

# PEDIATRIC EMERGENCY MEDICINE PRACTICE

AN EVIDENCE-BASED APPROACH TO PEDIATRIC EMERGENCY MEDICINE ▲ EB MEDICINE.NET

## Evidence-Based Assessment And Management Of Acute Bronchiolitis In The Emergency Department

*As your shift is winding down at 4 AM, a mother brings in her 9-month-old infant with a chief concern of "gaspings for air." The patient has had a runny nose and cough for a few days and a low-grade fever, but now he is breathing rapidly and wheezing with lower intercostal retractions. The mother states that the infant has had wheezing in the past, and she asks if he might have asthma since "it runs in the family." She also indicates that in the last 12 hours, the infant has not taken his usual amount of fluids. His oxygen saturation level is 87% on room air. You ask yourself, "Should I follow the path of treatment for bronchiolitis or asthma? Should I give the patient albuterol or epinephrine nebulizer treatment with oxygen? Does he need steroids? Which bronchodilator is best if he does not get better with the adrenergic nebulizer treatment and he requires continued care?" You also wonder if this patient is going to tire out and require assisted ventilation.*

Visits to the emergency department (ED) by infants and young children who are wheezing and in respiratory distress are anxiety-provoking for both parents and ED staff. Emergency clinicians should be aware of the causes of this true medical emergency in infants and children as well as management strategies for handling it prior to progression to respiratory failure. Bronchiolitis is the most common lower respiratory tract infection (LRTI) in infants and young children up to 2 years of age. More than 200,000 visits are made annually to EDs in the United States for bronchiolitis, with a

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### CME Objectives

Upon completion of this article, you should be able to:

1. Diagnose and assess bronchiolitis severity based on the patient's history and physical examination findings.
2. Identify risk factors associated with apnea due to bronchiolitis.
3. Discuss the controversies surrounding use of bronchodilators and corticosteroids in patients with bronchiolitis.
4. Identify criteria for hospitalization of patients with bronchiolitis.

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19% admission rate, making bronchiolitis the leading cause of hospitalization for infants.<sup>1,2</sup> Of note, the hospital charges for bronchiolitis alone are estimated at \$700 million annually.<sup>3</sup> The hospitalization rate for infants with bronchiolitis more than doubled between 1980 and 1996, and the proportion of infant hospitalizations due to bronchiolitis more than tripled.<sup>3</sup>

This issue of *Pediatric Emergency Medicine Practice* uses evidence-based medicine to recommend strategies for effective evaluation and treatment of bronchiolitis in pediatric patients. The definition of bronchiolitis, the clinical scoring systems, and outcome measures used in the bronchiolitis literature vary significantly, complicating interpretation of the data (See Table 1, page 3.) Although excellent published guidelines exist to help clinicians address this common disease, they often exclude the “high-risk” group for severe bronchiolitis (ie, patients who are at risk for serious complications such as apnea and who may need ventilatory support). Particularly helpful in this area is the American Academy of Pediatrics (AAP) Subcommittee on Diagnosis and Management of Bronchiolitis. (See Table 2, page 4.)<sup>4</sup> Novel treatments for acute bronchiolitis such as nebulized hypertonic saline, heliox, and nasal continuous positive airway pressure (nCPAP) are also available and will be discussed in this article.

## Critical Appraisal Of The Literature

Despite the high frequency of bronchiolitis, it remains a clinical diagnosis without a common international definition. In 2006, the AAP defined bronchiolitis as “rhinitis, tachypnea, wheezing, cough, crackles, use of accessory muscles, and/or nasal flaring in a child younger than 24

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months.”<sup>4</sup> Children presenting with these symptoms are often labeled with numerous diagnoses such as reactive airway disease, wheezing, cough, asthma, or pneumonia, as well as bronchiolitis.<sup>5</sup> A recent study by Jartti et al suggests that the diagnosis of bronchiolitis should be restricted either to children younger than 24 months who are having their first episode of wheezing or to children younger than 12 months.<sup>6</sup> Different cutoff ages for bronchiolitis, as well as the lack of a valid clinical scoring system that correlates with clinically significant improvement and the inclusion of testing for respiratory syncytial virus (RSV) or other viruses in the diagnosis, complicate a review and comparison of the literature.

A search of articles published on bronchiolitis from 1970 to the present was performed using Ovid MEDLINE® and PubMed. The areas of focus were bronchiolitis and pediatrics. Terms used in the search included *wheezing, bronchiolitis, lower respiratory tract infection, RSV, infant respiratory distress, bronchiolitis guidelines, steroids, and asthma*. More than 200 articles were analyzed, providing the background for further review. In addition, the Cochrane Database of Systematic Reviews was consulted. Three major current guidelines for the diagnosis and management of bronchiolitis were also reviewed and are summarized in Tables 1 and 2 on pages 3 and 4.<sup>4,7,8</sup>

## Pathophysiology

Bronchiolitis is usually due to a viral infection of the small airways. Infection of the bronchial respiratory and ciliated epithelial cells produces increased mucous secretion, cell death, and sloughing. This process is followed by a peribronchiolar lymphocytic infiltrate and submucosal edema, leading to critical narrowing and obstruction of the small airways. Hypoxia is due to the ventilation/perfusion mismatch caused by decreased ventilation of a portion of the lungs. The degree of obstruction may vary as these areas are cleared, resulting in rapidly changing clinical signs that confound an accurate assessment of the severity of the illness. (This is the reason examination findings can change from one minute to the next in a patient with bronchiolitis.) A decrease in lung compliance and an increase in the end-expiratory lung volume (secondary to air trapping) result in an increase in the work of breathing. In addition, atelectasis may be accelerated by the lack of collateral channels in young children and potentially by the administration of high concentrations of supplemental oxygen, which are absorbed more rapidly than room air. Smooth muscle constriction seems to have a limited role in explaining the lack of response to bronchodilators by patients with bronchiolitis.<sup>9</sup>

Recovery of pulmonary epithelial cells occurs after 3 to 4 days, but cilia do not regenerate for about 2

weeks, and debris is cleared by macrophages later on. This explains the median duration of illness of 12 days in children younger than 24 months with bronchiolitis; after 3 weeks, approximately 18% of these patients will remain ill, and after 4 weeks, 9% will remain ill.<sup>10</sup>

## Etiology

The number of viruses known to cause bronchiolitis has markedly expanded with the availability of sensitive diagnostic tests that use molecular amplification techniques. Respiratory syncytial virus (RSV) continues to account for 50% to 80% of cases.<sup>11</sup> However, the virus is a rare pathogen in older children hospitalized with bronchiolitis, because nearly all people are infected with RSV within the first 2 years of life, and the initial RSV infection is typically the most severe.<sup>12</sup> Annual epidemics of RSV usually begin in the late fall and peak between November and March. *Human metapneumovirus* (HMPV) accounts for an additional 3% to 19% of bronchiolitis cases<sup>16,17</sup> and appears to have a clinical course similar to that of RSV, with most

children infected during annual wintertime epidemics and a subset developing bronchiolitis.<sup>13,18,19</sup>

Other causes include the parainfluenza viruses (primarily parainfluenza virus type 3) and the influenza virus.<sup>13-15</sup>

The role of rhinoviruses in bronchiolitis is unclear compared to its well-documented role in triggering exacerbations of wheezing among patients with asthma.<sup>12,20,21</sup> A study by Jarrett et al focused on viral etiologies in young children with acute asthma and found that rhinovirus was an important agent (ie, it was identified in 65% of children aged 1-2 years and in 82% of children 3 years and older), with a recovery rate of 27% to 44%.<sup>23</sup> A multicenter ED-based study of children younger than 2 years diagnosed with bronchiolitis revealed that those infected with rhinovirus were more likely to be African-American, to have a previous history of wheezing, and to be treated with corticosteroids than infants with other viral infections.<sup>14</sup>

New molecular diagnostic techniques have also made it possible to determine if young children with bronchiolitis and other acute respiratory illnesses

