



## Community Acquired Pneumonia in children 60 days through 17 years of age<sup>a</sup>

Original Publication Date: July 11, 2000

Revision Publication Date: December 22, 2005

New search July, 2006 (see Development Process section)

### Target Population

**Inclusions:** Intended primarily for use in

- children 60 days through 17 years of age
- with signs, symptoms, or other findings suggesting a diagnosis of uncomplicated pneumonia
- acquired by exposure to organisms in the community.

**Exclusions:** The guidelines do not address all considerations needed to manage those with

- “toxic” appearance or requiring intensive care
- persistence of a neonatal cardiac or pulmonary disorder
- recent hospitalization with exposure to nosocomial flora
- likely aspiration of a foreign body or stomach contents
- congenital, acquired, or drug induced immunocompromise
- chronic conditions such as cystic fibrosis that uniquely alter pathophysiology and care options.

### Target Users

Include but are not limited to (in alphabetical order):

- Clinicians caring for inpatients
- Emergency Medicine physicians
- Infectious Diseases physicians

<sup>a</sup> Please cite as: **Community Acquired Pneumonia Guideline Team, Cincinnati Children's Hospital Medical Center:** Evidence-based care guideline for medical management of Community Acquired Pneumonia in children 60 days to 17 years of age, <http://www.cincinnatichildrens.org/svc/alpha/h/health-policy/ev-based/pneumonia.htm>, Guideline 14, pages 1-16, December 22, 2005.

- Patient Care staff, including:
  - nurses
  - respiratory therapists
- Patients and families
- Primary care providers
- Pulmonologists
- Radiologists
- Residents

### Introduction

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

This guideline revision presents new evidence concerning:

- etiology of community acquired pneumonia (CAP);
- a decline in the incidence of CAP due to *S. pneumoniae* as a result of the use of a heptavalent conjugated pneumococcal vaccine (PCV7, Prevnar<sup>®</sup>);
- refined clinical measures for identification of children with pneumonia;
- treatment of presumed bacterial pneumonia due to the increased prevalence of strains of *S. pneumoniae* which are either intermediately or highly resistant to penicillin.

Community acquired pneumonia (CAP) is an acute infection of the pulmonary parenchyma, acquired outside of a hospital setting. The diagnosis usually requires historical or physical evidence of an acute infectious process with fever and signs or symptoms of respiratory distress, or radiologic evidence of an acute pulmonary infiltrate (Leventhal 1982 [C], Bartlett 1998 [S,E]).

The literature on this subject is marked by inconsistent methodologies creating some uncertainties about the best methods for evaluating and treating these children.

The areas of uncertainty offering challenges in the management of CAP include:

- ability to make a clinical diagnosis,
- differentiation of viral versus bacterial infection,
- inability to determine the specific etiology of an infection, and
- selection of appropriate antibiotic therapy.

The objectives of this guideline are to:

- improve the use and interpretation of clinical signs and symptoms
- improve the appropriate use of diagnostic testing
- improve the use of appropriate antibiotic therapy
- improve the rate of hospitalized patients who meet admission criteria.

## Etiology

Direct culture of infected lung tissue requires invasive techniques. Because of this, published studies primarily use laboratory tests that provide only indirect evidence of pneumonia. These indirect techniques include nasopharyngeal culture, blood culture, polymerase chain reaction (PCR), and serology to establish the etiologies of CAP in study cohorts. These methods often fail to identify the etiology of infections and produce a degree of uncertainty about the true prevalence of specific organisms (*Wubbel 1999 [A], Juven 2000 [C]*).

Some consistent trends and conclusions can be derived from the literature (*Wubbel 1999 [A], Numazaki 2004 [C], Heiskanen-Kosma 1998 [C], Vuori 1998 [C], Korppi 1993 [C], Turner 1987 [C]*).

### • Bacterial causes

- *Streptococcus pneumoniae* accounted for 13% to 28% of CAP in children prior to the introduction of a heptavalent conjugated pneumococcal vaccine (PCV7, Prevnar®) in 2000 (*Overturf 2000 [S]*). PCV7 has reduced overall invasive disease due to *S. pneumoniae* (*Whitney 2003 [D]*). Though current prevalence has not been studied, *S. pneumoniae* continues to be the most commonly identified bacterial cause of community acquired pneumonia in children (*Heiskanen-Kosma 2003 [C]*).

**Note:** PCV7 is highly effective for covered serotypes (*Lucero 2005 [M], Klugman 2003 [A], Black 2004 [C], Black 2001 [C], Whitney 2003 [D]*).

- **Group A Streptococcus, S. aureus, and H. influenzae** cause pneumonias much less frequently (*Korppi 1993 [C]*).
- *Mycoplasma pneumoniae* and *Chlamydia (Chlamydophila) pneumoniae* are more common in school-age children (*Korppi 2004b [C]*); these organisms may be becoming increasingly prevalent in preschool children (*Esposito 2002 [C]*), but it is uncertain to what degree.
- **Viruses** are identified most often in children < 5 years of age. Respiratory syncytial virus (RSV) is the most common viral etiology in children < 3 years of age. In younger age groups, *Adenovirus*, *Parainfluenza virus*, *Influenza virus*, and the recently discovered *Human metapneumovirus* have also been identified (*Williams 2004 [C], Laundry 2003 [C], Murphy 1981 [C]*).
- **Mixed etiologies** are reported in 30% to 50% of children with CAP (*Korppi 2004b [C], Heiskanen-Kosma 2003 [C], Juven 2000 [C]*).

**Note:** Studies have found evidence that the etiology of a single case of CAP may be both *S. pneumoniae* and a virus, or *S. pneumoniae* and *M. pneumoniae*, or *S. pneumoniae* and *C. pneumoniae* (*Korppi 2004b [C], Heiskanen-Kosma 2003 [C], Juven 2000 [C]*).

## Guideline Recommendations

### Assessment and Diagnosis

#### General

The objective of the initial clinical assessment is to decide if the child's history and physical examination findings are suggestive of CAP.

#### Clinical Assessment

1. It is recommended that the initial history include:
  - age of child (*Juven 2000 [C]*)
  - season of the year (*Kim 1996 [C]*)
  - microorganisms currently circulating in the community (Cincinnati area information is posted on CCHMC's CenterLink webpage: "What's Bugging Us?") (*Local Expert Consensus [E]*)
  - immunization status, especially vaccines for *S. pneumoniae* and influenza virus if the child has an indication for these vaccines (*Lucero 2005 [M], Harper 2005 [S]*), and
  - exposure to tuberculosis, including personal or family travel in areas where tuberculosis is prevalent (*Local Expert Consensus [E]*).
2. It is recommended that a physical examination be initially performed for signs of respiratory illness and for fever (*Local Expert Consensus [E]*).

**Note 1:** Respiratory rates are best determined over a full 60-second period and inconsistencies require repeated observations. Respiratory patterns and rates in children are frequently modified by periodic behavioral and physiologic factors (*Taylor 1995 [C], Singhi 1994 [C], Morley 1990 [C], Zukin 1986 [C], Leventhal 1982 [C], Berman 1991 [S,E]*). See Table.

**Note 2:** Any single clinical finding is not useful in determining if a child does or does not have pneumonia; combinations of clinical findings are more predictive (*Margolis 1998 [M]*). See Appendix 1.

**Note 3:** The best individual examination measures in children less than 5 years are:

- nasal flaring (age < 12 months)
- oxygen saturation less than 94%

- tachypnea, and
- retractions

(Mahabee-Gittens 2005 [C], Redd 1994 [C], Harari 1991 [C]).

The best negative predictive value is obtained if there is an absence of:

- tachypnea alone, or
- all other signs of respiratory illness

(Margolis 1998 [M]).

See Appendix 1.

**Note 4:** See Appendix 2 for standardized lung sound nomenclature.

**Table: World Health Organization Age-Specific Criteria for Tachypnea \***

Age	Approximate normal respiratory rates (breaths/min)	Tachypnea threshold (breaths/min)
2 to 12 months	25 to 40	50
1 to 5 years	20 to 30	40
≥ 5 years	15 to 25	20

\*Tachypnea may not be present in a child with pronounced retractions or other signs of increased work of breathing (World Health Organization 1995 [E]).

