Cincinnati Children's Hospital Medical Center

Health Policy & Clinical Effectiveness Program

Evidence Based Clinical Practice Guideline

For medical management of

Bronchiolitis

in infants less than 1 year of age presenting with a first time episode[a]

Original Publication Date: **December 6, 1996**
Revision Publication Dates: November 28, 2001
August 15, 2005
New search May, 2006 (see Development Process section)

Target Population

Inclusion: Intended primarily for use in children:

- age less than 12 completed months and presenting for the first time with bronchiolitis typical in presentation and clinical course

Exclusion: Not intended for use in children:

- with a history of cystic fibrosis (CF)
- with a history of bronchopulmonary dysplasia (BPD)
- with immunodeficiencies
- admitted to an intensive care unit
- requiring ventilator care
- with other severe comorbid conditions complicating care

Target Users

Includes but is not limited to (in alphabetical order):

- Attending physicians
- Community physicians and practitioners
- Emergency department physicians
- Patient / family
- Patient care staff
- Residents

[a] Please cite as: **Bronchiolitis Guideline Team, Cincinnati Children's Hospital Medical Center:** Evidence based clinical practice guideline for medical management of bronchiolitis in infants 1 year of age or less presenting with a first time episode, http://www.cincinnatichildrens.org/svc/alpha/h/health-policy/ev-based/bronchiolitis.htm , Guideline 1, pages 1-13, August 15, 2005.

Introduction

References in parentheses ( ). Evidence strengths in [ ]. (See last page for definitions.)

Bronchiolitis is an acute inflammatory disease of the lower respiratory tract, resulting from obstruction of small airways. It is initiated by infection of the upper respiratory tract by any one of a number of seasonal viruses , the most common of which is respiratory syncytial virus (RSV) *(Williams 2004 [C], Andreoletti 2000 [C], Hall 2001 [S], Stark 1991 [S])*.

There is considerable confusion and variability with respect to the clinical management of infants with bronchiolitis. Typical bronchiolitis in infants is a self-limited disease, usually due to an acute viral infection that is little modified by aggressive evaluations, use of antibiotics or other therapies. The median duration of illness for children < 24 months with bronchiolitis is 12 days; after 21 days approximately 18% will remain ill, and after 28 days 9% will remain ill *(Swingler 2000 [C])*. Most infants who contract bronchiolitis recover without sequelae; however, up to 40% may have subsequent wheezing episodes through five years of age and approximately ten percent will have wheezing episodes after age five *(van Woensel 2000 [B])*.

Hospitalizations for bronchiolitis in U.S. infants less than one year of age have been increasing over the past decade *(Shay 1999 [O])*. The average duration of hospitalization is 3 to7 days *(Wang 1995 [C], Green 1989 [D])*. RSV-associated deaths account for less than 500 infant deaths per year in the U.S.; most of these children did not have concurrent cardiac or pulmonary disease *(Shay 1999 [O])*.

Several studies on the use of clinical guidelines for the management of infant bronchiolitis have shown a reduction in unnecessary resource utilization with a streamlining of medical care for these infants *(El-Radhi 1999 [C], Harrison 2001 [D], Perlstein 2000 [D], Liebelt 1999 [D], Perlstein 1999 [D], Muething 2004 [O], Kotagal 2002 [O])*.

In the target population, the objectives of this guideline are to:

- decrease the use of unnecessary diagnostic studies
- decrease the use of medications and respiratory therapy without observed improvement
- improve the rate of appropriate admission
- decrease the rate of nosocomial infection
- improve the use of appropriate monitoring activities
- decrease length of stay

Guideline Recommendations

Prevention

General

Infants less than three months of age, premature infants (<35 weeks gestation), and infants with chronic lung disease, congenital heart disease, or immune deficiency syndromes who are diagnosed with bronchiolitis may be at particular risk for hospitalization and significant morbidity *(Shay 2001 [D], Boyce 2000 [D], Joffe 1999 [D], Church 1984 [D], Shay 1999 [O])*. Prevention of hospitalization and significant morbidity is a high priority in the management of this lower respiratory tract infection.

Prevention Measures

1. It is recommended that measures to prevent acute bronchiolitis be reviewed with parents of newborns prior to discharge from the hospital and at follow-up visits in the first years of life. These specific measures include:
   - eliminating exposure to environmental tobacco smoke *(Mahabee-Gittens 2002 [O])*
   - limiting exposure to contagious settings and siblings (e.g. daycare centers)
   - an emphasis on handwashing in all settings
   - preventive medical therapies such as palivizumab (Synagis®, MedImmune); may be considered for selected high-risk patients *(IMpact-RSV Study Group 1998 [A], Celedon 1999 [C], Aitken 1998 [C], Wald 1991 [C])*.

     Note: A large, multicenter double-blind, randomized, controlled trial has shown that palivizumab (Synagis®, MedImmune) reduced the rates of hospitalization (not acute infection) for all infants studied, premature infants (<35 weeks) less than six months of age, and infants with BPD by 55%, 78%, and 39% respectively. The use of palivizumab has not been shown to be cost-effective in children regardless of prematurity or the presence of congenital heart disease due to the high cost of the medication and persistently low mortality rates associated with RSV-bronchiolitis *(IMpact-RSV Study Group 1998 [A], Heikkinen 2005 [C], Wegner 2004 [C], Shay 2001 [D], Yount 2004 [Q], Joffe 1999 [Q])*.

2. It is recommended, in patients with documented bronchiolitis, that masks covering the nose and eyes be worn and that contact isolation, including vigorous handwashing, be performed before and after entering the exam room *(Hall 1981 [C], Hall 2001 [S], Local Expert Consensus [E])*.

   Note 1: Viral transmission occurs by direct inoculation of contagious secretions from the hands or by large-particle aerosols into the eyes and nose, but rarely the mouth *(Hall 1981 [C], Hall 2001 [S], Local Expert Consensus [E])*.

   Note 2: Nosocomial infection may place medically fragile infants and children at increased risk for morbidity and mortality upon exposure to the hospital environment *(Langley 1997 [C])*.

   Note 3: Follow Respiratory/Contact precautions as described for bronchiolitis in the CCHMC Infection Control Manual (ICRM-735) *(Local Expert Consensus [E])*.

