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Pediatrics in Review

An Official Journal of the American Academy of Pediatrics

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Pediatrics in Review 2013;34;438

DOI: 10.1542/pir.34-10-438

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American Academy of Pediatrics

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Pneumonia

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Author Disclosure
Drs Gereige and Laufer have disclosed no financial relationships relevant to this article. This commentary does not contain discussion of unapproved/investigative use of a commercial product/device.

Practice Gap

The epidemiology of pneumonia is changing; chest radiographs and routine laboratory testing are unnecessary for routine diagnosis of community-acquired pneumonia in children who are candidates for outpatient treatment.

Objectives The readers of this article are expected to:

1. Know the cause, clinical manifestations, differential diagnosis, and general approach to the diagnosis, treatment, and prevention strategies of the different types of pneumonia in children of various age groups.
2. Be aware of the challenges that face the clinician in making an accurate diagnosis of pneumonia due to the inaccuracies and shortcomings of the various laboratory and imaging studies.
3. Know the complications of pneumonia in children and their appropriate diagnostic and therapeutic strategies.

Introduction

Pneumonia is commonly encountered by emergency department and primary care clinicians. Childhood pneumonia remains a significant cause of morbidity and mortality in developing countries, whereas mortality rates in the developed world have decreased secondary to new vaccines, antimicrobials, and advances in diagnostic and monitoring techniques. (1) This review focuses on pneumonia in children: its causes in various age groups, clinical manifestations, indications for hospitalization, and the challenges that clinicians face in making an accurate diagnosis despite the new and emerging diagnostic tests.

Epidemiology

The incidence of pneumonia varies by age groups and between developing and developed countries. Worldwide, the overall annual incidence of pneumonia in children younger than 5 years is 150 million to 156 million cases, (2)(3) leading to an estimated 2 million deaths per year, most of which occur in developing countries. (4) Forty percent of cases require hospitalization. (5) In developed countries, the annual incidence of pneumonia is estimated at 33 per 10,000 in children younger than 5 years and 14.5 per 10,000 in children ages 0 to 16 years. In the United States, pneumonia is estimated to occur in 2.6% of children younger than 17 years. Fortunately, the mortality rate in developed countries is less than 1 per 1000 per year. (3)

According to the World Health Organization (WHO), pneumonia is the single largest cause of death in children worldwide, leading to an annual death of an estimated 1.2 million children younger than 5 years. This accounts for 18% of all deaths of children younger than 5 years worldwide. (6)

Cases of pneumonia occur throughout the year; however, the incidence is increased during the colder months in

Abbreviations

BAL:	bronchoalveolar lavage
CAP:	community-acquired pneumonia
CA-MRSA:	community-associated methicillin-resistant <i>Staphylococcus aureus</i>
ELISA:	enzyme-linked immunosorbent assay
HIV:	human immunodeficiency virus
hMPV:	human metapneumovirus
IGRA:	interferon gamma release assay
LRTI:	lower respiratory tract infection
MRSA:	methicillin-resistant <i>Staphylococcus aureus</i>
MSSA:	methicillin-sensitive <i>Staphylococcus aureus</i>
PCR:	polymerase chain reaction
RSV:	respiratory syncytial virus
VATS:	video-assisted thoracoscopic surgery
WHO:	World Health Organization

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temperate climates for unknown reasons. It is presumed that person-to-person transmission of respiratory droplets enhanced by indoor crowding, impaired mucociliary clearance, and the peak of viral infections that led to viral pneumonias with secondary bacterial pneumonias are the cause of this peak. In tropical climates, peaks of respiratory infections are seen sporadically throughout the year. (4) Table 1 highlights the risk factors of pneumonia in neonates and older children and teens.

Definitions

Before further discussion of this topic, it is important to discuss the definitions of the various terms related to pneumonia.

Pneumonia

Pneumonia still remains a condition that is challenging to accurately diagnose. Therefore, no single definition that accurately describes childhood pneumonia currently exists. Pneumonia is defined as a lower respiratory tract infection (LRTI) typically associated with fever, respiratory symptoms, and evidence of parenchymal involvement by either physical examination or the presence of infiltrates on chest radiography. Pathologically, it represents an

inflammatory process of the lungs, including airways, alveoli, connective tissue, visceral pleura, and vascular structures. Radiologically, pneumonia is defined as an infiltrate on chest radiograph in a child with symptoms of an acute respiratory illness. (1)(7)

Walking Pneumonia

Walking pneumonia is a term typically used in school-aged children and young adults with clinical and radiographic evidence of pneumonia but with mild symptoms in which the respiratory symptoms do not interfere with normal activity. Typically, *Mycoplasma pneumoniae* has been implicated as the organism presumably responsible for walking pneumonia.

Community-Acquired Pneumonia

Community-acquired pneumonia (CAP) refers to an acute pulmonary infection in a previously healthy individual acquired in the community (as opposed to hospital-acquired or nosocomial pneumonia)(8)

Hospital-Acquired Pneumonia

A pneumonia that develops in a hospitalized child within 48 hours after admission is considered *hospital-associated*

Table 1. Risk Factors of Pneumonia (4)(29)(30)

