

Approach to Community-Acquired Pneumonia in Children

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Community-acquired pneumonia (CAP) in children represents a common problem and is a leading cause of morbidity and mortality for children worldwide. Pediatric CAP differs from adult disease in etiology, presentation, and course of illness. Although CAP is common, there are few evidence-based guidelines for diagnosis and management. Some authors define pediatric CAP using clinical criteria while others require radiologic data. Current limitations in diagnosis and management of this disease render CAP in children a challenge for the pediatrician and family physician. In addition, antimicrobial resistance has complicated treatment decisions. This article reviews the diagnosis and management of pediatric CAP and discusses the role of prevention.

Community-acquired pneumonia (CAP) is an acute infection of the lung parenchyma acquired outside the hospital. CAP is a common pediatric problem, with an annual incidence of approximately 40 cases per 1000 children in North America.¹ Children are probably at higher risk for pneumonia than adults of any age except perhaps the elderly.² Despite its frequency, pediatric CAP remains difficult to diagnose, evaluate, and manage, as many pathogens may be responsible, coinfections occur frequently, clinical features may vary widely, and laboratory testing to support the diagnosis is limited. Differentiating pneumonia from bronchiolitis, also common in young children, may be especially problematic.

ETIOLOGY OF INFECTION

Many pathogens cause pneumonia in children, including bacteria, viruses, parasites, and fungi. Because culture of lung parenchyma or pleural fluid requires an invasive procedure, most studies in children have relied on indirect methods such as nasopharyngeal culture, polymerase chain reaction assay, serology, and blood culture. As a result, the epidemiology of pneumonia in children is not well defined. The most common etiologies of pneumonia vary with the age of the patient. In neonates, group B streptococcus and gram-negative enteric bacteria are the most common bacterial pathogens and are generally acquired through vertical transmission.³ Viral pneumonia with cytomegalovirus and herpes simplex virus should be considered even without a suspicious maternal history. *Chlamydia trachomatis* infection, once a common cause of infection in infants,

has become much less common through prenatal screening and treatment of maternal infection.

The most common cause of bacterial pneumonia in children older than 3 weeks is *Streptococcus pneumoniae*. Before the pneumococcal vaccine was introduced in 2000, *Streptococcus pneumoniae* accounted for 13% to 28% of pediatric CAP.⁴ Group A streptococcus, *Staphylococcus aureus*, *Haemophilus influenzae* type B, and *Moraxella catarrhalis* are less common bacterial causes of pneumonia. The organisms *Mycoplasma pneumoniae* and *C. pneumoniae* commonly cause CAP in school-age children and teenagers, although they may infect preschool-age children more commonly than generally recognized. In one study, the age of patients with atypical infection ranged from 9 months to 13 years, with 47% occurring in those aged younger than 5 years.⁵ *Bordetella pertussis* should be considered in young or unimmunized children with paroxysmal cough, whoop, posttussive emesis, or apnea. Tuberculosis should also be considered if the patient has suggestive clinical signs, is incarcerated, has recently been to an endemic area, or has had contact with an individual with active tuberculosis.

Most cases of CAP in preschool-age children are caused by viruses, including respiratory syncytial virus (RSV), adenovirus, parainfluenza, influenza, and rhinoviruses. Mixed infections may occur in 30% to

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TAKE HOME POINTS

- Despite the high incidence of community-acquired pneumonia (CAP) in children, few guidelines exist for managing CAP in children.
- In well-appearing outpatients, neither chest radiographs nor other diagnostic tests are routinely indicated.
- Imaging should be considered in patients where the diagnosis is unclear, in those not responding to antibiotic therapy, and in those with possible complications.
- Treatment should be directed toward likely pathogens based on the patient's age.
- Because mixed infections are common, positive viral testing may not preclude a bacterial cause.
- "Atypical" organisms such as *Mycoplasma pneumoniae* may occur in children younger than 5 years, despite historical dogma.

50% of children with CAP, including *Streptococcus pneumoniae* and a virus, *Streptococcus pneumoniae* and *Mycoplasma pneumoniae*, and *Streptococcus pneumoniae* and *C. pneumoniae*.^{4,5} Viruses and *Streptococcus pneumoniae* may synergistically contribute to clinical illness.⁶

EVALUATION AND DIAGNOSIS

Children with fever, tachypnea, increased work of breathing, and abnormal lung examination require evaluation for pneumonia. Goals of this evaluation include diagnosis and determination of likely etiologies while recognizing limitations of diagnostic methods.