Assessment and Diagnosis

Clinical History and Physical Examination

3. It is recommended that the clinical history and physical examination be the basis for a diagnosis of bronchiolitis.

   The diagnosis of bronchiolitis and its severity is rooted in the clinician's interpretation of the constellation of characteristic findings and is not dependent on any specific clinical finding or diagnostic test *(Bordley 2004 [M])*. Infants with acute bronchiolitis may present with a wide range of clinical symptoms and severity, from mild upper respiratory infections (URI) to impending respiratory failure.

   Diagnostic criteria for bronchiolitis include, but are not limited to, the following:
   - preceding upper respiratory illness and/or rhinorrhea
   - signs of respiratory illness which may include the following common URI symptoms:
     - wheezing
     - retractions
     - shortness of breath
     - low O_2 saturation
     - tachypnea
     - color change
     - nasal flaring
   - signs of dehydration
   - exposure to persons with viral upper respiratory infection.

Laboratory and Radiologic Studies

4. It is recommended that routine diagnostic studies (RSV swab, chest X-rays, cultures, capillary or arterial blood gases, rapid influenza or other rapid

viral studies) **not** be performed to determine viral infection status or to rule out serious bacterial infections. Such studies are not generally helpful and may result in increased rates of unnecessary admission, further testing, and unnecessary therapies *(Bordley 2004 [M], Swingler 1998 [A], El-Radhi 1999 [C], Kuppermann 1997 [C], Liebelt 1999 [D], Antonow 1998 [D], Schwartz 1995 [S], Chiocca 1994 [S], Lugo 1993 [S], Stark 1991 [S])*.

Note 1: Chest X rays may be obtained as clinically indicated when the diagnosis of bronchiolitis is not clear *(Swingler 1998 [A], El-Radhi 1999 [C])*.

Note 2: Capillary or arterial blood gases and pulse oximetry may be obtained as clinically indicated for individual patients *(Local Expert Consensus [E])*.

Note 3: In selected very young infants, establishing a source through rapid viral testing may prevent unnecessary additional workup *(Bordley 2004 [M])*.

Management

General

The basic management of typical bronchiolitis is anchored in the provision of therapies that assures that the patient is clinically stable, well oxygenated, and well hydrated. The main benefits of hospitalization of infants with acute bronchiolitis are:

- the careful monitoring of clinical status,
- maintenance of a patent airway (through positioning, suctioning, and mucus clearance),
- maintenance of adequate hydration, and
- parental education

(Klassen 1997 [S], Lugo 1993 [S], Panitch 1993 [S], Nicolai 1990 [S], Local Expert Consensus [E]).

Medications and Oxygen

5. It is recommended to consider starting supplemental oxygen when the saturation is **consistently** less than 91% and consider weaning oxygen when **consistently** higher than 94% *(NIH 1997 [E], Local Expert Consensus [E])*.

   Oxygen therapy is frequently required in the treatment of bronchiolitis. See Monitoring section for recommendation regarding oxygen saturation monitoring to maintain blood oxygen levels within a normal range. This range is variable in definition and patient-specific.

6. It is recommended that scheduled or serial albuterol aerosol therapies **not** be **routinely** used *(Kellner 2005 [M], Flores 1997 [M], Kellner 1996 [M], Goh 1997 [A], Dobson 1998 [B], Chowdhury 1995 [B], Lugo 1998 [C], Lenney 1978 [D])*.

   Note 1: Although in some cases bronchiolitis may be a prelude to asthma *(Martinez 1995 [C], Stark 1991 [S])*, in the majority of cases the use of inhalation therapies and other treatments effective for treating the bronchospasm characteristic in asthma will not be efficacious for treating the airway edema typical of bronchiolitis *(Hall 2001 [S], Klassen 1997 [S])*.

   Note 2: Two meta-analyses of randomized, controlled trials have not shown dramatic effects on clinical scores or hospitalization rates from therapy with nebulized albuterol in children with bronchiolitis *(Flores 1997 [M], Kellner 1996 [M])*.

   Note 3: Deterioration and desaturation has been associated with inhalation therapies *(Flores 1997 [M], Ho 1991 [B])*.

7. It is recommended that a single administration trial inhalation using epinephrine or albuterol may be considered as an option, particularly when there is a family history for allergy, asthma, or atopy *(Hartling 2003 [M], Klassen 1997 [S])*.

   Note 1: Nebulized racemic epinephrine was shown to result in better improvement in pulmonary physiology and clinical scores compared with albuterol or placebo in several studies and one systematic review. These effects predominated in mildly ill children and were transient (30 to 60 minutes) in duration *(Hartling 2003 [M], Wainwright 2003 [A], Numa 2001 [O])*.

   Note 2: See Respiratory Care Therapy section regarding the **importance of suctioning** before any inhalation therapy.

   Note 3: The expected disposition of a patient may influence the choice of beta-agonist when a single administration trial is given. There is a lack of research regarding the appropriateness of routine epinephrine use outside the acute care setting *(Local Expert Consensus [E])*.

8. It is recommended that inhalation therapy **not** be repeated nor continued if there is no improvement in clinical appearance between 15 to 30 minutes after a trial inhalation therapy *(Klassen 1997 [S], Bausch & Lomb Pharmaceuticals 1999 [O])*.

   Note: In order to determine appropriateness of repeated therapy, use the Bronchiolitis Respiratory Sheet to record pre- and post-clinical score *(Conway 2004 [C])*.

9. It is recommended that antibiotics **not** be used in the absence of an identified bacterial focus.

   Note 1: The incidence of serious bacterial illness (SBI) has been reported to be less than 2% in bronchiolitis patients 60 days of age or younger *(Friis 1984 [B], Kuppermann 1997 [C], Purcell 2004 [D], Purcell 2002 [D], Liebelt 1999 [D], Antonow 1998 [D])*. See CCHMC Evidence Based Clinical Practice Guidelines for Fever of Uncertain Source 0-60 days or 2-36 months, Acute Otitis Media, Community-Acquired Pneumonia, and First Time Acute Urinary Tract Infection.

   Note 2: In almost 75% of patients with RSV infections, the virus may be isolated from the middle ear *(Heikkinen 1999 [C], Andrade 1998 [C], Pitkaranta 1998 [C])*. In patients with RSV and otitis media, a bacterial pathogen has been isolated in 25 out of 26 *(Andrade 1998 [C])* and one out of eight *(Pitkaranta 1998 [C])* middle ear fluid specimens after typanocentesis.