Risk factor for pneumonia in children	Risk factor for pneumonia in neonates
<ul style="list-style-type: none"> • Sex: M:F = 1.25:1–2:1 • Socioeconomic/environmental factors: <ul style="list-style-type: none"> ◦ Lower socioeconomic status (family size, crowding) ◦ Low maternal educational level ◦ Poor access to care ◦ Indoor air pollution ◦ Malnutrition ◦ Lack of breastfeeding ◦ Cigarette smoke (active and passive smoke exposure) ◦ Alcohol, drugs, and cigarettes use (increased risk of aspiration) in teens • Underlying cardiopulmonary disorders and medical conditions: <ul style="list-style-type: none"> ◦ Congenital heart disease ◦ Bronchopulmonary dysplasia and chronic lung disease ◦ Diabetes mellitus ◦ Cystic fibrosis ◦ Asthma ◦ Sickle cell disease ◦ Neuromuscular disorders (especially those associated with altered mental status) ◦ Some gastrointestinal disorders (eg, gastroesophageal reflux, tracheoesophageal fistula) ◦ Congenital and acquired immunodeficiency disorders 	<ul style="list-style-type: none"> Early-onset <ul style="list-style-type: none"> • Prolonged rupture of the fetal membranes (> 18 hours) • Maternal amnionitis • Premature delivery • Fetal tachycardia • Maternal intrapartum fever Late-onset <ul style="list-style-type: none"> • Assisted ventilation (4 times higher in intubated than in nonintubated) • Anomalies of the airway (eg, choanal atresia, tracheoesophageal fistula, and cystic adenomatoid malformations) • Severe underlying disease • Prolonged hospitalization • Neurologic impairment resulting in aspiration of gastrointestinal contents • Nosocomial infections due to poor hand washing or overcrowding

pneumonia. (9) Pneumonia that affects those individuals living in chronic care facilities and those who were recently hospitalized fall in this category as well.

Etiology

A large number of microorganisms cause pneumonia, ranging from viruses to bacteria and fungi (Table 2). The etiologic agents of pneumonia depend on the patient's age. In neonates (0-3 months of age), maternal flora, such as group B *streptococcus* and gram-negative bacteria, are common causes that are vertically transmitted. Overall, *Streptococcus pneumoniae* remains the most common bacterial cause of pneumonia in children older than 1 week, whereas viruses account for 14% to 35% of cases. (7) (10) In children ages 3 months to 5 years, 50% to 60% of cases are associated with viral respiratory infections. (11) In school-aged children (>5 years), atypical organisms, such as *M pneumoniae* and *Chlamydia pneumoniae* (previously known as *Chlamydia pneumoniae*), are more common. (12) *Mycoplasma pneumoniae* remains the leading cause of pneumonia in school-age children and young adults.

New vaccines and emerging antibiotic resistance led to a change in the pathogens implicated in pneumonia. The first vaccine that affected the epidemiology of pneumonia in the United States was the conjugated *Haemophilus influenzae* type b vaccine (1990). It drastically reduced invasive disease by this organism. In 2000, the pneumococcal conjugated 7-valent vaccine not only decreased the rates of invasive disease significantly (98.7 cases per 10,000 in 1998–1999 vs 23.4 cases per 10,000 in 2005) but also decreased the incidence of pneumonia that required hospitalization and ambulatory visits in children younger than 2 years. (10)(12)(13) The rates for children ages 1 to 18 years, however, remained stable. Conjugated vaccines reduce nasopharyngeal colonization. This effect benefited nonimmunized adults older than 65 years through herd immunity. As expected, the pneumococcal conjugated 7-valent vaccine led to a shift of the most common serotypes that cause disease in children, and the 13-valent pneumococcal conjugate vaccine introduced in 2010 provides additional coverage against common pneumococcal serotypes 1, 3, 5, 6A, 7F, and 19A, further decreasing the incidence of pneumonia that requires hospitalization. (10)(12)(13)

Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) should be considered in cases of complicated pneumonia with empyema and necrosis. The latter can be severe when associated with influenza infection. In the last few years, clinicians have encountered severe secondary bacterial infections after influenza

infection. This mechanism is still not clear, but animal models suggest that influenza A enhances transmission of bacteria such as *S aureus*. (13)

New viruses emerged in the past few years. The human metapneumovirus (hMPV) was described in 2001. Often considered to be a pathogen associated with bronchiolitis, it is described in association with pneumonia. Children younger than 5 years are susceptible to hMPV infection, and infants younger than 2 years with primary infection are particularly at risk of severe infection. Seroepidemiologic studies indicate that virtually all children are infected with hMPV by 5 to 10 years of age. In one series, hMPV was isolated in 8.3% (second only to respiratory syncytial virus [RSV]) of cases of radiologically diagnosed CAP. Children with hMPV were older than those with RSV (mean age of 19 vs 9 months) and had a higher incidence of gastrointestinal symptoms and wheeze. Indicators of severity (such as saturations on admission, respiratory rate, and duration of stay) were no different in hMPV compared with other viruses. (13) (14)

The human bocavirus is in the parvovirus family. Although it has not been cultured yet, it can be identified by electron microscopy. Initially, its role in pneumonia was unclear. Preliminary evidence suggests that nearly all children have produced antibodies to human bocavirus by school age, and most newborns receive antibodies from their mothers. (13)(14)

Clinical Manifestations

Pneumonia in children is a challenging diagnosis because the presenting signs and symptoms are nonspecific, might be subtle (particularly in infants and young children), and vary, depending on the patient's age, responsible pathogen, and severity of the infection. (1)(4)(7)(13)

In all age groups, fever and cough are the hallmark of pneumonia. (4) Other findings, such as tachypnea, increased work of breathing (eg, nasal flaring in infants), and hypoxia, may precede the cough. The WHO uses tachypnea and retractions to effectively diagnose pneumonia in children younger than 5 years but tachypnea becomes less sensitive and specific as age increases (in children >5 years). (4) Most of the clinical signs and symptoms have a low sensitivity and specificity except for cough, crackles (rales), retractions, rhonchi, and nasal flaring (in young infants), which are highly specific but not sensitive, meaning that their absence might help rule out the disease. (1) The rate of diagnosed pneumonia in patients with fever but no cough or tachypnea is 0.28%. Upper lobe pneumonias may present with a clinical picture suggestive of meningitis due to radiating neck pain.