Clinical Presentation

Children with pneumonia present with various clinical signs and symptoms. Symptoms and signs of pneumonia include fever, cough, tachypnea, nasal flaring, grunting, retractions, poor feeding, irritability, abnormal lung examination, and hypoxia, and the presence of these findings varies depending on the patient's age and the severity of illness. Although most present with respiratory symptoms and fever, some children with pneumonia present with less classic symptoms, such as abdominal pain, nausea, vomiting, or chest pain. In a study of children admitted for abdominal pain, pneumonia was ultimately found to be causative in 1.6% of patients.⁷ Multiple studies have sought to identify clinical variables that can be used to make

an accurate clinical diagnosis of pneumonia. These studies found that no single clinical variable offers significant accuracy, although tachypnea has the highest sensitivity (45%–80%) and specificity (54%–75%).^{8–10} Other signs of increased work of breathing, such as nasal flaring and retractions, increase the likelihood of pneumonia but are not highly sensitive or specific,⁹ as bronchiolitis may present similarly.

The World Health Organization (WHO) suggests that tachypnea and retractions are the most accurate signs for identifying pneumonia and should be used to guide management in areas with limited access to radiography. The WHO defines tachypnea as 50 breaths/min in infants 2 to 12 months of age, 40 breaths/min in children aged 1 to 5 years, and 20 breaths/min in children aged 5 years and older.¹¹ Respiratory rate should be measured over 60 seconds due to variations in respiratory rate from periodic breathing and behavioral factors. A 1997 Canadian study concluded that the absence of tachypnea, crackles, decreased breath sounds, and respiratory distress effectively excludes pneumonia.¹⁰ However, a subsequent study found that the sensitivity and specificity of these guidelines were only 45% and 66%, respectively.¹² No single clinical sign reliably predicts hypoxia, although inability to breastfeed, grunting, or central cyanosis suggests it.¹³ Oxygen saturation should be measured in patients with respiratory distress or ill appearance.

Historically, it was thought that "typical" bacterial pneumonia caused by pneumococcus could be differentiated from "atypical" pneumonia caused by *Mycoplasma pneumoniae* or *C. pneumoniae* based on clinical presentation. The presentation of typical bacterial CAP supposedly consisted of fever, pleuritic chest pain, and productive cough, while atypical pneumonia was described as featuring nonproductive cough, low-grade fever, and malaise. However, studies have shown that these presentations do not accurately reflect the etiology of bacterial pneumonia in children.⁵ An Italian study found no statistically significant differences in the clinical characteristics of pneumonia caused by *Streptococcus pneumoniae* versus pneumonia caused by atypical pathogens in terms of age, onset of symptoms, or presence of fever, cough, tachypnea, wheeze, or rales.⁴ Likewise, bacterial pneumonia can be difficult to distinguish from viral disease. In a study of hospitalized patients, high fever ($\geq 38.4^{\circ}\text{C}$) within 72 hours of admission and presence of pleural effusion were the only statistically significant clinical variables distinguishing bacterial (including mixed infections) from viral pneumonia.⁵ This study suggested that viral etiologies occur more commonly in younger children, while bacterial pneumonia occurs more frequently in older children.

Laboratory and Radiologic Assessment

Diagnosis of CAP in outpatients generally does not require laboratory studies or radiographs. Patients requiring hospitalization typically undergo diagnostic evaluation, although a standard laboratory work-up has not been defined. Most studies do not demonstrate a higher likelihood of bacterial infection in patients with high temperature or white blood cell count.^{4,14} Acute phase reactants such as C-reactive protein and erythrocyte sedimentation rate have low specificity for bacterial pneumonia.⁴ Although blood cultures are often obtained in hospitalized children with suspected pneumonia, the risk of bacteremia is extremely low in those older than 2 months with uncomplicated CAP.¹⁵

Testing outpatients with uncomplicated CAP to determine etiology generally is not indicated. Hospitalized patients with pneumonia are often tested with viral nasal washes or sputum cultures for cohorting purposes or to facilitate selection of targeted antibiotic therapy. Cultures of nasopharyngeal secretions have low accuracy because upper airway flora may differ significantly from lower airway pathogens.¹⁰ Older patients may be able to produce a high-quality sputum sample for sputum Gram stain and culture. Patients with symptomatic pleural effusions should have pleural fluid cultured prior to antibiotic administration when possible.