**Table 1. Major Guidelines For The Diagnosis And Management Of Bronchiolitis**

| Guideline  | Levels/Grades Of Recommendation  |
|--|--|
| <p><b>Clinical Practice Guidelines: Diagnosis and Management of Bronchiolitis (2006)</b></p> <p><b>American Academy of Pediatrics, Subcommittee on Diagnosis and Management of Bronchiolitis<sup>4</sup></b></p> <p><a href="http://aappolicy.aappublications.org/cgi/abstract/pediatrics;118/4/1774">http://aappolicy.aappublications.org/cgi/abstract/pediatrics;118/4/1774</a></p>    | <p>Levels of recommendation are based on the strength of evidence for each question:</p> <p><b>Level A:</b> Well-designed RCTs, or diagnostic studies on relevant populations</p> <p><b>Level B:</b> RCTs or diagnostic studies with minor limitations, overwhelming consistent evidence from observational studies</p> <p><b>Level C:</b> Observational studies (case-control and cohort design)</p> <p><b>Level D:</b> Expert opinion, case reports, reasoning from first principles</p> <p><b>Level X:</b> Exceptional situations in which validating studies cannot be performed and there is a clear preponderance of benefit or harm</p>   |
| <p><b>Bronchiolitis In Children: A National Clinical Guideline (2006)</b></p> <p><b>Scottish Intercollegiate Guidelines Network<sup>7</sup></b></p> <p><a href="http://www.sign.ac.uk/pdf/sign91.pdf">http://www.sign.ac.uk/pdf/sign91.pdf</a></p>   | <p>Evidence was evaluated for quality according to predefined, specified criteria and assigned to 1 of 8 levels (1++, 1+, 1-, 2++, 2+, 2-, 3, and 4). Recommendations were graded based on the strength of evidence for each question</p> <p><b>Grade A:</b> At least 1 meta-analysis, systemic review of RCTs, or RCT rated as 1++ and directly applicable to the target population; or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results</p> <p><b>Grade B:</b> A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+</p> <p><b>Grade C:</b> A body of evidence including studies rated as 2+, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++</p> <p><b>Grade D:</b> Evidence level 3 or 4; or extrapolated evidence from studies rated as 2+</p> <p><b>Good practice points:</b> Recommended best practice based on the clinical experience of the guideline development group</p> |
| <p><b>Evidence-Based Clinical Practice Guidelines For Infants With Bronchiolitis (2006)</b></p> <p><b>Bronchiolitis Guideline Team, Cincinnati Children's Hospital Medical Center<sup>8</sup></b></p> <p><a href="http://www.cincinnatichildrens.org/svc/alpha/h/health-policy/bronchiolitis.htm">http://www.cincinnatichildrens.org/svc/alpha/h/health-policy/bronchiolitis.htm</a></p> | <p>This document was developed by a bronchiolitis team consisting of Cincinnati Children's Hospital Medical Center physicians, a respiratory therapist, and members of the Division of Health Policy Clinical Effectiveness; a community physician; a nursing/patient services provider; and ad hoc advisors. This interdisciplinary working group performed systematic and critical literature reviews using a grading scale for quality, assigning each citation to 1 of 12 categories, and also examined current local practices. The recommendations are not graded.</p>   |

Abbreviations: randomized control trials, RCTs

are infected with more than 1 virus. Of note, rates of co-infection most commonly with RSV and either HMPV or rhinovirus range from 10% to 30% in samples of hospitalized children.<sup>24</sup> A recent large prospective study of children younger than 5 years hospitalized with RSV infection revealed a co-infection rate of 6%.<sup>25</sup> Whether concomitant infections increase the severity of bronchiolitis remains controversial. One small study did find that dual RSV and HMPV infections were associated with a 10-fold increase

**Table 2. AAP Clinical Practice Guidelines For The Diagnosis And Management Of Bronchiolitis<sup>4</sup>**

| Recommendation  | Grade/Level    |
|---|----------------|
| <b>1a.</b> For bronchiolitis, history and physical examination should be the basis for diagnosis and disease severity assessment. Laboratory and radiologic studies should not be ordered routinely.  | <b>Level B</b> |
| <b>1b.</b> When making decisions about management of children with bronchiolitis, the following risk factors for severe disease should be assessed: 1) age less than 12 weeks, 2) a history of prematurity, 3) underlying cardiopulmonary disease, and 4) immunodeficiency.   | <b>Level B</b> |
| <b>2a.</b> The management of bronchiolitis should not routinely include bronchodilators.  | <b>Level B</b> |
| <b>2b.</b> The use of alpha-adrenergic or beta-adrenergic medication is an option if given in a carefully monitored trial. The use of inhaled bronchodilators should be continued only if objective means of evaluation document a positive clinical response to the trial.   | <b>Level B</b> |
| <b>3.</b> The management of bronchiolitis should not routinely include the use of corticosteroid medications.   | <b>Level B</b> |
| <b>4.</b> Children with bronchiolitis should not be treated routinely with ribavirin.   | <b>Level B</b> |
| <b>5.</b> Only children with specific indications of bacterial infection should be given antibacterial medications. Treatment of the bacterial infection should be the same as it would be in the absence of bronchiolitis.   | <b>Level B</b> |
| <b>6A.</b> For infants with bronchiolitis, hydration and ability to take fluids orally should be assessed by clinicians.  | <b>Level X</b> |
| Indications for oxygen saturation monitoring and oxygen administration:<br><b>7A.</b> If SpO <sub>2</sub> falls persistently below 90% in infants who were previously healthy, supplemental oxygen is indicated. Adequate supplemental oxygen should be used to maintain SpO <sub>2</sub> ≥ 90%. If SpO <sub>2</sub> is ≥ 90% and the infant is feeding well and has minimal respiratory distress, supplemental oxygen may be discontinued. | <b>Level D</b> |

Abbreviations: oxyhemoglobin saturation, SpO<sub>2</sub>

in the risk of the need for mechanical ventilation.<sup>26</sup> Other studies have revealed no association between increased illness severity and the presence of more than 1 virus.<sup>24-27</sup>

## Differential Diagnosis

Cough, tachypnea, and wheezing are typical symptoms (the latter being the prominent presentation of acute bronchiolitis), but many other common and critical diseases should be considered when infants and young children present with wheezing. (See Table 3.)

Clues from the medical history that may facilitate diagnosis include family history, age at onset, pattern of wheezing, seasonal exacerbation, and sudden onset. Association of wheezing with feeding, cough, respiratory tract illnesses, and positional changes may also be helpful. Wheezing that is associated with feeding, coughing, and vomiting may indicate gastroesophageal reflux disease or tracheoesophageal fistula and should be evaluated with 24-hour pH monitoring, barium swallow, or both. When wheezing is associated with positional changes, there may be tracheomalacia or anomalies of the great vessels, warranting angiography, bronchoscopy, chest radiography, computed tomography (CT), or magnetic resonance imaging (MRI). When wheezing is exacerbated by neck flexion and relieved by neck hyperextension, the presumptive diagnosis is vascular ring, which may be diagnosed by angiography, barium swallow, bronchoscopy, chest radiography, CT, or MRI. Cystic fibrosis or immunodeficiency may be the cause of wheezing when the child has a history of multiple respiratory tract illnesses and a failure to thrive. In this case, ciliary function testing, immunoglobulin levels, and sweat chloride testing are appropriate. Heart murmurs, cardiomegaly, cyanosis without respiratory distress, and exertion and sweating associated with feeding might indicate cardiac diseases. The presence of drooling

**Table 3. Differential Diagnosis For Wheezing In Infancy**

| Life-Threatening Causes   |
|---|
| Infection: pneumonia, chlamydia, pertussis  |
| Foreign body: aspirated or esophageal   |
| Cardiac anomaly: congestive heart failure, vascular ring                                |
| Allergic reaction   |
| Bronchopulmonary disorder exacerbation  |
| Non-Life-Threatening Causes   |
| Congenital anomaly: tracheoesophageal fistula, bronchogenic cyst, laryngotracheomalacia |
| Gastroesophageal reflux disease   |
| Mediastinal mass  |
| Cystic fibrosis   |

with stridor, particularly if the child's immunizations are not up-to-date, should alert the emergency clinician to the possibility of epiglottitis. In addition, the sudden onset of wheezing and choking suggests foreign body aspiration.