   Note 3: Antibiotics have little, if any, effect on outcomes from otitis media *(Glasziou 2005 [M], Marcy 2001 [M], Del Mar 1997 [M], Rosenfeld 1994 [M])*.

10. It is recommended that antihistamines, oral decongestants, and nasal vasoconstrictors **not** be used for routine therapy.

    Note 1: There is no evidence to date for efficacy of these medications in reduction of cough or congestion in infants with upper and lower respiratory tract infections *(Clemens 1997 [B], Hutton 1991 [B], AAP 1997 [S], Gadomski 1992 [O])*.

    Note 2: Some components of these medications have been shown to be harmful to humans *(Kernan 2000 [D])*.

11. It is recommended that steroid therapy **not** be given (as inhalations, intravenously, orally, or intramuscularly) *(King 2004 [M], Garrison 2000 [M])*.

    Note: One well-conducted systematic review found a reduction in length of stay of 0.43 days (95% CI 0.8 to 0.05) with steroid therapy for bronchiolitis *(Garrison 2000 [M])*. However, when only the more methodologically rigorous studies with more specific definitions of bronchiolitis were analyzed in this meta-analysis, there was no significant effect of steroids on clinical status or length of stay.

Respiratory Care Therapy

12. It is recommended the infant be **suctioned,** when clinically indicated:
    - before feedings,
    - PRN, and
    - prior to each inhalation therapy

    (Local Expert Consensus [E]).

    In order to appropriately measure improvement in clinical status due to the therapeutic effects of the medication, the following reasons for suctioning are considered:
    - Suctioning itself may improve respiratory status such that inhalation therapy is not necessary. Thus, it is important to document the pre-and post-suction clinical score prior to treatment.
    - Suctioning may improve the delivery of the inhalation treatment.

    (Local Expert Consensus [E]).

    Note: Normal saline nose drops may be used prior to suctioning *(Local Expert Consensus [E])*.

13. It is recommended that other routine respiratory care therapies **not** be used, as they have not been found to be helpful. These include:
    - chest physiotherapy (CPT) *(Perrotta 2005 [M])*.
    - cool mist therapy *(Gibson 1974 [S])*.
    - aerosol therapy with saline *(Gadomski 1994 [A], Chowdhury 1995 [B], Ho 1991 [B])*.

Monitoring

14. It is recommended that repeated **clinical** assessment be conducted, as this is the most important aspect of monitoring for deteriorating respiratory status *(Local Expert Consensus [E])*.

15. It is recommended to consider cardiac and respiratory rate monitoring in hospitalized patients during the acute stage of bronchiolitis when the risk of apnea and/or bradycardia is greatest *(Anas 1982 [C], Church 1984 [D])*.

    Note 1: Premature infants, infants with underlying chronic conditions, and infants less than three months of age who contract RSV are at particular risk of severe complications such as apnea and mechanical ventilation *(Wang 1995 [C], Anas 1982 [C], Krasinski 1985 [D], Church 1984 [D])*.

    Note 2: Several studies have reported more severe progression of disease in children with bronchiolitis who present with low initial oxygen saturations *(Wang 1995 [C], Shaw 1991 [C], Mulholland 1990 [D])*.

16. It is recommended that scheduled spot checks of pulse oximetry be utilized in infants with bronchiolitis *(Local Expert Consensus [E])*.

    Note 1: Continuous oximetry measurement has been associated with increased length of stay of 1.6 days (95% CI 1.1 to 2.0) on average *(Schroeder 2004 [D])*.

    Note 2: Wide variability has been demonstrated in the manner in which clinicians use and interpret pulse oximetry readings in children with bronchiolitis. This variability has been shown to be associated with increased preferences for hospital admission and increased length of stay for children admitted with bronchiolitis *(Schroeder 2004 [D], Mallory 2003 [O])*.

    Note 3: In a prospective study of healthy, term infants, transient oxygen desaturation episodes were documented and were determined to be representative of normal breathing and oxygenation behavior. This study excluded any decreases in oxygen saturation related to the infants' movement which would interfere with measurement *(Hunt 1999 [C])*.

Discharge Criteria

17. It is recommended to begin discharge planning on admission *(Local Expert Consensus [E])*. Discharge criteria are:

    Respiratory Status
    - respirations less than 70 per minute and no clinical evidence of increased work of breathing
    - parent can clear the infant's airway using bulb suctioning
    - patient is either on room air or on stable oxygen therapy that is at a level considered consistent with being able to effectively continue the therapy at home

    Nutritional Status
    - the patient is on oral feedings at a level to prevent dehydration

    Social
    - home resources are adequate to support the use of any necessary home therapies
    - parent or guardian is confident they can provide care at home
    - family education complete

    Follow Up
    - when indicated, home care and durable medical supply (DMS) agencies have been notified and arrangements for visits finalized
    - primary care provider identified, notified, and agrees with discharge decision
    - follow-up appointments have been scheduled.

Education

18. It is recommended that the family be educated on the following topics regarding the care of a child with bronchiolitis:
    - basic pathophysiology and expected clinical course of bronchiolitis

      Note: The median duration of illness for children < 24 months with bronchiolitis is 12 days; after 21 days approximately 18% will remain ill, and after 28 days 9% will remain ill *(Swingler 2000 [C])*.
    - proper techniques for suctioning the nose and making breathing easier *(Local Expert Consensus [E])*
    - to call their primary care provider when the following signs of worsening clinical status are observed *(Local Expert Consensus [E])*
        a. increasing respiratory rate and/or work of breathing as indicated by accessory muscle use
        b. inability to maintain adequate hydration
        c. worsening general appearance.

19. It is recommended that the family be educated on the following topics regarding prevention of respiratory infection in infants:
    - eliminating exposure to environmental tobacco smoke *(Mahabee-Gittens 2002 [O])*
    - limiting exposure to contagious settings and siblings (e.g. daycare centers) *(Celedon 1999 [C])*
    - an emphasis on handwashing in all settings *(Hall 1981 [C])*.