Rapid tests are often used for RSV and influenza, while cultures are available for parainfluenza, adenovirus, and other pathogens. Testing for human metapneumovirus or bocavirus is available in some laboratories. Serologic tests for *Streptococcus pneumoniae*, *Mycoplasma pneumoniae*, and *C. pneumoniae* vary in sensitivity, do not correlate well with culture results, and are of limited clinical utility.¹⁰ Because multiple studies have demonstrated a high prevalence of coinfections or superinfections,^{5,16} isolation of a virus does not rule out the possibility of bacterial infection.

Although often considered the gold standard for diagnosis of pneumonia, chest radiography is not essential to diagnose pneumonia, particularly in outpatients. A 2005 Cochrane review found no evidence that chest radiographs improve outcome in ambulatory children with acute lower respiratory tract infections.¹⁷ Imaging should be considered in patients when the diagnosis is unclear, in those not responding to antibiotic therapy, and in those with possible complications such as effusion or empyema. Some studies suggest that chest radiographs alone do not accurately differentiate between etiologies,⁴ while others have found that lobar infiltrates usually reflect bacterial infection.¹⁴ In patients with complications of pneumonia, chest ul-

trasound or chest computed tomography may further guide management.

MANAGEMENT

Management of children with CAP depends on disease severity and patient age. All febrile neonates should be hospitalized and undergo a complete evaluation for serious bacterial infection, including blood, urine, and cerebrospinal fluid cultures. Antibiotic therapy with ampicillin and cefotaxime or gentamicin should be initiated to cover suspected pathogens, including group B streptococcus, *Escherichia coli*, and *Listeria* species. Afebrile, well-appearing infants with presumed *C. trachomatis* pneumonia can be managed as outpatients with macrolide therapy and close follow-up.¹⁰ Children older than 3 months with CAP can be managed as outpatients if they are not hypoxic, in respiratory distress, or dehydrated.¹⁸ Hospitalization should be considered if there is concern of respiratory failure, if the child cannot tolerate oral antibiotics, or if follow-up is not assured. A study comparing oral amoxicillin with intravenous penicillin showed no difference in duration of fever, hypoxia, or clinical symptoms.¹⁹ Outpatients should be seen 24 to 48 hours after diagnosis to monitor response to therapy and assess for complications such as empyema.

As there exist few criteria to accurately differentiate between viral and bacterial pneumonia, choosing which children to treat with antibiotics is difficult. Many researchers suggest close follow-up without antibiotic therapy for young children with mild disease, in whom a viral etiology is more likely.¹⁸ If antimicrobial therapy is desired, the choice of antibiotic is based on the most likely pathogen in a patient's age-group (**Table**).^{2,10} In outpatients aged 3 months to 5 years, oral amoxicillin 80 to 90 mg/kg/day divided 2 or 3 times daily is effective against most *Streptococcus pneumoniae* and is considered first-line therapy.^{18,20,21} Alternatives in penicillin-allergic patients include macrolides or cephalosporins, although cross-reactivity may occur with cephalosporins. A macrolide such as azithromycin may be added to amoxicillin, as atypical infections may be more common in younger children than generally recognized. For outpatient management of children over age 5 years, azithromycin is typically the drug of choice due to the prevalence of atypical pathogens. Azithromycin 10 mg/kg/day on day 1 followed by 4 additional days of 5 mg/kg/day is usually effective, although some experts suggest a 7- to 10-day course.² In the United States, approximately 15% of *Streptococcus pneumoniae* show resistance to macrolides; therefore, if the patient does not improve

Table. Common Bacterial Pathogens and Antimicrobial Therapy in Community-Acquired Pneumonia Based on Age

