Diagnosis and Treatment of Infants with Bronchiolitis

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Abstract

• Objective: To review the diagnosis and management of bronchiolitis.
• Methods: Qualitative review of the literature.
• Results: Bronchiolitis is a common disease that affects most children under 2 years of age. The most common etiology is respiratory syncytial virus (RSV) infection. The diagnosis is usually clinical, although rapid screening tests are available that can assist with early identification and decrease the use of unnecessary treatment. Observation, hydration, and oxygen remain the mainstays of treatment. Palivizumab has been a major advance in the control of RSV infection and has helped to decrease long-term complications in vulnerable populations.
• Conclusion: Acute management of bronchiolitis varies. Routine use of medications to treat bronchiolitis is not necessary.

Bronchiolitis is a common condition that affects 80% of the pediatric population in the United States younger than 12 months of age. Of affected children, 123,000 (2%–3%) will require hospitalization [1]. The most common etiology for bronchiolitis is respiratory syncytial virus (RSV) infection [2]. The virus has a worldwide distribution and infects almost all children by age 2 years. Children at high risk for developing complications and severe disease include premature infants, babies with history of chronic lung disease, immunodeficiencies, or congenital heart disease, infants with neurologic diseases, and healthy babies younger than 6 weeks [3,4]. Exposure to postnatal maternal smoking has been associated with increased severity [5]. The mortality resulting from RSV in the late 1990s was 2.0 per 100,000 live births in the United States [6], whereas in the United Kingdom it was 1.82 per 100,000 in the year 2000 [7].

Clinical Presentation

Typical findings in children with bronchiolitis include cough, nasal obstruction with or without rhinorrhea, fever, wheezing, and cough [8]. However, there are no standardized criteria for making a diagnosis. In a review of 65 studies by Bordley et al [9], most identified wheezing and tachypnea as the prominent diagnostic features. Mulholland et al [10] found that crackles and cyanosis correlate more with severity of disease than does respiratory rate, indicating that findings suggestive of bronchiolitis may not be as evident as thought. Auscultatory findings are variable and may include fine inspiratory crackles, expiratory wheeze, and prolonged expiration. Caution needs to be taken, as reliability of auscultation may be inconsistent among observers [11].

Patients with RSV bronchiolitis tend to have the worst symptoms on day 3; symptoms may last for 7 to 10 days [12]. Hypoxia maybe present for several weeks. In very young infants, premature, and low–birth weight babies, bronchiolitis may present with apneic episodes.

Diagnosis

In most cases, bronchiolitis is a clinical diagnosis and no further investigation is necessary [13,14]. Most children with bronchiolitis present with mild symptoms and are managed as outpatients with no routine diagnostic testing. However, children who develop significant shortness of breath may require continuous observation in the hospital. There is no consensus on when to admit children, and the decision is usually made in the emergency department (see Management discussion, below).

Chest radiographs are not needed to make the diagnosis and their use has not been shown to improve outcomes. They often yield nonspecific findings, including hyperinflation and areas of atelectasis. Atelectasis may be difficult to distinguish from a bacterial consolidation and may be seen in approximately 25% of patients with bronchiolitis [15]. Despite this, chest radiographs are done in 61% of emergency department visits in the United States for suspected bronchiolitis. A survey done by Christakis et al [16] revealed varied use of chest radiographs for diagnosis of bronchiolitis across 30 large hospitals. The test was associated with a longer length of stay as well as a more frequent use of antibiotics. In South Africa, Swingler et al [17] reviewed outcomes in a randomized study of children aged 2 to 59 months presenting with...
the World Health Organization definition of pneumonia who were randomly assigned to have a chest radiograph done or not. Even though bronchiolitis was the most common diagnosis in both groups, those who had a chest radiograph done were more frequently diagnosed with pneumonia and treated with antibiotics than those who did not have a chest radiograph done.