One of the most challenging illnesses to differentiate from bronchiolitis in infants and young children is asthma. Estimates vary, but approximately 80% to 90% of children with asthma experience symptoms before the age of 6 years (with 70% of children experiencing asthma-like symptoms before the age of 3 years). To avoid the overlap between the diagnosis of bronchiolitis and asthma, some authors recommended recently that the diagnosis of bronchiolitis should apply only to wheezing in patients 12 months of age or younger. In the past, some authors have extended the cutoff for upper limit age of making the diagnosis of bronchiolitis from 24 to 36 months. To differentiate between recurrent wheezing with bronchiolitis and asthma in younger children, Castro-Rodriguez et al developed the Modified Asthma Predictive Index (mAPI) on the basis of data from the Tucson Children's Respiratory Study.<sup>28</sup> A stringent index requires frequent wheezing in the first 3 years of life plus 1 of 2 major criteria (a parental diagnosis of asthma or a diagnosis of eczema in the child) or 2 of 3 minor criteria (a diagnosis of allergic rhinitis in the child, eosinophilia [ie, eosinophil count  $\geq$  4% of the total white blood cells], or wheezing apart from colds). Frequency of wheezing is determined by asking the parents whether the child's chest has ever sounded wheezy or whistling and how often the child has wheezed (on a scale of 1, or "very rarely," to 5, "on most days"). Patients are considered *frequent wheezers* if parents report a value greater than 3 on the scale. A loose index for the prediction of asthma requires any wheezing during the first 3 years of life plus 1 of the major criteria or 2 of the minor criteria. According to Castro-Rodriguez et al, children with a positive loose index were up to 5.5 times more likely than children with a negative loose index to have active asthma between 6 and 13 years of age.<sup>28</sup> Children with a positive stringent index were up to 9.8 times more likely than children with a negative index to have asthma later in childhood.<sup>28</sup>

The Prevention of Early Asthma in Kids (PEAK) criteria added more details to build upon the mAPI criteria. It specifies "frequent wheezing" as more than 3 exacerbations of wheezing in the past 12 months, with at least 1 physician-confirmed exacerbation. Additionally, it specifies allergic sensitization to 1 or more aeroallergens among the major criteria and replaces a diagnosis of allergic rhinitis as a minor criterion with allergic sensitization to milk, egg, or peanuts.<sup>29,30</sup> The PEAK study was designed to investigate the role of inhaled corticosteroids in preventing persistent asthma in children with a positive mAPI score.<sup>31</sup>

## Prehospital Care

The goals of prehospital care for the infant or young child with bronchiolitis must include timely assessment and recognition of the severity of the disease and initiation of appropriate treatment. Young age (ie, younger than 2 months) and a history that includes prematurity, chronic lung disease (CLD), or any cardiac or immune deficiencies as well as physical examination results including general appearance, vital signs, mental status, work of breathing, respiratory rate, and accessory muscle use can assist the prehospital provider in patient assessment. Special attention should be given to the occurrence of apnea spells, particularly if a previous episode was reported by the caregiver and if the patient is a neonate or is premature with a corrected gestational age less than 48 weeks. Cardiorespiratory monitoring and positioning of the infant or young child to facilitate respiratory efforts (ie, placing the patient in an upright posture) are essential. In addition, treatment should include administration of oxygen if the patient's oxygen saturation level is less than 90%, nasal suctioning, and possibly a trial of bronchodilators if the patient has increased work of breathing.

## Emergency Department Evaluation

### Important Historical Questions

It is crucial that emergency clinicians inquire about the patient's risk factors for severe bronchiolitis, which is characterized by persistently increased respiratory effort, apnea, and the need for intravenous hydration, supplemental oxygen, or mechanical ventilation.

### Risk Factors For Severe Bronchiolitis

Several studies have associated premature birth (< 35-37 weeks' gestation) and younger age (< 6-12 weeks of life) with an increased risk of severe bronchiolitis.<sup>32-34</sup> Other conditions predisposing the patient to severe disease or mortality include underlying respiratory illnesses such as bronchopulmonary dysplasia (also known as CLD) cystic fibrosis, and congenital anomalies. Hemodynamically significant congenital heart disease (CHD), an immune deficiency such as human immunodeficiency virus infection, organ or bone marrow transplants, and congenital immune deficiencies are also risk factors.<sup>35,36</sup> (See Table 4, page 6.)

The vast majority of studies addressing the risk factors for severe bronchiolitis and outcomes such as the need for mechanical ventilation and intensive care have involved hospitalized patients, which is a small subset of all children with bronchiolitis seen in the ED. The infrequent occurrence of these adverse events limits the power of these studies to predict bronchiolitis severity.

## Risk Factors For Apnea

Several factors have been identified to predict the group of patients with bronchiolitis who are at risk for the development of apnea in the course of their illness. (See Table 4.) They include young age, prematurity, a history of apnea of prematurity, and presentation with apnea.<sup>37-41</sup> Of note, these studies have focused on patients with confirmed bronchiolitis due to RSV, which could explain the high rates of apnea (16%-25%) reported in hospitalized patients with RSV infection.

In a recent retrospective study by Willwerth et al, the rate of apnea in young infants with clinically diagnosed bronchiolitis was determined.<sup>42</sup> In addition, a set of criteria for identifying patients at high risk for apnea was developed. Children were considered to be at high risk if: (1) they were full term at birth and were younger than 1 month, (2) they were preterm at birth (< 37 weeks' estimated gestation) and were younger than 48 weeks post conception, or (3) the child's parents or a clinician had already witnessed an apnea episode with this illness before admission. In all, 19 of 691 infants (2.7%) admitted with bronchiolitis developed apnea while hospitalized. All 19 patients with apnea were identified as high-risk by the risk criteria. Therefore, the risk criteria had perfect sensitivity (meaning that all patients who developed apnea were classified appropriately as high-risk). Seven percent of all patients considered high-risk by these criteria developed apnea. On the other hand, approximately two-thirds of the patients who did not develop apnea were classified as low-risk by the clinical rule. Due to the fact that the study included only hospitalized patients, this set of criteria cannot be applied to the patients with bronchiolitis who were discharged from the ED. The rate of apnea in this study is lower than the reported apnea rate of 16% to 25% in the RSV bronchiolitis study. That could be due to the fact that RSV testing was performed on disproportionately younger or sicker patients with bronchiolitis, a group naturally at higher risk of developing apnea.<sup>42</sup>

## Important Physical Findings

Serial examinations of respiratory status are very important in assessing overall patient status and reflecting variabilities in the disease state, from mucus plugging to progressive respiratory distress due to lower airway obstruction. Important elements of the physical examination include respiratory rate, increased work of breathing as evidenced by accessory muscle use and/or retractions, and auscultation findings such as wheezes or crackles. The impact of respiratory symptoms on feeding and hydration, particularly in young infants, is also critical.

Tachypnea, defined as a respiratory rate more than 70 breaths per minute, has been associated with increased risk for severe bronchiolitis in some stud-

ies but not others.<sup>33,43</sup> Of note, respiratory rates in otherwise healthy children change considerably over the first year of life, decreasing from a mean of approximately 50 breaths per minute in term newborns to approximately 40 breaths per minute at 6 months and 30 breaths per minute at 12 months.<sup>44,45</sup> Counting respiratory rate over 1 minute may be more accurate than extrapolating measurements to 1 minute but observing for shorter periods.<sup>46</sup> The absence of tachypnea correlates with the lack of LRTI or pneumonia (viral or bacterial) in infants.<sup>47</sup>

The most widely used clinical score, the Respiratory Distress Assessment Instrument,<sup>48</sup> is reliable with respect to scoring but has not been validated for clinical predictive value in bronchiolitis. There is no standard clinical score to assess bronchiolitis and many treatment trials use different variables to assess the medication's impact on the course of bronchiolitis such as respiratory rate, respiratory effort, severity of wheezing, and oxygenation. This was evident in a report by the Agency for Healthcare Research and Quality in which 43 of 52 treatment trials used different clinical scoring systems, making the comparison between these studies very difficult.<sup>49</sup>

Pulse oximetry is the fifth vital sign and is among the measures most strongly correlated with outcomes of bronchiolitis. In a recent prospective multicenter study, pulse oximetry level in the ED of less than 94% was associated with a greater than 5-fold increase in likelihood of hospitalization.<sup>50</sup>

## Table 4. Risk Factors For Severe Bronchiolitis And Apnea

### Risk factors for severe bronchiolitis:

1. History:
  - Age: < 6-12 weeks<sup>32-34</sup>
  - Prematurity: < 34-37 weeks' gestation <sup>32-34</sup>
  - Underlying respiratory illness such as CLD or BPD<sup>4</sup>
  - Significant congenital heart disease, immune deficiency including human immunodeficiency virus, organ or bone marrow transplants, or congenital immune deficiencies<sup>35,36</sup>
2. Physical examination:
  - General appearance: ill appearing<sup>33</sup>
  - Oxygen saturation level: < 94% on room air\*
  - Respiratory rate: > 70 breaths per minute or higher than normal rate for patient age<sup>4,33</sup>
  - Increased work of breathing: moderate to severe retractions and/or accessory muscle use<sup>4</sup>

### Risk factors for apnea:

- Full-term birth and < 1 month of age<sup>40,42</sup>
- Preterm birth (< 37 weeks' gestation) and age < 2 months post conception<sup>32-34,42</sup>
- History of apnea of prematurity<sup>42</sup>
- Emergency department presentation with apnea<sup>42</sup>
- Apnea witnessed by a caregiver<sup>42</sup>

\*See explanation in the Hypoxia section on page 13

Abbreviations: chronic lung disease, CLD; bronchopulmonary dysplasia, BPD

Arbitrary thresholds for oxygen therapy may also influence the physician's decision to admit patients with bronchiolitis. A survey of emergency physicians demonstrated that reducing the patient's pulse oximetry level from 94% to 92% in a clinical vignette significantly increased the likelihood of the physicians to recommend hospitalization.<sup>51</sup>

## Diagnostic Studies

In the acute care setting, acute bronchiolitis is primarily a clinical diagnosis. Diagnostic testing such as chest radiography, virologic testing, complete blood cell count, and urine analysis are not routinely recommended for infants with bronchiolitis.

