American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

CLINICAL PRACTICE GUIDELINE

Diagnosis and Management of Bronchiolitis

Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of All Children

Subcommittee on Diagnosis and Management of Bronchiolitis

Endorsed by the American Academy of Family Physicians, the American College of Chest Physicians, and the American Thoracic Society.

ABSTRACT

Bronchiolitis is a disorder most commonly caused in infants by viral lower respiratory tract infection. It is the most common lower respiratory infection in this age group. It is characterized by acute inflammation, edema, and necrosis of epithelial cells lining small airways, increased mucus production, and bronchospasm.

The American Academy of Pediatrics convened a committee composed of primary care physicians and specialists in the fields of pulmonology, infectious disease, emergency medicine, epidemiology, and medical informatics. The committee partnered with the Agency for Healthcare Research and Quality and the RTI International-University of North Carolina Evidence-Based Practice Center to develop a comprehensive review of the evidence-based literature related to the diagnosis, management, and prevention of bronchiolitis. The resulting evidence report and other sources of data were used to formulate clinical practice guideline recommendations.

This guideline addresses the diagnosis of bronchiolitis as well as various therapeutic interventions including bronchodilators, corticosteroids, antiviral and antibacterial agents, hydration, chest physiotherapy, and oxygen. Recommendations are made for prevention of respiratory syncytial virus infection with palivizumab and the control of nosocomial spread of infection. Decisions were made on the basis of a systematic grading of the quality of evidence and strength of recommendation. The clinical practice guideline underwent comprehensive peer review before it was approved by the American Academy of Pediatrics.

This clinical practice guideline is not intended as a sole source of guidance in the management of children with bronchiolitis. Rather, it is intended to assist clinicians in decision-making. It is not intended to replace clinical judgment or establish a protocol for the care of all children with this condition. These recommendations may not provide the only appropriate approach to the management of children with bronchiolitis.

www.pediatrics.org/cgi/doi/10.1542/peds.2006-2223

doi:10.1542/peds.2006-2223

All clinical practice guidelines from the American Academy of Pediatrics automatically expire 5 years after publication unless reaffirmed, revised, or retired at or before that time.

The recommendations in this guideline do not indicate an exclusive course of treatment or serve as a standard of care. Variations, taking into account individual circumstances, may be appropriate.

Key Word
bronchiolitis

Abbreviations
CAM—complementary and alternative medicine
LRTI—lower respiratory tract infection
AHRQ—Agency for Healthcare Research and Quality
RSV—respiratory syncytial virus
AAP—American Academy of Pediatrics
AAFP—American Academy of Family Physicians
RCT—randomized, controlled trial
CLD—chronic neonatal lung disease
SBI—serious bacterial infection
UTI—urinary tract infection
AOM—acute otitis media
Spo_2—oxyhemoglobin saturation
LRTD—lower respiratory tract disease

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275). Copyright © 2006 by the American Academy of Pediatrics

INTRODUCTION

THIS GUIDELINE EXAMINES the published evidence on diagnosis and acute management of the child with bronchiolitis in both outpatient and hospital settings, including the roles of supportive therapy, oxygen, bronchodilators, antiinflammatory agents, antibacterial agents, and antiviral agents and make recommendations to influence clinician behavior on the basis of the evidence. Methods of prevention

Downloaded from by guest on August 30, 2016

are reviewed, as is the potential role of complementary and alternative medicine (CAM).

The goal of this guideline is to provide an evidence-based approach to the diagnosis, management, and prevention of bronchiolitis in children from 1 month to 2 years of age. The guideline is intended for pediatricians, family physicians, emergency medicine specialists, hospitalists, nurse practitioners, and physician assistants who care for these children. The guideline does not apply to children with immunodeficiencies including HIV, organ or bone marrow transplants, or congenital immunodeficiencies. Children with underlying respiratory illnesses such as chronic neonatal lung disease (CLD; also known as bronchopulmonary dysplasia) and those with significant congenital heart disease are excluded from the sections on management unless otherwise noted but are included in the discussion of prevention. This guideline will not address long-term sequelae of bronchiolitis, such as recurrent wheezing, which is a field with distinct literature of its own.

Bronchiolitis is a disorder most commonly caused in infants by viral lower respiratory tract infection (LRTI). It is the most common lower respiratory infection in this age group. It is characterized by acute inflammation, edema and necrosis of epithelial cells lining small airways, increased mucus production, and bronchospasm. Signs and symptoms are typically rhinitis, tachypnea, wheezing, cough, crackles, use of accessory muscles, and/or nasal flaring.[1] Many viruses cause the same constellation of symptoms and signs. The most common etiology is the respiratory syncytial virus (RSV), with the highest incidence of RSV infection occurring between December and March.[2] Ninety percent of children are infected with RSV in the first 2 years of life,[3] and up to 40% of them will have lower respiratory infection.[4,5] Infection with RSV does not grant permanent or long-term immunity. Reinfections are common and may be experienced throughout life.[6] Other viruses identified as causing bronchiolitis are human metapneumovirus, influenza, adenovirus, and parainfluenza. RSV infection leads to more than 90 000 hospitalizations annually. Mortality resulting from RSV has decreased from 4500 deaths annually in 1985 in the United States[2,6] to an estimated 510 RSV-associated deaths in 1997[6] and 390 in 1999.[7] The cost of hospitalization for bronchiolitis in children less than 1 year old is estimated to be more than $700 million per year.[8]

Several studies have shown a wide variation in how bronchiolitis is diagnosed and treated. Studies in the United States,[9] Canada,[10] and the Netherlands[11] showed variations that correlated more with hospital or individual preferences than with patient severity. In addition, length of hospitalization in some countries averages twice that of others.[12] This variable pattern suggests a lack of consensus among clinicians as to best practices.

In addition to morbidity and mortality during the acute illness, infants hospitalized with bronchiolitis are more likely to have respiratory problems as older children, especially recurrent wheezing, compared with those who did not have severe disease.[13–15] Severe disease is characterized by persistently increased respiratory effort, apnea, or the need for intravenous hydration, supplemental oxygen, or mechanical ventilation. It is unclear whether severe viral illness early in life predisposes children to develop recurrent wheezing or if infants who experience severe bronchiolitis have an underlying predisposition to recurrent wheezing.

METHODS

To develop the clinical practice guideline on the diagnosis and management of bronchiolitis, the American Academy of Pediatrics (AAP) convened the Subcommittee on Diagnosis and Management of Bronchiolitis with the support of the American Academy of Family Physicians (AAFP), the American Thoracic Society, the American College of Chest Physicians, and the European Respiratory Society. The subcommittee was chaired by a primary care pediatrician with expertise in clinical pulmonology and included experts in the fields of general pediatrics, pulmonology, infectious disease, emergency medicine, epidemiology, and medical informatics. All panel members reviewed the AAP Policy on Conflict of Interest and Voluntary Disclosure and were given an opportunity to declare any potential conflicts.

The AAP and AAFP partnered with the AHRQ and the RTI International-University of North Carolina Evidence-Based Practice Center (EPC) to develop an evidence report, which served as a major source of information for these practice guideline recommendations.[1] Specific clinical questions addressed in the AHRQ evidence report were the (1) effectiveness of diagnostic tools for diagnosing bronchiolitis in infants and children, (2) efficacy of pharmaceutical therapies for treatment of bronchiolitis, (3) role of prophylaxis in prevention of bronchiolitis, and (4) cost-effectiveness of prophylaxis for management of bronchiolitis. EPC project staff searched Medline, the Cochrane Collaboration, and the Health Economics Database. Additional articles were identified by review of reference lists of relevant articles and ongoing studies recommended by a technical expert advisory group. To answer the question on diagnosis, both prospective studies and randomized, controlled trials (RCTs) were used. For questions related to treatment and prophylaxis in the AHRQ report, only RCTs were considered. For the cost-effectiveness of prophylaxis, studies that used economic analysis were reviewed. For all studies, key inclusion criteria included outcomes that were both clinically relevant and able to be abstracted. Initially, 744 abstracts were identified for possible inclusion, of which 83 were retained for systematic review. Results of the literature review were presented in evidence tables and published in the final evidence report.[1]

Downloaded from by guest on August 30, 2016

An additional literature search of Medline and the Cochrane Database of Systematic Reviews was performed in July 2004 by using search terms submitted by the members of the Subcommittee on the Diagnosis and Management of Bronchiolitis. The methodologic quality of the research was appraised by an epidemiologist before consideration by the subcommittee.

The evidence-based approach to guideline development requires that the evidence in support of a policy be identified, appraised, and summarized and that an explicit link between evidence and recommendations be defined. Evidence-based recommendations reflect the quality of evidence and the balance of benefit and harm that is anticipated when the recommendation is followed. The AAP policy statement "Classifying Recommendations for Clinical Practice Guidelines"[16] was followed in designating levels of recommendation (Fig 1; Table 1).

A draft version of this clinical practice guideline underwent extensive peer review by committees and sections within the AAP, American Thoracic Society, European Respiratory Society, American College of Chest Physicians, and AAFP, outside organizations, and other individuals identified by the subcommittee as experts in the field. Members of the subcommittee were invited to distribute the draft to other representatives and committees within their specialty organizations. The resulting comments were reviewed by the subcommittee and, when appropriate, incorporated into the guideline.

This clinical practice guideline is not intended as a sole source of guidance in the management of children with bronchiolitis. Rather, it is intended to assist clinicians in decision-making. It is not intended to replace clinical judgment or establish a protocol for the care of all children with this condition. These recommendations may not provide the only appropriate approach to the management of children with bronchiolitis.

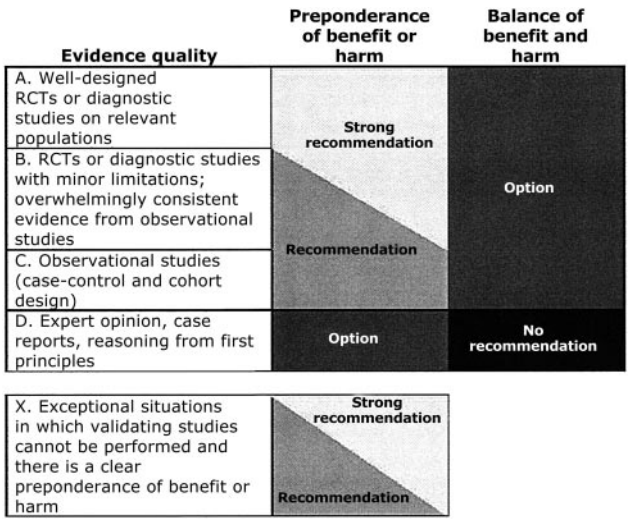

FIGURE 1
Integrating evidence quality appraisal with an assessment of the anticipated balance between benefits and harms if a policy is carried out leads to designation of a policy as a strong recommendation, recommendation, option, or no recommendation.

All AAP guidelines are reviewed every 5 years.

Definitions used in the guideline are:

- Bronchiolitis: a disorder most commonly caused in infants by viral LRTI; it is the most common lower respiratory infection in this age group and is characterized by acute inflammation, edema and necrosis of epithelial cells lining small airways, increased mucus production, and bronchospasm.
- CLD, also known as bronchopulmonary dysplasia: an infant less than 32 weeks' gestation evaluated at 36 weeks' postmenstrual age or one of more than 32 weeks' gestation evaluated at more than 28 days but less than 56 days of age who has been receiving supplemental oxygen for more than 28 days.[17]
- Routine: a set of customary and often-performed procedures such as might be found in a routine admission order set for children with bronchiolitis.
- Severe disease: signs and symptoms associated with poor feeding and respiratory distress characterized by tachypnea, nasal flaring, and hypoxemia.
- Hemodynamically significant congenital heart disease: children with congenital heart disease who are receiving medication to control congestive heart failure, have moderate to severe pulmonary hypertension, or have cyanotic heart disease.

RECOMMENDATION 1a

Clinicians should diagnose bronchiolitis and assess disease severity on the basis of history and physical examination. Clinicians should not routinely order laboratory and radiologic studies for diagnosis (recommendation: evidence level B; diagnostic studies with minor limitations and observational studies with consistent findings; preponderance of benefits over harms and cost).

RECOMMENDATION 1b

Clinicians should assess risk factors for severe disease such as age less than 12 weeks, a history of prematurity, underlying cardiopulmonary disease, or immunodeficiency when making decisions about evaluation and management of children with bronchiolitis (recommendation: evidence level B; observational studies with consistent findings; preponderance of benefits over harms).