- It is recommended that the severity of pneumonia be assessed based on overall clinical appearance and behavior, including an assessment of the child's degree of alertness and willingness to accept feedings. Subcostal retractions and other evidence of increased work of breathing increase the likelihood of a more severe form of pneumonia (World Health Organization 1995 [E]).
- It is recommended that children be assessed with an awareness that a small proportion of patients under five years of age may present without signs of respiratory illness (Bachur 1999 [D]). In acutely ill and febrile children, pneumonia also may present as pain referred to the abdomen or as fever without a source (Ravichandran 1996 [D], Jona 1976 [D], Local Expert Consensus [E]).

### Radiologic Assessment

- It is recommended, for children with clinical evidence of pneumonia, that chest X-rays be obtained when:
  - clinical findings are ambiguous,
  - a complication such as a pleural effusion is suspected, or
  - pneumonia is prolonged and unresponsive to antimicrobials
 (Swingler 1998 [A], Alario 1987 [C], Bachur 1999 [D]).

**Note 1:** In most studies of pneumonia, a positive chest X-ray was necessary to qualify a patient for study entry (Margolis 1998 [M], Redd 1994 [C]). This constraint makes it difficult to assess the degree to which chest X-rays are actually needed to diagnose pneumonia in a clinical setting, since the likelihood ratio of a reference standard cannot be measured.

**Note 2:** Chest X-rays have not consistently been shown to alter management decisions, nor to improve clinical outcomes (Swingler 1998 [A]).

**Note 3:** Chest X-rays have not been shown to differentiate viral from other etiologies (Virkki 2002 [C], Korppi 1993 [C], Alario 1987 [C], Bettenay 1988 [D]).

**Note 4:** The perceived need for and ordering of a chest X-ray is expected to be inversely and appropriately related to the clinician's experience with the diagnosis and treatment of CAP (Margolis 1998 [M], Local Expert Consensus [E]).

- It is recommended that chest X-rays be considered in children less than 5 years of age with high fevers and high white blood cell (WBC) counts of uncertain source (Bachur 1999 [D]).

### Laboratory Assessment

- It is recommended that a WBC count and differential be considered only when adjunctive information is necessary to help decide whether to use antibiotics (Korppi 2004a [C], Toikka 2000 [C], Bachur 1999 [D]).
 

**Note:** The likelihood of a bacterial cause generally increases as WBC counts increase above 15,000/mm<sup>3</sup>, especially above 20,000/mm<sup>3</sup> and when associated with fevers higher than 39°C (102.2°F) (Shuttleworth 1971 [C], Bachur 1999 [D]), but these relationships have not been documented in all studies (Wubbel 1999 [A], Ruuskanen 1999 [S,E]).
- It is recommended that blood cultures **not** be routinely obtained (Claesson 1989 [C], Hickey 1996 [D]).
 

**Note 1:** When pneumonia is diagnosed in an outpatient setting, the likelihood of a positive blood culture is less than 2.7% (Hickey 1996 [D]).

**Note 2:** Blood cultures may be helpful for inpatients with more severe, resistant, or other unusual forms of pneumonia. Their utility, however, is limited when antibiotics are administered prior to obtaining the specimen (Kuppermann 1997 [C], Local Expert Consensus [E]).

9. It is recommended that C reactive protein (CRP), erythrocyte sedimentation rate (ESR), and other measures of acute phase reactants **not** be performed, as these tests are not specific enough to be useful (*Korppi 2004a [C], Korppi 2003 [C], Virkki 2002 [C], Heiskanen-Kosma 2000 [C], Toikka 2000 [C], Korppi 1997 [C], Ruuskanen 1999 [S,E]*).
10. It is recommended that cultures, rapid viral studies or serologic testing for specific pathogens **not** be routinely performed, because the results, especially those that are not immediately available, usually do not affect initial management decisions (*Honda 2000 [D], Skerrett 1999 [S,E], Bartlett 1998 [S,E]*).
11. It is recommended that PPD and other skin testing be conducted in children with a history of exposure to tuberculosis, including personal or family travel in areas where tuberculosis is prevalent (*Alves dos Santos 2004 [D], Local Expert Consensus [E]*).
12. It is recommended that sputum Gram stain and culture on high quality specimens be considered when managing children with more severe disease (*Skerrett 1999 [S,E], Local Expert Consensus [E]*). See Consult and Referrals section.
 

**Note:** A high quality sputum is usually defined by the presence of less than 10 squamous epithelial cells and greater than 25 WBCs per low power field (*Skerrett 1999 [S,E]*).
13. It is recommended, that pleural cultures be considered prior to starting antibiotics when managing a child with an effusion (*Skerrett 1999 [S,E], Local Expert Consensus [E]*). See Consult and Referrals section.
14. It is recommended that when historical, physical, radiologic, or laboratory findings are inconsistent, additional studies be considered to evaluate for alternative or coincident conditions, such as foreign body aspiration or immunodeficiency (*Local Expert Consensus [E]*).

## **Management**

### **General**

There is substantial overlap in the clinical presentation of pneumonias caused by different etiologies, making prediction of etiology based on clinical presentation and radiologic and laboratory assessment very difficult. Choice of antibiotic in the treatment of CAP is generally based on age of patient and severity of illness.

### **Medications – age 60 days to 5 years**

15. It is recommended, for children 60 days to 5 years of age, that high dose amoxicillin (80 to 90 mg/kg/day) be used for 7 to 10 days when a bacterial cause for CAP is likely. This treatment will cover *S. pneumoniae*, the most common etiology for CAP for children in this age range (*Aurangzeb 2003 [A], Bartlett 1995 [S,E], Local Expert Consensus [E]*). See Appendix 3.

**Note 1:** The following resistance patterns have been reported:

- 16.7% to 35% of *S. pneumoniae* isolates from patients with community acquired respiratory tract infections (all ages) in the U.S. are resistant to penicillins (*Gordon 2003 [C]*).
- Twenty-six percent of *S. pneumoniae* isolates from blood/CSF specimens cultured at Cincinnati Children's Hospital Medical Center (CCHMC) in 2004 were resistant to penicillin (*Cincinnati Children's Hospital Medical Center 2004 [O]*).
- At least 15% of *S. pneumoniae* in the U.S. are resistant to macrolides (*Hyde 2001 [O]*).
- An organism resistant to penicillin is often resistant also to erythromycin. Erythromycin resistance generally suggests resistance to all macrolides (*Doern 1996 [C], Campbell 1998 [S]*).

**Note 2:** The effectiveness of high dose amoxicillin has been demonstrated for acute otitis media and is considered a reasonable option when treating other infections (*Piglansky 2003 [C], Jadavji 1997 [S,E], Local Expert Consensus [E]*). Resistance of *S. pneumoniae* to penicillin (including amoxicillin) is mediated through alterations in the penicillin-binding proteins. Using high doses of amoxicillin saturates the penicillin-binding proteins, and is therefore considered a reasonable antibiotic option (*Pallares 1995 [C]*).

**Note 3:** For children with allergies to penicillin, a macrolide or cephalosporin may be considered (*Dudas 2000 [C], Klein 1997 [S,E], Local Expert Consensus [E]*). See Consult and Referrals section if other antibiotics are being considered.

**Note 4:** Because *M. pneumoniae* or *C. pneumoniae* are a less common cause of CAP in children under age 5 years, macrolides are not considered first line therapy (*Esposito 2002 [C]*). A macrolide could be added to amoxicillin therapy at the 24 to 48 hour follow up if *M. pneumoniae* or *C. pneumoniae* is then suspected. This

practice will avoid overuse of macrolides in this age group while adequately protecting the young child from resistant *S. pneumoniae* (Wubbel 1999 [A], Harris 1998 [A], Local Expert Consensus [E]).