Table 2. Cause by Age Groups (7)(21)(30)

Pathogens	Neonates	Infants	Children <5 years	Children > 5 years
Viruses	Herpes simplex virus Enteroviruses Adenovirus Mumps Congenital rubella Cytomegalovirus	Cytomegalovirus (CMV)** Respiratory syncytial virus Parainfluenza Influenza Adenovirus Metapneumovirus	Respiratory syncytial virus Influenza A and B Parainfluenza viruses, usually type 3 Adenovirus serotypes (1, 2, 3, 4, 5, 7, 14, 21, and 35) Human metapneumovirus Rhinovirus Coronaviruses (including the severe acute respiratory syndrome virus and the New Haven coronavirus) Human bocavirus Human parechovirus types 1, 2, and 3	<ul style="list-style-type: none"> Respiratory viruses Rare causes of pneumonia: <ul style="list-style-type: none"> Coronavirus Varicella-zoster Epstein-Barr virus Mumps
Bacteria	Group B streptococci Gram-negative enteric bacteria <i>Ureaplasma urealyticum</i> <i>Listeria monocytogenes</i> <i>Chlamydia trachomatis</i> <i>Streptococcus pneumoniae</i> Group D <i>Streptococcus</i> Anaerobes	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Mycoplasma pneumoniae</i> <i>Mycobacterium tuberculosis</i> ** <i>Chlamydia trachomatis</i> ** <i>Mycoplasma hominis</i> ** <i>Ureaplasma urealyticum</i> ** <i>Bordetella pertussis</i>	<i>Streptococcus pneumoniae</i> <i>H influenzae</i> type b Nontypable <i>H influenzae</i> <i>Moraxella catarrhalis</i> <i>Staphylococcus aureus</i> (including CA-MRSA) <i>Streptococcus pyogenes</i> <i>Mycobacterium tuberculosis</i>	<i>Streptococcus pneumoniae</i> <i>Mycoplasma pneumoniae</i> <i>Chlamydia pneumoniae</i> <i>Mycobacterium tuberculosis</i> <i>Chlamydia psittaci</i> <i>Coxiella burnetii</i> <i>Klebsiella pneumoniae</i> <i>Legionella</i> <i>Streptococcus pyogenes</i> <i>Brucella abortus</i>
Fungi	<i>Candida</i> species <ul style="list-style-type: none"> Rate of colonization of gastrointestinal and respiratory tract of very low-birth-weight infants is 25% (during labor and delivery) Pneumonia in 70% of infants with systemic candidiasis 			<i>Coccidioides immitis</i> <i>Histoplasma capsulatum</i> <i>Blastomyces dermatitidis</i>
Other	Congenital toxoplasmosis Syphilis <ul style="list-style-type: none"> Early-onset pneumonia 			

Continued

Table 2. (Continued)

Pathogens	Neonates	Infants	Children <5 years	Children > 5 years
Comments	<ul style="list-style-type: none"> Herpes simplex virus <ul style="list-style-type: none"> Most common viral agent to cause early-onset pneumonia From the mother at time of birth 33%–55% of disseminated herpes simplex virus fatal despite treatment 	<p>**Causes of "afebrile pneumonia of infancy" seen between age 2 weeks to 3–4 months. Symptoms include:</p> <ul style="list-style-type: none"> Insidious onset of rhinorrhea and tachypnea Staccato cough Diffuse inspiratory crackles With or without conjunctivitis 	<p>Adenovirus serotypes 3, 7, and 21 have been associated with severe and complicated pneumonia</p> <p>Causes pneumonia complicated by necrosis and empyema. Frequently are seen after influenza and chickenpox</p>	
<p>CA-MRSA=community-acquired methicillin-resistant <i>Staphylococcus aureus</i>.</p>				

Lower lobe pneumonias may present as vague abdominal pain mimicking appendicitis.

In neonates, pneumonia can occur as early or late onset. (1) Early-onset pneumonia typically presents in the first 3 days of life. The infection is acquired from the mother either hematogenously through the placenta or through aspiration of infected amniotic fluid in utero or during or after birth. It commonly presents with respiratory distress beginning at or soon after birth. Newborns may also present with nonspecific symptoms, such as lethargy, apnea, tachycardia, and poor perfusion, occasionally progressing to septic shock or pulmonary hypertension. Other signs include temperature instability, metabolic acidosis, and abdominal distension. (2) Late-onset pneumonia occurs after birth during hospitalization or after discharge and is either nosocomial acquired or due to colonization or contaminated equipment. Late-onset pneumonia typically presents with nonspecific signs of apnea, tachypnea, poor feeding, abdominal distention, jaundice, emesis, respiratory distress, and circulatory collapse. Ventilator-dependent infants may have increased oxygen and ventilator requirements and/or purulent tracheal secretions.

It is virtually impossible to clinically differentiate bacterial from viral pneumonia except that bacterial pneumonia might have a more abrupt and severe onset after days of symptoms of an upper respiratory tract infection. The patient may be ill appearing and sometimes experience toxic effects, with moderate to severe respiratory distress and localized chest pain. Finally, complications are more likely to occur in bacterial pneumonia. (13)

Pneumococcal pneumonia is typically a lobar pneumonia that presents with fever, nonproductive cough, tachypnea, and decreased breath sounds over the affected lobe. (10)(12)

Atypical bacterial pneumonia caused by *M pneumoniae* or *C pneumoniae* usually presents with abrupt onset of fever, malaise, myalgia, headache, photophobia, sore throat, and gradually worsening prolonged nonproductive cough. Atypical bacterial pneumonia may be difficult to differentiate from viral pneumonia. Hoarseness is more frequently seen with *C pneumoniae* infection compared with a viral origin. Wheezing in a child older than 5 years might be associated with atypical bacterial (*Mycoplasma* or *Chlamydia*) and viral pneumonias and is unlikely to be due to other bacterial causes. (13) *Mycoplasma pneumoniae* may be asymptomatic or may present with minimal physical examination findings. In one review, 75% to 100% of patients with *M pneumoniae* infection have an intractable, nonproductive cough, whereas only 3% to 10% developed pneumonia. *M pneumoniae* is self-limited. A Cochran review found that there is still insufficient evidence that antibiotics

are effective against LRTI caused by *Mycoplasma* in children. (15) *Mycoplasma pneumoniae* may be also associated with a variety of extrapulmonary manifestations (Table 3). *Chlamydia pneumoniae* is indistinguishable from pneumonia caused by other factors. Extrapulmonary manifestations of *C pneumoniae* infections may include the following:

- Meningoencephalitis
- Guillain-Barré syndrome
- Reactive arthritis
- Myocarditis

Viral pneumonia has a gradual insidious onset. The patient usually experiences nontoxic effects, with upper respiratory tract symptoms, and auscultatory findings are more likely to be diffuse. Wheezing is more frequent in viral than bacterial pneumonia.