Age	Pathogens	Therapy	
		Outpatient	Inpatient
Birth–30 days*	Group B streptococci Gram-negative enteric bacteria <i>Listeria monocytogenes</i> <i>Staphylococcus aureus</i> †	Admit patient	Ampicillin + gentamicin or ampicillin + cefotaxime†
4 wk–4 mo	<i>Streptococcus pneumoniae</i> <i>Chlamydia trachomatis</i> ‡ <i>Bordetella pertussis</i>	Erythromycin or azithromycin‡	Cefotaxime ± macrolide
4 mo–4 yr	<i>S. pneumoniae</i> <i>Haemophilus influenzae</i> <i>Mycoplasma pneumoniae</i>	High-dose amoxicillin or amoxicillin-clavulanate ± azithromycin	Ampicillin or cefotaxime or cefuroxime
5–15 yr	<i>S. pneumoniae</i> <i>M. pneumoniae</i> <i>Chlamydia pneumoniae</i>	Erythromycin or azithromycin ± high-dose amoxicillin or amoxicillin-clavulanate	Ampicillin or cefotaxime or cefuroxime ± azithromycin†

*Patients younger than 30 days of age require inpatient management with intravenous antibiotics.

†Vancomycin or clindamycin should be considered if there is concern for methicillin-resistant *S. aureus*.

‡Macrolide therapy should be used if the pneumonia is believed to be caused by *C. trachomatis*. Erythromycin is generally avoided in patients aged 6 weeks or younger because of an association with pyloric stenosis.

after 48 hours of treatment, high-dose amoxicillin may be added.²²

Antimicrobial choice for inpatients is usually empiric and depends on the patient's age and most likely pathogen. Ampicillin, ampicillin-sulbactam, and cephalosporins such as ceftriaxone may be used in hospitalized children.² Fluoroquinolones are rarely used in young children. Trimethoprim-sulfamethoxazole is suggested by the WHO as first-line therapy for treatment of CAP in cases that are not severe, although a Cochrane review has shown it to be less effective than amoxicillin, which in turn was inferior to amoxicillin-clavulanate.²³ Methicillin-resistant *Staphylococcus aureus* (MRSA), while not a common cause of CAP, can cause a necrotizing pneumonia, especially in conjunction with influenza.²⁴ In cases where MRSA is suspected, clindamycin, vancomycin, or linezolid should be added.

PREVENTION

The leading causes of vaccine-preventable pneumonia in the United States are *Streptococcus pneumoniae* and influenza. Since routine childhood immunization with heptavalent pneumococcal conjugate vaccine began in the United States in 2000, the overall incidence of invasive pneumococcal disease has decreased, particularly the incidence of pneumococcal pneumonia.^{23,25} One study suggested that rates of pneumonia with a positive radiograph were reduced by 20.5%.¹ These declines

have been tempered by concern about the emergence of other pathogens or other pneumococcal serotypes, including invasive serotypes such as 19A.²⁶ The overall clinical significance of this shift remains uncertain.

Areas of the world without access to pneumococcal vaccine continue to see high rates of death caused by childhood pneumonia. A recent analysis suggested that pneumococcal vaccination in 72 developing countries could prevent 262,000 deaths per year in children aged 3 to 29 months.²⁷ In 68 of the countries studied, pneumococcal vaccination was found to be highly cost-effective.

In 2004–05, routine immunization for influenza was recommended for children aged 6 to 23 months. During seasons with good match between vaccine and circulating influenza strains, efficacy approaches 70% to 90%.²⁸ In 2003–04, a year without good match, the protective effect for children 6 months to 8 years was only 23% and 51% against influenza-like illness and bacterial or viral (including influenza) pneumonia, respectively.²⁹ This study found that previously unvaccinated children under the age of 8 years require 2 doses for maximal protection against influenza. The current recommendations, updated in 2008, now recommend annual immunization for children aged 5 years to 18 years, in addition to those aged 6 months to 4 years.³⁰ Children younger than age 9 years should receive 2 doses 4 weeks apart during their first immunization year.

CONCLUSION

CAP represents a common and challenging pediatric problem. Diagnosis may be difficult because of limited laboratory testing, the broad range of pathogens, and the frequency of coinfections. Treatment is typically empiric targeting the likely organism based on the patient's age. Future goals include establishing guidelines to guide treatment of children with CAP, studying the impact of antimicrobial resistance, and understanding the long-term impact of immunization campaigns, especially against pneumococcus. **HP**

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