**Note 5:** For an infant or child unable to tolerate liquids, a single initial dose of ceftriaxone may be considered prior to starting oral antibiotics (Baskin 1992 [C], Chumpa 1999 [D], Local Expert Consensus [E]).

### Medications – age 5 years and older

16. It is recommended, for children age 5 years and older, that a macrolide be used to treat CAP. This treatment will cover *M. pneumoniae* and *C. pneumoniae*, the most common etiologies of CAP for children in this age group. A macrolide may also cover *S. pneumoniae*, the most common bacterial cause of CAP in all age groups. Treatment duration is 7 to 10 days, although a five-day course of azithromycin may be used (Wubbel 1999 [A], Harris 1998 [A], Klein 1997 [S,E]). See Appendix 3.

**Note 1:** The following resistance patterns have been reported:

- At least 15% of *S. pneumoniae* in the U.S. are resistant to macrolides (Hyde 2001 [O]).
- 16.7% to 35% of *S. pneumoniae* isolates from patients with community acquired respiratory tract infections (all ages) in the U.S. are resistant to penicillins (Gordon 2003 [C]).
- Twenty-six percent of *S. pneumoniae* isolates from blood/CSF specimens cultured at Cincinnati Children's Hospital Medical Center (CCHMC) in 2004 were resistant to penicillin (Cincinnati Children's Hospital Medical Center 2004 [O]).
- An organism resistant to penicillin is often resistant also to erythromycin. Erythromycin resistance generally suggests resistance to all macrolides (Doern 1996 [C], Campbell 1998 [S]).
- For high dose amoxicillin discussion see the recommendation for the younger age group.

**Note 2:** There is no evidence that any macrolide is more efficacious than another for treating *M. pneumoniae* or *C. pneumoniae* (Wubbel 1999 [A], Harris 1998 [A], Block 1995 [A], Klein 1997 [S,E]).

### Medications – more severe disease

17. It is recommended, in a child with a more severe case of CAP (see recommendation #3), that the combination of both a macrolide and a  $\beta$ -lactam agent, (such as high dose amoxicillin or ceftriaxone) be considered. This will provide better coverage for resistant organisms and mixed infections (Korppi

2004b [C], Heiskanen-Kosma 2003 [C], Juven 2000 [C], Local Expert Consensus [E]).

**Note:** Mixed etiologies are reported in 30% to 50% of children with CAP (Korppi 2004b [C], Heiskanen-Kosma 2003 [C], Juven 2000 [C]).

### Other Therapies

18. It is recommended that therapies directed toward airway clearance, such as postural drainage and chest physiotherapy (CPT), **not** be used for the patient with uncomplicated pneumonia (Hardy 1994 [S,E], Local Expert Consensus [E]).

### Admission Criteria

19. It is recommended that hospital admission be especially considered for infants and children who:

- have oxygen saturation consistently less than 91%
- are severely dehydrated
- are moderately dehydrated and unable to hydrate themselves orally after IV hydration
- are in moderate or severe respiratory distress
- have failed outpatient antibiotic treatment, or
- the clinician or family have identified that it is unsafe to send home

(Local Expert Consensus [E]).

### Follow up

20. It is recommended that practitioners follow up within 24 to 48 hours all patients diagnosed with CAP, including those not initially started on antibiotics (Local Expert Consensus [E]).

**Note:** Evaluation of the child not following the expected clinical course may include consideration of:

- alternative diagnosis (Alves dos Santos 2004 [D]);
  - ineffective antibiotic treatment because of lack of antibiotic coverage for the actual etiology;
  - ineffective antibiotic treatment because of organisms resistant to either penicillins or macrolides (Hyde 2001 [O]);
  - complication(s); or
  - viral etiology
- (Local Expert Consensus [E]).

### Consults and Referrals

21. It is recommended that consultation with a specialist in pediatric infectious diseases be considered when allergies, comorbid conditions, or prior antibiotic non-responsiveness confound the choice of therapy for a specific patient (Local Expert Consensus [E]).

22. It is recommended that consultation with a specialist in pediatric pulmonary diseases is appropriate when uncertain about the management of an effusion (Byington 2002 [D], Hardie 1996 [D]).

### **Prevention and Education**

23. It is recommended that immunizations which prevent CAP be kept up-to-date, including:
- heptavalent conjugated pneumococcal vaccine (PCV7, Prevnar®), (AAP 2003 [O]); and
  - annual influenza vaccine for
    - all children 6 to 23 months of age, and
    - children aged  $\geq 6$  months with certain risk factors (including but not limited to asthma, cardiac disease, sickle cell disease, HIV and diabetes)
- (Harper 2005 [S]).
24. It is recommended that measures to prevent pneumonia infections be discussed with families, including:
- handwashing, especially when exposed to individuals with respiratory infections (Morton 2004 [A], Roberts 2000 [A]);
  - breastfeeding (Levine 1999 [C]);
  - limiting exposure to other children (Levine 1999 [C]);
- Note:** Spread of respiratory infections in daycare settings may be reduced by verifying the facility's handwashing policies and actual handwashing practices, selecting a setting with fewer children, and/or delaying entry into daycare (Roberts 2000 [A], Local Expert Consensus [E]).
- reducing exposure to smoke (Almirall 1999 [D]).

Health Topic on CCHMC's website <sup>b</sup>:

- [Pneumonia, Community Acquired](#)

---

### **Future Research Agenda**

---

Clinical questions related to guideline recommendations and of potential interest to CCHMC investigators:

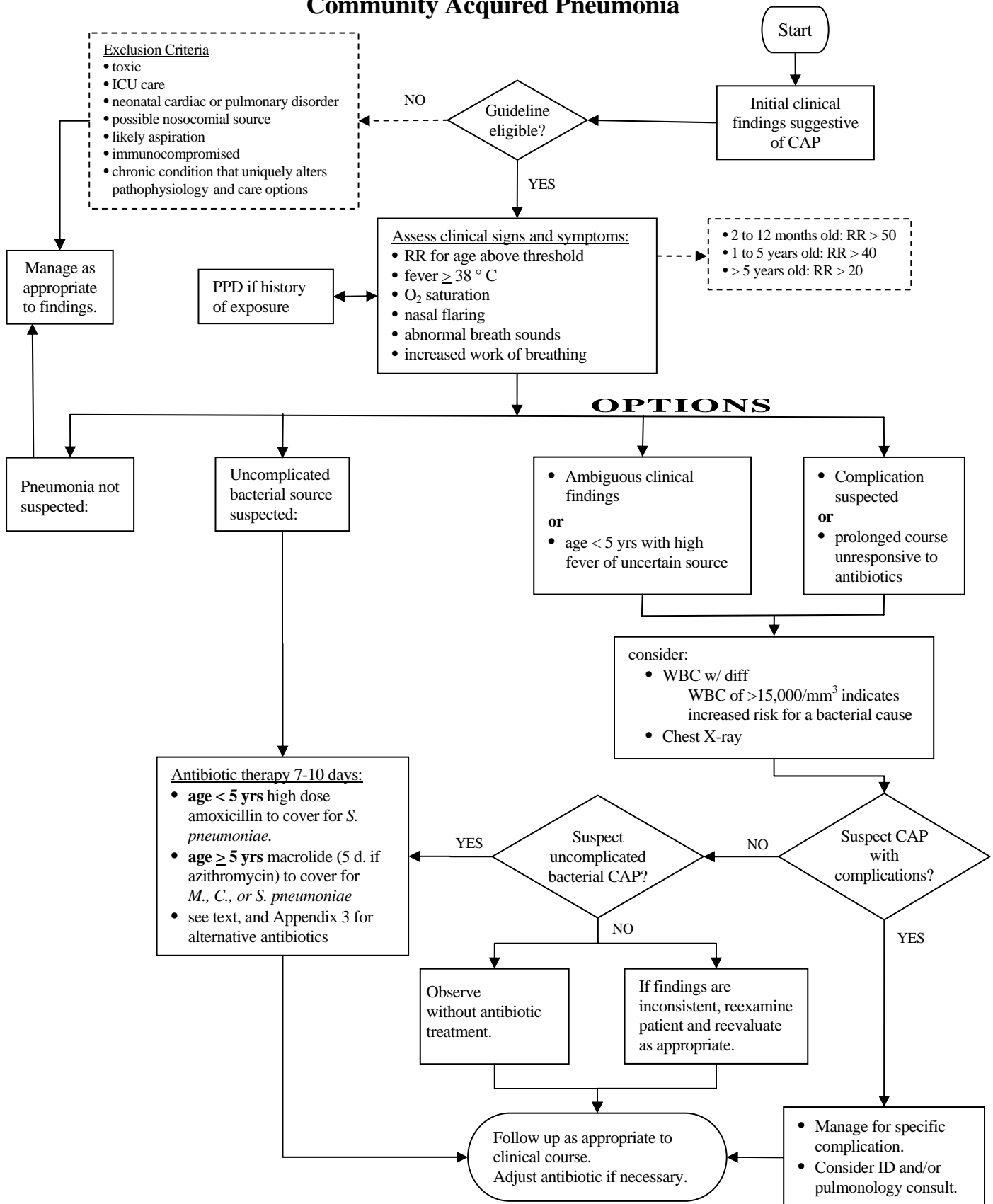
1. In what age group are *C. pneumoniae* and *M. pneumoniae* most likely to be found?
2. What is the evolving antibiotic resistance to CAP pathogens?
3. What is the ideal duration of antibiotic therapy (7 to 10 days versus less than 7 days) for the treatment of CAP?
4. What is the ideal dosing and frequency protocol for a short duration (1-, 3- or 5-day) course of azithromycin in the treatment of CAP?