General Approach

History and Physical Examination

The approach to the child with suspected pneumonia begins with a detailed history and careful physical examination. History is more likely to reveal fever, with associated respiratory symptoms, including cough and tachypnea. On physical examination, the clinician must pay special attention to the general appearance of the patient and assess for hypoxia

and cyanosis. Young infants may present with lethargy, poor feeding, or irritability. Although the presence of fever is not specific for pneumonia, it may be the only sign in occult pneumonia. In a systematic review, tachypnea was twice as frequent in children with vs without radiographic pneumonia, and its absence was the most valuable sign for ruling out the diagnosis, making it the most sensitive sign. Other signs of respiratory distress include increased work of breathing (intercostal, subcostal, or suprasternal retractions; nasal flaring; grunting, head bobbing; use of accessory muscles), apnea, and altered mental status. Signs of respiratory distress are more specific than fever or cough for LRTI but not as sensitive.

Lung examination is a key part of the assessment. Auscultation of all lung fields should be performed, listening for crackles (rales) or crepitations, the presence of which correlates with pneumonia. The absence of these findings does not rule out pneumonia. Other findings consistent with consolidated lung parenchyma might include decreased breath sounds, egophony, bronchophony, tactile fremitus, or dullness to percussion. Again, wheezing is more likely in viral or atypical pneumonia, but when wheezing is only heard unilaterally and is associated with fever, bronchial obstruction (intrinsic or extrinsic) and associated bacterial infection should be suspected. Splinting, dullness to percussion, distant breath sounds, and friction rub are suggestive of pleural effusion and must be confirmed by imaging. It is important to mention that many patients clinically suspected of having pneumonia are treated empirically with no need for imaging or laboratory workup except for severely ill children with hypoxia, respiratory distress, and inability to eat or drink.

Diagnostic Testing and Evaluation

RADIOGRAPHIC IMAGING. In a child with mild lower respiratory symptoms consistent with CAP who is a candidate for outpatient treatment, chest radiographs are not routinely needed to make the diagnosis. (7)(8)(16) The presence of infiltrates on chest radiograph in a child with fever and respiratory distress confirms the diagnosis of pneumonia; however, the absence of chest x-ray findings does not rule out pneumonia if there is high clinical suspicion. This is due to several factors: the radiographic findings may lag behind the clinical picture, dehydrated children may not have an infiltrate initially, and it is impossible to differentiate atelectasis from pneumonia on a single chest radiograph (an infiltrate that resolves in less than 48-72 hours is more likely atelectasis than pneumonia).

An initial chest radiograph may be indicated in the following situations (16):

Table 3. Clinical Manifestations of *Mycoplasma pneumoniae* Infections (7)

Respiratory tract disease

- Intractable nonproductive to mild cough (75%–100%)
- Pneumonia (3%–10%)
- Chills
- With or without wheezing and dyspnea
- Pharyngitis (6%–59%)
- Rhinorrhea (2%–40%)
- Ear pain (2%–35%)
- Severe earache secondary to bullous myringitis (5%)
- Sinusitis

Extrapulmonary disease

- Hemolytic anemia
- Rash (erythematous maculopapular rash, urticaria, Stevens–Johnson syndrome)
- Joint involvement (polyarthritis)
- Gastrointestinal (pancreatitis, hepatitis)
- Central nervous system
- Cardiac disease (pericarditis, myocarditis)

1. Severe disease, hypoxemia, or significant respiratory distress that requires hospitalization.
2. Inconclusive clinical findings.
3. To rule out other causes of respiratory distress (eg, foreign body, heart disease, underlying cardiopulmonary conditions).
4. Prolonged fever and worsening symptoms despite adequate antibiotic coverage to rule out complications (parapneumonic effusion, pneumothorax).
5. As part of the workup of a young infant with fever without a source and leukocytosis.

Follow-up chest radiographs are not routinely indicated in children who are adequately treated and recovered. Follow-up radiographs are indicated in complicated pneumonias that are clinically unstable, in patients receiving adequate antibiotic coverage for 48 to 72 hours with poor clinical improvement or worsening, and in recurrent pneumonias that involve the same lobe to rule out a suspected anomaly, chest mass, or foreign body. Children with complicated pneumonia treated with chest tube placement or video-assisted thoracoscopic surgery (VATS) do not require routine daily chest radiography if they are clinically stable and improving.

When indicated, chest radiographs should be obtained in the posteroanterior upright position in children younger than 4 years and in the supine anteroposterior position in younger children. A lateral view is preferred, and a lateral decubitus view (with affected side down) should be obtained when a pleural effusion is suspected.

Bedside ultrasonography of the chest was studied and compared with chest radiographs. In one prospective cohort study of 200 patients, ultrasonography had an overall sensitivity of 86% (95% CI, 71%-94%) and a specificity of 89% (95% CI, 83%-93%). Specificity increased to 97% in children with consolidation greater than 1 cm by chest radiographs. The authors concluded that bedside ultrasonography was found to be a highly specific, noninvasive, radiation-free test that can be used by clinicians to diagnose pneumonia. (17)

Laboratory Testing

Routine laboratory testing is not indicated to diagnose pneumonia, particularly in children who are stable, are nonhypoxic, and have suspected CAP and are candidates for outpatient treatment. Patients with hypoxemia, severe respiratory distress, possible complicated pneumonia, or associated comorbid conditions may need further workup.