Health Topics on CCHMC's website[b]:
- Bronchiolitis
- Bronchiolitis – Essential Facts
- Suctioning the Nose with a Bulb Syringe
- Second Hand Smoke Dangers

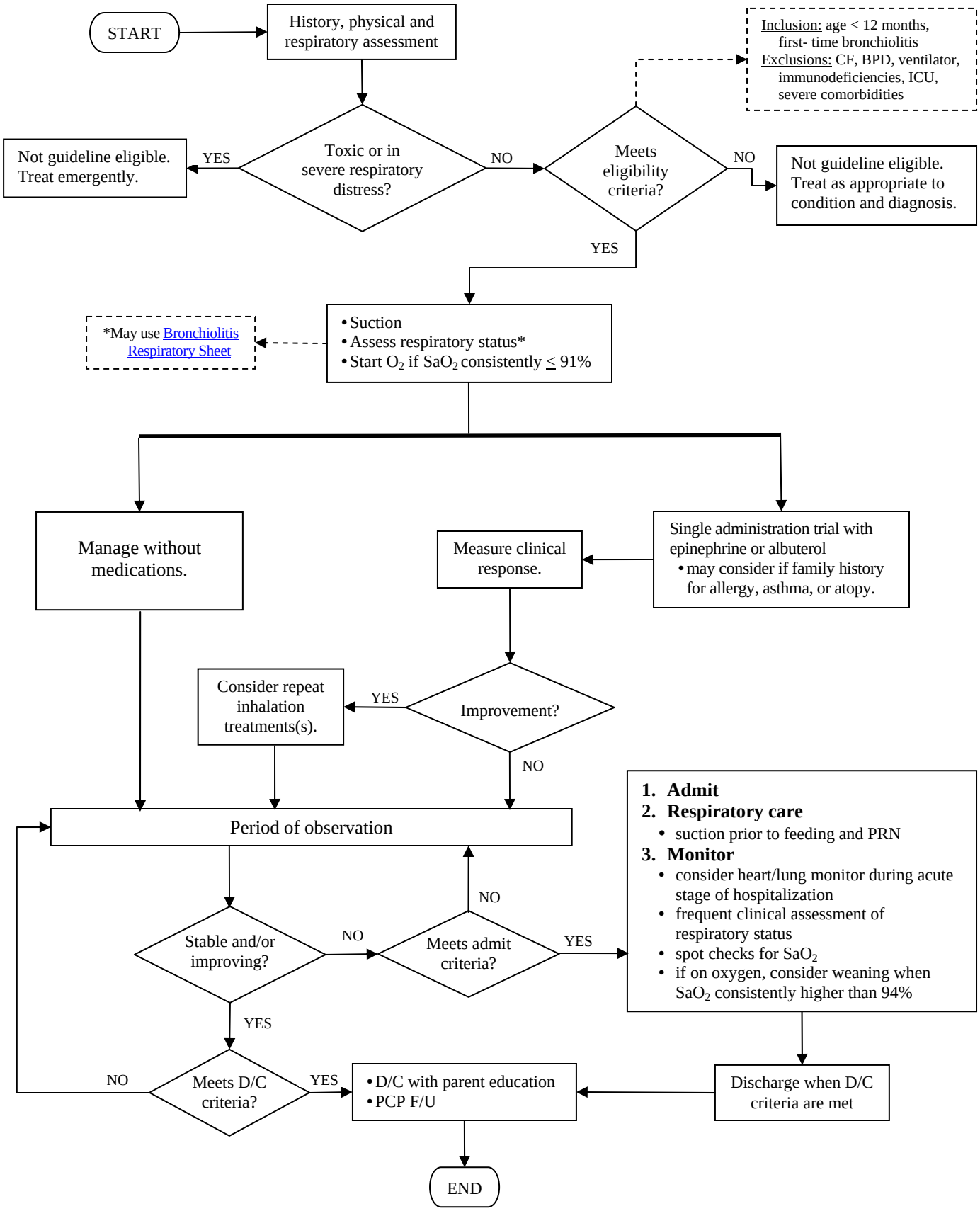
Future Research Agenda

Clinical questions related to guideline recommendations and of potential interest to CCHMC investigators in the population of bronchiolitic infants:
- What is the effect of suctioning on hospitalization rates?

[b] CCHMC Health Topic website: www.cincinnatichildrens.org/health/info

- What is the effect of continuous versus spot check pulse oximetry in bronchiolitic infants on safety and on length of stay?
- What is the role of epinephrine in management in the outpatient and home settings?
- What is the effect of the use of beta agonists on length of stay?
- What is the role of epinephrine versus albuterol in inpatient management?
- Is there a validated clinical scoring tool for measuring respiratory status?

Algorithm for medical management of Bronchiolitis
in infants less than 1 year of age presenting with a first time episode



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Development Process

The process by which this guideline was developed is documented in the Guideline Development Process Manual; a Team Binder maintains minutes and other relevant development materials. The recommendations contained in this guideline were formulated by an interdisciplinary working group which performed systematic and critical literature reviews, using the grading scale that follows, and examined current local clinical practices.

To select evidence for critical appraisal by the group, the Medline, EmBase and the Cochrane databases were searched for dates of October 2001 through October 2004 to generate an unrefined, "combined evidence" database using a search strategy focused on answering clinical questions relevant to bronchiolitis and employing a combination of Boolean searching on human-indexed thesaurus terms (MeSH headings using an OVID Medline interface) and "natural language" searching on words in the title, abstract, and indexing terms. The citations were reduced by: eliminating duplicates, review articles, non-English articles, and adult articles. The resulting abstracts were reviewed by a methodologist to eliminate low quality and irrelevant citations. During the course of the guideline development and revision, additional clinical questions were generated and subjected to the search process, and some relevant review articles were identified. August 2001 was the last date for which literature was searched for the previous version of the guideline. The details of previous review strategies are not documented. However, all citations carried from an earlier version were reviewed for appropriateness to this revision.

Evidence Grading Scale			
A	Randomized controlled trial: large sample	S	Review article
B	Randomized controlled trial: small sample	M	Meta-analysis
C	Prospective trial or large case series	Q	Decision analysis
D	Retrospective analysis	L	Legal requirement
E	Expert opinion or consensus	O	Other evidence
F	Basic laboratory research	X	No evidence

A search using the above criteria was conducted for dates of November, 2004 through May, 2006. Thirty-one relevant articles were selected as potential future citations for the guideline. However, none of these references were determined to require changes to the 2005 version of the recommendations.