---

<sup>b</sup> CCHMC Health Topic website:

[www.cincinnatichildrens.org/health/info](http://www.cincinnatichildrens.org/health/info)

## Algorithm for medical management of children 60 days through 17 years of age with Community Acquired Pneumonia



**Appendix 1: Likelihood Ratios (LR)**

**A. Definition**

When a health care provider evaluates a patient, he/she determines their own “best guess” for how likely a disease is present (or not present) at that time.

This “best guess” is dependent on:

- the disease prevalence in the community,
- the patient’s underlying medical status and current presentation, and
- the health care provider’s experience and knowledge of the literature.

This best guess is actually the **pre-test probability**.

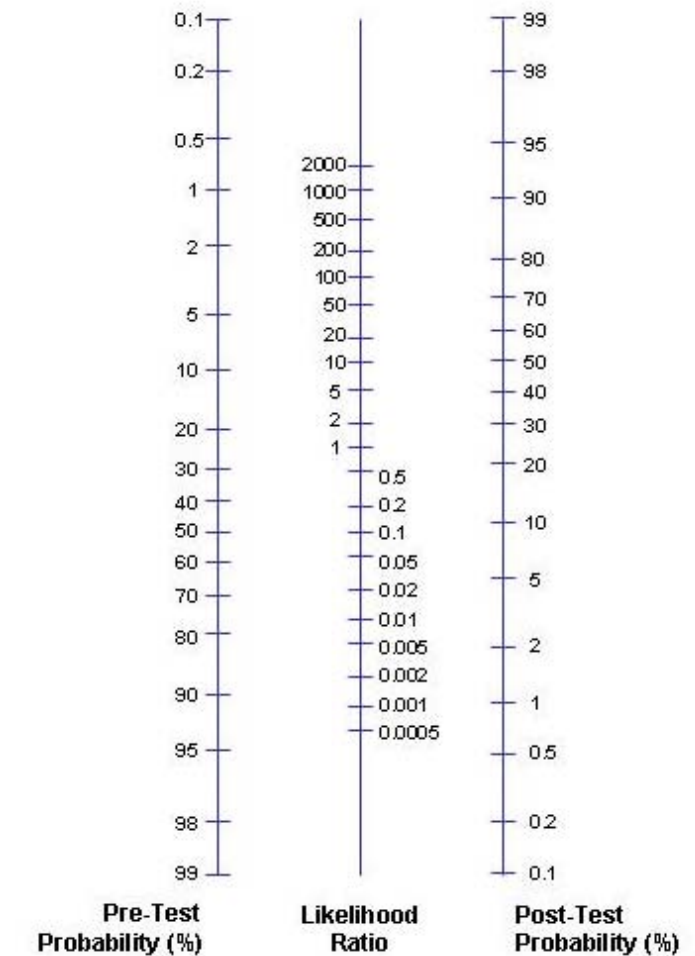
What health care providers are looking for is a test which will increase (or decrease) the **likelihood** of disease in that patient, thus allowing them to decide to treat, not treat, or pursue further diagnostic work up.

This change in “best guess” after diagnostic testing results in the **post-test probability** of disease.

Finding the post-test probability is done easily with **likelihood ratios** (see next page) and a **nomogram** (see figure).

What the likelihood ratio nomogram actually does is change pre-test probability to pre-test odds, multiply by the LR to get post-test odds, then change post-test odds back to post-test probability...all without having to manually perform complex calculations.

Fortunately, likelihood ratios (**LRs**) are determined by inherent properties of the diagnostic test, not the prevalence of disease in the population. By knowing the likelihood ratio(s) for any or all given tests, health care providers can determine which test is most informative and appropriate to use.



**Figure: Likelihood Ratio Nomogram**

**B. Rule of thumb:**

**An LR value**

- greater than 10 is very helpful in increasing diagnostic certainty  
the presence of clinical sign is 10 times more likely to be present in a child with CAP than in a child without CAP
- of 1 is not helpful  
the presence of clinical sign is just as likely to be present in child with CAP as in a child without CAP
- less than 0.2 is very helpful in ruling out the condition  
the presence of clinical sign is one-fifth as likely to be present in a child with CAP as in a child without CAP

For more information on LRs see: <http://www.cebm.utoronto.ca/glossary/lrs.htm#top>

See likelihood ratios for common signs and symptoms for use in diagnosing community acquired pneumonia next page.



**Appendix 1: Likelihood Ratios (LR), continued****C. Likelihood ratios (LRs) for common signs and symptoms  
for use in diagnosing community acquired pneumonia**

Sign/Symptom	Age range	LR (+) with 95% CIs <sup>c</sup>	LR (-) with 95% CIs <sup>c</sup>
Flaring	2 to 59 mo	2.94 (1.57, 5.52)	0.84 (0.71, 0.99)
Retractions	2 to 59 mo	1.07 (0.68, 1.68)	0.97 (0.79, 1.20)
Grunting	2 to 59 mo	0.56 (0.08, 4.07)	1.02 (0.97, 1.07)
Crackles (rales)	2 to 59 mo	1.51 (0.81, 2.83)	0.92 (0.79, 1.07)
RR $\geq$ 40	2 to 59 mo	1.36 (1.14, 1.63)	0.52 (0.30, 0.91)
RR $\geq$ 50	2 to 59 mo	1.74 (1.25, 2.41)	0.70 (0.52, 0.95)
RR $\geq$ 60	2 to 59 mo	2.60 (1.58, 4.27)	0.78 (0.63, 0.95)
RR $\geq$ 70	2 to 59 mo	2.12 (0.64, 7.04)	0.96 (0.89, 1.05)
O <sub>2</sub> sat $\leq$ 96%	2 to 59 mo	2.78 (2.09, 3.70)	0.48 (0.33, 0.71)
O <sub>2</sub> sat $\leq$ 95%	2 to 59 mo	3.54 (2.29, 5.45)	0.66 (0.51, 0.85)
O <sub>2</sub> sat $\leq$ 94%	2 to 59 mo	3.65 (1.98, 6.71)	0.80 (0.67, 0.96)
O <sub>2</sub> sat $\leq$ 93%	2 to 59 mo	2.95 (1.15, 7.54)	0.92 (0.82, 1.03)
Flaring	2 to 12 mo	5.22 (2.23, 12.21)	0.71 (0.50, 1.02)
RR $\geq$ 50 and O <sub>2</sub> sat $\leq$ 96%	13 to 59 mo	6.1 (2.7, 13.6)	Unable to calculate from data
RR $\geq$ 50 and O <sub>2</sub> sat $\leq$ 96%	2 to 12 mo	4.3 (2.6, 7.2)	Unable to calculate from data
RR $\geq$ 50 and O <sub>2</sub> sat $\leq$ 96% and flaring	2 to 12 mo	11.0 (2.4, 49.8)	Unable to calculate from data

