

## **Bronchiolitis: An Update in Diagnosis and Management**

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## **Disclosure**

**I, or an immediate family member including spouse/partner, have at present and/or have had within the last 12 months, or anticipate NO financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in context to the design, implementation, presentation, evaluation, etc. of CME activities**



## **Objectives**

- **Discuss updates to clinical practice guidelines for bronchiolitis**
  - **Diagnosis**
  - **Management**
  - **Prevention**



## **Bronchiolitis: Definition**

*Viral infection of the lower respiratory tract characterized by acute inflammation, edema, and necrosis of epithelial cells lining small airways, increased mucus production, and bronchospasm*

**AHRQ Evidence Report  
(Agency for Healthcare Research and Quality)**




Viral etiology*	URI (n= 175) n (%)	Croup (n= 18) n (%)	Bronchiolitis (n= 455) n (%)
Human rhinovirus	63 (36%)	5 (28%)	41 (9%)
RSV (A/B)	11 (6%)	3 (17%)	268 (59%)
Influenza virus (A/B)	10 (6%)	1 (6%)	10 (2%)
Human metapneumovirus	4 (2%)	0	5 (1%)
Human coronaviruses (HCOV OC43, 229E, NL)	8 (5%)	0	0
Parainfluenza viruses (PIV 1-3)	8 (5%)	3 (17%)	3 (1%)
HRV/RSV coinfection	7 (4%)	1 (6%)	30 (7%)
Other virus or other coinfection**	19 (11%)	3 (17%)	54 (12%)
Study virus negative	45 (26%)	2 (11%)	43 (9%)

Pediatr Infect Dis J. 2013;32(9):950–955


## Disease Burden

- **The most common cause of hospitalization during first 12 months of life**
- **100,000 bronchiolitis admissions annually (USA)**
- **Estimated annual cost \$1.73 billion**




## Bronchiolitis: Pathogenesis

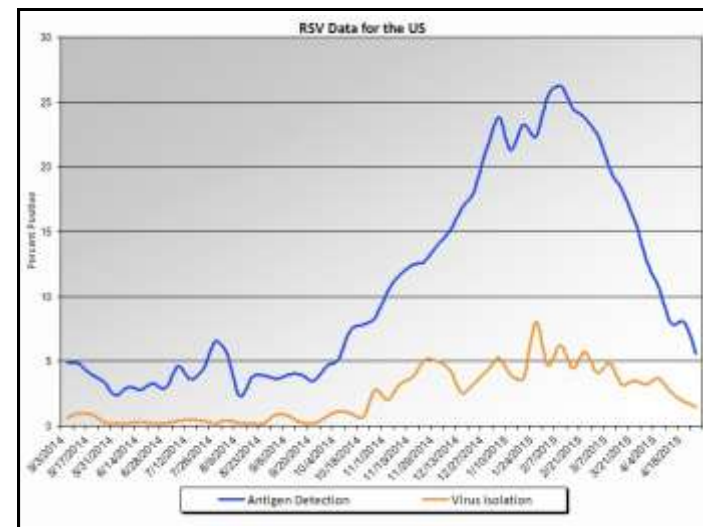
- **Acute inflammation**
- **Necrosis, sloughing of epithelium of small airways**
- **Edema**
- **Increased mucus secretion**
- **Bronchospasm**
- **All contribute to obstructed flow in small airways**