The 2 goals in the history and physical examination of infants presenting with cough and/or wheeze, particularly in the winter season, are the differentiation of infants with probable bronchiolitis from those with other disorders and the estimation of the severity of illness. Most clinicians recognize bronchiolitis as a constellation of clinical symptoms and signs including a viral upper respiratory prodrome followed by increased respi-

Downloaded from by guest on August 30, 2016

TABLE 1 **Guideline Definitions for Evidence-Based Statements**

Statement	Definition	Implication
Strong recommendation	A strong recommendation in favor of a particular action is made when the anticipated benefits of the recommended intervention clearly exceed the harms (as a strong recommendation against an action is made when the anticipated harms clearly exceed the benefits) and the quality of the supporting evidence is excellent. In some clearly identified circumstances, strong recommendations may be made when high-quality evidence is impossible to obtain and the anticipated benefits strongly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Recommendation	A recommendation in favor of a particular action is made when the anticipated benefits exceed the harms but the quality of evidence is not as strong. Again, in some clearly identified circumstances, recommendations may be made when high-quality evidence is impossible to obtain but the anticipated benefits outweigh the harms.	Clinicians would be prudent to follow a recommendation but should remain alert to new information and sensitive to patient preferences.
Option	Options define courses that may be taken when either the quality of evidence is suspect or carefully performed studies have shown little clear advantage to one approach over another.	Clinicians should consider the option in their decision-making, and patient preference may have a substantial role.
No recommendation	No recommendation indicates that there is a lack of pertinent published evidence and that the anticipated balance of benefits and harms is presently unclear.	Clinicians should be alert to new published evidence that clarifies the balance of benefit versus harm.

ratory effort and wheezing in children less than 2 years of age. Clinical signs and symptoms of bronchiolitis consist of rhinorrhea, cough, wheezing, tachypnea, and increased respiratory effort manifested as grunting, nasal flaring, and intercostal and/or subcostal retractions.

Respiratory rate in otherwise healthy children changes 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 of age and 30 breaths per minute at 12 months.[18–20] Counting respiratory rate over the course of 1 minute may be more accurate than measurements extrapolated to 1 minute but observed for shorter periods.[21] The absence of tachypnea correlates with the lack of LRTIs or pneumonia (viral or bacterial) in infants.[22,23]

The course of bronchiolitis is variable and dynamic, ranging from transient events such as apnea or mucus plugging to progressive respiratory distress from lower airway obstruction. Important issues to assess include the impact of respiratory symptoms on feeding and hydration and the response, if any, to therapy. The ability of the family to care for the child and return for further care should be assessed. History of underlying conditions such as prematurity, cardiac or pulmonary disease, immunodeficiency, or previous episodes of wheezing should be identified.

The physical examination reflects the variability in the disease state and may require serial observations over time to fully assess the child's status. Upper airway obstruction may contribute to work of breathing. Nasal suctioning and positioning of the child may affect the assessment. Physical examination findings of importance include respiratory rate, increased work of breathing as evidenced by accessory muscle use or retractions, and auscultatory findings such as wheezes or crackles.

The evidence relating the presence of specific findings in the assessment of bronchiolitis to clinical outcomes is limited. Most studies are retrospective and lack valid and unbiased measurement of baseline and outcome variables. Most studies designed to identify the risk of severe adverse outcomes such as requirement for intensive care or mechanical ventilation have focused on inpatients.[24–26] These events are relatively rare among all children with bronchiolitis and limit the power of these studies to detect clinically important risk factors associated with disease progression.

Several studies have associated premature birth (less than 37 weeks) and young age of the child (less than 6–12 weeks) with an increased risk of severe disease.[26–28] Young infants with bronchiolitis may develop apnea, which has been associated with an increased risk for prolonged hospitalization, admission to intensive care, and mechanical ventilation.[26] Other underlying conditions that have been associated with an increased risk of progression to severe disease or mortality include hemodynamically significant congenital heart disease,[26,29] chronic lung disease (bronchopulmonary dysplasia, cystic fibrosis, congenital anomaly),[26] and the presence of an immunocompromised state.[26,30]

Findings on physical examination have been less consistently associated with outcomes of bronchiolitis. Tachypnea, defined as a respiratory rate of 70 or more breaths per minute, has been associated with increased risk for severe disease in some studies[24,27,31] but not oth-

Downloaded from by guest on August 30, 2016

ers.[32] An AHRQ report[1] found 43 of 52 treatment trials that used clinical scores, all of which included measures of respiratory rate, respiratory effort, severity of wheezing, and oxygenation. The lack of uniformity of scoring systems made comparison between studies difficult.[1] The most widely used clinical score, the Respiratory Distress Assessment Instrument,[33] is reliable with respect to scoring but has not been validated for clinical predictive value in bronchiolitis. None of the other clinical scores used in the various studies have been assessed for reliability and validity. Studies that have assessed other physical examination findings have not found clinically useful associations with outcomes.[27,32] The substantial temporal variability in physical findings as well as potential differences in response to therapy may account for this lack of association. Repeated observation over a period of time rather than a single examination may provide a more valid overall assessment.

Pulse oximetry has been rapidly adopted into clinical assessment of children with bronchiolitis on the basis of data suggesting that it can reliably detect hypoxemia that is not suspected on physical examination.[27,34] Few studies have assessed the effectiveness of pulse oximetry to predict clinical outcomes. Among inpatients, perceived need for supplemental oxygen that is based on pulse oximetry has been associated with higher risk of prolonged hospitalization, ICU admission, and mechanical ventilation.[24,26,35] Among outpatients, available evidence differs on whether mild reductions in pulse oximetry (less than 95% on room air) predict progression of disease or need for a return visit for care.[27,32]

Radiography may be useful when the hospitalized child does not improve at the expected rate, if the severity of disease requires further evaluation, or if another diagnosis is suspected. Although many infants with bronchiolitis have abnormalities that show on chest radiographs, data are insufficient to demonstrate that chest radiograph abnormalities correlate well with disease severity.[16] Two studies suggest that the presence of consolidation and atelectasis on a chest radiograph is associated with increased risk for severe disease.[26,27] One study showed no correlation between chest radiograph findings and baseline severity of disease.[36] In prospective studies including 1 randomized trial, children with suspected LRTI who received radiographs were more likely to receive antibiotics without any difference in time to recovery.[37,38] Current evidence does not support routine radiography in children with bronchiolitis.

The clinical utility of diagnostic testing in infants with suspected bronchiolitis is not well supported by evidence.[39–41] The occurrence of serious bacterial infections (SBIs; eg, urinary tract infections [UTIs], sepsis, meningitis) is very low.[42,43] The use of complete blood counts has not been shown to be useful in either diagnosing bronchiolitis or guiding its therapy.[1]

Virologic tests for RSV, if obtained during peak RSV season, demonstrate a high predictive value. However, the knowledge gained from such testing rarely alters management decisions or outcomes for the vast majority of children with clinically diagnosed bronchiolitis.[1] Virologic testing may be useful when cohorting of patients is feasible.

Evidence Profile 1a: Diagnosis

- Aggregate evidence quality: B; diagnostic studies with minor limitations and observational studies with consistent findings
- Benefit: cost saving, limitation of radiation and blood tests
- Harm: risk of misdiagnosis
- Benefits-harms assessment: preponderance of benefit over harm
- Policy level: recommendation

Evidence Profile 1b: Risk Factors

- Aggregate evidence quality: B; observational studies with consistent findings
- Benefit: improved care of patients with risk factors for severe disease
- Harm: increased costs, increased radiation and blood testing
- Benefits-harms assessment: preponderance of benefit over harm
- Policy level: recommendation

RECOMMENDATION 2a

Bronchodilators should not be used routinely in the management of bronchiolitis (recommendation: evidence level B; RCTs with limitations; preponderance of harm of use over benefit).

RECOMMENDATION 2b

A carefully monitored trial of α-adrenergic or β-adrenergic medication is an option. Inhaled bronchodilators should be continued only if there is a documented positive clinical response to the trial using an objective means of evaluation (option: evidence level B; RCTs with limitations and expert opinion; balance of benefit and harm).

The use of bronchodilator agents continues to be controversial. RCTs have failed to demonstrate a consistent benefit from α-adrenergic or β-adrenergic agents. Several studies and reviews have evaluated the use of bronchodilator medications for viral bronchiolitis. A Cochrane systematic review[44] found 8 RCTs involving 394 children.[33,45–50] Some of the studies included infants who had a history of previous wheezing. Several used agents other than albuterol/salbutamol or epinephrine/adrenaline (eg, ipratropium and metaproterenol). Overall, results of the meta-analysis indicated that, at most, 1 in 4

Downloaded from by guest on August 30, 2016

children treated with bronchodilators might have a transient improvement in clinical score of unclear clinical significance. This needs to be weighed against the potential adverse effects and cost of these agents and the fact that most children treated with bronchodilators will not benefit from their use. Studies assessing the impact of bronchodilators on long-term outcomes have found no impact on the overall course of the illness.[1,44,51]

Albuterol/Salbutamol

Some outpatient studies have demonstrated modest improvement in oxygen saturation and/or clinical scores. Schweich et al[52] and Schuh et al[53] evaluated clinical scores and oxygen saturation after 2 treatments of nebulized albuterol. Each study showed improvement in the clinical score and oxygen saturation shortly after completion of the treatment. Neither measured outcomes over time. Klassen et al[47] evaluated clinical score and oxygen saturation 30 and 60 minutes after a single salbutamol treatment. Clinical score, but not oxygen saturation, was significantly improved at 30 minutes, but no difference was demonstrated 60 minutes after a treatment. Gadomski et al[54] showed no difference between those in groups on albuterol or placebo after 2 nebulized treatments given 30 minutes apart.

Studies of inpatients have not shown a clinical change that would justify recommending albuterol for routine care. Dobson et al[55] conducted a randomized clinical trial in infants who were hospitalized with moderately severe viral bronchiolitis and failed to demonstrate clinical improvement resulting in enhanced recovery or an attenuation of the severity of illness. Two meta-analyses[1,56] could not directly compare inpatient studies of albuterol because of widely differing methodology. Overall, the studies reviewed did not show the use of albuterol in infants with bronchiolitis to be beneficial in shortening duration of illness or length of hospital stay.

Epinephrine/Adrenaline

The AHRQ evidence report[1] notes that the reviewed studies show that nebulized epinephrine has "some potential for being efficacious." In contrast, a later multicenter controlled trial by Wainwright et al[51] concluded that epinephrine did not impact the overall course of the illness as measured by hospital length of stay. Analysis of outpatient studies favors nebulized epinephrine over placebo in terms of clinical score, oxygen saturation, and respiratory rate at 60 minutes[57] and heart rate at 90 minutes.[58] However, the differences were small, and it could not be established that they are clinically significant in altering the course of the illness. One study[59] found significant improvement in airway resistance (but no change in oxygen need), suggesting that a trial of this agent may be reasonable for such infants.

Several studies have compared epinephrine to albuterol (salbutamol) or epinephrine to placebo. Racemic epinephrine has demonstrated slightly better clinical effect than albuterol. It is possible that the improvement is related to the α effect of the medication.[60] Hartling et al[61] performed a meta-analysis of studies comparing epinephrine to albuterol and also participated in the Cochrane review of epinephrine.[62] The Cochrane report concluded: "There is insufficient evidence to support the use of epinephrine for the treatment of bronchiolitis among inpatients. There is some evidence to suggest that epinephrine may be favorable to salbutamol (albuterol) and placebo among outpatients."

Although there is no evidence from RCTs to justify routine use of bronchodilators, clinical experience suggests that, in selected infants, there is an improvement in the clinical condition after bronchodilator administration.[47,52,53,57,58] It may be reasonable to administer a nebulized bronchodilator and evaluate clinical response. Individuals and institutions should assess the patient and document pretherapy and posttherapy changes using an objective means of evaluation. Some of the documentation tools that have been used can be found in articles by Alario et al,[45] Bierman and Pierson,[63] Gadomski et al,[54] Lowell et al,[33] Wainwright et al,[51] Schuh et al,[64] and Gorelick et al.[65] In addition, a documentation tool has been developed by Cincinnati Children's Hospital (Cincinnati, OH).[66]

Extrapolation from the studies discussed above suggests that epinephrine may be the preferred bronchodilator for this trial in the emergency department and in hospitalized patients. In the event that there is documented clinical improvement, there is justification for continuing the nebulized bronchodilator treatments. In the absence of a clinical response, the treatment should not be continued.