Although radiographs may be useful in the ED when severe disease requires further evaluation or if foreign body aspiration, pneumonia, or congestive heart failure (CHF) is suspected based on history and physical examinations findings, current evidence does not support routine use in children with bronchiolitis.<sup>52</sup> Two studies suggest that the presence of consolidation and atelectasis on a chest radiograph is associated with an increased risk for severe disease,<sup>32,33</sup> whereas one study showed no correlation between chest radiograph findings and baseline disease severity.<sup>53</sup> Obtaining a chest radiograph could affect the emergency clinician's decision to start antibiotics. Numerous prospective studies, including a randomized trial, have shown that children with a suspected LRTI who were given radiographs were more likely to receive antibiotics without any difference in time to recovery.<sup>54,55</sup>

A subsequent prospective study of 265 children aged 2 to 23 months who presented to the ED with bronchiolitis analyzed use of routine radiography in patients with a simple form of the disease (defined in a child as coryza, cough, and respiratory distress accompanying a first episode of wheezing without underlying illness).<sup>56</sup> The authors identified findings inconsistent with bronchiolitis in only 2 cases, and in neither case did the findings change short-term management. On the other hand, clinicians were more likely to treat patients with antibiotics when ordering radiographs despite the fact that the radiographs findings did not support such treatment.<sup>56</sup>

Because most of the viruses that cause bronchiolitis have similar clinical presentations, identification of the specific agent in the ED setting has minimal effect on management. In addition, rapid viral antigen testing has variable sensitivity and specificity depending on the test used and its timing in relation to the respiratory season.<sup>57</sup> Emergency clinicians are most apt to obtain viral testing when encountering infants in the first few months of life who present with fever and typically recognized bronchiolitis signs and symptoms. A positive viral test result predicts a lower likelihood of a bacterial infection, with the exception of urinary tract infections (UTIs). Therefore, the fever

workup should include ruling out a UTI and avoiding unnecessary blood work. This does not apply during the newborn period, when the fever workup should include a complete septic analysis.

A large study of febrile infants less than 60 days of age with bronchiolitis and/or an RSV infection demonstrated that although the overall risk of serious bacterial infections (SBIs) in patients less than 28 days of age was significant, the risk was not different between RSV-positive and RSV-negative groups (10.1% vs 14.2%, respectively).<sup>43</sup> All SBIs in children between 28 and 60 days of age with RSV-positive bronchiolitis were UTIs. The rate of UTIs in the RSV-positive group was significantly lower than the rate in the RSV-negative group (5.5% vs 11.7%, respectively).<sup>58</sup> In another study of 2396 infants with RSV bronchiolitis, 69% of the 39 patients with an SBI had a UTI.<sup>59</sup>

Recently, low rates of co-infections also have been observed in studies using the "clinical diagnosis" of bronchiolitis without viral testing.<sup>60,61</sup>

## Treatment

Treatment for bronchiolitis is controversial and includes the followings therapies.

### Nasal Suction

Nasal suction should be used to clear secretions in infants with acute bronchiolitis, particularly if they exhibit respiratory distress or difficulties in feeding or sleeping. This is especially important in younger infants, who are obligatory nose breathers.

### Bronchodilators

#### Albuterol/Salbutamol

The AAP's Subcommittee on the Diagnosis and Management of Bronchiolitis recommends "a carefully monitored trial of adrenergic medication as an option and that inhaled bronchodilators should be continued only if there is a documented positive clinical response to the trial using an objective means of evaluation."<sup>4</sup> The use of bronchodilator agents continues to be controversial, with inconsistent results regarding their benefits in treating viral bronchiolitis. Numerous studies and systematic evidence-based reviews have attempted to summarize these results,<sup>62-65</sup> but they have been confounded by the variety of therapies used and outcome measures that range from effects of bronchodilators on oxygen saturation levels and clinical scores after 30 minutes and 60 minutes to effects on admission rates and length of hospital stay.<sup>66</sup> In addition, the use of bronchodilators should be weighed against their potential adverse effects and costs, especially given that most patients will not benefit from such treatment.

A recent Cochrane review of bronchodilators other than epinephrine found that the agents produce small, short-term improvements but do not affect rate of hospitalization or length of hospital stay.<sup>67</sup>

## Epinephrine

A meta-analysis of the treatment effects of nebulized epinephrine suggested a decrease in clinical symptoms when compared with either placebo or albuterol.<sup>68</sup> The dose is 0.9 mg/kg for racemic nebulized epinephrine or 0.03 mL/kg for the 2.25% solution, which is usually diluted in 3 mL of normal saline. A Cochrane review of inhaled epinephrine found no reduction in admission rates in the treatment group, with some studies demonstrating short-term improvements in clinical scores, oxygen saturation levels, and respiratory rates.<sup>69</sup>

## Anticholinergic Agents

Anticholinergic agents such as ipratropium are frequently given to children with wheezing because of their positive effects in the treatment of acute asthma exacerbation, but their role in the treatment of bronchiolitis is uncertain. A 2005 Cochrane review of the role of anticholinergic agents in the treatment of children younger than 2 years with wheezing identified 6 trials, only 2 of which involved patients with first-time wheezing.<sup>70</sup> Compared with beta2-agonist alone, the combination of ipratropium bromide and beta2-agonist was not associated with a difference in treatment response, respiratory rate, or oxygen saturation improvement in the ED. There was no significant difference in length of hospital stay between the ipratropium bromide and placebo groups or between patients receiving ipratropium bromide and a beta2-agonist combined and those receiving a beta2-agonist alone. At this point, use of anticholinergic agents either alone or in combination with beta-adrenergic agents for viral bronchiolitis is not justified in the ED.<sup>71-73</sup>

## Corticosteroids

Although consistent evidence of the efficacy of corticosteroids in the treatment of bronchiolitis is lacking,<sup>4,49,74</sup> it is estimated that up to 60% of infants hospitalized with the disease receive the medications.<sup>3,75-77</sup> Some studies have suggested benefits with corticosteroid therapy,<sup>78-81</sup> but a careful review of these studies, including sample size and methodology, demonstrated the inconclusive nature of the available evidence.<sup>49</sup> A Cochrane Collaboration review of 13 studies on the use of corticosteroids for bronchiolitis showed no significant differences between corticosteroid and placebo treatment groups in respiratory rates, oxygen saturation levels, initial admission rates, length of stay, subsequent visits, or readmission rates.<sup>74</sup>

Schuh and colleagues conducted a placebo-controlled trial involving 70 infants with moderate-to-severe bronchiolitis.<sup>82</sup> The authors found significant reductions in respiratory scores after 4 hours of observation in infants who received oral dexamethasone 1 mg/kg and 0.6 mg/kg (which was continued for patients discharged home for 5 days) compared

with those who received placebo. Moreover, the admission rate was 19% in the dexamethasone group compared with 44% in the placebo group.<sup>82</sup> The limitations of this study are the small sample size and the larger proportion of positive family history of atopy in infants in the dexamethasone group (increasing the risk of having asthma) compared to those in the placebo group. This could have affected the impact of corticosteroids on the course of their illness in the dexamethasone group.