Rapid viral tests are available in the United States. Direct immunofluorescence and enzyme immunoassays are commonly used in most hospitals, with a sensitivity of 80% to 90%. The use of these tests has helped to decrease the use of antibiotics [16,18]. RSV is found in 70% of patients with bronchiolitis, although other viral pathogens may be found [2]. Coexistence of more than 1 virus causing symptoms has been described. Human metapneumovirus has been reported as a cause of infection as well as coinfection with RSV since its discovery in 2001 [19,20]. Other organisms, such as adenovirus, influenza, and parainfluenza virus, may also be responsible for bronchiolitis epidemics [2]. Rhinovirus is the second most common causative pathogen of bronchiolitis and is associated with more severe disease [21].

Complications
Severe work of breathing leading to respiratory failure and mechanical ventilation may occur in 7% to 21% of children admitted with bronchiolitis, especially in those vulnerable to these complications (i.e., prematurity, cardiac disease, chronic lung disease) [22,23]. Studies have shown that fever may be a protective factor against serious bacterial infection except for urinary tract infections [24–26]. Caution must be taken with febrile infants younger than 2 months as they may be at increased risk of systemic sepsis [24].

Apnea may be present in 8% of infants with bronchiolitis and accounts for 20% of admissions to the intensive care unit [18]. The underlying reason for this presentation is not clear, but it is known that it is not a consequence of central nervous system infection by RSV [27].

Viral infections may also affect the epithelial lining of the upper airway, including the middle ear, leading to acute otitis media, which may be present in 50% of cases of bronchiolitis [28,20].

Patients admitted to the hospital may have a prolonged length of stay, usually due to persistent hypoxemia. Readmission to the hospital may occur. Kemper et al [28] reported a 3.7% readmission rate within a 30-day period. Median time between the 2 admissions was 2 days. Length of stay was usually longer in the second admission. The only risk factor for readmission was the lack of need for oxygen during the first hospitalization; the researchers hypothesized that these children might be at greater risk because they were seen early in the disease process and their disease eventually progressed to more severe illness.

Management
Acute management of bronchiolitis varies worldwide, even within countries [16,29,30]. This may be due in part to a lack of evidence delineating the ideal treatment of this common disorder. However, the published data support some basic recommendations of how to treat the symptoms of this infection. Cheney et al [31] and Muething et al [32] described how the use of a clinical pathway helped with discharge planning, reduced readmission rates, and avoided unnecessary invasive procedures.

When bronchiolitis is suspected, an assessment of the severity of disease should be made. Patients with mild disease will usually present with little or no respiratory distress, no hypoxemia, and no feeding difficulties. In this case, parents should be reassured and patients should be closely monitored [13,14,33]. Moderate disease is characterized by some retractions, hypoxemia corrected with oxygen, shortness of breath during feeding, and occasionally apneic spells [33]. Caution should be taken with these patients, and close observation or admission to the hospital should be considered. Intravenous fluids may be indicated if the patient is not feeding or there is significant tachypnea that may increase the risk of aspiration.

Admission to the hospital due to bronchiolitis has increased significantly over the last 20 years, likely due to the routine use of pulse oximeters [34,35]. Hypoxia is the main factor in deciding if a patient needs to stay. In a vignette-based survey in which the vignettes were identical except for given Sp02 values (94% or 92%) and respiratory rate (50 or 65 breaths/min), emergency department physicians were twice as likely to admit a child with saturations of 92% versus 94%. A respiratory rate greater than 65 breaths/min was not a finding that would prompt an admission [36]. The impact of pulse oximetry and oxygen therapy in infants with bronchiolitis needs further investigation in larger trials looking at outcomes of different levels and durations of oxygen desaturations [37].

In severe cases, individuals with bronchiolitis may present with severe respiratory distress, retractions, nasal flaring, and grunting. Increasing tiredness, persistent desaturation below 90% while receiving more than 40% to 50% of fractional inspired oxygen, and prolonged apnea warrants cardiorespiratory monitoring, ideally in an intensive care unit with the possibility of endotracheal intubation or positive pressure ventilation [33].