Because of a lack of studies, short duration of action, and potential adverse effects, epinephrine is usually not used in the home setting. Therefore, it would be more appropriate that a bronchodilator trial in the office or clinic setting use albuterol/salbutamol rather than racemic epinephrine. Parameters to measure its effectiveness include improvements in wheezing, respiratory rate, respiratory effort, and oxygen saturation.

Anticholinergic agents such as ipratropium have not been shown to alter the course of viral bronchiolitis. Although a minority of individual patients may show a positive clinical response to anticholinergic agents, studies have shown that the groups as a whole showed no significant improvement. At this point there is no justification for using anticholinergic agents, either alone or in combination with β-adrenergic agents, for viral bronchiolitis.[67–69]

Evidence Profile 2a: Routine Use of Bronchodilators

- Aggregate evidence quality: B; RCTs with limitations
- Benefit: short-term improvement in clinical symptoms

Downloaded from by guest on August 30, 2016

- Harm: adverse effects, cost of medications, cost to administer
- Benefits-harms assessment: preponderance of harm over benefit
- Policy level: recommendation

Evidence Profile 2b: Trial of Bronchodilators

- Aggregate evidence quality: B; RCTs with limitations
- Benefit: some patients with significant symptomatic improvement
- Harm: adverse effects, cost of medications, cost to administer
- Benefits-harms assessment: preponderance of benefit over harm in select patients
- Policy level: option

RECOMMENDATION 3

Corticosteroid medications should not be used routinely in the management of bronchiolitis (recommendation: evidence level B; based on RCTs with limitations and a preponderance of risk over benefit).

Reports indicate that up to 60% of infants admitted to the hospital for bronchiolitis receive corticosteroid therapy.[9,12,70] Systematic review and meta-analyses of RCTs involving close to 1200 children with viral bronchiolitis have not shown sufficient evidence to support the use of steroids in this illness.[1,71,72]

A Cochrane database review on the use of glucocorticoids for acute bronchiolitis[71] included 13 studies.[37,50,64,73–82] The 1198 patients showed a pooled decrease in length of stay of 0.38 days. However, this decrease was not statistically significant. The review concluded: "No benefits were found in either LOS [length of stay] or clinical score in infants and young children treated with systemic glucocorticoids as compared with placebo. There were no differences in these outcomes between treatment groups; either in the pooled analysis or in any of the sub analyses. Among the three studies evaluating hospital admission rates following the initial hospital visit there was no difference between treatment groups. There were no differences found in respiratory rate, hemoglobin oxygen saturation, or hospital revisit or readmission rates. Subgroup analyses were significantly limited by the low number of studies in each comparison. Specific data on the harm of corticosteroid therapy in this patient population are lacking. Available evidence suggests that corticosteroid therapy is not of benefit in this patient group."[71]

The 2 available studies that evaluated inhaled corticosteroids in bronchiolitis[83,84] showed no benefit in the course of the acute disease. Because the safety of high-dose inhaled corticosteroids in infants is still not clear, their use should be avoided unless there is a clear likelihood of benefit.

There are insufficient data to make a recommendation regarding the use of leukotriene modifiers in bronchiolitis. Until additional randomized clinical trials are completed, no conclusions can be drawn.

Evidence Profile 3: Corticosteroids

- Aggregate evidence quality: B; randomized clinical trials with limitations
- Benefit: possibility that corticosteroid may be of some benefit
- Harm: exposure to unnecessary medication
- Benefits-harms assessment: preponderance of harm over benefit
- Policy level: recommendation

RECOMMENDATION 4

Ribavirin should not be used routinely in children with bronchiolitis (recommendation: evidence level B; RCTs with limitations and observational studies; preponderance of harm over benefit).

The indications for specific antiviral therapy for bronchiolitis are controversial. A recent review of 11 randomized clinical trials of ribavirin therapy for RSV LRTIs, including bronchiolitis, summarized the reported outcomes.[85] Nine of the studies measured the effect of ribavirin in the acute phase of illness.[86–94] Two evaluated the effect on long-term wheezing and/or pulmonary function.[95,96] Three additional studies were identified with similar results. Two of these evaluated effectiveness in the acute phase[97,98] and one on subsequent respiratory status.[99]

Each of the 11 studies that addressed the acute treatment effects of ribavirin included a small sample size ranging from 26 to 53 patients and cumulatively totaling 375 subjects. Study designs and outcomes measured were varied and inconsistent. Seven of the trials demonstrated some improvement in outcome attributed to ribavirin therapy, and 4 did not. Of those showing benefit, 4 documented improved objective outcomes (eg, better oxygenation, shorter length of stay), and 3 reported improvement in subjective findings such as respiratory scores or subjective clinical assessment. The quality of the studies was highly variable.

Of the studies that focused on long-term pulmonary function, one was an RCT assessing the number of subsequent wheezing episodes and LRTIs over a 1-year period.[96] Two others were follow-up studies of previous randomized trials and measured subsequent pulmonary function as well as wheezing episodes.[95,99] The first study[96] found fewer episodes of wheezing and infections in the ribavirin-treated patients, and the latter 2 studies[95,99] found no significant differences between groups.

Downloaded from by guest on August 30, 2016

No randomized studies of other antiviral therapies of bronchiolitis were identified.

Specific antiviral therapy for RSV bronchiolitis remains controversial because of the marginal benefit, if any, for most patients. In addition, cumbersome delivery requirements,[100] potential health risks for caregivers,[101] and high cost[102] serve as disincentives for use in the majority of patients. Nevertheless, ribavirin may be considered for use in highly selected situations involving documented RSV bronchiolitis with severe disease or in those who are at risk for severe disease (eg, immunocompromised and/or hemodynamically significant cardiopulmonary disease).

Evidence Profile 4: Ribavirin

- Aggregate evidence quality: B; RCTs with limitations and observational studies
- Benefit: some improvement in outcome
- Harm: cost, delivery method, potential health risks to caregivers
- Benefits-harms assessment: preponderance of harm over benefit
- Policy level: recommendation

RECOMMENDATION 5

Antibacterial medications should be used only in children with bronchiolitis who have specific indications of the coexistence of a bacterial infection. When present, bacterial infection should be treated in the same manner as in the absence of bronchiolitis (recommendation: evidence level B; RCTs and observational studies; preponderance of benefit over harm).

Children with bronchiolitis frequently receive antibacterial therapy because of fever,[103] young age,[104] or the concern over secondary bacterial infection.[105] Early RCTs[106,107] showed no benefit from antibacterial treatment of bronchiolitis. However, concern remains regarding the possibility of bacterial infections in young infants with bronchiolitis; thus, antibacterial agents continue to be used.

Several retrospective studies[41,108–113] identified low rates of SBI (0%–3.7%) in patients with bronchiolitis and/or infections with RSV. When SBI was present, it was more likely to be a UTI than bacteremia or meningitis. In a study of 2396 infants with RSV bronchiolitis, 69% of the 39 patients with SBI had a UTI.[110]

Three prospective studies of SBI in patients with bronchiolitis and/or RSV infections also demonstrated low rates of SBI (1%–12%).[42,43,114] One large study of febrile infants less than 60 days of age[43] with bronchiolitis and/or RSV infections demonstrated that the overall risk of SBI in infants less than 28 days of age, although significant, was not different between RSV-positive and RSV-negative groups (10.1% and 14.2%, respectively). All SBIs in children between 29 and 60 days of age with RSV-positive bronchiolitis were UTIs. The rate of UTIs in RSV-positive patients between 28 and 60 days old was significantly lower than those who were RSV-negative (5.5% vs 11.7%).

Approximately 25% of hospitalized infants with bronchiolitis will have radiographic evidence of atelectasis or infiltrates, often misinterpreted as possible bacterial infection.[115] Bacterial pneumonia in infants with bronchiolitis without consolidation is unusual.[116]

Although acute otitis media (AOM) in bronchiolitic infants may be caused by RSV alone, there are no clinical features that permit viral AOM to be differentiated from bacterial. Two studies address the frequency of AOM in patients with bronchiolitis. Andrade et al[117] prospectively identified AOM in 62% of 42 patients who presented with bronchiolitis. AOM was present in 50% on entry to the study and developed in an additional 12% within 10 days. Bacterial pathogens were isolated from 94% of middle-ear aspirates, with *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* being the most frequent isolates. A subsequent report[118] followed 150 children hospitalized for bronchiolitis for the development of AOM. Seventy-nine (53%) developed AOM, two thirds within the first 2 days of hospitalization. Tympanocentesis was performed on 64 children with AOM, and 33 middle-ear aspirates yielded pathogens. *H influenzae*, *S pneumoniae*, and *M catarrhalis* were the ones most commonly found. AOM did not influence the clinical course or laboratory findings of bronchiolitis. When found, AOM should be managed according to the AAP/AAFP guidelines for diagnosis and management of AOM.[119]

Evidence Profile 5: Antibacterial Therapy

- Aggregate evidence quality: B; RCTs and observational studies with consistent results
- Benefit: appropriate treatment of bacterial infections, decreased exposure to unnecessary medications and their adverse effects when a bacterial infection is not present, decreased risk of development of resistant bacteria
- Harm: potential to not treat patient with bacterial infection
- Benefits-harms assessment: preponderance of benefit over harm
- Policy level: recommendation

RECOMMENDATION 6a

Clinicians should assess hydration and ability to take fluids orally (strong recommendation: evidence level X; validating studies cannot be performed; clear preponderance of benefit over harm).

Downloaded from by guest on August 30, 2016

RECOMMENDATION 6b

Chest physiotherapy should not be used routinely in the management of bronchiolitis (recommendation: evidence level B; RCTs with limitations; preponderance of harm over benefit).

The level of respiratory distress caused by bronchiolitis guides the indications for use of other treatments.

Intravenous Fluids

Infants with mild respiratory distress may require only observation, particularly if feeding remains unaffected. When the respiratory rate exceeds 60 to 70 breaths per minute, feeding may be compromised, particularly if nasal secretions are copious. Infants with respiratory difficulty may develop nasal flaring, increased intercostal or sternal retractions, and prolonged expiratory wheezing and be at increased risk of aspiration of food into the lungs.[120] Children who have difficulty feeding safely because of respiratory distress should be given intravenous fluids. The possibility of fluid retention related to production of antidiuretic hormone has been reported in patients with bronchiolitis.[121,122] Clinicians should adjust fluid management accordingly.

Airway Clearance

Bronchiolitis is associated with airway edema and sloughing of the respiratory epithelium into airways, which results in generalized hyperinflation of the lungs. Lobar atelectasis is not characteristic of this disease, although it can be seen on occasion. A Cochrane review[123] found 3 RCTs that evaluated chest physiotherapy in hospitalized patients with bronchiolitis.[124–126] No clinical benefit was found using vibration and percussion techniques. Suctioning of the nares may provide temporary relief of nasal congestion. There is no evidence to support routine "deep" suctioning of the lower pharynx or larynx.

Evidence Profile 6a: Fluids

- Aggregate evidence quality: evidence level X; validating studies cannot be performed
- Benefit: prevention of dehydration
- Harm: overhydration, especially if syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is present
- Benefits-harms assessment: clear preponderance of benefit over harm
- Policy level: strong recommendation

Evidence Profile 6b: Chest Physiotherapy

- Aggregate evidence quality: B; RCTs with limitations
- Benefit: clearance of secretions, prevention of atelectasis
- Harm: stress to infant during procedure, cost of administering chest physiotherapy
- Benefits-harms assessment: preponderance of harm over benefit
- Policy level: recommendation

RECOMMENDATION 7a

Supplemental oxygen is indicated if oxyhemoglobin saturation (Spo_2) falls persistently below 90% in previously healthy infants. If the Spo_2 does persistently fall below 90%, adequate supplemental oxygen should be used to maintain Spo_2 at or above 90%. Oxygen may be discontinued if Spo_2 is at or above 90% and the infant is feeding well and has minimal respiratory distress (option: evidence level D; expert opinion and reasoning from first principles; some benefit over harm).

RECOMMENDATION 7b

As the child's clinical course improves, continuous measurement of Spo_2 is not routinely needed (option: evidence level D; expert opinion; balance of benefit and harm).

RECOMMENDATION 7c

Infants with a known history of hemodynamically significant heart or lung disease and premature infants require close monitoring as the oxygen is being weaned (strong recommendation: evidence level B; observational studies with consistent findings; preponderance of benefit over harm).

Healthy infants have an Spo_2 greater than 95% on room air, although transient decreases to an Spo_2 of less than 89% occur.[127,128] 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).