*(Mahabee-Gittens 2005 [C])*

Sign/Symptom	Age range	LR (+) with 95% CIs <sup>c</sup>	LR (-) with 95% CIs <sup>c</sup>
Flaring	3 to 59 mo	2.96 (1.66, 5.27)	0.74 (0.58, 0.93)
Retractions	3 to 59 mo	2.33 (1.45, 3.73)	0.70 (0.53, 0.93)

*(Redd 1994 [C])*

Sign/Symptom	Age range	LR (+) with 95% CIs <sup>c</sup>	LR (-) with 95% CIs <sup>c</sup>
Flaring	2 to 71 mo	3.74 (1.64, 8.53)	0.82 (0.70, 0.95)
Retractions	2 to 71 mo	2.59 (1.42, 4.70)	0.78 (0.64, 0.94)
RR $\geq$ 50	2 to 71 mo	2.12 (1.51, 2.97)	0.53 (0.37, 0.76)
Temp $>$ 38° C	2 to 71 mo	1.16 (0.70, 1.92)	0.95 (0.77, 1.16)

*(Harari 1991 [C])*mo = months; RR = respiratory rate; O<sub>2</sub> sat = oxygen saturation; Temp = temperature

<sup>c</sup> 95%CI: 95% Confidence Interval expresses the uncertainty (precision) of a measured value; it is the range of values within which we can be 95% sure that the true value lies. A study with a larger sample size will generate more precise measurements, resulting in a narrower confidence interval.

**Appendix 2: Standardized Lung Sound Nomenclature**

Description	Term
Discontinuous Fine (high pitched, low amplitude, short duration)	Fine crackles
Coarse (low pitched, high amplitude, long duration)	Coarse crackles
Continuous High pitched	Wheezes
Low pitched	Rhonchus

(Mikami 1987 [E])

**Appendix 3: Antibiotics for the Outpatient Treatment of Community Acquired Pneumonia**

Antibiotic	Dose, Frequency & Max Daily Dose	Oral Dosage Forms	Relative Cost	Comments
<b>First Line Therapy</b>				
<b>Amoxicillin</b>	80 to 90 mg / kg / day Max daily dose 2 gm taken as: 40 to 45 mg / kg BID or 25 to 30 mg / kg TID	Suspension (per 5mL): 125, 200, 250 or 400mg  250 or 500 mg capsules	Low	<ul style="list-style-type: none"> <li>1<sup>st</sup> line for patients 60 days to 5 years of age</li> <li>High dose for resistant <i>S. pneumoniae</i></li> <li>400mg/5ml formulation not covered by Ohio Medicaid (Oct, 2005)</li> </ul>
<b>Azithromycin (Zithromax®)</b>	day 1 = 10 mg / kg Max dose: 500mg  day 2 to 5 = 5 mg / kg Max dose: 250mg  taken: once a day	Suspension (per 5mL): 100 or 200 mg  250 mg capsules	High	<ul style="list-style-type: none"> <li>1<sup>st</sup> line for patients age 5 years and older</li> <li><i>S. pneumoniae</i> (15% resistant)</li> <li><i>Chlamydia (Chlamydophila) pneumoniae</i></li> <li><i>Mycoplasma pneumoniae</i></li> <li>Not covered by Kentucky Medicaid (Oct, 2005)</li> </ul>
<b>Second Line Therapy</b>				
<b>Cephalosporins</b>				
<b>Cefprozil (Cefzil®)</b>	30 mg / kg / day Max daily dose: 1 gm taken as: 15 mg / kg BID	Suspension (per 5mL): 125 or 250mg	High	<ul style="list-style-type: none"> <li><i>S. pneumoniae</i></li> </ul>
<b>Ceftriaxone (Rocephin®)</b>	50 mg / kg / day (IM) Max daily dose: 1 gm taken: once a day	N/A	High	<ul style="list-style-type: none"> <li>Intramuscular</li> <li>Often used as treatment on day 1 and followed with oral therapy</li> </ul>
<b>Cefuroxime (Ceftin®)</b>	30 mg / kg / day Max daily dose: 1 gm taken as: 15 mg / kg BID	Suspension (per 5 ml): 125 or 250 mg  125, 250, and 500 mg tablets	High	<ul style="list-style-type: none"> <li><i>S. pneumoniae</i></li> <li>Unpleasant taste (Steele 1997 [O])</li> </ul>
<b>Macrolide</b>				
<b>Clarithromycin (Biaxin®)</b>	15 mg / kg / day Max daily dose: 1gm taken as: 7.5 mg / kg BID	Suspension (per 5 ml): 125 or 250 mg  250 and 500 mg tablets	High	<ul style="list-style-type: none"> <li><i>S. pneumoniae</i></li> <li><i>Chlamydia (Chlamydophila) pneumoniae</i></li> <li><i>Mycoplasma pneumoniae</i></li> <li>Not covered by Ohio Medicaid (Oct, 2005)</li> <li>Unpleasant taste (Steele 1997 [O])</li> </ul>

CCHMC Formulary

## Community Acquired Pneumonia Team Members 2005

### Community Physicians

\*Joseph Gibbons, MD, Chair

### CCHMC Physicians and Practitioners

\*Melinda Mahabee-Gittens MD, Emergency Medicine

\*William Hardie MD, Pulmonary Medicine

\*Rebecca Brady, MD, Infectious Disease

\*Alan Brody, MD, Radiology

\*Omer Berger, MD, General Pediatrics

### Residents

Katie Kerrey, MD, Chief

Tracie Butler, MD

### Patient Services

Dawn Butler, PharmD, Pharmacy

\*Scott Pettinichi, RRT, Dir. Respiratory Care

Shirley Salway, RN, BS

### Division of Health Policy & Clinical Effectiveness Support

Eloise Clark, MPH, Facilitator

Danette Stanko, MA, MPH, Epidemiologist

\*Kate Rich, Lead Decision Support Analyst

Detrice Barry, RN, MSN, Education Coordinator

Debbie Hacker, RN, Medical Reviewer

Gary Geis, MD, Methodologist, Emergency Medicine

Edward Donovan, MD, Medical Director, Clinical Effectiveness

Eduardo Mendez, RN, MPH, Dir. Evidence-Based Practice

All Team Members and Clinical Effectiveness support staff listed above have signed a conflict of interest declaration.

### Ad Hoc Advisors

\*Uma Kotagal, MBBS, MSc, VP, Division Director

Kieran Phelan, MD, General Pediatrics & Clinical Effectiveness

Mel Rutherford, Esq, VP, Risk Management

\*Richard Ruddy, MD, Dir. Emergency Medicine

\*Beverly Connelly, MD, Dir. Ped Infectious Diseases

\*Thomas DeWitt, MD, Dir. General & Community Pediatrics

\*Michael Farrell, MD, Chief of Staff

\*Dorine Seaquist RN, VP, Patient Services

Raouf Amin, MD, Dir. Pulmonary Medicine

Joel Mortensen, PhD, Dir. Microbiology & Virology

\*Member of previous Community Acquired Pneumonia guideline development Team

## 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.

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

To select evidence for critical appraisal by the group, the Medline, EmBase and the Cochrane databases were searched for dates of January, 2000 through August, 2005, to generate an unrefined, “combined evidence” database using a search strategy focused on answering clinical questions relevant to community acquired pneumonia 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, additional clinical questions were generated and subjected to the search process, and some relevant review articles were identified. December, 1999 was the last date for which literature was reviewed for the previous version of this guideline. The details of previous review strategies are not documented. However, all original citations were reviewed for appropriateness to this revision.

A search using the above criteria was conducted for dates of September, 2005 through June, 2006. Three 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 implementation of the original publication of this guideline has provided learnings which have been incorporated into this revision. The outcome measure monitored as of the revision publication date is: percent of guideline-eligible CAP patients receiving antibiotics in the Emergency Department who receive an etiology-appropriate antibiotic (age-dependent).