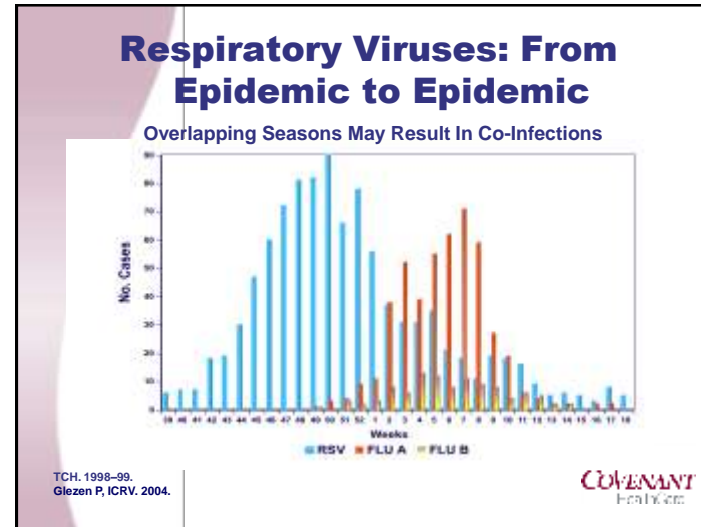
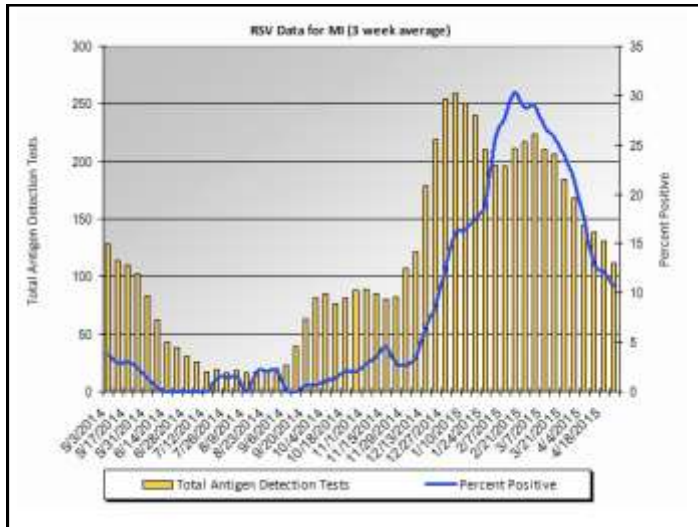


(Hematoxylin and Eosin, x40)



C Hall, N Engl J Med 344:1917, June 21, 2001





- ## Presentation
- Rhinitis
  - Cough
  - Tachypnea
  - Wheezing
  - Use of accessory muscle use
  - Nasal flaring
  - Fever +/-
  - Tachycardia
  - Dehydration
  - Otitis media
  - Apnea / Apparent life threatening event (ALTE)
  - May progress to respiratory failure
- COVENANT**  
Pediatrics

- ## Physical Exam
- Hydration status
  - Level of alertness
  - Respiratory rate
  - Accessory muscle use
  - Retractions
  - Wheezes
  - Crackles
  - Grunting
  - Nasal flaring
  - Head bobbing
  - Pulse oximetry
- 
- COVENANT**  
Pediatrics

## Bronchiolitis: Differential Diagnosis

- Infections
- Foreign body
- Vascular ring
- Congenital mass
- Tracheomalacia
- Cardiac failure (left→right shunt, myocarditis)



## Children at Highest Risk for Severe RSV

- |                          |  |
|--------------------------|--|
| Premature birth          | <ul style="list-style-type: none"><li>• Altered airway anatomy</li><li>• Absence of maternal antibody</li></ul>  |
| Chronic lung disease     | <ul style="list-style-type: none"><li>• Bronchial hyperresponsiveness</li><li>• Reduced lung capacity</li></ul>  |
| Congenital heart disease | <ul style="list-style-type: none"><li>• Pulmonary vascular hyperresponsiveness</li><li>• Pulmonary hypertension</li><li>• Increased pulmonary blood flow</li></ul> |
| Neuromuscular disease    | <ul style="list-style-type: none"><li>• Decreased respiratory muscle strength and endurance</li></ul>  |
| Immune deficiency        | <ul style="list-style-type: none"><li>• Decreased host defenses</li><li>• Impaired capacity to eliminate virus</li></ul>   |

Weisman L. Presented at: 1st International Congress on Respiratory Syncytial Virus; June 2002; Washington, DC.



## Additional Susceptibility and Exposure Factors for Severe RSV Disease

- Tobacco smoke exposure
- Living with school aged children
- Minimal breast feeding
- Genetic predisposition



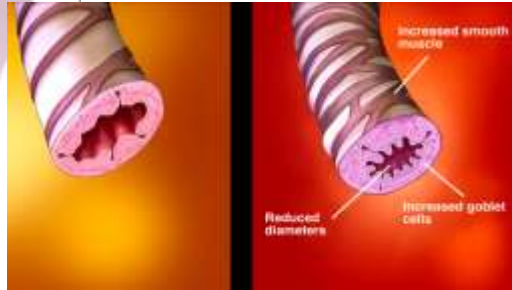
## Premature Birth Can Alter Airway Anatomy

- Altered airway development, even in the absence of clinical respiratory disease
- Even without mechanical ventilation or oxygen use
- Altered development is evidenced by:
  - ↓ diameters of major airways = ↑ obstruction
  - ↑ bronchial muscle = ↑ airway hyperreactivity
  - ↑ number of goblet cells = ↑ mucus production and plugging

Hoo A-F et al. *J Pediatr*. 2002;141:652-658; Hislop AA, Haworth SG. *Am Rev Respir Dis*. 1989;140:1717-1726; Mansell AL et al. *J Pediatr*. 1987;110:111-115; Hjalmarson O, Sandberg K. *Am J Respir Crit Care Med*. 2002;165:83-87.