Appropriate companion documents have been developed to assist in the effective dissemination and implementation of the guideline. Experience with the implementation of earlier version of this guideline has provided learnings which have been incorporated into this revision *(Conway 2004 [C], Perlstein 2000 [D], Perlstein 1999 [D], Muething 2004 [O], Kotagal 2002 [O]).*

Once the guideline has been in place for three years, the development team reconvenes to explore the continued validity of the guideline. This phase can be initiated at any point that evidence indicates a critical change is needed.

Recommendations have been formulated by a consensus process directed by best evidence, patient and family preference and clinical expertise. During formulation of these recommendations, the team members have remained cognizant of controversies and disagreements over the management of these patients. They have tried to resolve controversial issues by consensus where possible and, when not possible, to offer optional approaches to care in the form of information that includes best supporting evidence of efficacy for alternative choices.

The guidelines have been reviewed and approved by clinical experts not involved in the development process, senior management, Risk Management & Corporate Compliance, the Institutional Review Board, other appropriate hospital committees, and other individuals as appropriate to their intended purposes.

The guideline was developed without external funding. All Team Members and Clinical Effectiveness support staff listed have declared whether they have any conflict of interest and none were identified.

NOTE: These recommendations result from review of literature and practices current at the time of their formulations. This protocol does not preclude using care modalities proven efficacious in studies published subsequent to the current revision of this document. This document is not intended to impose standards of care preventing selective variances from the guidelines to meet the specific and unique requirements of

individual patients. Adherence to this pathway is voluntary. The physician in light of the individual circumstances presented by the patient must make the ultimate judgment regarding the priority of any specific procedure.

For more information about these guidelines, their supporting evidences and the guideline development process, contact the Health Policy & Clinical Effectiveness office at: 513-636-2501 or HPCEInfo@cchmc.org.

References

1. **AAP:** Committee on Drugs. Use of codeine- and dextromethorphan-containing cough remedies in children. *Pediatrics*, 99(6): 918-20, 1997, *[S]* _____ ☜.
2. **Aitken, M., and Taylor, J. A.:** Prevalence of clinical sinusitis in young children followed up by primary care pediatricians. *Arch Pediatr Adolesc Med*, 152(3): 244-8, 1998, *[C]* _____ ☜.
3. **Anas, N.; Boettrich, C.; Hall, C. B.; and Brooks, J. G.:** The association of apnea and respiratory syncytial virus infection in infants. *J Pediatr*, 101(1): 65-8, 1982, *[C]* _____ ☜.
4. **Andrade, M. A.; Hoberman, A.; Glustein, J.; Paradise, J. L.; and Wald, E. R.:** Acute otitis media in children with bronchiolitis. *Pediatrics*, 101(4 Pt 1): 617-9, 1998, *[C]* _____ ☜.
5. **Andreoletti, L.; Lesay, M.; Deschildre, A.; Lambert, V.; Dewilde, A.; and Wattre, P.:** Differential detection of rhinoviruses and enteroviruses RNA sequences associated with classical immunofluorescence assay detection of respiratory virus antigens in nasopharyngeal swabs from infants with bronchiolitis. *J Med Virol*, 61(3): 341-6, 2000, *[C]* _____ ☜.
6. **Antonow, J. A.; Hansen, K.; McKinstry, C. A.; and Byington, C. L.:** Sepsis evaluations in hospitalized infants with bronchiolitis. *Pediatr Infect Dis J*, 17(3): 231-6., 1998, *[D]* _____ ☜.
7. **Bausch & Lomb Pharmaceuticals, I.:** *Albuterol Sulfate Inhalation Solution, 0.5%*. Clinical Pharmacology, Clinical Trials Tampa, FL, 1999, *[O]*.
8. **Bordley, W. C.; Viswanathan, M.; King, V. J.; Sutton, S. F.; Jackman, A. M.; Sterling, L.; and Lohr, K. N.:** Diagnosis and testing in bronchiolitis: a systematic review. *Arch Pediatr Adolesc Med*, 158(2): 119-26, 2004, *[M]* _____ ☜.
9. **Boyce, T. G.; Mellen, B. G.; Mitchel, E. F., Jr.; Wright, P. F.; and Griffin, M. R.:** Rates of hospitalization for respiratory syncytial virus infection among children in medicaid. *J Pediatr*, 137(6): 865-70, 2000, *[D]* _____ ☜.
10. **Celedon, J. C.; Litonjua, A. A.; Weiss, S. T.; and Gold, D. R.:** Day care attendance in the first year of life and illnesses of the upper and lower respiratory tract in children with a familial history of atopy. *Pediatrics*, 104(3 Pt 1): 495-500, 1999, *[C]* _____ ☜.
11. **Chiocca, E. M.:** RSV and the high-risk infant. *Pediatr Nurs*, 20(6): 565-8., 1994, *[S]* _____ ☜.
12. **Chowdhury, D.; al Howasi, M.; Khalil, M.; al-Frayh, A. S.; Chowdhury, S.; and Ramia, S.:** The role of bronchodilators in the management of bronchiolitis: a clinical trial. *Ann Trop Paediatr*, 15(1): 77-84, 1995, *[B]* _____ ☜.
13. **Church, N. R.; Anas, N. G.; Hall, C. B.; and Brooks, J. G.:** Respiratory syncytial virus-related apnea in infants. Demographics and outcome. *Am J Dis Child*, 138(3): 247-50, 1984, *[D]* _____ ☜.
14. **Clemens, C. J.; Taylor, J. A.; Almquist, J. R.; Quinn, H. C.; Mehta, A.; and Naylor, G. S.:** Is an antihistamine-decongestant combination effective in temporarily relieving symptoms of the common cold in preschool children? *J Pediatr*, 130(3): 463-6., 1997, *[B]* _____ ☜.
15. **Conway, E.; Schoettker, P. J.; Moore, A.; Britto, M. T.; Kotagal, U. R.; and Rich, K.:** Empowering respiratory therapists to take a more active role in delivering quality care for infants with bronchiolitis. *Respir Care*, 49(6): 589-99, 2004, *[C]* _____ ☜.
16. **Del Mar, C.; Glasziou, P.; and Hayem, M.:** Are antibiotics indicated as initial treatment for children with acute otitis media? A meta-analysis. *BMJ*, 314(7093): 1526-9, 1997, *[M]* _____ ☜.
17. **Dobson, J. V.; Stephens-Groff, S. M.; McMahon, S. R.; Stemmler, M. M.; Brallier, S. L.; and Bay, C.:** The use of albuterol in hospitalized infants with bronchiolitis. *Pediatrics*, 101(3 Pt 1): 361-8, 1998, *[B]* _____ ☜.
18. **El-Radhi, A. S.; Barry, W.; and Patel, S.:** Association of fever and severe clinical course in bronchiolitis. *Arch Dis Child*, 81(3): 231-4, 1999, *[C]* _____ ☜.
19. **Flores, G., and Horwitz, R. I.:** Efficacy of beta2-agonists in bronchiolitis: a reappraisal and meta-analysis. *Pediatrics*, 100(2 Pt 1): 233-9, 1997, *[M]* _____ ☜.
20. **Friis, B. et al.:** Antibiotic treatment of pneumonia and bronchiolitis. A prospective randomised study. *Arch Dis Child*, 59(11): 1038-45., 1984, *[B]* _____ ☜.
21. **Gadomski, A., and Horton, L.:** The need for rational therapeutics in the use of cough and cold medicine in infants. *Pediatrics*, 89(4 Pt 2): 774-6., 1992, *[O]* _____ ☜.
22. **Gadomski, A. M.; Aref, G. H.; el Din, O. B.; el Sawy, I. H.; Khallaf, N.; and Black, R. E.:** Oral versus nebulized albuterol in the management of bronchiolitis in Egypt. *J Pediatr*, 124(1): 131-8, 1994, *[A]* _____ ☜.
23. **Garrison, M. M.; Christakis, D. A.; Harvey, E.; Cummings, P.; and Davis, R. L.:** Systemic corticosteroids in infant bronchiolitis: A meta-analysis. *Pediatrics*, 105(4): E44, 2000, *[M]* _____ ☜.
24. **Gibson, L. E.:** Use of water vapor in the treatment of lower respiratory disease. *Am Rev Respir Dis*, 110(6 Pt 2): 100-3, 1974, *[S]* _____ ☜.
25. **Glasziou, P. P.; Del Mar, C. B.; Sanders, S. L.; and Hayem, M.:** Antibiotics for acute otitis media in children. *Cochrane Database Syst Rev*, (1), 2005, *[M]* _____ ☜.
26. **Goh, A.; Chay, O. M.; Foo, A. L.; and Ong, E. K.:** Efficacy of bronchodilators in the treatment of bronchiolitis. *Singapore Med J*, 38(8): 326-8, 1997, *[A]* _____ ☜.
27. **Green, M.; Brayer, A. F.; Schenkman, K. A.; and Wald, E. R.:** Duration of hospitalization in previously well infants with respiratory syncytial virus infection. *Pediatr Infect Dis J*, 8(9): 601-5, 1989, *[D]* _____ ☜.
28. **Hall, C. B.:** Respiratory syncytial virus and parainfluenza virus. *N Engl J Med*, 344(25): 1917-28, 2001, *[S]* _____ ☜.