The degree of hypoxemia determines the need for oxygen. There are no validated studies that show giving oxygen will improve outcomes, but it is considered standard of care. There is no consensus on ideal oxygen saturation, although 2006 guidelines from the American Academy of Pediatrics [38] recommend an oxygen saturation of 90% or greater. In published studies, oxygen is used to keep saturation in the
Montelukast, a novel therapy, was examined by Bisgaard [52] in a randomized, double-blind, placebo-controlled; parallel-group study of 130 infants aged 3 to 36 months. A daily dose of a 5-mg chewable tablet was administered within 7 days of the onset of illness for 28 days. Children taking montelukast were symptom-free on 22% of the days and nights compared with 4% of the days and nights for infants on placebo. This medication needs to be investigated in a larger cohort to confirm its effects.

Caffeine has been poorly studied as therapy for apnea associated with bronchiolitis. There are 3 publications involving a total of 10 preterm infants presenting with bronchiolitis-related apnea. The use of caffeine reduced the incidence of apnea as well as the need for mechanical intubation [53–55].

Other therapies, including helium [56], immunoglobulin, interferon, vitamin A, and surfactant are still being investigated with no conclusive results [33].

**Prevention**

The most important preventive measure to stop the spread of infection is frequent and adequate handwashing. Studies have not shown that the use of gowns, masks, gloves, and goggles help stop the spread of RSV; however, a lower incidence of transmission was identified [57–59].

In 1994, RSV-IGIV was introduced as an effective monthly infusion to help decrease the symptoms and recurrence of RSV bronchiolitis [60]. This led to the production of palivizumab, which has been the major advance in the control of RSV infection. Palivizumab is a human recombinant monoclonal antibody against a surface glycoprotein of RSV administered by monthly injection during the prevalent months (October–April) [13]. The costs versus benefits of this vaccine has been a subject of controversy [61], with some studies showing the cost of palivizumab prophylaxis high relative to benefits realized [62]. The average cost per child per season is $5000 to $6000. In a cost-effectiveness study, palivizumab was most cost-effective for babies born at 32 weeks or less, who had a long-term oxygen requirement, and who were discharged home between September and November [63]. The estimated cost per admission forestalled was calculated at $12,000. Infants born with congenital heart disease were also found to have a 45% reduction in admission rate. The American Academy of Pediatrics has issued recommendations on appropriate candidates for RSV prophylaxis [64] (Table). Palivizumab is likely changing the populations that are affected by RSV. Prais et al [65] found that children requiring admission to the intensive care unit were term babies who did not have chronic lung disease and were not candidates for RSV prophylaxis according to the current recommendations.

**Outcomes**

Outcomes of children who develop RSV bronchiolitis seem

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range of 90% to 94%. Bajaj et al [39] proposed that patients with hypoxia and uncomplicated bronchiolitis be sent home on oxygen after an 8-hour period on observation in the emergency department. The authors proved that it is safe, and the frequency of readmission was low. Larger trials need to be done to identify safety issues.

Pharmacologic interventions are widely used despite poor evidence of their usefulness. The use of bronchodilators has been controversial. Bronchodilators are prescribed to most infants with bronchiolitis in the United States and Europe [30,40]. A Cochrane review revealed that several studies showed significant bronchodilator responsiveness in children affected with bronchiolitis [41]. The results were questionable, as infants older than 12 months were included and the likelihood of asthma is increased in this group. Lenney and Milner [42] concluded that there is no significant responsiveness to bronchodilators in infants younger than 18 months of age with bronchiolitis by using modified forced oscillation and plethysmography. Tepper et al [43] found a subgroup of infants with bronchodilator response by applying end-tidal rapid thoracoabdominal compression technique. Moll et al [44] looked at the same population but used the raised thoracoabdominal compression method and found that bronchodilator response is not age-dependant. Regardless of these findings, the overall consensus was that bronchodilators do not produce a clinically relevant response, with only a short-term recovery, and they do not improve oxygenation or hospital admission rates [41,45].