One landmark study of the use of corticosteroids in treating bronchiolitis was conducted by the Bronchiolitis Study Group of the Pediatric Emergency Care Applied Research Network, which enrolled patients at 20 medical center EDs from 2004 to 2006.<sup>83</sup> The participants were 2 to 12 months old and presented with a first episode of bronchiolitis. None of the infants had experienced prior wheezing or asthma, and they were enrolled during the first 7 days of the index illness. The infants also had "moderate" or "severe" symptoms as measured by a standard assessment rubric. Patients received 1 mg/kg of dexamethasone solution or the same volume of placebo fluid. Investigators assessed symptom scores and vital signs and examined the patients at entry, 1 hour, and 4 hours after receipt of the study medication or placebo. Other ED care and laboratory testing were left to the discretion of the local providers. Families were contacted within 1 week after the ED visit to obtain information on side effects and rates of revisiting medical care. In all, 600 patients were randomly assigned to the treatment groups, and roughly equal numbers in the 2 arms had complete data. The patients in both groups received very similar treatment by the providers; 77% of the intervention group and 80.3% of the placebo group received albuterol, and the mean number of treatments was the same per group. Similarly, there was no statistically significant difference in the percentages admitted to the hospital (ie, 39.7% of patients in the dexamethasone group were admitted vs 41% in the placebo group). Even after adjustments for patient age, history of atopy, and positive RSV test results, dexamethasone did not improve admission rates or secondary outcomes of interest. Mean length of stay was 2.55 days for the treatment group compared with 2.27 days for the placebo group, a difference that did not reach statistical significance. In addition, there was no difference in readmission rates (ie, 4.2% for the treatment group vs 3.8% for the placebo group). The authors concluded that use of dexamethasone in the ED did not improve outcomes in first-time wheezers with bronchiolitis. This study did not address the question of steroid effectiveness in infants with bronchiolitis and prior wheezing or in older children with bronchiolitis.<sup>84</sup>

## Inhaled Steroids

Two available studies that evaluated use of inhaled

corticosteroids in the treatment of bronchiolitis showed no benefit in the course of the acute disease.<sup>85,86</sup> Unless there is a clear likelihood of benefit, high-dose inhaled corticosteroids should not be used in infants because of safety concerns.

### **Combination Of Epinephrine And Dexamethasone**

Pediatric Emergency Research Canada conducted a double-blind, placebo-controlled multicenter trial involving 800 infants (6 weeks to 12 months of age) with bronchiolitis at 8 Canadian pediatric EDs.<sup>86</sup> Patients were randomly assigned to 1 of 4 study groups: (1) the epinephrine-dexamethasone group received 2 treatments of nebulized epinephrine and a total of 6 oral doses of dexamethasone (1.0 mg/kg in the ED and 0.6 mg/kg for an additional 5 days), (2) the epinephrine group received nebulized epinephrine and oral placebo, (3) the dexamethasone group received nebulized placebo and oral dexamethasone, and (4) the placebo group received nebulized placebo and oral placebo. The primary outcome was hospital admission within 7 days after the ED visit.

Of interest, the epinephrine-dexamethasone group had a lower admission rate over 7 days than the placebo group (17.1% vs 26.4%, respectively). The study authors did not anticipate this potential interaction in the design, and after adjustment for multiple comparisons, the difference did not reach statistical significance. These results must undergo further investigation before they can be implemented in routine practice. If they are confirmed, the moderate effect (ie, 11 infants need to be treated for 1 not to be admitted) could represent a potentially important relative reduction in the number of hospitalizations for this common disorder.<sup>86</sup> The synergy between adrenergic agents and corticosteroids has been well described in the asthma literature and has been observed in other small studies of bronchiolitis.<sup>87,88</sup>

### **Hypertonic Saline**

Some studies have shown that hypertonic saline improves mucociliary clearance in pediatric patients with cystic fibrosis.<sup>89</sup> Airway edema and mucus plugging are the predominant pathologic features in infants with acute viral bronchiolitis, and several studies have assessed the ability of nebulized hypertonic saline solution to reduce these pathologic effects and decrease airway obstruction. A 2008 Cochrane review of the use of hypertonic saline in bronchiolitis included 4 randomized trials involving 254 infants (2-24 months of age; 189 inpatients and 65 outpatients) with acute viral bronchiolitis.<sup>90</sup> Patients treated with nebulized 3% saline had a significantly shorter mean length of hospital stay than those treated with nebulized 0.9% saline (mean difference, 0.94 day). The 3% saline group also had a significantly lower post-inhalation clinical score than the 0.9% saline group in the first 3 days of treatment. The improvement in clinical scores was greater among inpatients than outpatients. No adverse events related to 3% saline inhala-

tion were reported. The authors concluded that use of nebulized 3% saline may significantly reduce the length of hospital stay and improve the clinical severity score in infants with acute viral bronchiolitis. This review had several limitations. First, there was clinical heterogeneity among the trials; various bronchodilators were used with the normal and hypertonic saline solutions, and the frequency of inhalation delivery ranged from once every 8 hours to use of nebulizers every 2 hours for 3 treatments. Second, the generalizability of the results to the ED setting is limited because only a single small study addressed the ED-relevant outcome of admission rate, which did not improve with use of nebulized hypertonic saline.<sup>91,92</sup>

Recently, a randomized, double-blind, placebo-controlled trial was conducted at a single pediatric ED to determine whether nebulized 3% hypertonic saline with epinephrine is more effective than nebulized 0.9% saline with epinephrine in the treatment of infants younger than 12 months with mild-to-moderate bronchiolitis. The primary outcome measure was the change from baseline to 120 minutes in respiratory distress, as measured by the Respiratory Assessment Change Score (RACS). The change in oxygen saturation levels was also determined. Secondary outcome measures included the rates of hospital admission and return to the ED. A total of 46 patients were enrolled and their conditions evaluated. No improvements were noted in oxygen saturation levels and RACs assessed at baseline and 120 minutes in the hypertonic saline group compared with the normal saline control group. In addition, rates of admission and return visits to the ED were similar between groups. The authors concluded that in the emergency setting, treatment of acute bronchiolitis with hypertonic saline and epinephrine did not improve clinical outcomes any more than treatment with normal saline and epinephrine. This finding differs from previously published results of outpatient and inpatient populations and merits further evaluation.<sup>93</sup>

## **Controversies And Cutting Edge Treatment**

New therapies are being investigated, particularly regarding treatment of critically ill patients with bronchiolitis. These treatments include nasal continuous positive airway pressure (nCPAP), heliox, or a combination of heliox and nCPAP.

### **Nasal Continuous Positive Airway Pressure**

By decreasing inspiratory muscle workload, preventing or relieving atelectasis, and preventing airway collapse, nCPAP could help in the treatment of bronchiolitis. Thia et al recruited children younger than 1 year with bronchiolitis and a capillary PCO<sub>2</sub> level greater than 6 kPa and randomly assigned them to either nCPAP or standard treatment groups and then crossed them over to the alternative treatment after 12 hours.<sup>94</sup> Standard treatment included

# Clinical Pathway For Assessment And Management Of Acute Bronchiolitis

Obtain a brief history, physical examination, vital signs, pulse oximetry reading, and respiratory status. Assess the risk for severe bronchiolitis and apnea. Assess the patient frequently because of the variable disease course. Consider nasal suction prior to repeated examinations.

## History:

- Age: < 12 weeks\*; full-term birth and < 1 month of age\*\*
- Prematurity: < 34-35 weeks' gestation\*; Preterm birth (< 37 weeks' gestation) and < 2 months post conception\*\*
- History of apnea of prematurity\*\*
- Underlying respiratory illnesses (eg, chronic lung disease), congenital heart disease, or immune deficiencies\*
- Emergency department presentation with apnea\*\*
- Apnea witnessed by a caregiver\*\*