Blood Tests

A complete blood cell count with differential does not allow differentiation among bacterial, atypical, or viral

origins or dictate management, particularly in the outpatient setting. (7)(8) A complete blood cell count with differential is typically performed in children who are candidates for hospitalization (Table 4). Peripheral eosinophilia suggests *Chlamydia trachomatis* in infants with afebrile pneumonia of infancy. Acute phase reactants, such as erythrocyte sedimentation rate, C-reactive protein, and serum procalcitonin, should not be routinely measured in fully immunized children with mild disease but may be useful in monitoring response to treatment in children hospitalized with severe or complicated pneumonia. (11)(16) Other blood tests might include serum electrolytes to assess for degree of dehydration and to rule out hyponatremia secondary to syndrome of inappropriate antidiuretic hormone secretion.

Microbiologic Tests

BLOOD CULTURES

- Not routinely indicated in the outpatient setting in children who have nontoxic effects and fully immunized due to low yield (only positive in 10%-12% of children). (8)
- In patients with parapneumonic effusion or empyema the yield increases to 30% to 40%.
- Should be obtained in children hospitalized with severe disease, who fail to demonstrate response despite adequate antibiotic coverage, or in children with complicated pneumonia. (16)
- Follow-up blood cultures are not necessary in patients with clear improvement.

NASOPHARYNGEAL SAMPLES. Nasopharyngeal cultures do not provide useful information because the bacteria recovered are usually normal upper respiratory tract flora and do not necessarily correlate with the cause of pneumonia. Polymerase chain reaction (PCR) is now available for the detection of several pathogens in nasopharyngeal samples as discussed below. The identification of bacteria by PCR in nasopharyngeal samples is not as useful for the same reason expressed above.

SPUTUM CULTURES

- Difficult to obtain and induce in young children (<5 years) and in outpatient setting.
- Should be obtained in older hospitalized children, children who are in intensive care, those who have complicated pneumonia, or those who do not respond to empiric therapy; good-quality sputum samples can be obtained.
- An adequate sputum specimen for examination is one with:

Table 4. Indications for Hospitalization (8)(16)

- Hypoxia (oxygen saturations <90%–92%)
- Infants <3–6 months with suspected bacterial infection (unless a viral cause or *Chlamydia trachomatis* is suspected and they are normoxemic and relatively asymptomatic)
- Tachypnea:
 - Infants <12 months of age: respiratory rate >70 breaths/min
 - Children: respiratory rate >50 breaths/min
- Respiratory distress: apnea, grunting, difficulty breathing, and poor feeding
- Signs of dehydration
- Inability to maintain hydration or oral intake
- Capillary refill time >2 seconds
- Infants and children with toxic appearance or suspected or confirmed to have infection with a virulent organism (CA-MRSA or group A *Streptococcus*)
- Underlying conditions comorbidities that:
 - May predispose patients to a more serious course (eg, cardiopulmonary disease, genetic syndromes, neurocognitive disorders)
 - May be worsened by pneumonia (eg, metabolic disorder)
 - May adversely affect response to treatment (eg, immunocompromised host, sickle cell disease)
- Complications (eg, effusion/empyema)
- Failure of outpatient therapy (48–72 hours with no response)
- Caretaker unable to provide appropriate observation or to comply with prescribed home therapy

Indications for intensive care admission include:

- Severe respiratory distress or impending respiratory failure requiring
 - Intubation and mechanical ventilation
 - Positive pressure ventilation
- Recurrent apnea or slow irregular respirations
- Cardiopulmonary monitoring due to cardiovascular compromise secondary to:
 - Sustained tachycardia
 - Inadequate blood pressure
 - Requires pharmacologic support of blood pressure or perfusion
 - Altered mental status due to hypercarbia or hypoxemia
- Pediatric Early Warning Score >6

CA-MRSA=community-acquired methicillin-resistant *Staphylococcus aureus*.

- 10 or fewer epithelial cells
- And 25 or more polymorphonuclear leukocytes under low power ($\times 100$).
- A predominant microorganism and/or intracellular organisms suggest the etiologic agent.

PLEURAL FLUID

- When pleural fluid is more than minimal in amount, it should be obtained through a diagnostic (and possibly therapeutic) thoracentesis and sent for Gram stain and culture ideally before administration of antibiotics.
- Because most children have already received antibiotics by the time the pleural fluid is sampled, thereby significantly reducing the yield of conventional cultures, antigen testing and PCR may be helpful in identifying the causative agent.
- Studies such as pH, glucose, protein, and lactate dehydrogenase rarely change management and are not recommended, except for white blood cell count with differential to differentiate bacterial from mycobacterial causes and from malignancy. (16) Table 5 highlights the laboratory findings in empyema.

Rapid Tests

Nasopharyngeal swab specimen for rapid testing by PCR or immunofluorescence may be useful. (8) A positive rapid test result for viruses in inpatient and outpatient settings might decrease the need for further testing or for starting antibiotic therapy; it may also give the opportunity for starting antiviral therapy early. (16) Rapid tests exist for the following microorganisms:

- RSV
- Influenza viruses
- Parainfluenza viruses
- Adenovirus
- *Mycoplasma pneumoniae*
- *Chlamydophila pneumoniae*
- Coronaviruses
- Bordetella pertussis
- Picornavirus (rhinovirus and enterovirus)
- hMPV (can only be identified by PCR)

The PCR tests for pneumococcus in sputum and blood are not recommended because their sensitivity and specificity in children have not been conclusively established.

Antigen Detection and Serologic Testing

Urinary antigen detection tests have low sensitivity and high false-positive rates. (8)(16) Hence, they are not recommended for the diagnosis of pneumococcal pneumonia in children. (16)

Pleural fluid antigen detection: In children with parapneumonic effusion or empyema whose pleural fluid

Table 5. Laboratory Findings in Empyema (2)(4)(16)

Studies	Empyema
pH	<7.1
Glucose	<40 mg/dL
Lactate dehydrogenase	>1000 IU/mL
Gram stain and culture with or without polymerase chain reaction	Bacteria
Gross appearance	Purulent

culture was obtained after antibiotic therapy, a positive pneumococcal antigen in the pleural fluid can be helpful in confirming the cause.