In the clinical setting, pulse oximeters are convenient, safe tools to measure oxygenation status. Clinicians ordering pulse oximetry should understand that the shape of the oxyhemoglobin dissociation curve dictates that when Spo_2 is above 90%, large increases in Pao_2 are associated with small increases in Spo_2. In contrast, when Spo_2 is below 90%, a small decrease in Pao_2 is associated with large decreases in Spo_2 (Fig 2). This raises the question of whether there is a single value for Spo_2 that can serve as a decision point to hospitalize or initiate supplemental oxygen in infants with bronchiolitis.

In studies that examined treatment for bronchiolitis in hospitalized infants, some investigators started supplemental oxygen when Spo_2 fell below 90%, and others started oxygen before the Spo_2 reached 90%.[98,129]

Although data are lacking to codify a single value of Spo_2 to be used as a cutoff point for initiating or discontinuing supplemental oxygen, these studies and the relationship between Pao_2 and Spo_2 support the position that otherwise healthy infants with bronchiolitis who have Spo_2 at or above 90% at sea level while breathing

Downloaded from by guest on August 30, 2016

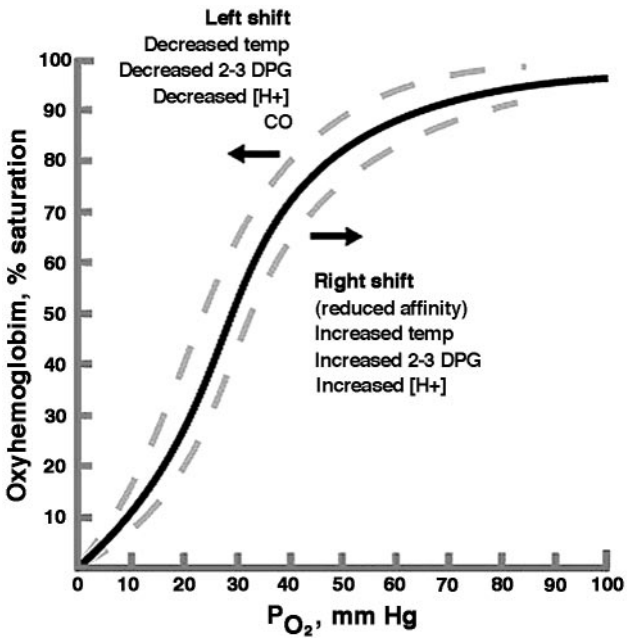

FIGURE 2
Oxyhemoglobin dissociation curve showing percent saturation of hemoglobin at various partial pressures of oxygen. Note that the position of the curve and the affinity of hemoglobin for oxygen changes with changing physiologic conditions. (Reproduced with permission from the educational website www.anaesthesiauk.com.)

room air likely gain little benefit from increasing Pa_{O_2} with supplemental oxygen, particularly in the absence of respiratory distress and feeding difficulties. Because several factors including fever, acidosis, and some hemoglobinopathies shift the oxyhemoglobin dissociation curve so that large decreases in Pa_{O_2} begin to occur at an Sp_{O_2} of more than 90%, clinicians should consider maintaining a higher Sp_{O_2} in children with these risk factors.[130,131]

Although widely used pulse oximeters have some shortcomings, under normal circumstances the accuracy of Sp_{O_2} may vary slightly (most oximeters are accurate to $\pm 2\%$). More importantly, poorly placed probes and motion artifact will lead to inaccurate measurements and false readings and alarms.[132] Before instituting O_2 therapy, the accuracy of the initial reading should be verified by repositioning the probe and repeating the measurement. The infant's nose and, if necessary, oral airway should be suctioned. If Sp_{O_2} remains below 90%, O_2 should be administered. The infant's clinical work of breathing should also be assessed and may be considered as a factor in a decision to use oxygen supplementation.

Premature or low birth weight infants and infants with bronchopulmonary dysplasia or hemodynamically significant congenital heart disease merit special attention because they are at risk to develop severe illness that requires hospitalization, often in the ICU.[7,29,133–135] These infants often have abnormal baseline oxygenation coupled with an inability to cope with the pulmonary inflammation seen in bronchiolitis. This can result in more severe and prolonged hypoxia compared with normal infants, and clinicians should take this into account when developing strategies for using and weaning supplemental oxygen.

Evidence Profile 7a: Supplemental Oxygen

- Aggregate evidence quality: D; expert opinion and reasoning from first principles
- Benefit: use of supplemental oxygen only when beneficial, shorter hospitalization
- Harm: inadequate oxygenation
- Benefits-harms assessment: some benefit over harm
- Policy level: option

Evidence Profile 7b: Measurement of Sp_{O_2}

- Aggregate evidence quality: D; expert opinion
- Benefit: shorter hospitalization
- Harm: inadequate oxygenation between measurements
- Benefits-harms assessment: some benefit over harm
- Policy level: option

Evidence Profile 7c: High-Risk Infants

- Aggregate evidence quality: B; observational studies with consistent findings
- Benefit: improved care of high-risk infants
- Harm: longer hospitalization, use of oxygen when not beneficial
- Benefits-harms assessment: preponderance of benefit over harm
- Policy level: Strong recommendation

RECOMMENDATION 8a

Clinicians may administer palivizumab prophylaxis to selected infants and children with CLD or a history of prematurity (less than 35 weeks' gestation) or with congenital heart disease (recommendation: evidence level A; RCT; preponderance of benefit over harm).

RECOMMENDATION 8b

When given, prophylaxis with palivizumab should be given in 5 monthly doses, usually beginning in November or December, at a dose of 15 mg/kg per dose administered intramuscularly (recommendation: evidence level C; observational studies and expert opinion; preponderance of benefit over cost).

The 2006 Report of the Committee on Infectious Disease (*Red Book*) included the following recommendations for the use of palivizumab[136]:

- Palivizumab prophylaxis should be considered for infants and children younger than 24 months of age with chronic lung disease of prematurity who have

Downloaded from by guest on August 30, 2016

required medical therapy (supplemental oxygen, bronchodilator or diuretic or corticosteroid therapy) for CLD within 6 months before the start of the RSV season. Patients with more severe CLD who continue to require medical therapy may benefit from prophylaxis during a second RSV season. Data are limited regarding the effectiveness of palivizumab during the second year of life. Individual patients may benefit from decisions made in consultation with neonatologists, pediatric intensivists, pulmonologists, or infectious disease specialists.

- Infants born at 32 weeks of gestation or earlier may benefit from RSV prophylaxis, even if they do not have CLD. For these infants, major risk factors to consider include their gestational age and chronologic age at the start of the RSV season. Infants born at 28 weeks of gestation or earlier may benefit from prophylaxis during their first RSV season, whenever that occurs during the first 12 months of life. Infants born at 29 to 32 weeks of gestation may benefit most from prophylaxis up to 6 months of age. For the purpose of this recommendation, 32 weeks' gestation refers to an infant born on or before the 32nd week of gestation (ie, 32 weeks, 0 days). Once a child qualifies for initiation of prophylaxis at the start of the RSV season, administration should continue throughout the season and not stop at the point an infant reaches either 6 months or 12 months of age.
- Although palivizumab has been shown to decrease the likelihood of hospitalization in infants born between 32 and 35 weeks of gestation (ie, between 32 weeks, 1 day and 35 weeks, 0 days), the cost of administering prophylaxis to this large group of infants must be considered carefully. Therefore, most experts recommend that prophylaxis should be reserved for infants in this group who are at greatest risk of severe infection and who are younger than 6 months of age at the start of the RSV season. Epidemiologic data suggest that RSV infection is more likely to lead to hospitalization for these infants when the following risk factor are present: child care attendance, school-aged siblings, exposure to environmental air pollutants, congenital abnormalities of the airways, or severe neuromuscular disease. However, no single risk factor causes a very large increase in the rate of hospitalization, and the risk is additive as the number of risk factors for an individual infant increases. Therefore, prophylaxis should be considered for infants between 32 and 35 weeks of gestation only if 2 or more of these risk factors are present. Passive household exposure to tobacco smoke has not been associated with an increased risk of RSV hospitalization on a consistent basis. Furthermore, exposure to tobacco smoke is a risk factor that can be controlled by the family of an infant at increased risk of severe RSV disease, and preventive measures will be far less costly than palivizumab prophylaxis. High-risk infants never should be exposed to tobacco smoke. In contrast to the well-documented beneficial effect of breastfeeding against many viral illnesses, existing data are conflicting regarding the specific protective effect of breastfeeding against RSV infection. High-risk infants should be kept away from crowds and from situations in which exposure to infected individuals cannot be controlled. Participation in group child care should be restricted during the RSV season for high-risk infants whenever feasible. Parents should be instructed on the importance of careful hand hygiene. In addition, all high-risk infants and their contacts should be immunized against influenza beginning at 6 months of age.
- In the Northern hemisphere and particularly within the United States, RSV circulates predominantly between November and March. The inevitability of the RSV season is predictable, but the severity of the season, the time of onset, the peak of activity, and the end of the season cannot be predicted precisely. There can be substantial variation in timing of community outbreaks of RSV disease from year to year in the same community and between communities in the same year, even in the same region. These variations, however, occur within the overall pattern of RSV outbreaks, usually beginning in November or December, peaking in January or February, and ending by the end of March or sometime in April. Communities in the southern United States tend to experience the earliest onset of RSV activity, and Midwestern states tend to experience the latest. The duration of the season for western and northeast regions typically occurs between that noted in the South and the Midwest. In recent years, the national median duration of the RSV season has been 15 weeks and even in the South, with a seasonal duration of 16 weeks, the range is 13 to 20 weeks. Results from clinical trials indicate that palivizumab trough serum concentrations >30 days after the fifth dose will be well above the protective concentration for most infants. If the first dose is administered in November, 5 monthly doses of palivizumab will provide substantially more than 20 weeks of protective serum antibody concentrations for most of the RSV season, even with variation in season onset and end. Changes from this recommendation of 5 monthly doses require careful consideration of the benefits and costs.
- Children who are 24 months of age or younger with hemodynamically significant cyanotic and acyanotic congenital heart disease will benefit from palivizumab prophylaxis. Decisions regarding prophylaxis with palivizumab in children with congenital heart disease should be made on the basis of the degree of physiologic cardiovascular compromise. Children younger

Downloaded from by guest on August 30, 2016

than 24 months of age with congenital heart disease who are most likely to benefit from immunoprophylaxis include:

- Infants who are receiving medication to control congestive heart failure
- Infants with moderate to severe pulmonary hypertension
- Infants with cyanotic heart disease

Results from 2 blinded, randomized, placebo-controlled trials with palivizumab involving 2789 infants and children with prematurity, CLD, or congenital heart disease demonstrated a reduction in RSV hospitalization rates of 39% to 78% in different groups.[137,138] Results from postlicensure observational studies suggest that monthly immunoprophylaxis may reduce hospitalization rates to an even greater extent than that described in the prelicensure clinical trials.[139] Palivizumab is not effective in the treatment of RSV disease and is not approved for this indication.

Several economic analyses of RSV immunoprophylaxis have been published.[140–147] The primary benefit of immunoprophylaxis with palivizumab is a decrease in the rate of RSV-associated hospitalization. None of the 5 clinical RCTs have demonstrated a significant decrease in rate of mortality attributable to RSV infection in infants who receive prophylaxis. Most of the economic analyses fail to demonstrate overall savings in health care dollars because of the high cost if all at-risk children were to receive prophylaxis. Estimates of cost per hospitalization prevented have been inconsistent because of considerable variation in the baseline rate of hospitalization attributable to RSV in different high-risk groups. Other considerations that will influence results include the effect of prophylaxis on outpatient costs and a resolution of the question of whether prevention of RSV infection in infancy decreases wheezing and lower respiratory tract problems later in childhood.

Evidence Profile 8a: Palivizumab Prophylaxis

- Aggregate evidence quality: A; RCTs
- Benefit: prevention of morbidity and mortality in high-risk infants
- Harm: cost
- Benefits-harms assessment: preponderance of benefit over harm
- Policy level: recommendation

Evidence Profile 8b: Five-Dose Regimen

- Aggregate evidence quality: C; observational studies and expert opinion
- Benefit: decreased cost resulting from using minimal number of needed doses
- Harm: risk of illness from RSV outside the usual season
- Benefits-harms assessment: preponderance of benefit over harm
- Policy level: recommendation

RECOMMENDATION 9a

Hand decontamination is the most important step in preventing nosocomial spread of RSV. Hands should be decontaminated before and after direct contact with patients, after contact with inanimate objects in the direct vicinity of the patient, and after removing gloves (strong recommendation: evidence level B; observational studies with consistent results; strong preponderance of benefit over harm).

