B (RSVB).² The two transmembrane glycoproteins, F (fusion) and G (**Figure 1**), play critical roles in the entry of the virus into the host cell.¹ The G protein is the most varying structure among RSV strains, and this variability dictates the antigenic nature between RSVA and RSVB groups.²

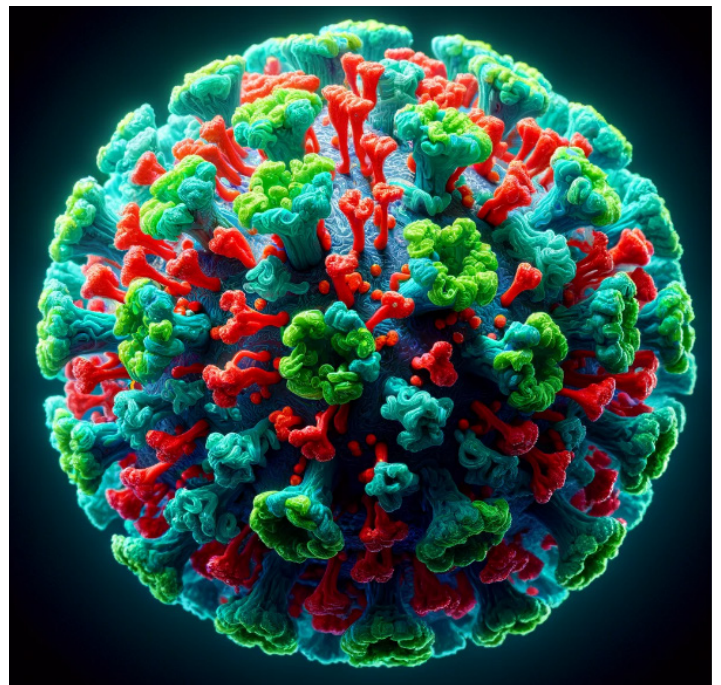


Figure 1. RSV with G and F transmembrane proteins.

The F protein is critical for infecting the host cell.¹ Unlike the G protein, the sequence of the F protein is highly conserved between RSVA and RSVB, with less than 10% sequence diversity between the two groups.² The F protein exists in two major forms based on its fusion to the host cell, the less stable prefusion (Pre-F) and the stable post-fusion (Post-F).¹ The F protein, specifically Pref, plays an important role in immunity and is the target for currently available vaccines and monoclonal antibodies.

Did you know?

Prior to the COVID-19 pandemic, RSV infections followed a seasonal pattern of peaking during late fall or early winter (mid-December to early February).³ A low number of RSV infections had occurred during the first year of the pandemic, along with increases in RSV cases out of season.¹ This may be explained by reduced RSV exposure during the first year of the pandemic, creating an 'immunity debt', making the population more vulnerable to another RSV infection.¹

Epidemiology and Burden of Disease Infants

Most children will experience at least one RSV infection by 2 years of age.³ In fact, RSV is the leading cause of lower respiratory tract infection (LRTI) in Canadian children.⁴ LRTI affects more than one in three children in the first 2 years of life and is the most common cause of hospital admission in their first year of life.⁴ Hospitalization rates due to RSV have increased from 1% to 3% of all infants.⁴ Mortality due to RSV is rare among children receiving supportive care, with an estimated case-fatality rate of less than 0.5%.⁵

Older Adults

RSV is increasingly recognized as a significant cause of severe respiratory disease in older adults.⁶ Older adults experience a variety of factors (e.g. immunosenescence, weaker respiratory muscles, and lower lung compliance) associated with a higher risk of complications from RSV.² The incidence of RSV LRTI in people ≥65 years has been estimated to be 6.7 cases per 1000 people per year.¹ Although the individual risk of severe RSV LRTI is lower in older adults than in infants, the impact of this infection in this group is significant.¹ A recent publication, compared

outcomes of individuals aged ≥ 60 years hospitalized for COVID-19, influenza, or RSV.⁶ They reported that RSV was associated with a lower risk of hospitalization, when compared to influenza and COVID-19; however, it had a higher risk of requiring:⁶

- Supplemental oxygen
- Mechanical ventilation
- ICU admission

Patients infected with RSV also report a lower quality of life, including an increase in fatigue, difficulty in social functioning, and limitations due to emotional problems.⁸

Practice Pearl

One Canadian study found that adults aged ≥65 years comprised only 22% of all RSV-related hospitalizations, yet were associated with 85% of RSV-related deaths.⁹ Findings of the study indicated that 1 in 9 older adults hospitalized due to RSV, die from this infection and its complications.⁹

Clinical Presentation and Diagnosis

Patients infected with RSV will typically experience mild to moderate nasal congestion and low-grade fever within a few days of exposure and transmission, followed within a few days by a productive cough.² A portion of infected individuals will progress to LRTI and develop symptoms requiring hospitalization.² The timeline for a typical RSV infection is illustrated in **Figure 2**.