Routine serologic testing for specific pathogens (eg, *S pneumoniae*, *M pneumoniae*, *C pneumoniae*) is not indicated because results do not usually influence management. Viral serologic testing is not practical because acute and convalescent specimens are needed. Serologic testing for *Chlamydia* species is not readily available.

Mycoplasma pneumoniae, when suspected in an older child, is often treated empirically. However, serologic and PCR testing can be helpful in evaluating the younger child or in establishing the diagnosis in patients with extrapulmonary (particularly central nervous system) manifestations. The most widely used serodiagnostic test is enzyme-linked immunosorbent assay (ELISA); however, the complement fixation test has better specificity. It measures early IgM (predominantly) and IgG antibodies (to a lesser extent) to *M pneumoniae*. A positive result is defined as follows:

- A 4-fold or greater increase in titer in paired sera OR
- A single titer of greater than or equal to 1:32

Antibody titers rise 7 to 9 days after infection and peak at 3 to 4 weeks. A 4-fold decline in titer also is diagnostic if late samples are obtained. The presence of antibodies either by enzyme immunoassay or complement fixation is highly sensitive for the detection of *M pneumoniae* infection. A major disadvantage of these tests is their false-positive results, particularly during inflammatory reactions, such as neurologic syndromes, bacterial meningitis, and acute pancreatitis.

Less commonly used diagnostic tests are as follows:

1. Tuberculin skin testing or Quantiferon gold (children >5 years old): If pulmonary tuberculosis is suspected, either tuberculin skin testing (purified protein derivative) or interferon gamma release assays (IGRAs) can be used. There are 2 available IGRAs:

- a. Quantiferon Gold: Measures interferon gamma produced by lymphocytes
- b. ELISA spot: Measures the number of lymphocytes producing interferon gamma both in response to specific *M tuberculosis* antigens.

IGRAs measure response to antigens not present in BCG or *Mycobacterium avium*; therefore, it has better specificity than tuberculin skin testing, especially in children who had received BCG vaccine in whom frequent purified protein derivatives can cause a boosting effect.

2. Urine antigen testing for legionellosis due to serogroup 1.
3. Serum and urine antigen testing for histoplasmosis.
4. Histoplasmosis serologic testing (immunodiffusion and complement fixation).
5. *Cryptococcus* antigen detection in serum.
6. The following tests can be used as part of the workup of the immunocompromised patient with suspected pneumonia:
 - a. β -D-Glucan levels: β -D-Glucan is part of the cell wall of yeast and fungi and even *Pneumocystis jirovecii* and can be elevated in fungal pneumonias. (18)
 - b. Galactomannan levels: Galactomannan is part of the cell wall of molds, such as aspergillus. Antigen levels in bronchoalveolar lavage (BAL) or serum are positive in suspected pneumonia due to aspergillus. (19)

The clinician must be aware that certain antibiotics, such as piperacillin-tazobactam or transfusion with blood or blood-derived products such as intravenous immunoglobulin, may induce false-positive test results. (20)

Invasive Studies

Invasive studies to establish the cause of pneumonia in children are reserved for the critically ill child or the child with significant comorbidity whose initial diagnostic workup is inconclusive and in whom the risk of establishing the diagnosis outweighs the risk of the invasive procedure. (16) Invasive studies are rarely needed. Invasive studies include the following:

- Bronchoscopy with BAL - Quantitative culture techniques differentiate true infection from upper airway contamination.
- Morning gastric lavage through a nasogastric tube for acid fast bacilli stain and culture is used in the diagnosis of tuberculosis.
- The BAL technique for obtaining cultures in intubated patients uses a catheter inside a catheter, avoiding

sampling the upper airway and directly obtaining cultures from the alveoli. Because of the anatomy of the lungs, samples are obtained from the right lower lobe.

- Computed tomography or ultrasonography-guided percutaneous needle aspiration of the affected lung tissue.
- Lung biopsy either by a thoracoscopic or thoracotomy approach is rarely used in United States, but open biopsy yields diagnostic information that may affect medical management in up to 90% of patients. In one study, open lung biopsy confirmed the infectious cause in 10 of 33 patients, 8 of whom had a prior non-diagnostic BAL. Lung biopsy is commonly used in immunocompromised patients.

Differential Diagnosis

When the clinician is faced with a child presenting with fever, tachypnea, cough, respiratory distress, and infiltrates on chest radiograph, the diagnosis of pneumonia is highly likely. (7) Other diagnoses, however, must be considered. In a neonate with respiratory distress, congenital anatomical cardiopulmonary anomalies must be ruled out, such as tracheoesophageal fistula, congenital heart disease, and sepsis. In infants and young children, foreign body aspiration (even if no history of any witnessed aspiration), bronchiolitis, heart failure, sepsis, and metabolic acidosis may all cause tachypnea. In these cases, a careful history and physical examination and a supportive imaging study can distinguish pneumonia from other conditions.

In adolescents and young adults, Lemierre syndrome (jugular vein suppurative thrombophlebitis) must be considered. Lemierre syndrome is typically caused by *Fusobacterium* species that infect the carotid sheath and spread to lungs and mediastinum.

Children who present with respiratory distress and wheezing may have CAP; however, first-time wheezing of asthma with or without bronchiolitis can be the true diagnosis. A patient with asthma or bronchiolitis may have a radiographic picture that is normal or has infiltrates that could potentially be due to atelectasis.

Other entities that may mimic pneumonia on clinical examination or on radiographs in children are listed in Table 6

Treatment

Treatment of pneumonia varies between inpatient and outpatient settings. In either setting, supportive care includes the use of antipyretics, suctioning, and hydration when needed. Mucolytics and cough suppressants have

no role in the treatment of pneumonia. (21)(22) Zinc supplementation has been studied and found to be an effective adjunct to decreasing the incidence and prevalence of pneumonia in children 2 to 59 months. (23)(24) In most cases of CAP, the chances of having a specific etiologic diagnosis are low, leading the clinician to treat empirically. The **Figure** gives highlights of the decision tree of the approach to the child with suspected pneumonia.

