NYSMPEP Respiratory Syncytial Virus (RSV) Bronchiolitis Module

Key Message 3:

- **Infants with pulmonary abnormalities or neuromuscular disease which impairs their ability to clear lung secretions MAY be considered eligible for respiratory syncytial virus (RSV) prophylaxis with palivizumab in their first year of life. Such prophylaxis is not likely to be of benefit in the second year of life.**
- **Immunocompromised infants and children MAY be considered eligible for RSV prophylaxis using palivizumab if they are <24 months of age at season onset**

Pulmonary abnormalities, neuromuscular disease[1]

- Risk of RSV related hospitalizations is not well defined for this population.
- These conditions include nonproductive cough, recurrent gastroesophageal tract reflux, malformation of the lungs, tracheoesophageal fistula, and upper-airway conditions - especially those requiring a tracheostomy.

Immunosuppression[1,2]

- A severe clinical course of RSV has been demonstrated in children receiving chemotherapy or immunosuppressed for other reasons.
- RSV in these patients may progress to further complications including death.
- More specific risk factors include age ≤2 years, lymphopenia, early presentation of lower respiratory tract symptoms, and corticosteroid therapy.
- Underlying diagnosis, degree of immunosuppression, RSV load, and concentration of anti-RSV antibodies have NOT been shown to correlate with poor outcomes.

Summary of changes in RSV prophylaxis recommendations from the AAP.[3,4]

Previous Guidelines (2009)	Recent Guidance (2014)
Infants with anatomic pulmonary abnormalities or neuromuscular disease	
• GA <35 weeks and chronologic age <12 months at season onset[a] • Impaired clearance of secretions from upper respiratory tract	• Chronologic age <12 months at season onset • Otherwise consistent
Immunocompromised infants and children	
• Chronologic age <24 months at season onset • Profoundly immunocompromised	• Consistent

[a]New York State Department of Health designates RSV season as October 16 – March 31

References: 1. Bocchini Jr JA. Pediatrics. 2009;124:1694. 2. Brady MT. Pediatrics. 2014;134.e620. 3. Committee on Infectious Diseases and Bronchiolitis Guidelines Committee. Pediatrics. 2014;134:415. 4. Wilkesmann A. Pediatr Infect Dis J. 2007;26:485. 5. El Saleeby CM. Pediatrics. 2008;121:235. 6. Asner S. Pediatr Infect Dis J. 2013;32:1073. 7. Kim YJ. J Infect Dis. 2014;209:1195.

Literature Summary

Limited data exist for the following populations. The following studies indicate that immunocompromised infants may benefit from prophylaxis if they are in their first 24 months of life, as they are likely to experience adverse outcomes associated with RSV progression. This is especially true for those exposed to smoke, radiation, or who present with an absolute lymphocyte count (ALC) ≤100 cells/mm. Infants with neuromuscular impairment or pulmonary abnormalities are more likely to require intensive care and mechanical ventilation associated with RSV, and may therefore be considered for prophylaxis in their first year of life.

Trial	Design	Population	Endpoints	Results	Conclusions
Pulmonary abnormalities/neuromuscular disease					
Wilkesmann 2007[4]	P, MC cohort	n=1,541 with clinically relevant NMI identified based on physician recommendations, compared to those without NMI over 6 consecutive RSV seasons (1999-2005), in Germany	Clinically relevant aspects of the management of NMI inpatients with RSV infection • PICU admission • Acute otitis media infection • Seizures • Apnea • Fever • Hypoxemia • Tachypnea • Wheezing	Total of 1,568 RSV infections NMI vs. Without NMI • PICU admission 45% vs 10%, P<0.001 OR 4.94, 95% CI 2.69 to 8.94 • Acute otitis media infection 10% vs 5%, P<0.07 • Seizures 15% vs 2%, P<0.001 • Apnea 11% vs 11%, P=0.92 • Fever 23% vs 25%, P=0.8 • Hypoxemia 34% vs 27%, P=0.19 • Tachypnea 63% vs 0.46%, P=0.01 • Wheezing 67% vs 55%, P=0.03 • Mechanical ventilation requirement 9.6% vs 1.9% OR 3.85, 95% CI 1.28 to 10.22	Children with clinically relevant NMI hospitalized with RSV infection are more likely to be admitted to the PICU and require mechanical ventilation.
Immunocompromised					
El Saleeby 2007[5]	Retrospective cohort	n=58 patients aged <21 yr with neoplasias, hematologic disorders, immunodeficiency syndromes, or HSCTs with RSV, between 1997 and 2005, at hospital in Tennessee	Risk factors for severe RSV infection and death (multivariate and univariate regression, respectively)	Risk factors for LRTI: Diagnosis • ALL: 8.7% (reference) • HSCT/AML/SCIDS: 42%, OR 2.84, 95% CI 0.43 to 18.7 • Solid tumor: 36.4%, OR 1.72, 95% CI 0.19 to 15.9 Age >2 yr: 14.6% (reference) • 0-2 yr: 58.8%, OR 9.84, 95% CI 1.95 to 49.8 Profound lymphopenia (ALC ≤100 cells/mm^3 at diagnosis) • No: 20.8% (reference)	Profound lymphopenia and young age are independently associated with RSV LRTI. LRTI may progress to death, particularly in HSCT patients age 2 years or less being treated for AML