29. **Hall, C. B.; Douglas, R. G., Jr.; Schnabel, K. C.; and Geiman, J. M.:** Infectivity of respiratory syncytial virus by various routes of inoculation. *Infect Immun*, 33(3): 779-83, 1981, *[C]* _____ ☜.

30. **Harrison, A. M.; Boeing, N. M.; Domachowske, J. B.; Piedmonte, M. R.; and Kanter, R. K.:** Effect of RSV bronchiolitis practice guidelines on resource utilization. *Clinical Pediatrics*, 40(9): 489-495, 2001, *[D]* _____ ☜.

31. **Hartling, L.; Wiebe, N.; Russell, K.; Patel, H.; and Klassen, T. P.:** A meta-analysis of randomized controlled trials evaluating the efficacy of epinephrine for the treatment of acute viral bronchiolitis. *Arch Pediatr Adolesc Med*, 157(10): 957-64, 2003, *[M]* _____ ☜.

32. **Heikkinen, T.; Thint, M.; and Chonmaitree, T.:** Prevalence of various respiratory viruses in the middle ear during acute otitis media. *N Engl J Med*, 340(4): 260-4, 1999, *[C]* _____ ☜.

33. **Heikkinen, T.; Valkonen, H.; Lehtonen, L.; Vainionpaa, R.; and Ruuskanen, O.:** Hospital admission of high risk infants for respiratory syncytial virus infection: implications for palivizumab prophylaxis. *Arch Dis Child Fetal Neonatal Ed*, 90(1): F64-8, 2005, *[C]* _____ ☜.

34. **Ho, L.; Collis, G.; Landau, L. I.; and Le Souef, P. N.:** Effect of salbutamol on oxygen saturation in bronchiolitis. *Arch Dis Child*, 66(9): 1061-4, 1991, *[B]* _____ ☜.

35. **Hunt, C. E.; Corwin, M. J.; Lister, G.; Weese-Mayer, D. E.; Neuman, M. R.; Tinsley, L.; Baird, T. M.; Keens, T. G.; and Cabral, H. J.:** 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*, 135(5): 580-6, 1999, *[C]* _____ ☜.

36. **Hutton, N.; Wilson, M. H.; Mellits, E. D.; Baumgardner, R.; Wissow, L. S.; Bonuccelli, C.; Holtzman, N. A.; and DeAngelis, C.:** Effectiveness of an antihistamine-decongestant combination for young children with the common cold: a randomized, controlled clinical trial. *J Pediatr*, 118(1): 125-30., 1991, *[B]* _____ ☜.

37. **IMpact-RSV Study Group:** Palivizumab, a Humanized Respiratory Syncytial Virus Monoclonal Antibody, Reduces Hospitalization From Respiratory Syncytial Virus Infection in High-risk Infants. *Pediatrics*, 102(3): 531-7, 1998, *[A]* _____ ☜.

38. **Joffe, S.; Escobar, G. J.; Black, S. B.; Armstrong, M. A.; and Lieu, T. A.:** Rehospitalization for respiratory syncytial virus among premature infants. *Pediatrics*, 104(4 Pt 1): 894-9, 1999, *[D]* _____ ☜.