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 guidelines, 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, 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.

Copies of this Evidence-Based Care Guideline (EBCG) and its companion documents are available online and may be distributed by any organization for the global purpose of improving child health outcomes. Website address:

<http://www.cincinnatichildrens.org/svc/alpha/h/health-policy/ev-based/default.htm>. Examples of approved uses of the EBCG include the following:

- copies may be provided to anyone involved in the organization's process for developing and implementing evidence-based care guidelines;
- hyperlinks to the CCHMC website may be placed on the organization's website;
- the EBCG may be adopted or adapted for use within the organization, provided that CCHMC receives appropriate attribution on all written or electronic documents; and
- copies may be provided to patients and the clinicians who manage their care.

Notification of CCHMC at [HPCEInfo@cchmc.org](mailto:HPCEInfo@cchmc.org) for any EBCG, or its companion documents, adopted, adapted, implemented or hyperlinked by the organization is appreciated.

**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](mailto:HPCEInfo@cchmc.org).*

---

**REFERENCES**


---

1. **AAP:** American Academy of Pediatrics Red Book. 26th Edition, 2003, [O] \_\_\_\_\_ ☞.
2. **Alario, A. J.; McCarthy, P. L.; Markowitz, R.; Kornguth, P.; Rosenfield, N.; and Leventhal, J. M.:** Usefulness of chest radiographs in children with acute lower respiratory tract disease. *J Pediatr*, 111(2): 187-93, 1987, [C] \_\_\_\_\_ ☞.
3. **Almirall, J.; Gonzalez, C. A.; Balanzo, X.; and Bolibar, I.:** Proportion of community-acquired pneumonia cases attributable to tobacco smoking. *Chest*, 116(2): 375-9, 1999, [D] \_\_\_\_\_ ☞.
4. **Alves dos Santos, J. W.; Torres, A.; Michel, G. T.; de Figueiredo, C. W.; Mileto, J. N.; Foletto, V. G., Jr.; and de Nobrega Cavalcanti, M. A.:** Non-infectious and unusual infectious mimics of community-acquired pneumonia. *Respir Med*, 98(6): 488-94, 2004, [D] \_\_\_\_\_ ☞.
5. **Aurangzeb, B., and Hameed, A.:** Comparative efficacy of amoxicillin, cefuroxime and clarithromycin in the treatment of community -acquired pneumonia in children. *JCPSP, J College Phys & Surg - Pakistan*, 13(12): 704-7, 2003, [A] \_\_\_\_\_ ☞.
6. **Bachur, R.; Perry, H.; and Harper, M. B.:** Occult pneumonias: empiric chest radiographs in febrile children with leukocytosis. *Ann Emerg Med*, 33(2): 166-73, 1999, [D] \_\_\_\_\_ ☞.
7. **Bartlett, J. G.; Breiman, R. F.; Mandell, L. A.; and File, T. M.:** Community-acquired pneumonia in adults: guidelines for management. The Infectious Diseases Society of America. *Clin Infect Dis*, 26(4): 811-38, 1998, [S,E] \_\_\_\_\_ ☞.
8. **Bartlett, J. G., and Mundy, L. M.:** Community-acquired pneumonia. *N Engl J Med*, 333(24): 1618-24, 1995, [S,E] \_\_\_\_\_ ☞.
9. **Baskin, M. N.; O'Rourke, E. J.; and Fleisher, G. R.:** Outpatient treatment of febrile infants 28 to 89 days of age with intramuscular administration of ceftriaxone. *J Pediatr*, 120(1): 22-7, 1992, [C] \_\_\_\_\_ ☞.
10. **Berman, S.; Simoes, E. A.; and Lanata, C.:** Respiratory rate and pneumonia in infancy. *Arch Dis Child*, 66(1): 81-4, 1991, [S,E] \_\_\_\_\_ ☞.
11. **Bettenay, F. A.; de Campo, J. F.; and McCrossin, D. B.:** Differentiating bacterial from viral pneumonias in children. *Pediatr Radiol*, 18(6): 453-4, 1988, [D] \_\_\_\_\_ ☞.
12. **Black, S.; Shinefield, H.; Baxter, R.; Austrian, R.; Bracken, L.; Hansen, J.; Lewis, E.; and Fireman, B.:** Postlicensure surveillance for pneumococcal invasive disease after use of heptavalent pneumococcal conjugate vaccine in Northern California Kaiser Permanente. *Pediatr Infect Dis J*, 23(6): 485-9, 2004, [C] \_\_\_\_\_ ☞.
13. **Black, S. B.; Shinefield, H. R.; Hansen, J.; Elvin, L.; Laufer, D.; and Malinoski, F.:** Postlicensure evaluation of the effectiveness of seven valent pneumococcal conjugate vaccine. *Pediatr Infect Dis J*, 20(12): 1105-7, 2001, [C] \_\_\_\_\_ ☞.
14. **Block, S.; Hedrick, J.; Hammerschlag, M. R.; Cassell, G. H.; and Craft, J. C.:** Mycoplasma pneumoniae and Chlamydia pneumoniae in pediatric community-acquired pneumonia: comparative efficacy and safety of clarithromycin vs. erythromycin ethylsuccinate. *Pediatr Infect Dis J*, 14(6): 471-7, 1995, [A] \_\_\_\_\_ ☞.
15. **Byington, C. L. et al.:** An epidemiological investigation of a sustained high rate of pediatric parapneumonic empyema: risk factors and microbiological associations. *Clin Infect Dis*, 34(4): 434-40, 2002, [D] \_\_\_\_\_ ☞.
16. **Campbell, G. D., and Silberman, R.:** Drug-resistant Streptococcus pneumoniae. *Clin Infect Dis*, 26(5): 1188-95, 1998, [S] \_\_\_\_\_ ☞.
17. **Chumpa, A.; Bachur, R. G.; and Harper, M. B.:** Bacteremia-associated pneumococcal pneumonia and the benefit of initial parenteral antimicrobial therapy. *Pediatr Infect Dis J*, 18(12): 1081-5, 1999, [D] \_\_\_\_\_ ☞.
18. **Cincinnati Children's Hospital Medical Center:** Antibiotic Susceptibility Report. 2004, [O].
19. **Claesson, B. A. et al.:** Etiology of community-acquired pneumonia in children based on antibody responses to bacterial and viral antigens. *Pediatr Infect Dis J*, 8(12): 856-62, 1989, [C] \_\_\_\_\_ ☞.
20. **Doern, G. V.; Brueggemann, A.; Holley, H. P., Jr.; and Rauch, A. M.:** Antimicrobial resistance of Streptococcus pneumoniae recovered from outpatients in the United States during the winter months of 1994 to 1995: results of a 30-center national surveillance study. *Antimicrob Agents Chemother*, 40(5): 1208-13, 1996, [C] \_\_\_\_\_ ☞.
21. **Dudas, V.; Hopefl, A.; Jacobs, R.; and Guglielmo, B. J.:** Antimicrobial selection for hospitalized patients with presumed community-acquired pneumonia: a survey of nonteaching US community hospitals. *Annals of Pharmacotherapy*, 34(4): 446-52, 2000, [C] \_\_\_\_\_ ☞.
22. **Esposito, S.; Bosis, S.; Cavagna, R.; Faelli, N.; Begliatti, E.; Marchisio, P.; Blasi, F.; Bianchi, C.; and Principi, N.:** Characteristics of Streptococcus pneumoniae and atypical bacterial infections in children 2-5 years of age with community-acquired pneumonia. *Clin Infect Dis*, 35(11): 1345-52, 2002, [C] \_\_\_\_\_ ☞.
23. **Gordon, K. A.; Biedenbach, D. J.; and Jones, R. N.:** Comparison of Streptococcus pneumoniae and Haemophilus influenzae susceptibilities from community-acquired respiratory tract infections and hospitalized patients with pneumonia: five-year results for the SENTRY Antimicrobial Surveillance Program. *Diagn Microbiol Infect Dis*, 46(4): 285-9, 2003, [C] \_\_\_\_\_ ☞.