## Premature Birth Can Alter Airways



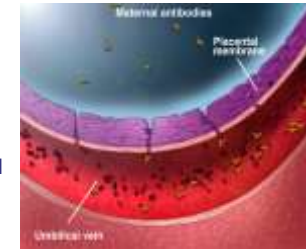
Term Infant Lung      Premature Infant Lung

Hislop AA, Haworth SG. *Am Rev Respir Dis.* 1989;140:1717-1726; Hoo A-F et al. *J Pediatr.* 2002;141:652-658; Mansell AL et al. *J Pediatr.* 1987;110:111-115.



## Premature Infants Have Decreased Maternal Antibody Transfer

- Antibody transfer occurs during the third trimester (after 28 weeks)
- Antibody levels at birth are proportional to GA
- Antibody levels are also influenced by birth weight, independent of GA



GA = gestational age.

Okoko JB et al. *Trop Med Int Health.* 2001;6:529-534; Yeung CY, Hobbs JR. *Lancet.* 1968;7553:1167-1170.



# PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

### Clinical Practice Guideline: The Diagnosis, Management, and Prevention of Bronchiolitis

Shawn L. Ralston, Allan S. Lieberthal, H. Cody Meissner, Brian K. Alvenson, Jill E. Baley, Anne M. Gadomski, David W. Johnson, Michael J. Light, Nizar F. Maraqa, Eneida A. Mendonca, Kieran J. Phelan, Joseph J. Zorc, Danette Stanko-Lopp, Mark A. Brown, Ian Nathanson, Elizabeth Rosenblum, Stephen Sayles III and Sinsi Hernandez-Cancio

*Pediatrics*; originally published online October 27, 2014;  
DOI: 10.1542/peds.2014-2742

## Guideline Overview

- Update to the 2006 AAP Guidelines
- Greater evidence
- Addresses newer therapies
- Stronger recommendations
- Revised use of palivizumab for prevention



## Guidelines

- **Management of bronchiolitis 1 mos to 23 mos of age**
- **Does not apply to children with**
  - **Immunodeficiencies**
  - **Underlying lung disease (including recurrent wheezes)**
  - **Chronic neonatal lung disease (BPD)**
  - **Neuromuscular disease**
  - **Cystic fibrosis**
  - **Significant congenital heart disease**



- **Not intended to replace clinical judgment**
- **Not intended to establish a protocol for the care of ALL children with bronchiolitis**



## Diagnosis

- **Diagnosis and disease severity based on history and physical examination**
- **Laboratory studies and imaging should not be obtained routinely**



## Virologic Testing

- **Routine virologic testing not recommended**
- **Viral co-infections in nearly 1/3 of patients**
- **Often detect prolonged viral shedding from a previous unrelated illness (especially rhinovirus)**
- **Value in identifying specific virus not demonstrated**



## Rapid RSV Antigen Detection

- Nasopharyngeal wash
- Prevents excessive use of antibiotics
  - Severe bacterial infections with RSV are rare
- Provides early diagnosis, proper care, cohorting
- Provides prognostic information
- Identifies etiology of nosocomial infections
- Provides important epidemiology for start and stop of RSV season

Andrade MA et al. *Pediatrics*. 1998;101:617-619; Friis B et al. *Arch Dis Child*. 1984;59:1038-1045; Hall CB et al. *J Pediatr*. 1988;113:266-271; Presented by KJ Henrickson, MD:ICRV 2003; Levine DA et al. *Pediatrics*. 2004; 113:1728-1734; Purcell K et al. *Arch Pediatr Adolesc Med*. 2002;156:322-324.



## Chest Radiograph

- Routine chest radiographs not recommended
- CXR often abnormal
- Rarely correlates with disease severity
- More likely to use (inappropriate) antibiotics
- Reserve for cases severe enough to warrant ICU admission



## Evaluation

- Diagnose
- Assess severity
- Assess risk for severe disease
  - Age less than 12 weeks
  - History of prematurity
  - Chronic lung disease
  - Hemodynamically significant congenital heart disease
- Assess feeding and hydration
- Previous episodes of wheezing
- Physical exam requires serial observations over time



## Albuterol

- Several RCTs fail to demonstrate a significant benefit from  $\alpha$ - or  $\beta$ -adrenergic agents
  - May improve clinical symptom scores
  - Does not affect resolution, need to hospitalize, or LOS
- Potential risk and cost outweigh potential benefit