The clinical presentation of RSV cannot be distinguished from other respiratory viruses, including influenza.¹⁰ The challenge in older adults is that the clinical signs of RSV overlap with signs of heart failure and chronic obstructive pulmonary disease (COPD).¹⁰

Did you know?

Repeat infections with RSV are common throughout life.³ Approximately 30–75% of children <2 years of age who have been infected with RSV in their first 12 months of life will experience a reinfection the following season. When reinfected with RSV, most older children and adults will typically present with an upper respiratory tract infection.³

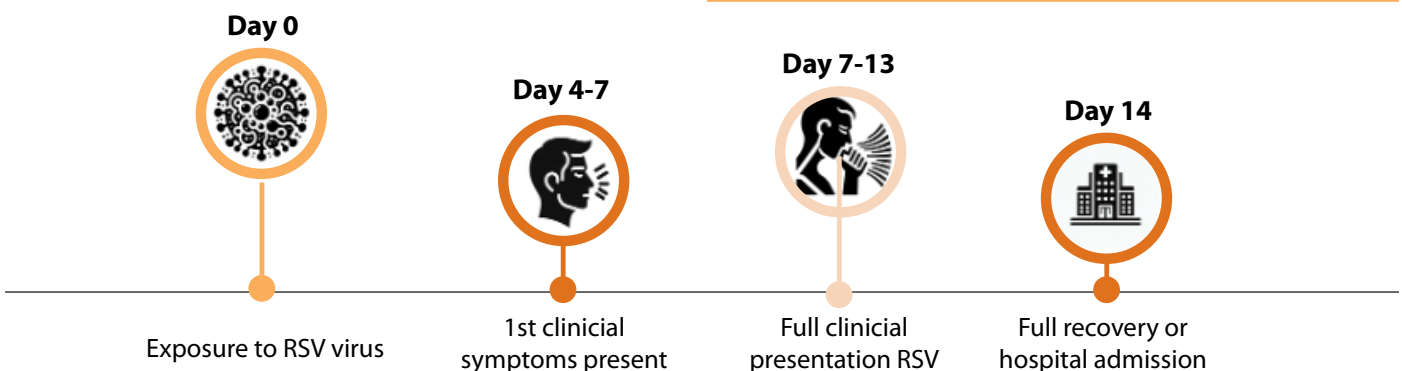


Figure 2 - Median Timeline for an RSV Infection; adapted from Kaler et al.²

Vaccine	Components	Dose	Efficacy – prevention of medically attending LRTI*	Safety	Other
Arexvy® (GSK)	Antigen: 120 µg PreF3 Adjuvant: AS01 _E	0.5 mL IM (deltoid)	77.5% (57.9–89.0) for season 1 and interim season 2	Common: Pain at the injection site (61%), Fatigue (34%), Myalgia (29%) Headache (27%)	Optimal timing for vaccine: Onset of fall and winter RSV season, though could be administered any time Coadministration: ACIP recommends coadministration with other vaccines at the same visit
Abrysvo® (Pfizer)	Antigen: 60 µg PreF A 60 µg PreF B	0.5 mL IM (deltoid)	81.0% (43.5–95.2) for season 1 and interim season 2	Common: Fatigue (16%), Headache (13%), Pain at the injection site (11%)	

Table 1. Summary of Subunit RSV Vaccines¹³⁻¹⁵

Abbreviations: **ACIP:** Advisory Committee on Immunization Practices; **IM:** intramuscular; **LRTI:** lower respiratory tract infection; **PreF3:** Pre-fusion protein 3; **RSV:** respiratory syncytial virus.