References: 1. Brady MT. *Pediatrics*. 2014;134:e620. 2. Hall CB. *N Engl J Med*. 2009;360:588. 3. Committee on Infectious Diseases and Bronchiolitis Guidelines Committee. *Pediatrics*. 2014;134:415. 4. Bocchini Jr JA. *Pediatrics*. 2009;124:1694. 5. Stevens TP. *Arch Pediatr Adolesc Med*. 2000;154:55. 6. Boyce TG. *J Pediatr*. 2000;137:865. 7. Winterstein AG. *JAMA Pediatr*. 2013;167:1118. 8. IMPACT RSV Study Group. *Pediatrics*. 1998;102:531. 9. Feltes TF. *J Pediatr*. 2003;143:532. 10. Chang RK and Chen AY. *Pediatr Cardiol*. 2010;31:90.

Trial	Design	Population	Endpoints	Results	Conclusions
Immunocompromised (continued)					
				• Yes: 60.0% OR 7.17, 95% CI 1.17 to 44.03 Occurrence of death: 8.6% Risk factors for death: • LRTI and HSCT: death rate 100% • <2 years of age: OR 12.3, 95% CI 1.26 to 120 AML: death rate 100%	
Asner 2013[6]	Retrospective cohort	n=117 RSV-positive immunocompromised pediatric inpatients age <18 years between 2006 and 2011 in Toronto	Risk factors for acquisition and outcomes from RSV infections in this population	• 45.9% patients presented with N-RSV • >1/3 presented with a LRTI • 28% ICU admission rate • 5% mortality rate, all CA-RSV patients LRTI: • N-RSV: 13 (31%) • CA-RSV: 39 (52%) OR 2.5, 95% CI 1.1 to 5.6 Prolonged hospital stay: • OR 0.7; 95% CI 0.5 to 0.8 Median duration of stay: • N-RSV: 24 days • CA-RSV: 11.5 days OR 0.96, 95% CI 0.93 to 0.98	N-RSV patients were more likely to require a prolonged hospital stay while those with CA-RSV were more likely to progress to LRTI. Differences among those with CA-RSV compared with N-RSV warrant further study.
Kim 2014[7]	Retrospective cohort	n=181 HSCT recipients with RSV upper respiratory tract infection	The significance of various factors in the progression to LRTI: • Lymphocyte engraftment dynamics • Lung function • Smoking history • Corticosteroid • Antiviral treatment • Viral subtypes • RSV-specific neutralizing antibodies	Progression to LRTI: Smoking history: • Smoke exposure vs none: OR 2.5, 95% CI 1.1 to 5.6 Irradiation: • High-dose total body irradiation vs none: OR 2.5, 95% CI 1.1 to 5.6 • None/low irradiation: OR 2.1, 95% CI 0.8 to 5.2 Lymphopenia at URTI onset vs. ALC> 500: • ALC ≤100/mm^3: OR 6.0, 95% CI 1.9 to 18.9 ALC >100: OR 2.1, 95% CI 0.7 to 5.8	Host and transplant related factors appear to determine the risk of progression to LRTI more than viral factors, specifically lymphopenia, smoke exposure, and radiation exposure.

ALC=absolute lymphocyte count; CA=community-acquired; HSCT=hematopoietic stem cell transplant; LRTI=lower respiratory tract infection; N=nosocomial; NMI=neuromuscular impairment; PICU=pediatric intensive care unit; SCIDS=severe combined immunodeficiency syndrome; URTI=upper respiratory tract infection

References: 1. Synagis [package insert]. Gaithersburg, MD: MedImmune, LLC; 2014. 2. Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. *Pediatrics*. 2014;134:415. 3. Webinar – Updated AAP Guidance for Palivizumab Prophylaxis among Infants and Young Children at Increased Risk of RSV Hospitalization. www.aapredbook.org/site/resources/webinars.xhtml. 4. Modified recommendations for use of palivizumab for prevention of respiratory syncytial virus infection. *Pediatrics*. 2009;124:1694.