39. **Joffe, S.; Ray, G. T.; Escobar, G. J.; Black, S. B.; and Lieu, T. A.:** Cost-effectiveness of respiratory syncytial virus prophylaxis among preterm infants. *Pediatrics*, 104(3 Pt 1): 419-27, 1999, *[Q]* _____ ☜.

40. **Kellner, J. D.; Ohlsson, A.; Gadomski, A. M.; and Wang, E. E.:** Efficacy of bronchodilator therapy in bronchiolitis. A meta-analysis. *Arch Pediatr Adolesc Med*, 150(11): 1166-72, 1996, *[M]* _____ ☜.

41. **Kellner, J. D.; Ohlsson, A.; Gadomski, A. M.; and Wang, E. E. L.:** Bronchodilators for bronchiolitis. *Cochrane Database Syst Rev*, (2), 2005, *[M]* _____ ☜.

42. **Kernan, W. N.; Viscoli, C. M.; Brass, L. M.; Broderick, J. P.; Brott, T.; Feldmann, E.; Morgenstern, L. B.; Wilterdink, J. L.; and Horwitz, R. I.:** Phenylpropanolamine and the risk of hemorrhagic stroke. *N Engl J Med*, 343(25): 1826-32., 2000, *[D]* _____ ☜.

43. **King, V. J.; Viswanathan, M.; Bordley, W. C.; Jackman, A. M.; Sutton, S. F.; Lohr, K. N.; and Carey, T. S.:** Pharmacologic treatment of bronchiolitis in infants and children: a systematic review. *Arch Pediatr Adolesc Med*, 158(2): 127-37, 2004, *[M]* _____ ☜.

44. **Klassen, T. P.:** Recent advances in the treatment of bronchiolitis and laryngitis. *Pediatr Clin North Am*, 44(1): 249-61., 1997, *[S]* _____ ☜.

45. **Kotagal, U. R.; Robbins, J. M.; Kini, N. M.; Schoettker, P. J.; Atherton, H. D.; and Kirschbaum, M. S.:** Impact of a bronchiolitis guideline: a multisite demonstration project. *Chest*, 121(6): 1789-97, 2002, *[O]* _____ ☜.

46. **Krasinski, K.:** Severe respiratory syncytial virus infection: clinical features, nosocomial acquisition and outcome. *Pediatr Infect Dis*, 4(3): 250-7, 1985, *[D]* _____ ☜.

47. **Kuppermann, N.; Bank, D. E.; Walton, E. A.; Senac, M. O., Jr.; and McCaslin, I.:** Risks for bacteremia and urinary tract infections in young febrile children with bronchiolitis. *Arch Pediatr Adolesc Med*, 151(12): 1207-14, 1997, *[C]* _____ ☜.

48. **Langley, J. M. et al.:** Nosocomial respiratory syncytial virus infection in Canadian pediatric hospitals: a Pediatric Investigators Collaborative Network on Infections in Canada Study. *Pediatrics*, 100(6): 943-6, 1997, *[C]* _____ ☜.

49. **Lenney, W., and Milner, A. D.:** Alpha and beta adrenergic stimulants in bronchiolitis and wheezy bronchitis in children under 18 months of age. *Arch Dis Child*, 53(9): 707-9., 1978, *[D]* _____ ☜.

50. **Liebelt, E. L.; Qi, K.; and Harvey, K.:** Diagnostic testing for serious bacterial infections in infants aged 90 days or younger with bronchiolitis. *Arch Pediatr Adolesc Med*, 153(5): 525-30, 1999, *[D]* _____ ☜.

51. **Local Expert Consensus:** During guideline development timeframe. *[E]*.

52. **Lugo, R. A., and Nahata, M. C.:** Pathogenesis and treatment of bronchiolitis. *Clin Pharm*, 12(2): 95-116., 1993, *[S]* _____ ☜.

53. **Lugo, R. A.; Salyer, J. W.; and Dean, J. M.:** Albuterol in acute bronchiolitis--continued therapy despite poor response? *Pharmacotherapy*, 18(1): 198-202, 1998, *[C]* _____ ☜.

54. **Mahabee-Gittens, M.:** Smoking in parents of children with asthma and bronchiolitis in a pediatric emergency department. *Pediatr Emerg Care*, 18(1): 4-7, 2002, *[O]* _____ ☜.

55. **Mallory, M. D.; Shay, D. K.; Garrett, J.; and Bordley, W. C.:** Bronchiolitis management preferences and the influence of pulse oximetry and respiratory rate on the decision to admit. *Pediatrics*, 111(1): e45-51, 2003, *[O]* _____ ☜.

56. **Marcy, M. et al.:** Management of acute otitis media. Evidence Report/Technology Assessment No. 15. *AHRQ Publication*, No. 01-E010: 1- 379, 2001, *[M]* _____ ☜.

57. **Martinez, F. D.; Wright, A. L.; Taussig, L. M.; Holberg, C. J.; Halonen, M.; and Morgan, W. J.:** Asthma and wheezing in the first six years of life. The Group Health Medical Associates. *N Engl J Med*, 332(3): 133-8, 1995, *[C]* _____ ☜.

58. **Muething, S.; Schoettker, P. J.; Gerhardt, W. E.; Atherton, H. D.; Britto, M. T.; and Kotagal, U. R.:** Decreasing overuse of therapies in the treatment of bronchiolitis by incorporating evidence at the point of care. *J Pediatr*, 144(6): 703-10, 2004, *[O]* _____ ☜.

59. **Mulholland, E. K.; Olinsky, A.; and Shann, F. A.:** Clinical findings and severity of acute bronchiolitis. *Lancet*, 335(8700): 1259-61, 1990, *[D]* _____ ☜.

60. **Nicolai, T., and Pohl, A.:** Acute viral bronchiolitis in infancy: epidemiology and management. *Lung*, 168(Suppl): 396-405., 1990, *[S]* _____ ☜.

61. **NIH:** NIH Guidelines for the diagnosis and management of asthma (Expert Panel Report 2). 112, 1997, *[E]* ____ ☜.

62. **Numa, A. H.; Williams, G. D.; and Dakin, C. J.:** The effect of nebulized epinephrine on respiratory mechanics and gas exchange in bronchiolitis. *Am J Respir Crit Care Med*, 164(1): 86-91, 2001, *[O]* _____ ☜.