*LRTI prompting one or more inpatient or outpatient healthcare services

Vaccine	Contains	C	Efficacy	Safety	Other
Sinagis® (Palivizumab)	Monoclonal antibody targeting the F protein	50mg for infants <5 kg 100 mg for infants ≥5 kg Single IM injection in anterolateral aspect of thigh	38 to 86% reduction in the risk of RSV hospital admissions	Common: Rash Pyrexia	Option in premature infants who will not benefit as significantly from maternal RSV vaccination Nirsevimab has been used in the second RSV season in those at high risk NACI has advised to consider these options in infants at elevated risk due to prematurity or comorbid illness
Beyfortus® (Nirsevimab)		15 mg/kg of body weight IM in anterolateral aspect of thigh every 28–30 days during RSV season	79% reduction in the risk of medically attended RSV LRTI	Common: Rash Pyrexia	

Table 2. Summary of Subunit RSV Monoclonal Antibodies.^{5,20-22}

Abbreviations: **IM:** intramuscular; **LRTI:** lower respiratory tract infection; **NACI:** National Advisory Council on Immunization; **RSV:** respiratory syncytial virus

Did you know?

The shedding of RSV is highly variable and begins within a day of exposure and can persist for 3–7 days for adults, up to 14–21 days for infants, and up to several months for immunocompromised individuals.²

Risk Factors for Severe Respiratory Syncytial Virus Infection and Hospitalization

A variety of factors are associated with a higher risk of severe RSV infections. In children, these higher risk groups include prematurity, chronic lung disease of prematurity, congenital heart disease, trisomy 21, and neuromuscular disease.³ In older adults, age and comorbidities (e.g. asthma, diabetes, coronary heart disease, heart failure, and COPD) increase the risk of severe RSV outcomes.¹¹

Practice Pearl

It is challenging to predict which infants and older adults will develop severe RSV infections. At least half of all infants hospitalized with RSV were previously healthy without any of the established risk factors.³

Respiratory Syncytial Virus Prevention – Vaccination**Older Adults**

Two subunit vaccines have been developed to prevent lower respiratory tract disease caused by RSV in adults aged ≥60 years. The two vaccines contain a stabilized version of the RSV Pre-F protein.¹² The National Advisory Committee on Immunization (NACI) has not provided recommendations for RSV immunization in older adults. The CDC recommends clinicians consider vaccination in adults aged ≥60 years using shared decision making. A summary of these two vaccines is provided in **Table 1**.

Infants

Immunization during pregnancy is another common strategy to reduce the risk of infectious disease in infants. The administration of Abrysvo® in pregnant persons between 24 and 36 weeks of pregnancy was evaluated to determine the efficacy in reducing RSV infections in infants.¹⁶ Administration of the vaccine reduced the risk of:¹⁷

- The baby being hospitalized for RSV by 68% and having a healthcare visit for RSV by 57% within 3 months after birth
- The baby being hospitalized for RSV by 57% and having a healthcare visit for RSV by 51% within 6 months after birth
- Severe RSV disease by 82% within 3 months and by 69% within 6 months after birth

The most common adverse effects reported were similar to those reported in older adults, with pain at the injection site, headache, myalgia, and nausea.¹⁷ More preterm births occurred when the vaccine was administered during 24 through 36 weeks of pregnancy; however, the difference was not statistically significant.¹⁷ An increase in preterm births was not observed when the vaccine was administered between weeks 32 through 36 of pregnancy.¹⁷

ACIP recommends pregnant people between 32 through 36 weeks of pregnancy receive the RSV vaccine during the RSV season.¹⁷ The vaccine is approved in Canada for the active immunization of pregnant individuals from 32 through 36 weeks gestational age. They also state that coadministration of the RSV vaccine with other adult vaccines including Tdap, COVID-19 and influenza can occur at the same visit, when recommended.¹⁷

Respiratory Syncytial Virus Prevention – Monoclonal Antibodies

Another strategy to reduce the risk of severe RSV in infants is the administration of monoclonal antibodies targeting the F protein. These antibodies provide passive protection to high-risk infants who are at risk of severe RSV outcomes.¹⁸ These monoclonal antibodies bind to the F protein of RSV, thus preventing a key component of human cell infection by the virus.¹⁹ These antibodies are used in infants at high-risk of infection such as those who are premature, and those with risk factors discussed above. **Table 2** provides a summary of these therapies.

Role of the Primary Care Clinician

Until recently, the options to reduce the impact of RSV infections in patients at risk were limited to public health interventions (e.g. social distancing, masking, and handwashing). With the introduction of vaccines and monoclonal antibodies, clinicians have options to reduce the impact of RSV in vulnerable patients. The key is to identify patients who can benefit from these interventions in clinical practice. Having a discussion with the patient about the benefits and risks of prevention options can help clinicians recommend the most effective strategies to reduce the patient's risk.

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