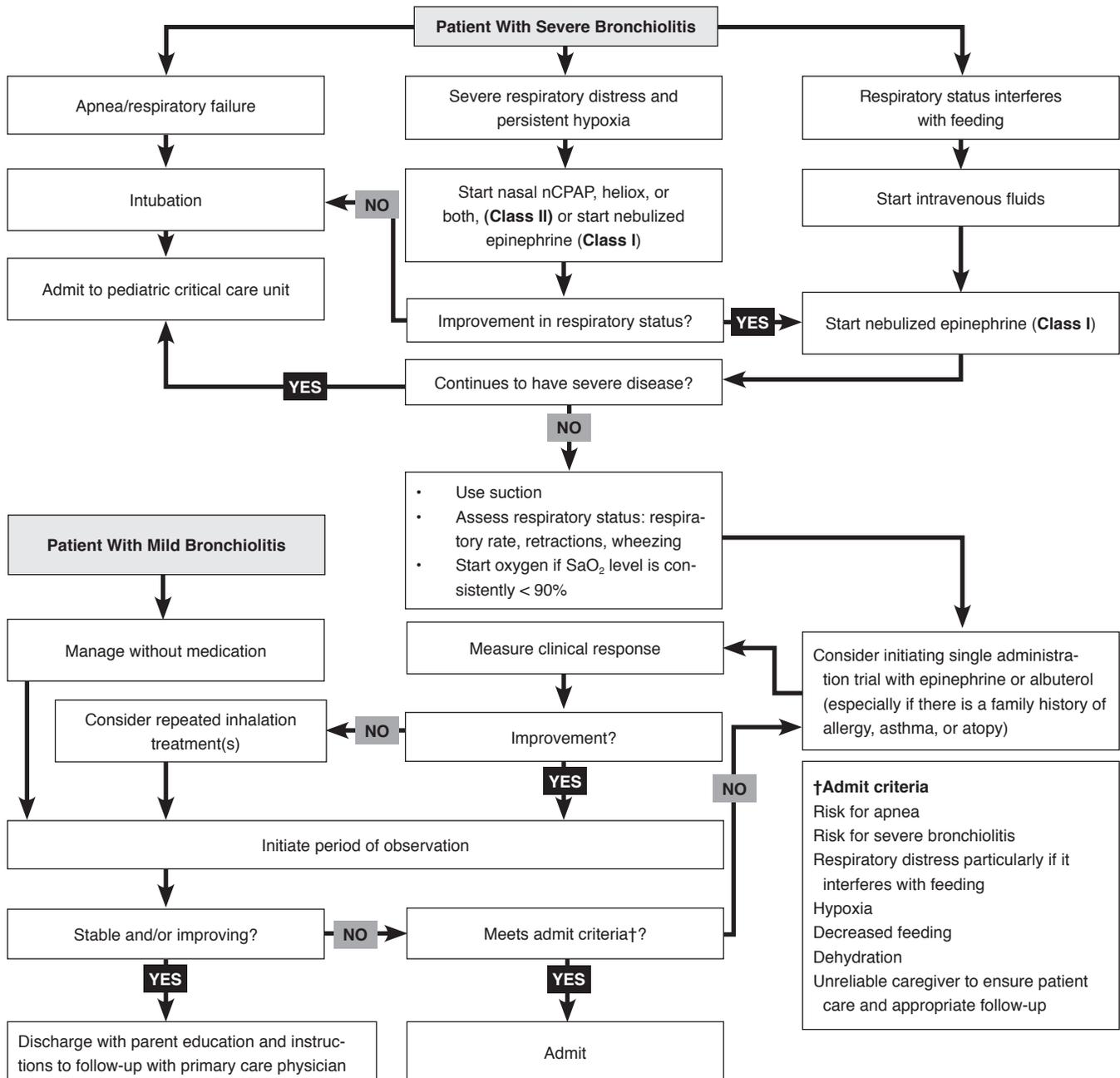
\*risk factor for severe bronchiolitis

\*\*apnea risk

## Physical examination:

- General appearance: ill looking\*
- Oxygen saturation level: < 90% on room air in previously healthy infants, < 94% in patients with comorbidities\*
- Respiratory rate: >70 breaths per minute or higher than normal rate for patient age\*
- Increased work of breathing: moderate to severe retractions and/or accessory muscle use\*
- Dehydration\*

Class definitions are available on page 20.



intravenous fluids and supplemental oxygen by nasal prongs or face mask. The changes in  $\text{PCO}_2$  levels were compared between the groups after 12 and 24 hours. After 12 hours, the  $\text{PCO}_2$  level decreased by 0.92 kPa in children treated with nCPAP compared with an increase of 0.04 kPa in those receiving standard treatment. Patients who used nCPAP in the first half of the study experienced a significantly better reduction in  $\text{PCO}_2$  level than those who used it during the second half. Of interest, there were no differences in capillary pH, respiratory rate, pulse rate, and the need for invasive ventilatory support. Overall, nCPAP was well-tolerated, with no complications identified. Study results suggest that nCPAP improves ventilation in children with bronchiolitis and hypercapnia when compared with standard treatment.<sup>94</sup>

### Heliox Use In Acute Bronchiolitis

Heliox is a mixture of helium (naturally inert gas with a low molecular weight) with 21% oxygen, producing a mixed gas one-third as dense as air. Its benefits in the treatment of obstructive airway diseases include reducing gaseous flow resistance and subsequently reducing respiratory effort and improving gaseous exchange and alveolar ventilation. In addition, heliox increases the elimination of carbon dioxide through its high diffusion coefficient.<sup>96</sup>

Cambonie et al conducted a prospective, randomized, double-blind study to determine the effects of heliox on respiratory distress symptoms in young infants (< 3 months of age) admitted to the pediatric intensive care unit (PICU) with moderate to severe acute RSV bronchiolitis. All infants were randomly and blindly assigned to inhale either heliox or an air-oxygen mixture for 1 hour under an oxyhood. The mean respiratory distress score was significantly lower in the heliox group than in the air-oxygen group (3.05 vs 5.5, respectively), with a significant reduction in accessory muscle use and expiratory wheezing in the heliox group. In contrast, inspiratory breath sounds and incidence of cyanosis did not significantly differ between groups. The respiratory distress score at baseline was higher in previously premature infants in the heliox group than in term infants in this group (5.8 vs 5.2, respectively;  $P < .05$ ), with comparable decreases in the scores at 1 hour. The authors concluded that heliox breathing induced a rapid reduction in accessory muscle use and expiratory wheezing even in premature patients.<sup>96</sup>

### Heliox And Nasal Continuous Positive Airway Pressure

The potential synergy between nCPAP and heliox is due to nCPAP's promotion of heliox distribution within the obstructed airways by decreasing atelectasis and preventing airway collapse. In addition, the use of nCPAP may reduce the required fraction

of inspired oxygen ( $\text{FIO}_2$ ) and further augment the actual helium concentration delivered to the patient. On the other hand, heliox actions reduce the risk of barotrauma from gas trapping, limiting the potential detrimental effects of nCPAP.

Recently, Martín-Torres et al conducted a prospective, interventional, crossover study involving infants 1 month to 2 years of age admitted to the PICU for treatment of severe, acute bronchiolitis unresponsive to therapy.<sup>97</sup> Patients with a clinical score (ie, Modified Wood's Clinical Asthma Score) greater than 5, an arterial oxygen saturation ( $\text{SaO}_2$ ) level less than 92% or transcutaneous  $\text{CO}_2$  pressure greater than 50 mm Hg despite supportive therapy, and using nebulized L-epinephrine and heliox therapy through a non-rebreathing reservoir face mask were included. Patients were randomly assigned to either 30 minutes of treatment with heliox with nCPAP or to air-oxygen with nCPAP, and measurements were taken at baseline and after 30 minutes of treatment. Mean baseline values for both groups combined were as follows: nCPAP of 7.2 cm  $\text{H}_2\text{O}$ , clinical score of 7.7, transcutaneous  $\text{CO}_2$  pressure of 61.6 mm Hg, and  $\text{SaO}_2$  level of 88.6% with the  $\text{FIO}_2$  at 35.4%. Despite the fact that the clinical scores, transcutaneous  $\text{CO}_2$  pressure, and  $\text{SaO}_2$  levels improved during the study with use of both heliox with nCPAP and air-oxygen with nCPAP, more significant results were achieved with the use of heliox and nCPAP than with air-oxygen and nCPAP. In fact, improvement in clinical score was doubled in the heliox/nCPAP group than with air-oxygen and nCPAP. On the other hand, there was no difference in  $\text{SaO}_2$  between the groups after 30 minutes of treatment. No patients required endotracheal intubation.<sup>97</sup>

The beneficial effects of heliox and nCPAP demonstrated in these studies in infants with severe bronchiolitis are encouraging, especially given that improvements in the patients' clinical condition and blood gas status were obtained in a safe and noninvasive manner. The treatment may provide time for other therapeutic agents to work or for the disease to resolve naturally and might help to avoid more aggressive interventions such as endotracheal intubation and mechanical ventilation. In addition, the response to heliox is seen rapidly (ie, within the first hour) and is maintained during treatment, consistent with its mechanism of action. Therefore, nonrespondents can be readily detected, and other treatments can be promptly initiated. Multicenter research is needed to validate the results of these studies, because of their limited number and small size. Other issues that need to be addressed are the optimal timing of intervention, the ideal initial and maintenance parameters, and the duration of treatment.

Other therapies currently being explored as treatments for bronchiolitis include use of the leukotriene receptor antagonist montelukast. Benefits in time-to-resolution of symptoms with this therapy are not apparent.<sup>98-100</sup>

## Bronchiolitis And Vitamin D Deficiency

Recent reports have related the increased incidence of severe bronchiolitis to the increased incidence of vitamin D deficiency.<sup>101</sup> Low levels of vitamin D are quite common among US newborns<sup>102,103</sup> and have been associated with an increased incidence of pneumonia and LRTI requiring hospitalization.<sup>104-106</sup>

The pathophysiology of these observations may relate to the role of vitamin D in the activity of the innate immune system.<sup>107</sup> Camargo et al recently found that lower maternal intake of vitamin D during pregnancy had a statistically significant, independent association with increased risk of recurrent childhood wheeze.<sup>108</sup> This finding was replicated in 5-year-old Scottish children.<sup>109</sup> In addition, Camargo et al confirmed this finding in a separate birth cohort from New Zealand in whom low vitamin D levels in cord blood were associated with increased risks of respiratory infections at 3 months and wheezing in early childhood.<sup>110</sup> Further research is needed to investigate the relationship between bronchiolitis and vitamin D deficiency and has the potential to help prevent this common illness.