## Epinephrine

- **Studies typically compare with placebo or albuterol**
- **Lack of efficacy**
- **Longer LOS when used on fixed schedule (as opposed to PRN)**



## Systemic Steroids

- **Steroids are beneficial in other respiratory diseases (croup, asthma)**
- **No improvement in**
  - **LOS**
  - **Clinical score**
  - **Admission rate to hospital**
  - **Respiratory rate**
  - **Oxygen saturations**
  - **Steroids may prolong viral shedding**



THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

May 14, 2009

### Epinephrine and Dexamethasone in Children with Bronchiolitis

Amy C. Plint, M.D., M.Sc., David W. Johnson, M.D., Hema Patel, M.D., M.Sc.,  
Natasha Wiebe, M.Math., Rhonda Correll, H.B.Sc.N., Rollin Brant, Ph.D.,  
Craig Mitton, Ph.D., Serge Gouin, M.D., Maala Bhatt, M.D., M.Sc.,  
Gary Joubert, M.D., Karen J.L. Black, M.D., M.Sc., Troy Turner, M.D.,  
Sandra Whitehouse, M.D., and Terry P. Klassen, M.D., M.Sc.,  
for Pediatric Emergency Research Canada (PERC)



## Nebulized Hypertonic Saline

- **Increases mucociliary clearance**
- **Rehydration of airway surface liquid**
- **Does not demonstrate benefit when LOS is short**
- **May be considered in cases where LOS > 3 days**
- **Not effective in ED**





## 2014 AAP Guidelines Medication – Summary

- **Clinicians should not administer to patients with bronchiolitis**
  - **Albuterol**
  - **Nebulized epinephrine**
  - **Hypertonic saline**
  - **Systemic steroids**



## Oxygen

- **Pulse oximetry has been erroneously used as proxy for respiratory distress**
- **Continuous pulse oximetry shown to prolong hospitalization**
- **Transient hypoxia likely not harmful**



## Oxygen

- **In otherwise healthy infants:**
  - **Supplemental oxygen is indicated if SpO<sub>2</sub> falls below 90%**
  - **Oxygen may be discontinued if SpO<sub>2</sub> at or above 90%, feeding well, and with minimal respiratory distress**
- **Infants with a history of hemodynamically significant heart or lung disease and premature infants require close monitoring as oxygen is being weaned**
- **Absolute numbers should not be the only factor dictating decision making**



## 2014 AAP Guidelines Oxygen – Summary

- **Clinicians may choose not to use supplemental oxygen if SpO<sub>2</sub> exceeds 90%**
- **May choose not to use continuous pulse oximetry**



## Apnea – Risk Factors

- **Age < 1 month for full term infants**
- **Age < 48 weeks postconceptional age for preterm infants**
- **Previous apneic event upon presentation to hospital**

**Large study showed zero apnic events if none of these risk factors present**

Ann Emerg Med. 2006;48(4):441–447



## Chest Physiotherapy

- **Bronchiolitis a risk for atelectasis**
- **5 RCT evaluating CPT (vibration or percussion) → No clinical benefit**
  
- **Routine CPT is not helpful**
  - **Stress to the infant**
  - **Cost and labor**



## Nasopharyngeal Suctioning

- **Preferential nasal breathing**
- **Removing secretions relieves obstruction, agitates patient, mobilizes secretions, maximizes air flow**
- **Lapses of external suctioning < 4 hours resulted in decreased LOS**
- **Routine deep suctioning associated with prolonged LOS**

JAMA Pediatr. 2013;167(5): 414–421



## Nasal Suctioning



## Antibiotics

- **Febrile infants 30-90 days with distinct viral syndrome have very low risk of serious bacterial infection SBI (much less than 1%)**
- **Abnormal WBC not useful in predicting SBI in infants with RSV**
- **Routine screening for bacteremia is not justified**
- **Antibiotics should not be used**



## Hydration

- **Hydration – needs to be assessed**
  - **If very tachypnic, may have difficulties maintaining oral hydration**
  - **IV fluids may be warranted, although not necessarily routine**
  - **RSV has been associated with SIADH and hyponatremia. If IV hydration is utilized, isotonic fluids are probably the safest**



## Prevention

- **Palivizumab**
  - **Tightened guidelines**
- **Hand Hygiene**
  - **Alcohol based rubs**
  - **Disinfect before and after**
  - **Contact with inanimate objects**
  - **After removing gloves**