24. **Harari, M.; Shann, F.; Spooner, V.; Meisner, S.; Carney, M.; and de Campo, J.:** Clinical signs of pneumonia in children. *Lancet*, 338(8772): 928-30, 1991, [C] \_\_\_\_\_ ↗.
25. **Hardie, W.; Bokulic, R.; Garcia, V. F.; Reising, S. F.; and Christie, C. D.:** Pneumococcal pleural empyemas in children. *Clin Infect Dis*, 22(6): 1057-63, 1996, [D] \_\_\_\_\_ ↗.
26. **Hardy, K. A.:** A review of airway clearance: new techniques, indications, and recommendations. *Respiratory Care*, 39(5): 440-55, 1994, [S,E] \_\_\_\_\_ ↗.
27. **Harper, S. A.; Fukuda, K.; Uyeki, T. M.; Cox, N. J.; and Bridges, C. B.:** Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*, 54(RR-8): 1-40, 2005, [S] \_\_\_\_\_ ↗.
28. **Harris, J. A.; Kolokathis, A.; Campbell, M.; Cassell, G. H.; and Hammerschlag, M. R.:** Safety and efficacy of azithromycin in the treatment of community-acquired pneumonia in children. *Pediatr Infect Dis J*, 17(10): 865-71, 1998, [A] \_\_\_\_\_ ↗.
29. **Heiskanen-Kosma, T., and Korppi, M.:** Serum C-reactive protein cannot differentiate bacterial and viral aetiology of community-acquired pneumonia in children in primary healthcare settings. *Scand J Infect Dis*, 32(4): 399-402, 2000, [C] \_\_\_\_\_ ↗.
30. **Heiskanen-Kosma, T. et al.:** Etiology of childhood pneumonia: serologic results of a prospective, population-based study. *Pediatr Infect Dis J*, 17(11): 986-91, 1998, [C] \_\_\_\_\_ ↗.
31. **Heiskanen-Kosma, T.; Korppi, M.; and Leinonen, M.:** Serologically indicated pneumococcal pneumonia in children: a population-based study in primary care settings. *APMIS*, 111(10): 945-50, 2003, [C] \_\_\_\_\_ ↗.
32. **Hickey, R. W.; Bowman, M. J.; and Smith, G. A.:** Utility of blood cultures in pediatric patients found to have pneumonia in the emergency department. *Ann Emerg Med*, 27(6): 721-5, 1996, [D] \_\_\_\_\_ ↗.
33. **Honda, J.; Yano, T.; Kusaba, M.; Yonemitsu, J.; Kitajima, H.; Masuoka, M.; Hamada, K.; and Oizumi, K.:** Clinical use of capillary PCR to diagnose Mycoplasma pneumoniae. *J Clin Microbiol*, 38(4): 1382-4, 2000, [D] \_\_\_\_\_ ↗.
34. **Hyde, T. B. et al.:** Macrolide resistance among invasive Streptococcus pneumoniae isolates. *JAMA*, 286(15): 1857-62, 2001, [O] \_\_\_\_\_ ↗.
35. **Jadavji, T.; Law, B.; Lebel, M. H.; Kennedy, W. A.; Gold, R.; and Wang, E. E.:** A practical guide for the diagnosis and treatment of pediatric pneumonia. *CMAJ*, 156(5): S703-11, 1997, [S,E] \_\_\_\_\_ ↗.
36. **Jona, J. Z., and Belin, R. P.:** Basilar pneumonia simulating acute appendicitis in children. *Arch Surg*, 111(5): 552-3, 1976, [D] \_\_\_\_\_ ↗.
37. **Juven, T.; Mertsola, J.; Waris, M.; Leinonen, M.; Meurman, O.; Roivainen, M.; Eskola, J.; Saikku, P.; and Ruuskanen, O.:** Etiology of community-acquired pneumonia in 254 hospitalized children. *Pediatr Infect Dis J*, 19(4): 293-8, 2000, [C] \_\_\_\_\_ ↗.
38. **Kim, P. E.; Musher, D. M.; Glezen, W. P.; Rodriguez-Barradas, M. C.; Nahm, W. K.; and Wright, C. E.:** Association of invasive pneumococcal disease with season, atmospheric conditions, air pollution, and the isolation of respiratory viruses. *Clin Infect Dis*, 22(1): 100-6, 1996, [C] \_\_\_\_\_ ↗.
39. **Klein, J. O.:** History of macrolide use in pediatrics. *Pediatr Infect Dis J*, 16(4): 427-31, 1997, [S,E] \_\_\_\_\_ ↗.
40. **Klugman, K. P.; Madhi, S. A.; Huebner, R. E.; Kohberger, R.; Mbelle, N.; and Pierce, N.:** A trial of a 9-valent pneumococcal conjugate vaccine in children with and those without HIV infection. *N Engl J Med*, 349(14): 1341-8, 2003, [A] \_\_\_\_\_ ↗.
41. **Korppi, M.:** Non-specific host response markers in the differentiation between pneumococcal and viral pneumonia: what is the most accurate combination? *Pediatrics International*, 46(5): 545-50, 2004a, [C] \_\_\_\_\_ ↗.
42. **Korppi, M.; Heiskanen-Kosma, T.; Jalonen, E.; Saikku, P.; Leinonen, M.; Halonen, P.; and Makela, P. H.:** Aetiology of community-acquired pneumonia in children treated in hospital. *Eur J Pediatr*, 152(1): 24-30, 1993, [C] \_\_\_\_\_ ↗.
43. **Korppi, M.; Heiskanen-Kosma, T.; and Kleemola, M.:** Incidence of community-acquired pneumonia in children caused by Mycoplasma pneumoniae: serological results of a prospective, population-based study in primary health care. *Respirology*, 9(1): 109-14, 2004b, [C] \_\_\_\_\_ ↗.
44. **Korppi, M.; Heiskanen-Kosma, T.; and Leinonen, M.:** White blood cells, C-reactive protein and erythrocyte sedimentation rate in pneumococcal pneumonia in children. *Eur Respir J*, 10(5): 1125-9, 1997, [C] \_\_\_\_\_ ↗.
45. **Korppi, M.; Remes, S.; and Heiskanen-Kosma, T.:** Serum procalcitonin concentrations in bacterial pneumonia in children: a negative result in primary healthcare settings. *Pediatric Pulmonology*, 35(1): 56-61, 2003, [C] \_\_\_\_\_ ↗.
46. **Kuppermann, N.; Bank, D. E.; Walton, E. A.; Senac, M. O.; 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] \_\_\_\_\_ ↗.
47. **Laundy, M.; Ajayi-Obe, E.; Hawrami, K.; Aitken, C.; Breuer, J.; and Booy, R.:** Influenza A community-acquired pneumonia in East London infants and young children. *Pediatric Infectious Disease Journal*, 22(10 Suppl): S223-7, 2003, [C] \_\_\_\_\_ ↗.