Several studies as well as a Cochrane review did not find that ipratropium bromide had any usefulness in patients presenting with bronchiolitis [41,46].

Nebulized epinephrine has been one of the medications of choice for acute bronchiolitis in emergency departments [30]. Its use has been controversial, as it has been shown to cause short-term responses compared with placebo and may mislead to early discharges [47,48].

There is little proof that systemic steroids are helpful in bronchiolitis. Schuh et al [49] demonstrated an acquiescent response to high-dose dexamethasone in patients aged 2 to 24 months with mild to moderate bronchiolitis. However, this study contradicts a systematic review of 13 trials, which did not demonstrate any benefit in clinical outcomes in the use of steroids in bronchiolitis [50].

Ribavirin has been used extensively as antiviral therapy in the treatment of bronchiolitis. Trials of ribavirin for RSV have been unreliable in estimating its effects. A Cochrane review of 12 studies showed that in 3 small trials ribavirin may reduce the duration of mechanical ventilation, length of stay, and the long-term incidence of recurrent wheezing following RSV disease [51]. There are several practical issues limiting the use of ribavirin, including difficult administration, high cost, and occupational hazard exposure [33].

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Bronchiolitis

Table. American Academy of Pediatrics Recommended Candidates for RSV Prophylaxis

<table>
<thead>
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<th>Consider for:</th>
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<tr>
<td>Infants and children younger than 2 years with chronic lung disease who have</td>
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<tr>
<td>required medical therapy (ie, supplemental oxygen, bronchodilator, diuretic or</td>
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<tr>
<td>corticosteroid therapy) within 6 months before the start of RSV season</td>
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<tr>
<td>Infants born at 32 weeks’ gestation or earlier without chronic lung disease</td>
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<tr>
<td>Infants born between 32 and 35 weeks of gestation if 2 or more risk factors</td>
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<tr>
<td>present (ie, child care attendance, school-aged siblings, exposure to</td>
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<tr>
<td>environmental air pollutants, congenital abnormalities of the airways, or</td>
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<tr>
<td>severe neuro-muscular disease)</td>
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<td>Children who are 24 months or younger with hemodynamically significant cyanotic</td>
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<tr>
<td>and acyanotic congenital heart disease will benefit from 5 monthly intramuscular</td>
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<tr>
<td>injections of palivizumab (15 mg/kg)</td>
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Adapted with permission from American Academy of Pediatrics Committee on Infectious Diseases and Committee on Fetus and Newborn. Revised indications for the use of palivizumab and respiratory syncytial virus immune globulin intravenous for the prevention of respiratory syncytial virus infections. Pediatrics 2003;112:1442–6.

This information can vary depending on severity of disease, exposure to allergens, geographic location, and genetic makeup. It is known that premature infants who have worse lung function prior to neonatal unit discharge are more likely to develop symptomatic RSV and other respiratory illnesses later [66].

Children with severe bronchiolitis secondary to RSV are more likely to develop recurrent episodes of lower respiratory tract diseases, wheezing, and abnormal lung function later in childhood [67]. In a 20-year prospective study, Piippo-Savolainen et al [68] observed an increased risk of persistent asthma and abnormal lung function until adulthood after bronchiolitis in infancy.

Conclusion

Bronchiolitis is a common disease that affects most children under 2 years of age. Its diagnosis is still not standardized, but rapid screening tests are available that can assist with early identification and decrease the use of unnecessary treatment. Observation, hydration, and supplemental oxygen remain the mainstays of treatment. The introduction of palivizumab has helped to decrease long-term complications in vulnerable populations.

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References