RECOMMENDATION 9b

Alcohol-based rubs are preferred for hand decontamination. An alternative is hand-washing with antimicrobial soap (recommendation: evidence level B; observational studies with consistent results; preponderance of benefit over harm).

RECOMMENDATION 9c

Clinicians should educate personnel and family members on hand sanitation (recommendation: evidence level C; observational studies; preponderance of benefit over harm).

Efforts should be made to decrease the spread of RSV and other causative agents of bronchiolitis in medical settings, especially in the hospital. RSV RNA has been identified in air samples as much as 22 feet from the patient's bedside.[148] Secretions from infected patients can be found on beds, crib railings, tabletops, and toys. Organisms on fomites may remain viable and contagious for several hours.[149]

It has been shown that RSV as well as many other viruses can be carried and spread to others on the hands of caregivers.[150] Frequent hand-washing by health care workers has been shown to reduce RSV's nosocomial spread.[150] The Centers for Disease Control and Prevention published an extensive review of the hand-hygiene literature and made recommendations as to indications for hand-washing and hand antisepsis.[151] Among the recommendations are that hands should be decontaminated before and after direct contact with patients, after contact with inanimate objects in the direct vicinity of the patient, and after removing gloves. If hands are not visibly soiled, an alcohol-based rub is preferred. An alternative is to wash hands with an antimicrobial soap. The guideline also describes the appropriate technique for using these products.

Other methods that have been shown to be effective in controlling the spread of RSV are education of personnel and family members; surveillance for the onset of RSV season; use of gloves, with frequent changes to avoid the spread of organisms on the gloves; and wearing gowns for direct contact with the patient. It has not

Downloaded from by guest on August 30, 2016

been clearly shown that wearing masks offers additional benefit to the above-listed measures.[149] Isolation and/or cohorting of RSV-positive patients, including assignment of personnel to care only for these patients, is effective[152,153] but may not be feasible. Strict hand decontamination and education of staff and families about prevention of spread of organisms is essential regardless of whether isolation is used.

Programs that implement the above-mentioned principles have been shown to decrease the nosocomial spread of RSV. Johns Hopkins Hospital (Baltimore, MD) instituted a program of pediatric droplet precaution for all children less than 2 years old with respiratory symptoms during RSV season until the child is shown to not have RSV. Nosocomial transmission of RSV decreased by approximately 50%. Before intervention, a patient was 2.6 times more likely to have nosocomially transmitted RSV than after the intervention.[154] A similar program at Children's Hospital of Philadelphia (Philadelphia, PA) resulted in a decrease of nosocomial RSV infections of 39%.[155]

Evidence Profile 9a: Hand Decontamination

- Aggregate evidence quality: B; observational studies with consistent findings
- Benefit: decreased spread of infection
- Harm: time
- Benefits-harms assessment: strong preponderance of benefit over harm
- Policy level: strong recommendation

Evidence Profile 9b: Alcohol-Based Rubs

- Aggregate evidence quality: B; observational studies with consistent findings
- Benefit: decreased spread of infection
- Harm: irritative effect of alcohol-based rubs
- Benefits-harms assessment: preponderance of benefit over harm
- Policy level: recommendation

Evidence Profile 9c: Education

- Aggregate evidence quality: C; observational studies
- Benefit: decreased spread of infection
- Harm: time, cost of gloves and gowns if used, barriers to parental contact with patient
- Benefits-harms assessment: preponderance of benefit over harm
- Policy level: recommendation

RECOMMENDATION 10a

Infants should not be exposed to passive smoking (strong recommendation: evidence level B; observational studies with consistent results; strong preponderance of benefit over harm).

RECOMMENDATION 10b

Breastfeeding is recommended to decrease a child's risk of having lower respiratory tract disease (LRTD) (recommendation: evidence level C; observational studies; preponderance of benefit over harm).

Tobacco Smoke

Passive smoking increases the risk of having an RSV infection with a reported odds ratio of 3.87.[156] There have been numerous studies on the effect of passive smoking on respiratory illness in infants and children. In a systematic review of passive smoking and lower respiratory illness in infants and children, Strachan and Cook[157] showed a pooled odds ratio of 1.57 if either parent smoked and an odds ratio of 1.72 if the mother smoked. Stocks and Dezateux[158] reviewed 20 studies of pulmonary function in infants. These studies showed a significant decrease in pulmonary function in infants of mothers who smoked during and after pregnancy. Forced expiratory flow was decreased by approximately 20%. Other measures of pulmonary function were likewise abnormal.

Paternal smoking also has an effect. The prevalence of upper respiratory tract illness increased from 81.6% to 95.2% in infants under 1 year of age in households where only the father smoked.[159]

Breastfeeding

Breast milk has been shown to have immune factors to RSV including immunoglobulin G and A antibodies[160] and interferon-α.[161] Breast milk has also been shown to have neutralizing activity against RSV.[162] In one study the relative risk of hospital admission with RSV was 2.2 in children who were not being breastfed.[163] In another study, 8 (7%) of 115 children hospitalized with RSV were breastfed, and 46 (27%) of 167 controls were breastfed.[164]

A meta-analysis of the relationship of breastfeeding and hospitalization for LRTD in early infancy[165] examined 33 studies, all of which showed a protective association between breastfeeding and the risk of hospitalization for LRTD. Nine studies met all inclusion criteria for analysis. The conclusion was that infants who were not breastfed had almost a threefold greater risk of being hospitalized for LRTD than those exclusively breastfed for 4 months (risk ratio: 0.28).

Evidence Profile 10a: Secondhand Smoke

- Aggregate evidence quality: B; observational studies with consistent findings
- Benefit: decreased risk of LRTI

Downloaded from by guest on August 30, 2016

- Harm: none
- Benefits-harms assessment: strong preponderance of benefit over harm
- Policy level: strong recommendation

Evidence Profile 10b: Breastfeeding

- Aggregate evidence quality: C; observational studies
- Benefit: improved immunity, decreased risk of LRTI, improved nutrition
- Harm: implied inadequacy of mothers who cannot or prefer to not breastfeed
- Benefits-harms assessment: preponderance of benefit over harm
- Policy level: recommendation

RECOMMENDATION 11

Clinicians should inquire about use of CAM (option: evidence level D; expert opinion; some benefit over harm).

No recommendations for CAM for treatment of bronchiolitis are made because of limited data. Clinicians now recognize that an increasing number of parents/caregivers are using various forms of nonconventional treatment for their children. Treatments that have been used specifically for bronchiolitis include homeopathy, herbal remedies, osteopathic manipulation, and applied kinesiology. Substantially more data are available regarding the use of homeopathic and herbal remedies for the treatment of bronchitis and the common cold. Whether these therapies would prevent the development of bronchiolitis is unknown. A single recent trial indicated that an herbal preparation containing *Echinacea*, propolis, and vitamin C prevented the development of upper respiratory infections in children between the ages of 1 and 5 years.[166] Bronchiolitis was not specifically studied.

To date, there are no studies that conclusively show a beneficial effect of alternative therapies used for the treatment of bronchiolitis. Recent interest in the use of CAM has led to research efforts to investigate its efficacy. It is difficult to design and conduct studies on certain forms of CAM because of the unique nature of the treatment. Any study conducted will need to show proof of effectiveness of a specific therapy when compared with the natural history of the disease. Conclusions regarding CAM cannot be made until research evidence is available. However, because of the widespread use of CAM, clinicians should ask parents what alternative forms of treatment they are using and be ready to discuss potential benefits or risks.

Evidence Profile 11: Asking About CAM

- Aggregate evidence quality: D; expert opinion
- Benefit: improved parent-physician communication, awareness of other, possibly harmful treatments being used
- Harm: time required for discussion, lack of knowledge about CAM by many pediatricians
- Benefits-harms assessment: some benefit over harm
- Policy level: option

FUTURE RESEARCH

The AHRQ evidence report[1] points out that outcomes measured in future studies of bronchiolitis should be clinically relevant and of interest to parents, clinicians, and health systems. Among the recommended outcomes are rates of hospitalization, need for more intensive services in the hospital, costs of care, and parental satisfaction with treatment.[1] One of the difficulties with the bronchiolitis literature is the absence of validated clinical scoring scales that are objective, replicable, and can be easily be performed in the hospital, emergency department, and outpatient settings. Studies should also be of sufficient size to be able to draw meaningful conclusions for the above-mentioned outcomes. Because bronchiolitis is a self-limited disease, large numbers of patients would need to be enrolled to observe small changes in outcome. This would necessitate large multicenter study protocols. Currently, such multicentered studies are being conducted in the United States and Canada on the use of corticosteroids in the emergency department.

Future research should include:

- development of rapid, cost-effective tests for viruses other than RSV that may also play a role in bronchiolitis;
- studies to determine if there are selected patients who may benefit from bronchodilators or corticosteroids;
- clinical studies of the target Spo_2 for the most efficient use of oxygen and oxygen monitoring;
- development of new therapies including new antiviral medications;
- continued research into the development of an RSV vaccine; and
- continued development of immunoprophylaxis that would require fewer doses and decreased cost.

SUMMARY

This clinical practice guideline provides evidence-based recommendations on the diagnosis and management of bronchiolitis in infants less than 2 years of age. It emphasizes using only diagnostic and management modalities that have been shown to affect clinical outcomes.

Bronchiolitis is a clinical diagnosis that does not require diagnostic testing. Many of the commonly used management modalities have not been shown to be effective in improving the clinical course of the illness. This includes the routine use of bronchodilators, corti-

Downloaded from by guest on August 30, 2016

costeroids, ribavirin, antibiotics, chest radiography, chest physiotherapy, and complementary and alternative therapies. Options for the appropriate use of oxygen and oxygen monitoring have been presented. Specific prevention with palivizumab and general prevention, particularly the use of hand decontamination to prevent nosocomial spread, were also discussed.

CONCLUSIONS

1a. Clinicians should diagnose bronchiolitis and assess disease severity on the basis of history and physical examination. Clinicians should not routinely order laboratory and radiologic studies for diagnosis (recommendation).

1b. Clinicians should assess risk factors for severe disease such as age less than 12 weeks, a history of prematurity, underlying cardiopulmonary disease, or immunodeficiency when making decisions about evaluation and management of children with bronchiolitis (recommendation).

2a. Bronchodilators should not be used routinely in the management of bronchiolitis (recommendation).

2b. A carefully monitored trial of α-adrenergic or β-adrenergic medication is an option. Inhaled bronchodilators should be continued only if there is a documented positive clinical response to the trial using an objective means of evaluation (option).

3. Corticosteroid medications should not be used routinely in the management of bronchiolitis (recommendation).

4. Ribavirin should not be used routinely in children with bronchiolitis (recommendation).

5. Antibacterial medications should only be used in children with bronchiolitis who have specific indications of the coexistence of a bacterial infection. When present, bacterial infection should be treated in the same manner as in the absence of bronchiolitis (recommendation).

6a. Clinicians should assess hydration and ability to take fluids orally (strong recommendation).

6b. Chest physiotherapy should not be used routinely in the management of bronchiolitis (recommendation).

7a. Supplemental oxygen is indicated if Spo_2 falls persistently below 90% in previously healthy infants. If the Spo_2 does persistently fall below 90%, adequate supplemental oxygen should be used to maintain an Spo_2 at or above 90%. Oxygen may be discontinued if Spo_2 is at or above 90% and the infant is feeding well and has minimal respiratory distress (option).

7b. As the child's clinical course improves, continuous measurement of Spo_2 is not routinely needed (option).

7c. Infants with a known history of hemodynamically significant heart or lung disease and premature infants require close monitoring as oxygen is being weaned (strong recommendation).

8a. Clinicians may administer palivizumab prophylaxis for selected infants and children with CLD or a history of prematurity (less than 35 weeks' gestation) or with congenital heart disease (recommendation).

8b. When given, prophylaxis with palivizumab should be given in 5 monthly doses, usually beginning in November or December, at a dose of 15 mg/kg per dose administered intramuscularly (recommendation).

9a. Hand decontamination is the most important step in preventing nosocomial spread of RSV. Hands should be decontaminated before and after direct contact with patients, after contact with inanimate objects in the direct vicinity of the patient, and after removing gloves (strong recommendation).

9b. Alcohol-based rubs are preferred for hand decontamination. An alternative is hand-washing with antimicrobial soap (recommendation).

9c. Clinicians should educate personnel and family members on hand sanitation (recommendation).

10a. Infants should not be exposed to passive smoking (strong recommendation).