48. **Leventhal, J. M.:** Clinical predictors of pneumonia as a guide to ordering chest roentgenograms. *Clin Pediatr (Phila)*, 21(12): 730-4, 1982, [C] \_\_\_\_\_ ↗.
49. **Levine, O. S.; Farley, M.; Harrison, L. H.; Lefkowitz, L.; McGeer, A.; and Schwartz, B.:** Risk factors for invasive pneumococcal disease in children: a population-based case-control study in North America. *Pediatrics*, 103(3): E28, 1999, [C] \_\_\_\_\_ ↗.
50. **Local Expert Consensus:** During guideline development timeframe. [E].
51. **Lucero, M. G.; Dulalia, V. E.; Parreno, R. N.; Lim-Quianzon, D. M.; Nohynek, H.; Makela, H.; and Williams, G.:** Pneumococcal conjugate vaccines for preventing vaccine-type invasive pneumococcal disease and pneumonia with consolidation on x-ray in children under two years of age. *Cochrane Database of Systematic Reviews*, (1), 2005, [M] \_\_\_\_\_ ↗.
52. **Mahabee-Gittens, E. M.; Grupp-Phelan, J.; Brody, A. S.; Donnelly, L. F.; Allen Bracey, S. E.; Duma, E. M.; Mallory, M. L.; and Slap, G. B.:** Identifying children with pneumonia in the emergency department. *Clin Pediatr (Phila)*, 44(5): 427-35, 2005, [C] \_\_\_\_\_ ↗.
53. **Margolis, P., and Gadomski, A.:** Does this infant have pneumonia? *JAMA*, 279(4): 308-13, 1998, [M] \_\_\_\_\_ ↗.
54. **Mikami, R.; Murao, M.; Cugell, D. W.; Chretien, J.; Cole, P.; Meier-Sydow, J.; Murphy, R. L.; and Loudon, R. G.:** International Symposium on Lung Sounds. Synopsis of proceedings. *Chest*, 92(2): 342-5, 1987, [E] \_\_\_\_\_ ↗.
55. **Morley, C. J.; Thornton, A. J.; Fowler, M. A.; Cole, T. J.; and Hewson, P. H.:** Respiratory rate and severity of illness in babies under 6 months old. *Arch Dis Child*, 65(8): 834-7, 1990, [C] \_\_\_\_\_ ↗.
56. **Morton, J. L., and Schultz, A. A.:** Healthy Hands: Use of alcohol gel as an adjunct to handwashing in elementary school children. *J Sch Nurs*, 20(3): 161-7, 2004, [A] \_\_\_\_\_ ↗.
57. **Murphy, T. F.; Henderson, F. W.; Clyde, W. A.; Collier, A. M.; and Denny, F. W.:** Pneumonia: an eleven-year study in a pediatric practice. *Am J Epidemiol*, 113(1): 12-21, 1981, [C] \_\_\_\_\_ ↗.
58. **Numazaki, K. et al.:** Etiological agents of lower respiratory tract infections in Japanese children. *In Vivo*, 18(1): 67-71, 2004, [C] \_\_\_\_\_ ↗.
59. **Overturf, G. D.:** American Academy of Pediatrics. Committee on Infectious Diseases. Technical report: prevention of pneumococcal infections, including the use of pneumococcal conjugate and polysaccharide vaccines and antibiotic prophylaxis. *Pediatrics*, 106(2 Pt 1): 367-76, 2000, [S] \_\_\_\_\_ ↗.
60. **Pallares, R.; Linares, J.; Vadillo, M.; Cabellos, C.; Manresa, F.; Viladrich, P. F.; Martin, R.; and Gudiol, F.:** Resistance to penicillin and cephalosporin and mortality from severe pneumococcal pneumonia in Barcelona, Spain. *N Engl J Med*, 333(8): 474-80, 1995, [C] \_\_\_\_\_ ↗.
61. **Piglansky, L.; Leibovitz, E.; Raiz, S.; Greenberg, D.; Press, J.; Leiberman, A.; and Dagan, R.:** Bacteriologic and clinical efficacy of high dose amoxicillin for therapy of acute otitis media in children. *Pediatr Infect Dis J*, 22(5): 405-13, 2003, [C] \_\_\_\_\_ ↗.
62. **Ravichandran, D., and Burge, D. M.:** Pneumonia presenting with acute abdominal pain in children. *Br J Surg*, 83(12): 1707-8, 1996, [D] \_\_\_\_\_ ↗.
63. **Redd, S. C.; Patrick, E.; Vreuls, R.; Metsing, M.; and Motetee, M.:** Comparison of the clinical and radiographic diagnosis of paediatric pneumonia. *Trans R Soc Trop Med Hyg*, 88(3): 307-10, 1994, [C] \_\_\_\_\_ ↗.
64. **Roberts, L.; Smith, W.; Jorm, L.; Patel, M.; Douglas, R. M.; and McGilchrist, C.:** Effect of infection control measures on the frequency of upper respiratory infection in child care: a randomized, controlled trial. *Pediatrics*, 105(4 Pt 1): 738-42, 2000, [A] \_\_\_\_\_ ↗.
65. **Ruuskanen, O., and Mertsola, J.:** Childhood community-acquired pneumonia. *Semin Respir Infect*, 14(2): 163-72, 1999, [S,E] \_\_\_\_\_ ↗.
66. **Shuttleworth, D. B., and Charney, E.:** Leukocyte count in childhood pneumonia. *Am J Dis Child*, 122(5): 393-6, 1971, [C] \_\_\_\_\_ ↗.
67. **Singhi, S.; Dhawan, A.; Kataria, S.; and Walia, B. N.:** Validity of clinical signs for the identification of pneumonia in children. *Ann Trop Paediatr*, 14(1): 53-8, 1994, [C] \_\_\_\_\_ ↗.
68. **Skerrett, S. J.:** Diagnostic testing for community-acquired pneumonia. *Clin Chest Med*, 20(3): 531-48, 1999, [S,E] \_\_\_\_\_ ↗.
69. **Steele, R. W.; Estrada, B.; Begue, R. E.; Mirza, A.; Travillion, D. A.; and Thomas, M. P.:** A double-blind taste comparison of pediatric antibiotic suspensions. *Clin Pediatr (Phila)*, 36(4): 193-9, 1997, [O] \_\_\_\_\_ ↗.
70. **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] \_\_\_\_\_ ↗.
71. **Taylor, J. A.; Del Beccaro, M.; Done, S.; and Winters, W.:** Establishing clinically relevant standards for tachypnea in febrile children younger than 2 years. *Arch Pediatr Adolesc Med*, 149(3): 283-7, 1995, [C] \_\_\_\_\_ ↗.

72. **Toikka, P.; Irjala, K.; Juven, T.; Virkki, R.; Mertsola, J.; Leinonen, M.; and Ruuskanen, O.:** Serum procalcitonin, C-reactive protein and interleukin-6 for distinguishing bacterial and viral pneumonia in children. *Pediatr Infect Dis J*, 19(7): 598-602, 2000, [C] \_\_\_\_\_ ↗.
73. **Turner, R. B.; Lande, A. E.; Chase, P.; Hilton, N.; and Weinberg, D.:** Pneumonia in pediatric outpatients: cause and clinical manifestations. *J Pediatr*, 111(2): 194-200, 1987, [C] \_\_\_\_\_ ↗.
74. **Virkki, R.; Juven, T.; Rikalainen, H.; Svedstrom, E.; Mertsola, J.; and Ruuskanen, O.:** Differentiation of bacterial and viral pneumonia in children. *Thorax*, 57(5): 438-41, 2002, [C] \_\_\_\_\_ ↗.
75. **Vuori, E.; Peltola, H.; Kallio, M. J.; Leinonen, M.; and Hedman, K.:** Etiology of pneumonia and other common childhood infections requiring hospitalization and parenteral antimicrobial therapy. SE-TU Study Group. *Clin Infect Dis*, 27(3): 566-72, 1998, [C] \_\_\_\_\_ ↗.
76. **Whitney, C. G. et al.:** Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine. *N Engl J Med*, 348(18): 1737-46, 2003, [D] \_\_\_\_\_ ↗.
77. **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] \_\_\_\_\_ ↗.
78. **World Health Organization:** The management of acute respiratory infections in children: Practical guidelines for outpatient care. 1995, [E].
79. **Wubbel, L.; Muniz, L.; Ahmed, A.; Trujillo, M.; Carubelli, C.; McCoig, C.; Abramo, T.; Leinonen, M.; and McCracken, G. H.:** Etiology and treatment of community-acquired pneumonia in ambulatory children. *Pediatr Infect Dis J*, 18(2): 98-104, 1999, [A] \_\_\_\_\_ ↗.
80. **Zukin, D. D.; Hoffman, J. R.; Cleveland, R. H.; Kushner, D. C.; and Herman, T. E.:** Correlation of pulmonary signs and symptoms with chest radiographs in the pediatric age group. *Ann Emerg Med*, 15(7): 792-6, 1986, [C] \_\_\_\_\_ ↗.