## Bronchiolitis And Asthma

The relationship between bronchiolitis and the development of asthma has been studied for years. It has been estimated that 50% of children with bronchiolitis have recurrent wheezing (as assessed by the parents) or asthma (as diagnosed by a physician during the following 2 decades of life).<sup>9</sup> This is particularly true in rhinovirus bronchiolitis. In a study by Kotaniemi-Syrjänen et al comparing the development of asthma after infections with RSV and rhinovirus, asthma was present in 10% of patients in the RSV group compared with 60% of patients in the rhinovirus group.<sup>111</sup>

The results from a small trial of prednisolone use for 3 days versus placebo in children hospitalized with their first or second episode of wheezing due to rhinovirus bronchiolitis are of particular interest. In this trial, Jartti and colleagues found that children who had rhinovirus bronchiolitis and received prednisolone had reduced relapses during a 2-month period after hospitalization and reduced recurrent wheezing at 1 year.<sup>112</sup>

## Risk Management Pitfalls In The Treatment of Pediatric Bronchiolitis

(continued on page 13)

1. **"The 'happy wheezer' did not respond to the first albuterol nebulizer treatment. Let's continue the albuterol treatment until the patient is completely clear."**

The AAP's Subcommittee on the Diagnosis and Management of Bronchiolitis recommends "a carefully monitored trial of adrenergic medication as an option and that inhaled bronchodilators should be continued only if there is a documented positive clinical response to the trial using an objective means of evaluation."<sup>4</sup> This recommendation reflects the fact that use of bronchodilator agents remains controversial, and results regarding their benefits for viral bronchiolitis are inconsistent. In addition, continuous albuterol treatment will expose the patient to side effects and unnecessary prolonged stays in the ED without benefits.

2. **"Let's send this wheezer home on steroids."**  
In contrast to dexamethasone's demonstrated effectiveness in treating asthma and croup, to date no conclusive evidence has shown that use of systemic dexamethasone improves outcomes in first-time wheezers with bronchiolitis. In addition, because of safety concerns with use of high-dose inhaled corticosteroids in infants, they should be avoided unless there is a clear likelihood of benefit.

3. **"We need to get a radiograph because this wheezer has a fever."**

In the ED, radiographs should not be routinely obtained for diagnosis of bronchiolitis because no literature supports the practice. Radiographs may be useful in cases of severe disease that require further evaluation or if another diagnosis such as foreign body aspiration, pneumonia, or CHF is suspected on the basis of history and physical examination findings.

4. **"We need to admit all first-time wheezers with bronchiolitis if they do not clear in the ED."**

One of the main reasons to admit patients with bronchiolitis is the concern regarding the development of apnea. Risk factors for apnea include young age (< 6-12 weeks old), prematurity, a history of apnea of prematurity, presentation with apnea, or apnea witnessed by a parent or healthcare provider. In addition, patients with bronchiolitis may be admitted because of respiratory distress, hypoxia, or dehydration related to the inability to take fluids secondary to increased work of breathing. Wheezing alone is not a criterion for admission unless it is associated with other risk factors for severe disease or apnea. Social factors such as parental comfort and reliability in ensuring appropriate care and follow-up should be taken into consideration when disposition decisions are made in the ED.

Further research should focus on clarifying the potential benefits of identifying and treating rhinovirus bronchiolitis in order to prevent the development of asthma.<sup>113</sup>

## Disposition

Most children with bronchiolitis have mild disease and are discharged home.<sup>114</sup> Some patients with bronchiolitis will have a severe course manifested by dehydration, respiratory distress, respiratory failure, apnea, or death. The most challenging task for emergency clinicians is to determine the appropriate disposition for a young infant, as the disease course is extremely variable.

Infants with bronchiolitis are frequently hospitalized because of respiratory distress, hypoxia, or dehydration due to their inability to take fluids secondary to the increased work of breathing. In addition, concerns about apnea will affect the emergency clinician's decision to admit the patient. (See Table 5, page 14.)

## Hypoxia

Pulse oximetry has been adopted into the clinical assessment of children with bronchiolitis on the basis of data that it can reliably detect hypoxemia that is not detected on physical examination.<sup>33</sup> Healthy infants have an oxygen saturation as measured by pulse oximetry ( $SpO_2$ ) greater than 95% on room air, although transient decreases to an  $SpO_2$  level less than 89% do occur.<sup>115-116</sup> In bronchiolitis, airway edema and sloughing of respiratory epithelial cells cause mismatching of ventilation and perfusion and subsequent reductions in oxygenation ( $PaO_2$  and  $SpO_2$ ). Of note, when the  $SpO_2$  level is above 90%, large increases in  $PaO_2$  are associated with small increases in  $SpO_2$ . In contrast, when the  $SpO_2$  level is below 90%, a small decrease in  $PaO_2$  is associated with a large decrease in  $SpO_2$ . Therefore, in otherwise healthy infants with bronchiolitis who have a  $SpO_2$  level at or above 90% at sea level while breathing room air, increasing  $PaO_2$  with supplemental oxygen will likely provide little benefit, particularly in the absence of respiratory distress and feeding difficulties. Nevertheless, because

## Risk Management Pitfalls In The Treatment of Pediatric Bronchiolitis

(continued from page 12)

5. **"The 'happy wheezer's' pulse oximetry reading is 90% on room air. We need to immediately provide supplemental oxygen."**

In a wheezer who has no respiratory distress but has low  $SpO_2$ , the first priority is to ensure that pulse oximetry probes are placed appropriately, particularly in the active infant/child. Poorly placed probes and motion artifact will lead to inaccurate measurements and false alarms. Before instituting oxygen therapy, the initial reading should be verified by repositioning the probe and repeating the measurement. The infant's nose should also be suctioned. If the  $SpO_2$  level remains below 90%, oxygen should be administered. The infant's clinical work of breathing should also be assessed and may be a factor in the decision to use oxygen supplementation.

6. **"This neonate is wheezing; she must have bronchiolitis."**

Other life-threatening causes of wheezing should be considered. Clues from the history and physical examination such as sweating and exertion with feeding, heart murmur, and hepatomegaly should be elicited to rule out CHF and "cardiac wheezing." This determination is important before starting a trial of nebulized adrenergic treatment.

7. **"This 2-month-old patient with 30 weeks' gestation has mild wheezing and a respiration rate of 60 breaths per minute. Her pulse oximetry reading is 92% on room air after an nebulized adrenergic treatment. I can send him home with albuterol and frequent bulb suctioning."**

Bronchiolitis presentation is variable, and tachypnea and increased work of breathing can proceed wheezing. This patient has 3 risk factors for severe disease, including young age, prematurity, and hypoxia. In addition, he has a risk factor for apnea (ie, < 48 months post conception, considering his prematurity). Close observation is warranted.

8. **"The mother states that this neonate has had a runny nose and cough for 2 days. The nurse called because the baby turned blue for a brief period. He is now breathing at a rate of 60 breaths per minute, and his pulse oximetry reading is 96% on room air, so I can send him home."**

Young age (< 1 month old) and witnessed apnea by a healthcare provider are major risk factors for developing another apneic episode or persistent apnea. Admission of this neonate to a monitored bed (with apnea monitor) is indicated.

factors such as fever, acidosis, and some hemoglobinopathies shift the oxyhemoglobin dissociation curve so that large decreases in PaO<sub>2</sub> begin to occur at a SpO<sub>2</sub> level of more than 90%, clinicians should consider maintaining a higher SpO<sub>2</sub> in children with these risk factors.<sup>117</sup>

In addition, the patient's work of breathing should be assessed and considered in the decision to use oxygen supplementation. Premature or low-birth-weight infants and infants with bronchopulmonary dysplasia or hemodynamically significant CHD merit special attention because they are at risk of developing a severe illness that requires hospitalization, often in the intensive care unit (ICU).<sup>118</sup> These infants often have abnormal baseline oxygenation coupled with an inability to cope with the pulmonary inflammation seen in bronchiolitis. This combination can result in hypoxia that is more severe and prolonged than that experienced by otherwise healthy infants, and clinicians should take this into account when developing strategies for using and weaning supplemental oxygen.