10b. Breastfeeding is recommended to decrease a child's risk of having LRTD (recommendation).

11. Clinicians should inquire about use of CAM (option).

SUBCOMMITTEE ON THE DIAGNOSIS AND MANAGEMENT OF BRONCHIOLITIS, 2004–2006

Allan S. Lieberthal, MD, Chairperson
Howard Bauchner, MD
Caroline B. Hall, MD
David W. Johnson, MD
Uma Kotagal, MD
Michael J. Light, MD (on the AstraZeneca and MedImmune speakers' bureaus; research grant from MedImmune)
Wilbert Mason, MD (on the MedImmune speakers' bureau)
H. Cody Meissner, MD
Kieran J. Phelan, MD
Joseph J. Zorc, MD

Downloaded from by guest on August 30, 2016

LIASONS

Mark A. Brown, MD (on the GlaxoSmithKline, AstraZeneca, and MedImmune speakers' bureaus)
American Thoracic Society

Richard D. Clover, MD (continuing medical education presenter for institutions that received unrestricted educational grants from Sanofi Pasteur and Merck)
American Academy of Family Physicians

Ian T. Nathanson, MD
American College of Chest Physicians

Matti Korppi, MD
European Respiratory Society

CONSULTANTS

Richard N. Shiffman, MD

Danette Stanko-Lopp, MA, MPH

STAFF

Caryn Davidson, MA

REFERENCES

1. Agency for Healthcare Research and Quality. *Management of Bronchiolitis in Infants and Children.* Evidence Report/Technology Assessment No. 69. Rockville, MD: Agency for Healthcare Research and Quality; 2003. AHRQ Publication No. 03-E014
2. Mullins JA, Lamonte AC, Bresee JS, Anderson LJ. Substantial variability in community respiratory syncytial virus season timing. *Pediatr Infect Dis J.* 2003;22:857–862
3. Greenough A, Cox S, Alexander J, et al. Health care utilisation of infants with chronic lung disease, related to hospitalisation for RSV infection. *Arch Dis Child.* 2001;85:463–468
4. Parrott RH, Kim HW, Arrobio JO, et al. Epidemiology of RSV infection in Washington DC II: infection and disease with respect to age, immunologic status, race and sex. *Am J Epidemiol.* 1973;98:289–300
5. Meissner HC. Selected populations at increased risk from respiratory syncytial virus infection. *Pediatr Infect Dis J.* 2003; 22(2 suppl):S40–S44; discussion S44–S45
6. Shay DK, Holman RC, Roosevelt GE, Clarke MJ, Anderson LJ. Bronchiolitis-associated mortality and estimates of respiratory syncytial virus-associated deaths among US children, 1979–1997. *J Infect Dis.* 2001;183:16–22
7. Leader S, Kohlhase K. Recent trends in severe respiratory syncytial virus (RSV) among US infants, 1997 to 2000. *J Pediatr.* 2003;143(5 suppl):S127–S132
8. Stang P, Brandenburg N, Carter B. The economic burden of respiratory syncytial virus-associated bronchiolitis hospitalizations. *Arch Pediatr Adolesc Med.* 2001;155:95–96
9. Willson DF, Horn SD, Hendley JO, Smout R, Gassaway J. Effect of practice variation on resource utilization in infants for viral lower respiratory illness. *Pediatrics.* 2001;108: 851–855
10. Wang EE, Law BJ, Boucher FD, et al. Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC) study of admission and management variation in patients hospitalized with respiratory syncytial viral lower respiratory tract infection. *J Pediatr.* 1996;129:390–395
11. Brand PLP, Vaessen-Verberne AAPH. Differences in management of bronchiolitis between hospitals in the Netherlands. *Eur J Pediatr.* 2000;159:343–347
12. Behrendt CE, Decker MD, Burch DJ, Watson PH. International variation in the management of infants hospitalized with respiratory syncytial virus. International RSV Study Group. *Eur J Pediatr.* 1998;157:215–220
13. Martinez FD. Respiratory syncytial virus bronchiolitis and the pathogenesis of childhood asthma. *Pediatr Infect Dis J.* 2003; 22(2 suppl):S76–S82
14. Stein RT, Sherrill D, Morgan WJ, et al. Respiratory syncytial virus in early life and risk of wheeze and allergy by age 13 years. *Lancet.* 1999;354:541–545
15. Schauer U, Hoffjan S, Bittscheidt J, et al. RSV bronchiolitis and risk of wheeze and allergic sensitization in the first year of life. *Eur Respir J.* 2002;20:1277–1283
16. American Academy of Pediatrics, Steering Committee on Quality Improvement and Management. Classifying recommendations for clinical practice guidelines. *Pediatrics.* 2004; 114:874–877
17. Jobe AH, Bancalari E. Bronchopulmonary dysplasia. *Am J Respir Crit Care Med.* 2001;163:1723–1729
18. Ashton R, Connolly K. The relation of respiration rate and heart rate to sleep states in the human newborn. *Dev Med Child Neurol.* 1971;13:180–187
19. Iliff A, Lee VA. Pulse rate, respiratory rate, and body temperature of children between two months and eighteen years of age. *Child Dev.* 1952;23:237–245
20. Rogers MC. Respiratory monitoring. In: Rogers MC, Nichols DG, eds. *Textbook of Pediatric Intensive Care*. Baltimore, MD: Williams & Wilkins; 1996:332–333
21. Berman S, Simoes EA, Lanata C. Respiratory rate and pneumonia in infancy. *Arch Dis Child.* 1991;66:81–84
22. Margolis P, Gadomski A. The rational clinical examination: does this infant have pneumonia? *JAMA.* 1998;279:308–313
23. Mahabee-Gittens EM, Grupp-Phelan J, Brody AS, et al. Identifying children with pneumonia in the emergency department. *Clin Pediatr (Phila).* 2005;44:427–435
24. Brooks AM, McBride JT, McConnochie KM, Aviram M, Long C, Hall CB. Predicting deterioration in previously healthy infants hospitalized with respiratory syncytial virus infection. *Pediatrics.* 1999;104:463–467
25. Navas L, Wang E, de Carvalho V, Robinson J. Improved outcome of respiratory syncytial virus infection in a high-risk hospitalized population of Canadian children. Pediatric Investigators Collaborative Network on Infections in Canada. *J Pediatr.* 1992;121:348–354
26. Wang EE, Law BJ, Stephens D. Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC) prospective study of risk factors and outcomes in patients hospitalized with respiratory syncytial viral lower respiratory tract infection. *J Pediatr.* 1995;126:212–219
27. Shaw KN, Bell LM, Sherman NH. Outpatient assessment of infants with bronchiolitis. *Am J Dis Child.* 1991;145:151–155
28. Chan, PW, Lok FY, Khatijah SB. Risk factors for hypoxemia and respiratory failure in respiratory syncytial virus bronchiolitis. *Southeast Asian J Trop Med Public Health.* 2002;33: 806–810
29. MacDonald NE, Hall CB, Suffin SC, Alexson C, Harris PJ, Manning JA. Respiratory syncytial viral infection in infants with congenital heart disease. *N Engl J Med.* 1982;307: 397–400
30. Hall CB, Powell KR, MacDonald NE, et al. Respiratory syncytial viral infection in children with compromised immune function. *N Engl J Med.* 1986;315:77–81
31. McMillan JA, Tristram DA, Weiner LB, Higgins AP, Sandstrom C, Brandon R. Prediction of the duration of hospitalization in patients with respiratory syncytial virus infection: use of clinical parameters. *Pediatrics.* 1988;81:22–26
32. Roback MG, Baskin MN. Failure of oxygen saturation and clinical assessment to predict which patients with bronchioli-

Downloaded from by guest on August 30, 2016

tis discharged from the emergency department will return requiring admission. *Pediatr Emerg Care.* 1997;13:9–11
33. Lowell DI, Lister G, Von Koss H, McCarthy P. Wheezing in infants: the response to epinephrine. *Pediatrics.* 1987;79: 939–945
34. Hall CB, Hall WJ, Speers DM. Clinical and physiological manifestations of bronchiolitis and pneumonia: outcome of respiratory syncytial virus. *Am J Dis Child.* 1979;133:798–802
35. Schroeder AR, Marmor AK, Pantell RH, Newman TB. Impact of pulse oximetry and oxygen therapy on length of stay in bronchiolitis hospitalizations. *Arch Pediatr Adolesc Med.* 2004; 158:527–530
36. Dawson KP, Long A, Kennedy J, Mogridge N. The chest radiograph in acute bronchiolitis. *J Paediatr Child Health.* 1990; 26:209–211
37. Roosevelt G, Sheehan K, Grupp-Phelan J, Tanz RR, Listernic R. Dexamethasone in bronchiolitis: a randomized controlled trial. *Lancet.* 1996;348:292–305
38. Swingler GH, Hussey GD, Zwarenstein M. Randomised controlled trial of clinical outcome after chest radiograph in ambulatory acute lower-respiratory infection in children. *Lancet.* 1998;351:404–408
39. Mallory MD, Shay DK, Garrett J, Bordley WC. Bronchiolitis management preferences and the influence of pulse oximetry and respiratory rate on the decision to admit. *Pediatrics.* 2003; 111(1). Available at: www.pediatrics.org/cgi/content/full/111/1/e45
40. Bordley WC, Viswanathan M, King VJ, et al. Diagnosis and testing in bronchiolitis: a systematic review. *Arch Pediatr Adolesc Med.* 2004;158:119–126
41. Liebelt E, Qi K, Harvey K. Diagnostic testing for serious bacterial infections in infants aged 90 days or younger with bronchiolitis. *Arch Pediatr Adolesc Med.* 1999;153:525–530
42. Kuppermann N, Bank DE, Walton EA, Senac MO Jr, McCaslin I. Risks for bacteremia and urinary tract infections in young febrile children with bronchiolitis. *Arch Pediatr Adolesc Med.* 1997;151:1207–1214
43. Levine DA, Platt SL, Dayan PS, et al. Risk of serious bacterial infection in young febrile infants with respiratory syncytial virus infections. *Pediatrics.* 2004;113:1728–1734
44. Kellner JD, Ohlsson A, Gadomski AM, Wang EE. Bronchodilators for bronchiolitis. *Cochrane Database Syst Rev.* 2000;(2): CD001266
45. Alario AJ, Lewander WJ, Dennehy P, Seifer R, Mansell AL. The efficacy of nebulized metaproterenol in wheezing infants and young children. *Am J Dis Child.* 1992;146:412–418
46. Henry RL, Milner AD, Stokes GM. Ineffectiveness of ipratropium bromide in acute bronchiolitis. *Arch Dis Child.* 1983;58: 925–926
47. Klassen TP, Rowe PC, Sutcliffe T, Ropp LJ, McDowell IW, Li MM. Randomized trial of salbutamol in acute bronchiolitis. *J Pediatr.* 1991;118:807–811
48. Lines DR, Kattampallil JS, Liston P. Efficacy of nebulized salbutamol in bronchiolitis. *Pediatr Rev Commun.* 1990;5: 121–129
49. Mallol J, Barrueo L, Girardi G, et al. Use of nebulized bronchodilators in infants under 1 year of age: analysis of four forms of therapy. *Pediatr Pulmonol.* 1987;3:298–303
50. Tal A, Bavilski C, Yohai D, Bearman JE, Gorodischer R, Moses SW. Dexamethasone and salbutamol in the treatment of acute wheezing in infants. *Pediatrics.* 1983;71:13–18
51. Wainwright C, Altamirano L, Cheney M, et al. A multicenter, randomized, double-blind, controlled trial of nebulized epinephrine in infants with acute bronchiolitis. *N Engl J Med.* 2003;349:27–35
52. Schweich PJ, Hurt TL, Walkley EI, Mullen N, Archibald LF. The use of nebulized albuterol in wheezing infants. *Pediatr Emerg Care.* 1992;8:184–188
53. Schuh S, Canny G, Reisman JJ, et al. Nebulized albuterol in acute bronchiolitis. *J Pediatr.* 1990;117:633–637
54. Gadomski AM, Lichtenstein R, Horton L, King J, Keane V, Permutt T. Efficacy of albuterol in the management of bronchiolitis. *Pediatrics.* 1994;93:907–912
55. Dobson JV, Stephens-Groff SM, McMahon SR, Stemmler MM, Brallier SL, Bay C. The use of albuterol in hospitalized infants with bronchiolitis. *Pediatrics.* 1998;101:361–368
56. Flores G, Horwitz RI. Efficacy of beta2-agonists in bronchiolitis: a reappraisal and meta-analysis. *Pediatrics.* 1997;l00: 233–239
57. Kristjansson S, Lodrup Carlsen KC, Wennergren G, Strannegard IL, Carlsen KH. Nebulised racemic adrenaline in the treatment of acute bronchiolitis in infants and toddlers. *Arch Dis Child.* 1993;69:650–654
58. Menon K, Sutcliffe T, Klassen TP. A randomized trial comparing the efficacy of epinephrine with salbutamol in the treatment of acute bronchiolitis. *J Pediatr.* 1995;126:1004–1007
59. Numa AH, Williams GD, Dakin CJ. The effect of nebulized epinephrine on respiratory mechanics and gas exchange in bronchiolitis. *Am J Respir Crit Care Med.* 2001;164:86–91
60. Wohl ME, Chernick V. State of the art: bronchiolitis. *Am Rev Respir Dis.* 1978;118:759–781
61. Hartling L, Wiebe N, Russell K, Patel H, Klassen T. A meta-analysis of randomized controlled trials evaluating the efficacy of epinephrine for the treatment of acute viral bronchiolitis. *Arch Pediatr Adolesc Med.* 2003;157:957–967
62. Hartling L, Wiebe N, Russell K, Patel H, Klassen TP. Epinephrine for bronchiolitis. *Cochrane Database Syst Rev.* 2004;(1): CD003123
63. Bierman CW, Pierson WE. The pharmacological management of status asthmaticus in children. *Pediatrics.* 1974;54:245–247
64. Schuh S, Coates AL, Binnie R, et al. Efficacy of oral dexamethasone in outpatients with acute bronchiolitis. *J Pediatr.* 2002;140:27–32
65. Gorelick MH, Stevens MW, Schultz TR, Scribano PV. Performance of a novel clinical score, the Pediatric Asthma Severity Score (PASS) in the evaluation of acute asthma. *Acad Emerg Med.* 2004;11:10–18
66. Cincinnati Children's Hospital Medical Center. Evidence-based clinical practice guideline for the medical management of infants less than 1 year with a first episode of bronchiolitis. Available at: www.cincinnatichildrens.org/NR/rdonlyres/B3EC347E-65AC-490A-BC4C-55C3AF4B76D5/0/BronchRS.pdf. Accessed June 21, 2006
67. Goh A, Chay OM, Foo AL, Ong EK. Efficacy of bronchodilators in the treatment of bronchiolitis. *Singapore Med J.* 1997; 38:326–328
68. Chowdhury D, al Howasi M, Khalil M, al-Frayh AS, Chowdhury S, Ramia S. The role of bronchodilators in the management of bronchiolitis: a clinical trial. *Ann Trop Paediatr.* 1995;15:77–84
69. Wang EE, Milner R, Allen U, Maj H. Bronchodialtors for treatment of mild bronchiolitis: a factorial randomized trial. *Arch Dis Child.* 1992;67:289–293
70. Shay DK, Holman RC, Newman RD, Liu LL, Stout JW, Anderson LJ. Bronchiolitis associated hospitalizations among US children, 1980–1996. *JAMA.* 1999;282:1440–1446
71. Patel H, Platt R, Lozano JM, Wang EE. Glucocorticoids for acute viral bronchiolitis in infants and young children. *Cochrane Database Syst Rev.* 2004;(3):CD004878
72. Garrison MM, Christakis DA, Harvey E, Cummings P, Davis RL. Systemic corticosteroids in infant bronchiolitis: a meta-analysis. *Pediatrics.* 2000;105(4). Available at: www.pediatrics.org/cgi/content/full/105/4/e44