Outpatient Management

EMPIRIC THERAPY. Antimicrobial therapy is not routinely recommended in preschool children with pneumonia (viruses are more common). (21) Because *S pneumoniae* remains the most commonly implicated pathogen, amoxicillin or amoxicillin-clavulanate remains the most appropriate first-line antimicrobial agent used empirically for CAP in fully immunized, healthy, young preschool children with mild to moderate symptoms. (25) Clavulanate adds the benefit of action against β -lactamase-producing organisms (*H influenzae* and *Moraxella catarrhalis*). *S pneumoniae* resistance to penicillin is due to a penicillin-binding protein (PBP2x) that has decreased affinity to β -lactams. Increasing the dose of amoxicillin (90-100 mg/kg daily) may overcome this mechanism of resistance and should be prescribed if the clinician suspects resistance (eg, children in day care or siblings in day care, history of frequent infections). Amoxicillin-clavulanate is dispensed in 2 different amoxicillin-clavulanate ratios: 7:1 and 14:1. The 14:1 ratio should be used when high-dose amoxicillin is required to reduce the possibility of antibiotic-associated diarrhea.

In school-aged children and teens with a clinical picture compatible with atypical CAP, coverage using a macrolide (azithromycin or clarithromycin) should be considered. A systematic review of studies in developing countries found no significant difference in the treatment failures or relapse rates between 3- and 5-day courses of antibiotics in children ages 2 to 59 months with outpatient management of CAP. (26)

In children with moderate to severe CAP suspected of having influenza infection and because early antiviral therapy provides the maximum benefit, treatment with antiviral therapy should not be delayed until confirmation of a positive influenza test result. It is also worth noting that treatment after 48 hours of symptoms might still provide clinical benefits in severe cases of influenza. (16)

Inpatient Management

Table 4 highlights the indications for hospitalizations and intensive care admission.

Table 6. Mimickers of Pneumonia in Children

Anatomical considerations

- Prominent thymus
- Breast shadows
- Bronchogenic cyst
- Vascular ring
- Pulmonary sequestration
- Congenital lobar emphysema
- Atelectasis (due to a foreign body or mucous plug)

Aspiration of gastric contents secondary to

- Gastroesophageal reflux
- Tracheoesophageal fistula
- Cleft palate
- Neuromuscular disorders

Chronic pulmonary disorders

- Asthma
- Bronchiectasis
- Bronchopulmonary dysplasia
- Cystic fibrosis
- Pulmonary fibrosis
- α_1 -Antitrypsin deficiency
- Pulmonary hemosiderosis
- Alveolar proteinosis
- Desquamative interstitial pneumonitis
- Sarcoidosis
- Histiocytosis X

Drugs and chemicals

- Nitrofurantoin
- Bleomycin
- Cytotoxic drugs
- Opiates
- Radiation therapy
- Smoke inhalation
- Lipoid pneumonia

Vasculitis

- Systemic lupus erythematosus
- Granulomatosis with polyangiitis (Wegener)
- Juvenile idiopathic arthritis

Others

- Hypersensitivity pneumonitis
- Neoplasm
- Pulmonary edema due to heart failure
- Pulmonary infarction
- Acute respiratory distress syndrome
- Graft-vs-host disease
- Poor inspiratory film
- Near drowning
- Underpenetrated film

Adapted from Barson WJ. Clinical Features and Diagnosis of Community-Acquired Pneumonia in Children. UpToDate®. June 2012.

EMPIRIC THERAPY. It is helpful for the clinician to be familiar with the antibiograms of the local community hospitals when deciding on empiric therapy. Fully immunized infants or school-aged children hospitalized with CAP must be empirically prescribed an antibiotic regimen that provides coverage for *S pneumoniae* using ampicillin or penicillin G (if no significant local resistant strains in community data). Ampicillin-sulbactam provides additional coverage against *H influenzae*, *M catarrhalis*, or methicillin-sensitive *S aureus* (MSSA). The currently available intravenous formulations of ampicillin-sulbactam do not permit high-dose ampicillin (300-400 mg/kg daily) when pneumococci with high ampicillin mean inhibitory concentration is suspected. If this dose is desired, a combination of ampicillin-sulbactam at 300 mg/kg daily (dosing ampicillin at 200 mg/kg daily) and regular ampicillin at 100 to 200 mg/kg daily is a recommended regimen. The alternative is third-generation cephalosporin (ceftriaxone at 100 mg/kg daily or cefotaxime at 200 mg/kg daily) used in infants and children who are not fully immunized, in regions with high rates of invasive penicillin-resistant pneumococcal strains, and in infants and children with severe life-threatening infections and/or pneumonia complications, such as empyema. In patients with suspected *M pneumoniae* or *C pneumoniae*, the addition of an oral or parenteral macrolide to empiric cephalosporin or β -lactam antibiotic should be considered. In hospitalized patients with other comorbidities or clinical or radiographic findings suggestive of *S aureus*, vancomycin, linezolid, or clindamycin should be added to the regimen (Table 7). (16) Ceftaroline, a fifth-generation cephalosporin, may provide an attractive alternative in those patients with complicated pneumonia. Ceftaroline does not yet have an indication in pediatrics hence, data on dosing is limited. Ceftaroline is the first cephalosporin with proven efficacy against *S aureus* expressing the penicillin-binding protein PBP2a and pneumococci expressing PBP2x. Even though ceftaroline is indicated for use, it has not been approved for treating lung infections due to MRSA, but it is indicated for MSSA. There is no evidence that chest physiotherapy plays a beneficial role in the management of pneumonia or leads to a decrease in the length of stay or a change in the outcome. (27)

Complicated pneumonia (eg, parapneumonic effusion, lung abscess) is an indication for hospitalization. The antibiotic choice in these patients must provide a broader coverage for β -lactam resistant bacteria and CA-MRSA. In addition, coverage for anaerobes must be provided in children with lung abscess or aspiration pneumonia until a specific etiologic agent is identified.

SPECIFIC THERAPY. When a bacterial pathogen is identified on blood or pleural fluid cultures, susceptibility testing should guide the antibiotic choice (Table 8).