## RSV Transmission

- **Transmitted by droplets, large particles, and fomites**
- **Can survive for as long as 6 hours on stethoscopes and up to 12 hours on hard, nonporous surfaces**
- **More than 50% of medical personnel are infected with RSV when RSV is prevalent in the community**
- **Nosocomial infection remains a serious problem**

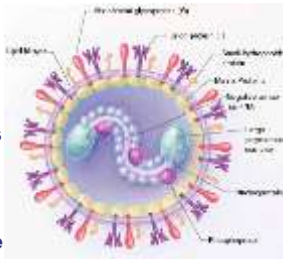


Blydt-Hansen T et al. *Pediatr Infect Dis J.* 1999;18:164-165; Cohen B et al. *Pediatr Infect Dis J.* 2003;22:494-499; Hall CB. *Clin Infect Dis.* 2000;31:590-596; Hall CB et al. *J Infect Dis.* 1980;141:98-102.



## RSV Infection

- Incubation 2-8 days
- Virus detected in secretions 4 days before symptoms appear and up to 7 days after symptoms resolve
- Viral shedding may continue up to 4 weeks
- Spread by close or direct contact: inoculation of eyes, nose
- No permanent or long-term immunity
- By age two years, 97% of children have been infected



## RSV Reinfection

- Between 50% and 75% of children followed each year (birth to 5 years old) have been reinfected each
- Reinfection more than once within the same season is common
- Reinfection tends to be more mild
- Antibody response is not sufficient to prevent subsequent RSV reinfection

Glezen WP et al. *Am J Dis Child.* 1986;140:543-546; Hall CB et al. *J Infect Dis.* 1991;163:693-698.



## Tobacco Smoke Exposure

- Passive smoke exposure increases the risk and severity of bronchiolitis
- Counsel parents about exposure and cessation programs
- Engage parents as partners in their child's health



## Breast Feeding

- 2012 AAP recommendations for exclusive breast feeding for first 6 months
- Significantly fewer respiratory infections



## Intensive Therapy

- CPAP
- Heliox
- Mechanical ventilation
  - Conventional
  - High Frequency
- Surfactant
- Inhaled Nitric Oxide
- ECMO



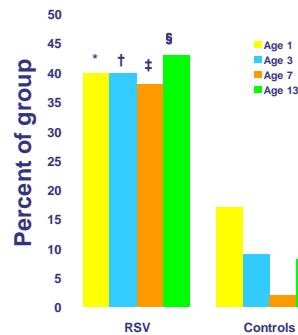
## Humidified High Flow Nasal Cannula

- Flow rates that exceed inspiratory flow rates
- Thermally controlled
- >95% relative humidity
- Precise and titratable oxygen delivery
- May also deliver heliox, iNO, or continuously nebulized medications



## Risk Factor for Asthma/Recurrent Wheezing by 13 Years of Age

- 47 children hospitalized for RSV LRTI in the first year of life
- 93 controls with no RSV LRTI
- Compared to previous data, risk for wheeze was significantly higher at 13 years compared with controls ( $P < 0.001$ )



\*  $P=0.003$ ; †  $P<0.001$ ; ‡  $P<0.0001$ ; §  $P<0.001$ ;  
LRTI = lower respiratory tract infection.

Sigurs N et al. *Am J Respir Crit Care Med.* 2000;161:1501-1507;  
Sigurs N et al. *Am J Respir Crit Care Med.* 2005;171:137-41



## Host Response to RSV

- T Helper cell 2 (TH2)
  - Associated with allergen response and disease progression
- TH1
  - Attenuates host response and cytotoxic lymphocytes
- Interleukin 18 (IL-18) plays important role in adjusting balance of TH1/TH2 immune response in viral infections
- Genetic polymorphisms in IL-18 associated with severity of RSV infection



## Summary

- Routine virology, lab work, cultures, or chest radiographs are not indicated
- Routine use of corticosteroids, bronchodilators, nebulized epinephrine, antibiotics, is of no benefit
- Therapeutic options remain largely supportive, with attention to superficial nasal suctioning, judicious use of supplemental oxygen, and attention to hydration status
- The best available options are prevention and prophylaxis



## Future Research Needs

- Better algorithms to predict course of illness
- Further studies evaluating combined inhaled epinephrine and steroids
- Better designed studies for hypertonic saline
- Use of home oxygen
- Oxygen delivered by high-flow cannula
- RSV vaccine
- Antivirals



## Thank You

**Michael Fiore, MD FAAP**

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**Covenant Health Care Pediatric  
Intensive Care Unit – 583-5437**

**Covenant Health Care RSV Prevention  
Program – 583-5418**

**One Call Transfer Center 1-877-606-  
1225**