63. **Panitch, H. B.; Callahan, C. W.; and Schidlow, D. V.:** Bronchiolitis in children. *Clin Chest Med*, 14(4): 715-31., 1993, *[S]* _____ ☜.

64. **Perlstein, P. H.; Kotagal, U. R.; Bolling, C.; Steele, R.; Schoettker, P. J.; Atherton, H. D.; and Farrell, M. K.:** Evaluation of an evidence-based guideline for bronchiolitis. *Pediatrics*, 104(6): 1334-41, 1999, *[D]* _____ ☜.

65. **Perlstein, P. H.; Kotagal, U. R.; Schoettker, P. J.; Atherton, H. D.; Farrell, M. K.; Gerhardt, W. E.; and Alfaro, M. P.:** Sustaining the implementation of an evidence-based guideline for bronchiolitis. *Arch Pediatr Adolesc Med*, 154(10): 1001-7, 2000, *[D]* _____ ☜.

66. **Perrotta, C.; Ortiz, Z.; and Roque, M.:** Chest physiotherapy for acute bronchiolitis in paediatric patients between 0 and 24 months old. *Cochrane Database Syst Rev*, (2): CD004873, 2005, *[M]* _____ ☜.

67. **Pitkaranta, A.; Jero, J.; Arruda, E.; Virolainen, A.; and Hayden, F. G.:** Polymerase chain reaction-based detection of rhinovirus, respiratory syncytial virus, and coronavirus in otitis media with effusion. *J Pediatr*, 133(3): 390-4, 1998, *[C]* _____ ☜.

68. **Purcell, K., and 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*, 23(3): 267-9, 2004, *[D]* _____ ☜.

69. **Purcell, K., and Fergie, J.:** Concurrent serious bacterial infections in 2396 infants and children hospitalized with respiratory syncytial virus lower respiratory tract infections. *Arch Pediatr Adolesc Med*, 156(4): 322-4, 2002, *[D]* _____ ☜.

70. **Rosenfeld, R. M.; Vertrees, J. E.; Carr, J.; Cipolle, R. J.; Uden, D. L.; Giebink, G. S.; and Canafax, D. M.:** Clinical efficacy of antimicrobial drugs for acute otitis media: metaanalysis of 5400 children from thirty-three randomized trials. *J Pediatr*, 124(3): 355-67, 1994, *[M]* _____ ☜.

71. **Schroeder, A. R.; Marmor, A. K.; Pantell, R. H.; and Newman, T. B.:** Impact of pulse oximetry and oxygen therapy on length of stay in bronchiolitis hospitalizations. *Arch Pediatr Adolesc Med*, 158(6): 527-30, 2004, *[D]* _____ ☜.

72. **Schwartz, R.:** Respiratory syncytial virus in infants and children. *Nurse Pract*, 20(9): 24-9., 1995, *[S]* _____ ☜.

73. **Shaw, K. N.; Bell, L. M.; and Sherman, N. H.:** Outpatient assessment of infants with bronchiolitis. *Am J Dis Child*, 145(2): 151-5, 1991, *[C]* _____ ☜.

74. **Shay, D. K.; Holman, R. C.; Newman, R. D.; Liu, L. L.; Stout, J. W.; and Anderson, L. J.:** Bronchiolitis-associated hospitalizations among US children, 1980-1996. *JAMA*, 282(15): 1440-6, 1999, *[O]* _____ ☜.

75. **Shay, D. K.; Holman, R. C.; Roosevelt, G. E.; Clarke, M. J.; and Anderson, L. J.:** Bronchiolitis-associated mortality and estimates of respiratory syncytial virus-associated deaths among US children, 1979-1997. *J Infect Dis*, 183(1): 16-22, 2001, *[D]* _____ ☜.

76. **Stark, J. M., and Busse, W. W.:** Respiratory virus infection and airway hyerreactivity in children. *Pediatr Allergy Immunol*, 2: 95-110, 1991, *[S]*.

77. **Swingler, G. H.; Hussey, G. D.; and Zwarenstein, M.:** Duration of illness in ambulatory children diagnosed with bronchiolitis. *Arch Pediatr Adolesc Med*, 154(10): 997-1000, 2000, *[C]* _____ ☜.

78. **Swingler, G. H.; Hussey, G. D.; and Zwarenstein, M.:** Randomised controlled trial of clinical outcome after chest radiograph in ambulatory acute lower-respiratory infection in children. *Lancet*, 351(9100): 404-8., 1998, *[A]* _____ ☜.

79. **van Woensel, J. B.; Kimpen, J. L.; Sprikkelman, A. B.; Ouwehand, A.; and van Aalderen, W. M.:** Long-term effects of prednisolone in the acute phase of bronchiolitis caused by respiratory syncytial virus. *Pediatr Pulmonol*, 30(2): 92-6, 2000, *[B]* _____ ☜.

80. **Wainwright, C. et al.:** A multicenter, randomized, double-blind, controlled trial of nebulized epinephrine in infants with acute bronchiolitis. *N Engl J Med*, 349(1): 27-35, 2003, *[A]* _____ ☜.

81. **Wald, E. R.; Guerra, N.; and Byers, C.:** Upper respiratory tract infections in young children: duration of and frequency of complications. *Pediatrics*, 87(2): 129-33, 1991, *[C]* _____ ☜.

82. **Wang, E. E.; Law, B. J.; and 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*, 126(2): 212-9, 1995, *[C]* _____ ☜.

83. **Wegner, S.; Vann, J. J.; Liu, G.; Byrns, P.; Cypra, C.; Campbell, W.; and Stiles, A.:** Direct cost analyses of palivizumab treatment in a cohort of at-risk children: evidence from the North Carolina Medicaid Program. *Pediatrics*, 114(6): 1612-9, 2004, *[C]* _____ ☜.

84. **Williams, J. V.; Harris, P. A.; Tollefson, S. J.; Halburnt-Rush, L. L.; Pingsterhaus, J. M.; Edwards, K. M.; Wright, P. F.; and Crowe, J. E., Jr.:** Human metapneumovirus and lower respiratory tract disease in otherwise healthy infants and children. *N Engl J Med*, 350(5): 443-50, 2004, *[C]* _____ ☜.

85. **Yount, L. E., and Mahle, W. T.:** Economic analysis of palivizumab in infants with congenital heart disease. *Pediatrics*, 114(6): 1606-11, 2004, *[Q]* _____ ☜.