Downloaded from by guest on August 30, 2016

73. Berger I, Argaman Z, Schwartz SB, et al. Efficacy of corticosteroids in acute bronchiolitis: short-term and long-term follow-up. *Pediatr Pulmonol.* 1998;26:162–166
74. Bulow SM, Nir M, Levin E, et al. Prednisolone treatment of respiratory syncytial virus infection: a randomized controlled trial of 147 infants. *Pediatrics.* 1999;104(6). Available at: www.pediatrics.org/cgi/content/full/105/6/e77
75. Connolly JH, Field CMB, Glasgoe JFT, Slattery M, MacLynn DM. A double blind trial of prednisolone in epidemic bronchiolitis due to respiratory syncytial virus. *Acta Paediatr Scand.* 1969;58:116–120
76. Dabbous JA, Tkachyk JS, Stamm SJ. A double blind study on the effects of corticosteroids in the treatment of bronchiolitis. *Pediatrics.* 1966;37:477–484
77. DeBoeck K, Van der Aa N, Van Lierde S, Corbeel L, Eeckels R. Respiratory syncytial virus bronchiolitis: a double-blind dexamethasone efficacy study. *J Pediatr.* 1997;131:919–921
78. Goebel J, Estrada B, Quinonez J, Nagji N, Sanford D, Boerth RC. Prednisolone plus albuterol versus albuterol alone in mild to moderate bronchiolitis. *Clin Pediatr (Phila).* 2000;39:213–220
79. Klassen TP, Sutcliffe T, Watters LK, Wells GA, Allen UD, Li MM. Dexamethasone in salbutamol-treated inpatients with acute bronchiolitis: a randomized controlled trial. *J Pediatr.* 1997;130:191–196
80. Leer JA, Bloomfield N, Green JL, et al. Corticosteroid treatment in bronchiolitis. *Am J Dis Child.* 1969;117:495–503
81. Springer C, Bar-Yishay E, Uwayyed K, Avital A, Vilozni D, Godfrey S. Corticosteroids do not affect the clinical or physiological status of infants with bronchiolitis. *Pediatr Pulmonol.* 1990;9:181–185
82. Van Woensel JBM, Wolfs TFW, van Aaldersen WMC, Brand PLP, Kimpen JLL. Randomised double blind placebo controlled trial of prednisolone in children admitted to hospital with respiratory syncytial virus bronchiolitis. *Thorax.* 1997;52:634–637
83. de Blic J. Use of corticoids in acute bronchiolitis in infants [in French]. *Arch Pediatr.* 2001;9 (suppl 1):49S–54S
84. Chao LC, Lin YZ, Wu WF, Huang FY. Efficacy of nebulized budesonide in hospitalized infants and children younger than 24 months with bronchiolitis. *Acta Paediatr Taiwan.* 2003;44:332–335
85. King VJ, Viswanathan M, Bordley WC, et al. Pharmacologic treatment of bronchiolitis in infants and children. *Arch Pediatr Adolesc Med.* 2004;158:127–137
86. Hall CB, McBride JT, Walsh EE, et al. Aerosolized ribavirin treatment of infants with respiratory syncytial viral infection: a randomized double-blind study. *N Engl J Med.* 1983;308:1443–1447
87. Taber LH, Knight V, Gilbert BE, et al. Ribavirin aerosol treatment of bronchiolitis associated with respiratory syncytial virus infection in infants. *Pediatrics.* 1983;72:613–618
88. Barry W, Cockburn F, Cornall R, et al. Ribavirin aerosol for acute bronchiolitis. *Arch Dis Child.* 1986;61:593–597
89. Rodriguez WJ, Kim HW, Brandt CD, et al. Aerosolized ribavirin in the treatment of patients with respiratory syncytial virus disease. *Pediatr Infect Dis J.* 1987;6:159–163
90. Smith DW, Frankel LR, Mathers LH, Tang AT, Ariagno RL, Prober CG. A controlled trial of aerosolized ribavirin in infants receiving mechanical ventilation for severe respiratory syncytial virus infection. *N Engl J Med.* 1991;325:24–29
91. Janai HK, Stutman HR, Zeleska M, et al. Ribavirin effect on pulmonary function in young infants with respiratory syncytial virus bronchiolitis. *Pediatr Infect Dis J.* 1993;12:214–218
92. Meert KL, Sarnaik AP, Gelmini MJ, Lieh-Lai MW. Aerosolized ribavirin in mechanically ventilated children with respiratory syncytial virus lower respiratory tract disease: a double-blind, randomized trial. *Crit Care Med.* 1994;22:566–572
93. Guerguerian AM, Gauthier M, Lebel MH, Farrell CA, Lacroix J. Ribavirin in ventilated respiratory syncytial virus bronchiolitis. *Am J Respir Crit Care Med.* 1999;160:829–834
94. Everard ML, Swarbrick A, Rigby AS, Milner AD. The effect of ribavirin to treat previously healthy infants admitted with acute bronchiolitis on acute and chronic respiratory morbidity. *Respir Med.* 2001;95:275–280
95. Rodriguez WJ, Arrobio J, Fink R, Kim HW, Milburn C. Prospective follow-up and pulmonary functions from a placebo-controlled randomized trial of ribavirin therapy in respiratory syncytial virus bronchiolitis. *Arch Pediatr Adolesc Med.* 1999;153:469–474
96. Edell D, Khoshoo V, Ross G, Salter K. Early ribavirin treatment of bronchiolitis. *Chest.* 2002;122:935–939
97. Hall CB, McBride JT, Gala CL, Hildreth SW, Schnabel KC. Ribavirin treatment of respiratory syncytial viral infection in infants with underlying cardiopulmonary disease. *JAMA.* 1985;254:3047–3051
98. Groothuis JR, Woodin KA, Katz R, et al. Early ribavirin treatment of respiratory syncytial virus infection in high-risk children. *J Pediatr.* 1990;117:792–798
99. Long CE, Voter KZ, Barker WH, Hall CB. Long term follow-up of children hospitalized with respiratory syncytial virus lower respiratory tract infection and randomly treated with ribavirin and placebo. *Pediatr Infect Dis J.* 1997;16:1023–1028
100. Bradley JS, Conner JD, Compagiannis LS, Eiger LL. Exposure of health care workers to ribavirin during therapy for respiratory syncytial virus infections. *Antimicrob Agents Chemother.* 1990;34:668–670
101. Rodriguez WJ, Bui RHD, Conner JD, et al. Environmental exposure of primary care personnel to ribavirin aerosol when supervising treatment of infants with respiratory syncytial virus infections. *Antimicrob Agents Chemother.* 1987;31:1143–1146
102. Feldstein TJ, Swegarden JL, Atwood GF, Peterson CD. Ribavirin therapy: implementation of hospital guidelines and effect on usage and cost of therapy. *Pediatrics.* 1995;96:14–17
103. Putto A, Ruuskanen O, Meruman O. Fever in respiratory virus infections. *Am J Dis Child.* 1986;140:1159–1163
104. LaVia W, Marks MI, Stutman HR. Respiratory syncytial virus puzzle: clinical features, pathophysiology, treatment, and prevention. *J Pediatr.* 1992;121:503–510
105. Nichol KP, Cherry JD. Bacterial-viral interrelations in respiratory infections in children. *N Engl J Med.* 1967;277:667–672
106. Field CM, Connolly JH, Murtagh G, Slattery CM, Turkington EE. Antibiotic treatment of epidemic bronchiolitis. *Br Med J.* 1966;5479:83–85
107. Friis B, Andersen P. Brenoe E, et al. Antibiotic treatment of pneumonia and bronchiolitis. A prospective randomised study. *Arch Dis Child.* 1984;59:1038–1045
108. Antonow JA, Hansen K, McKinstry CA, Byington CL. Sepsis evaluations in hospitalized infants with bronchiolitis. *Pediatr Infect Dis J.* 1998;17:231–236
109. Greenes DS, Harper MB. Low risk of bacteremia in febrile children with recognizable viral syndromes. *Pediatr Infect Dis J.* 1999;18:258–261
110. Purcell K, Fergie J. Concurrent serious bacterial infections in 2396 infants and children hospitalized with respiratory syncytial virus lower respiratory tract infections. *Arch Pediatr Adolesc Med.* 2002;156:322–324
111. Purcell K, Fergie J. Concurrent serious bacterial infections in 912 infants and children hospitalized for treatment of respiratory syncytial virus lower respiratory tract infection. *Pediatr Infect Dis J.* 2004;23:267–269
112. Titus MO, Wright SW. Prevalence of serious bacterial infec-