Infants with SpO<sub>2</sub> levels less than 92% require close observation and hospitalization. The AAP recommends that oxygen therapy be initiated judiciously when SpO<sub>2</sub> levels fall consistently below 90% and that the intensity of monitoring SpO<sub>2</sub> levels be reduced as the infant improves.<sup>4</sup> Decisions regarding hospitalization of infants with SpO<sub>2</sub> levels between

### Table 5. Criteria For Hospitalization

A. Patients with bronchiolitis should be considered for admission if they have:

1. Risk for apnea (See Table 4)
2. Risk for severe bronchiolitis (See Table 4)
3. Respiratory distress, particularly if it interferes with feeding
4. Hypoxia
5. Decreased feeding and/or dehydration
6. An unreliable caregiver (ie, unable to ensure patient care and appropriate follow-up)

B. All patients with severe bronchiolitis should be admitted.

92% and 94% should be supported by a detailed clinical assessment and consideration of the phase of the illness and should take social factors into account. A recent British study revealed that the mean lag time for SpO<sub>2</sub> levels to normalize was 66 hours after all other problems had resolved.<sup>119</sup> Of note, as a result of continuous pulse oximetry monitoring, a substantial proportion of infants remain in the hospital for administration of oxygen after other abnormalities have improved.<sup>120</sup>

Novel approaches such as the use of home oxygen therapy have been studied in some populations, and further research on the use of oxygen in treating bronchiolitis is needed.<sup>121,122</sup>

### Dehydration

Infants with a respiratory rate exceeding 60 breaths per minute are at risk for compromised feeding, particularly if nasal secretions are copious. Infants with respiratory difficulty may develop nasal flaring, increased work of breathing, and prolonged expiratory wheezing and are at increased risk of aspiration of food into the lungs.<sup>123</sup> Children who have difficulty feeding safely because of respiratory distress should be given intravenous fluids.

### Risk Factors For Unscheduled Return ED Visits

Norwood et al recently conducted a prospective cohort study of patients younger than 2 years with bronchiolitis who were discharged from 30 EDs in 15 states from 2004 to 2006. The Multicenter Airway Research Collaboration was used to determine predictors of unscheduled visits within 2 weeks after the ED visit. Of 722 patients eligible for the analysis, 717 (99%) had unscheduled visit data; of these, 121 patients (17%, or 1 in 6 children) had unscheduled visits. Independent predictors of unscheduled visits were age < 2 months, male sex, and history of hospitalization. Two-thirds of the unscheduled visits occurred within 2 days of the ED visit, with 13% of patients returning to the ED and 6% admitted.<sup>124</sup>

## Cost-Effective Strategies

- Avoid routine radiographs and laboratory studies in the diagnosis of acute bronchiolitis to decrease costs, radiation exposure, and blood testing in infants and young children presenting to the ED with the classic form of the disease. Radiographs should be obtained only if the disease severity requires it or if there is suspicion of a different etiology for the wheezing or respiratory distress.
- Avoid routine use of bronchodilators in the management of bronchiolitis, especially when the disease is mild to moderate (ie, in well hydrated/

happy wheezers with no hypoxia or respiratory distress). These medications provide inconsistent benefits, and their use should be weighed against their potential side effects and costs.

- Avoid the continuation of inhaled bronchodilators when objective assessments before and after therapy show no clinical response to the initial treatment. Discontinuation decreases the unnecessary administration of multiple bronchodilator treatments, avoids medication side effects, and decreases the length of stay in the ED.

The admission of well-appearing children with bronchiolitis who are at high risk for unscheduled visits is debatable, as the goals of admission are mainly close observation and supportive therapy. On the other hand, close follow-up with the primary care physician and strict anticipatory guidance instructions could eliminate the need for hospitalization. Research is needed to validate this approach.

## Summary

Acute bronchiolitis is mainly a clinical diagnosis; diagnostic laboratory and radiographic tests play a limited role in typical cases. In cases of severe bronchiolitis manifested by respiratory distress, increased work of breathing that leads to decreased feeding and dehydration, hypoxia, respiratory failure, and apnea, emergency clinicians have the opportunity to assess patients for risk factors. These factors include age less than 6 to 12 weeks, prematurity, and underlying comorbidities such as CLD, cardiac disease, and immunodeficiency. Pulse oximetry drives the use of healthcare resources. Supplemental oxygen is indicated if the patient's SpO<sub>2</sub> level is consistently below 90% or at higher pulse oximetry readings if the patient is in respiratory distress or has an underlying disease that causes abnormal baseline oxygenation.

Numerous large recent trials have demonstrated the lack of efficacy of bronchodilators and corticosteroids in the treatment of acute first-time bronchiolitis. Other recent studies suggest the potential future role of combination therapies. Emergency clinicians can help to decrease the financial burden of this disease by using history and physical examination findings and strict criteria for diagnostic testing to assess and manage bronchiolitis in young children.

## Case Conclusion

*You rapidly identify severe bronchiolitis in your patient and recognize that aggressive management is required. You place the patient on pulse oximetry and start a trial of nebulized epinephrine with oxygen while closely monitoring his clinical response to treatment. Your patient's respiratory rate decreases after the treatment, with decrease in the work of breathing as well. His pulse oximetry level is 90% on room air, so you administer supplemental oxygen via nasal cannula. The patient starts to cry without tears, and you notice his dry mucous membranes. You administer intravenous fluids and give him a second epinephrine nebulizer treatment. His respiratory rate is 55 breaths per minute with no retractions, and he is able to take his bottle for only a brief period even after the nurse suctioned his nasal secretions. His SpO<sub>2</sub> level remains at 90% on room air. You call the hospitalist to admit the patient because his tachypnea is leading to compromised oral intake and because of his consistent hypoxia.*

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Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study, will be included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, will be noted by an asterisk (\*) next to the number of the reference.

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## CME Questions



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1. Which of the following symptoms is not consistent with the clinical definition of bronchiolitis?
  - a. Tachypnea
  - b. Wheezing
  - c. Stridor
  - d. Use of accessory muscles
2. Which of the following disorders should not be considered in the differential diagnosis of bronchiolitis?
  - a. Gastroenteritis
  - b. Pneumonia
  - c. CHF
  - d. Asthma
3. Which of the following historical findings is not a risk factor for severe bronchiolitis?
  - a. Hypoglycemia
  - b. Age: < 12 weeks
  - c. Prematurity (< 34–35 weeks' gestation)
  - d. Significant CHD and an immune deficiency
4. Which of the following findings is not considered a risk factor for apnea with bronchiolitis?
  - a. Full-term birth and < 1 month of age
  - b. Apnea witnessed by a caregiver
  - c. Fever
  - d. Preterm birth (< 48 weeks' gestation) and < 2 months post conception
5. In a well-appearing young infant with high fever and bronchiolitis, which of the following bacterial infections should also be evaluated?
  - a. Pneumonia
  - b. UTI
  - c. Bacteremia
  - d. Meningitis
6. Which of the following physical examination findings is not a risk factor for severe bronchiolitis?
  - a. Oxygen saturation level < 90% on room air
  - b. Umbilical hernia
  - c. Respiratory rate > 70 breaths per minute or a higher than normal rate for the patient's age
  - d. Increased work of breathing (ie, moderate to severe retractions and or accessory muscle use)

## Coming In Future Issues

Abuse  
Lower GI Bleeding  
Endocrine Disorders  
Testicular Torsion

### Class Of Evidence Definitions

Each action in the clinical pathways section of *Pediatric Emergency Medicine Practice* receives a score based on the following definitions.

#### Class I

- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

#### Level of Evidence:

- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

#### Class II

- Safe, acceptable
- Probably useful

#### Level of Evidence:

- Generally higher levels of evidence
- Non-randomized or retrospective studies: historic, cohort, or case control studies
- Less robust RCTs
- Results consistently positive

#### Class III

- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

#### Level of Evidence:

- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

This clinical pathway is intended to supplement, rather than substitute for, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

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#### Indeterminate

- Continuing area of research
- No recommendations until further research

#### Level of Evidence:

- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

Significantly modified from: The Emergency Cardiovascular Care Committees of the American Heart Association and representatives from the resuscitation councils of ILCOR: How to Develop Evidence-Based Guidelines for Emergency Cardiac Care: Quality of Evidence and Classes of Recommendations; also: Anonymous. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency Cardiac Care Committee and Subcommittees, American Heart Association. Part IX. Ensuring effectiveness of community-wide emergency cardiac care. *JAMA*. 1992;268(16):2289-2295.

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