Downloaded from by guest on August 30, 2016

tions in febrile infants with respiratory syncytial virus infections. *Pediatrics.* 2003;112:282–284
113. Melendez E, Harper MB. Utility of sepsis evaluation in infants 90 days of age or younger with fever and clinical bronchiolitis. *Pediatr Infect Dis J.* 2003;22:1053–1056
114. Hall CB, Powell KR, Schnabel KC, Gala CL, Pincus PH. Risk of serious bacterial infection in infants hospitalized with respiratory syncytial viral infection. *J Pediatr.* 1988;113:266–271
115. Hall CB. Respiratory syncytial virus: a continuing culprit and conundrum. *J Pediatr.* 1999;135(2 pt 2):2–7
116. Davies HD, Matlow A, Petric M, Glazier R, Wang EE. Prospective comparative study of viral, bacterial and atypical organisms identified in pneumonia and bronchiolitis in hospitalized Canadian infants. *Pediatr Infect Dis J.* 1996;15:371–375
117. Andrade MA, Hoberman A, Glustein J, Paradise JL, Wald ER. Acute otitis media in children with bronchiolitis. *Pediatrics.* 1998;101:617–619
118. Shazberg G, Revel-Vilk S, Shoseyov D, Ben-Ami A, Klar A, Hurvitz H. The clinical course of bronchiolitis associated with otitis media. *Arch Dis Child.* 2000;83:317–319
119. American Academy of Pediatrics, Subcommittee on Management of Acute Otitis Media. Diagnosis and management of acute otitis media. *Pediatrics.* 2004;113:1451–1465
120. Khoshoo V, Edell D. Previously healthy infants may have increased risk of aspiration during respiratory syncytial viral bronchiolitis. *Pediatrics.* 1999;104:1389–1390
121. Gozal D, Colin AA, Jaffe M, Hochberg Z. Water, electrolyte, and endocrine homeostasis in infants with bronchiolitis. *Pediatr Res.* 1990;27:204–209
122. van Steensel-Moll HA, Hazelzet JA, van der Voort E, Neijens HJ, Hackeng WH. Excessive secretion of antidiuretic hormone in infections with respiratory syncytial virus. *Arch Dis Child.* 1990;65:1237–1239
123. Perotta C, Ortiz Z, Roque M. Chest physiotherapy for acute bronchiolitis in paediatric patients between 0 and 24 months old. *Cochrane Database Syst Rev.* 2005;(2):CD004873
124. Nicholas KJ, Dhouieb MO, Marshal TG, Edmunds AT, Grant MB. An evaluation of chest physiotherapy in the management of acute bronchiolitis: changing clinical practice. *Physiotherapy.* 1999;85:669–674
125. Webb MS, Martin JA, Cartlidge PH, Ng YK, Wright NA. Chest physiotherapy in acute bronchiolitis. *Arch Dis Child.* 1985;60:1078–1079
126. Bohe L, Ferrero ME, Cuestas E, Polliotto L, Genoff M. Indications of conventional chest physiotherapy in acute bronchiolitis [in Spanish]. *Medicina (B Aires).* 2004;64:198–200
127. O'Brien LM, Stebbens VA, Poets CF, Heycock EG, Southall DP. Oxygen saturation during the first 24 hours of life. *Arch Dis Child Fetal Neonatal Ed.* 2000;83:F35–F38
128. Hunt CE, Corwin MJ, Lister G, et al. Longitudinal assessment of hemoglobin oxygen saturation in healthy infants during the first 6 months of age. Collaborative Home Infant Monitoring Evaluation (CHIME) Study Group. *J Pediatr.* 1999;135:580–586
129. Young S, O'Keeffe PT, Arnott J, Landau LI. Lung function, airway responsiveness, and respiratory symptoms before and after bronchiolitis. *Arch Dis Child.* 1995;72:16–24
130. Forster RE II, Dubois AB, Briscoe WA, Fisher AB. *The Lung: Physiologic Basis of Pulmonary Function Tests*. Chicago, IL: Year Book Medical Publishers, Inc; 1986
131. Chernick V, Boat TF. *Kendig's Disorders of the Respiratory Tract in Children*. Philadelphia, PA: W. B. Saunders Co; 1998
132. Salyer JW. Neonatal and pediatric pulse oximetry. *Respir Care.* 2003;48:386–396; discussion 397–398
133. Groothuis JR, Gutierrez KM, Lauer BA. Respiratory syncytial virus infection in children with bronchopulmonary dysplasia. *Pediatrics.* 1988;82:199–203
134. Grimaldi M, Gouyon B, Michaut F, Huet F, Gouyon J; Burgundy Perinatal Network. Severe respiratory syncytial virus bronchiolitis: epidemiologic variations associated with the initiation of palivizumab in severely premature infants with bronchopulmonary dysplasia. *Pediatr Infect Dis J.* 2004;23:1081–1085
135. Horn SD, Smout RJ. Effect of prematurity on respiratory syncytial virus hospital resource use and outcomes. *J Pediatr.* 2003;143(5 suppl):S133–S141
136. American Academy of Pediatrics. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006
137. The IMpact-RSV study group. Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants. *Pediatrics.* 1998;102:531–537
138. Feltes TF, Cabalka AK, Meissner HC, et al. Palivizumab prophylaxis reduces hospitalization due to respiratory syncytial virus in young children with hemodynamically significant congenital heart disease. *J Pediatr.* 2003;143:532–540
139. Romero JR. Palivizumab prophylaxis of respiratory syncytial virus disease from 1998 to 2002: results from four years of palivizumab usage. *Pediatr Infect Dis J.* 2003;22(2 suppl):S46–S54
140. Hay JW, Ernst RL, Meissner HC. RSV-IGIV: a cost effectiveness analysis. *Am J Manag Care.* 1996;2:851–861
141. O'Shea TM, Sevick MA, Givner LB. Costs and benefits of respiratory syncytial virus immunoglobulin to prevent hospitalization for lower respiratory tract illness in very low birth weight infants. *Pediatr Infect Dis J.* 1998;17:587–593
142. Robbins JM, Tilford JM, Jacobs RF, Wheeler JG, Gillaspy SR, Schutze GE. A number-needed-to-treat analysis of respiratory syncytial virus immune globulin intravenous to prevent hospitalization [published correction appears in *Arch Pediatr Adolesc Med*. 1998;152:577]. *Arch Pediatr Adolesc Med.* 1998;152:358–366
143. Atkins JT, Karimi P, Morris BH, McDavid G, Shim S. Prophylaxis for RSV with RSV-IGIV among preterm infants of thirty-two weeks gestation and less: reduction in incidence, severity of illness and cost. *Pediatr Infect Dis J.* 2002;19:138–143
144. Thomas M, Bedford-Russell A, Sharland M. Hospitalization for RSV infection in ex-preterm infants: implications for use of RSV-IGIV. *Arch Dis Child.* 2000;83:122–127
145. Joffe S, Ray GT, Escobar GJ, Black SB, Lieu TA. Cost-effectiveness of RSV prophylaxis among preterm infants. *Pediatrics.* 1999;104:419–427
146. Stevens TP, Sinkin RA, Hall CB, Maniscalco WM, McConnochie KM. Respiratory syncytial virus and premature infants born at 32 weeks' gestation or earlier: hospitalization and economic implications of prophylaxis. *Arch Pediatr Adolesc Med.* 2000;154:55–61
147. Kamal-Bahl S, Doshi J, Campbell J. Economic analysis of respiratory syncytial virus immunoprophylaxis in high-risk infants. *Arch Pediatr Adolesc Med.* 2002;156:1034–1041
148. Aintablian N, Walpita P, Sawyer MH. Detection of *Bordetella pertussis* and respiratory synctial virus in air samples from hospital rooms. *Infect Control Hosp Epidemiol.* 1998;19:918–923
149. Hall CB. Nosocomial respiratory syncytial virus infections: the "Cold War" has not ended. *Clin Infect Dis.* 2000;31:590–596
150. Sattar SA, Terro J, Vashon R, Keswick B. Hygienic hand antiseptics: should they not have activity and label claims against viruses? *Am J Infect Control.* 2002;30:355–372
151. Boyce JM, Pittet D; Healthcare Infection Control Practices Advisory Committee, HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. Guideline for hand hygiene in health-care settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/

Downloaded from by guest on August 30, 2016

APIC/IDSA Hand Hygiene Task Force. Society for Healthcare Epidemiology of America/Association for Professionals in Infection Control/Infectious Diseases Society of America. *MMWR Recomm Rep*. 200225;51(RR-16):1–45; quiz CE1–CE4
152. Isaacs D, Dickson H, O'Callaghan C, Sheaves R, Winter A, Moxon ER. Handwashing and cohorting in prevention of hospital acquired infections with respiratory syncytial virus. *Arch Dis Child.* 1991;66:227–231
153. Krasinski K, LaCouture R, Holzman RS, Waithe E, Bonk S, Hanna B. Screening for respiratory syncytial virus and assignment to a cohort at admission to reduce nosocomial transmission. *J Pediatr.* 1990;116:894–898
154. Karanfil LV, Conlon M, Lykens K, et al. Reducing the rate of nosocomially transmitted respiratory syncytial virus [published correction appears in *Am J Infect Control*. 1999;27:303]. *Am J Infect Control.* 1999;27:91–96
155. Macartney KK, Gorelick MH, Manning ML, Hodinka RL, Bell LM. Nosocomial respiratory syncytial virus infections: the cost-effectiveness and cost-benefit of infection control. *Pediatrics.* 2000;106:520–526
156. McConnochie KM, Roghmann KJ. Breast feeding and maternal smoking as predictors of wheezing in children age 6 to 10 years. *Pediatr Pulmonol.* 1986;2:260–268
157. Strachan DP, Cook DG. Health effects of passive smoking. 1. Parental smoking and lower respiratory illness in infancy and early childhood. *Thorax.* 1997;52:905–914
158. Stocks J, Dezateux C. The effect of parental smoking on lung function and development during infancy. *Respirology.* 2003; 8:266–285
159. Shiva F, Basiri M, Sadeghi B, Padyab M. Effects of passive smoking on common respiratory symptoms in young children. *Acta Paediatr.* 2003;92:1394–1397
160. Nandapalan N, Taylor C, Scott R, Toms GL. Mammary immunity in mothers of infants with respiratory syncytial virus infection. *J Med Virol.* 1987;22:277–287
161. Chiba Y, Minagawa T, Mito K, et al. Effect of breast feeding on responses of systemic interferon and virus-specific lymphocyte transformation in infants with respiratory syncytial virus infection. *J Med Virol.* 1987;21:7–14
162. Laegreid A, Kolsto Otnaess AB, Orstavik I, Carlsen KH. Neutralizing activity in human milk fractions against respiratory syncytial virus. *Acta Paediatr Scand.* 1986;75:696–701
163. Pullan CR, Toms GL, Martin AJ, Gardner PS, Webb JK, Appleton DR. Breastfeeding and respiratory syncytial virus infection. *Br Med J.* 1980;281:1034–1036
164. Downham MAPS, Scott R, Sims DG, Webb JKG, Gardner PS. Breast-feeding protects against respiratory syncytial virus infections. *Br Med J.* 1976;2(6030):274–276
165. Bachrach VR, Schwarz E, Bachrach LR. Breastfeeding and the risk of hospitalization for respiratory disease in infancy: a meta-analysis. *Arch Pediatr Adolesc Med.* 2003;157:237–243
166. Cohen HA, Varsano I, Kahan E, Sarrell EM, Uziel Y. Effectiveness of an herbal preparation containing echinacea, propolis, and vitamin C in preventing respiratory tract infections in children: a randomized, double-blind, placebo-controlled, multicenter study. *Arch Pediatr Adolesc Med.* 2004; 158:217–221

Downloaded from by guest on August 30, 2016

Diagnosis and Management of Bronchiolitis
Subcommittee on Diagnosis and Management of Bronchiolitis
Pediatrics 2006;118;1774
DOI: 10.1542/peds.2006-2223

Updated Information & Services	including high resolution figures, can be found at: /content/118/4/1774.full.html
References	This article cites 156 articles, 45 of which can be accessed free at: /content/118/4/1774.full.html#ref-list-1
Citations	This article has been cited by 100 HighWire-hosted articles: /content/118/4/1774.full.html#related-urls
Post-Publication Peer Reviews (P^{3}Rs)	One P^{3}R has been posted to this article: /cgi/eletters/118/4/1774
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): **Subcommittee on Diagnosis and Management of Bronchiolitis** /cgi/collection/subcommittee_on_diagnosis_and_management_of_bronchiolitis **Pulmonology** /cgi/collection/pulmonology_sub
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: /site/misc/Permissions.xhtml
Reprints	Information about ordering reprints can be found online: /site/misc/reprints.xhtml

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2006 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Downloaded from by guest on August 30, 2016

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Diagnosis and Management of Bronchiolitis

Subcommittee on Diagnosis and Management of Bronchiolitis

Pediatrics 2006;118;1774
DOI: 10.1542/peds.2006-2223

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/118/4/1774.full.html

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2006 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Downloaded from by guest on August 30, 2016