The treatment regimen for uncomplicated cases must be continued for a total of 7 to 10 days (parenteral and oral therapy). In hospitalized cases whose baseline inflammatory markers are checked, some centers recommend continuing antibiotics until the erythrocyte sedimentation rate falls below 20 mm/h. Longer antibiotic regimen is recommended in complicated cases, starting parenterally and continuing orally. Suggested antibiotic courses are 4 weeks total or 2 weeks after defervescence and clinical improvement.

Children receiving adequate antibiotic coverage for 48 to 72 hours without clinical improvement or with deterioration of clinical picture should undergo further investigation to rule out alternative diagnosis (foreign body), antibiotic resistance, or complicated pneumonia. (16)

Children with allergy to β -lactams become a therapeutic challenge. History is essential in this situation because many children whose parents report penicillin allergy are not necessarily truly allergic. If real allergy is suspected, options are carbapenems (meropenem, 20-40 mg/kg per dose every 8 hours), which rarely cross react with penicillins or cephalosporins, or clindamycin (even in hospitals with reported clindamycin resistance >30% on antibiograms), or combination of antibiotics, such as vancomycin or linezolid plus aztreonam. Quinolones such as levofloxacin will cover most respiratory pathogens that cause pyogenic and walking pneumonia.

Complications and Sequelae

Children with pneumonia might experience several complications. (7)(13)The complications are more likely due to bacterial pneumonias than atypical or viral pneumonias. The rate of complications in hospitalized children with pneumococcal pneumonia is estimated at 40% to 50%.

Patients with chronic illness or comorbid conditions are more subject to complications that result in increased

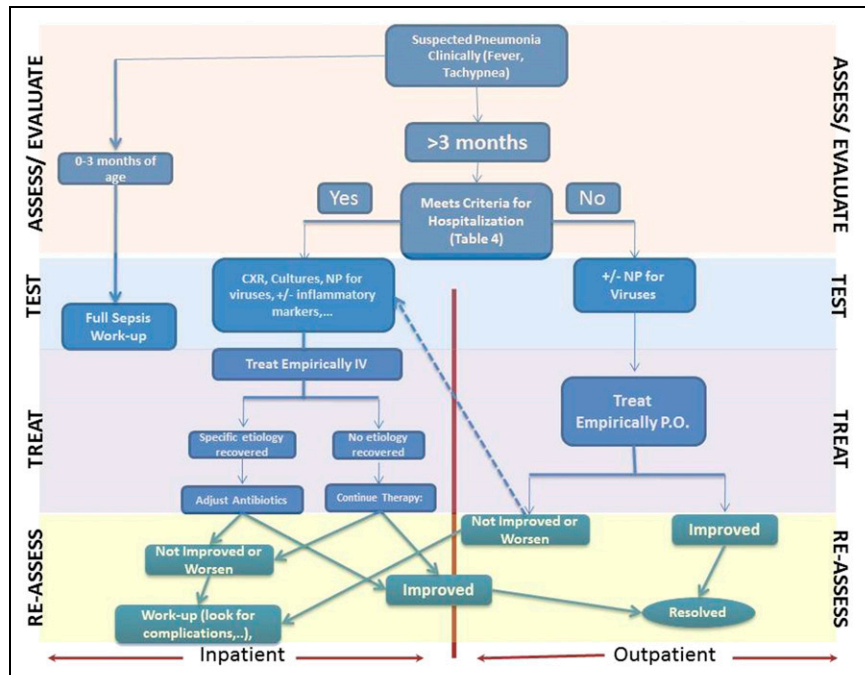


Figure. General approach to childhood pneumonia.

length of stay. Prolonged or persistent fever or worsening of symptoms despite adequate antibiotic coverage in a child is suspect for complications. Table 9 lists the complications of pneumonias

Necrotizing pneumonia is suspected when a translucent lesion is seen on chest radiography in a child with prolonged fever or septic appearance. Diagnosis is confirmed with contrast-enhanced computed tomography. Most necrotizing pneumonias in pediatrics are caused by

Table 7. Empiric Antibiotic Regimen (4)(7)

Outpatient	Inpatient
First line • Young children ○ Amoxicillin • Adolescent: ○ Azithromycin	First line • Ampicillin • Cephalosporin + • Azithromycin
Second line (adolescent) • Macrolide or doxycycline • Fluoroquinolones (eg, levofloxacin, moxifloxacin) – Also used for adolescent or older child with type 1 hypersensitivity to β -lactam antibiotics	Second line • Vancomycin • Clindamycin • Linezolid

Table 8. Specific Antibiotic Regimen (7)(31)

Pathogen	Antibiotic(s)	Comments
<i>Streptococcus pneumoniae</i>		
• Penicillin susceptible	<ul style="list-style-type: none"> • Penicillin or ampicillin (drug of choice) • Cefuroxime • Cefotaxime • Ceftriaxone • Clindamycin (oral or intravenous) 	50–90 mg/kg daily For patients allergic to β -lactam antibiotics
• Intermediate and resistant strains	<ul style="list-style-type: none"> • Cefotaxime • Ceftriaxone • Linezolid and • Clindamycin • Cefdinir 	Most active oral cephalosporin in vitro against penicillin-resistant strains
○ Pneumococcal serotype 19A	<ul style="list-style-type: none"> • Vancomycin, linezolid, or levofloxacin 	Multidrug resistant to penicillin, macrolides, clindamycin, and trimethoprim-sulfamethoxazole
<i>Mycoplasma pneumoniae</i>	<ul style="list-style-type: none"> • Azithromycin • Clarithromycin • Erythromycin • Tetracycline • Doxycycline • Doxycycline or a fluoroquinolone 	<ul style="list-style-type: none"> • 10 mg/kg in 1 dose on the first day and 5 mg/kg in 1 dose for 4 days • 15 mg/kg per day in 2 divided doses for 10 days • 30 to 40 mg/kg per day in 4 divided doses for 10 days • 20 to 50 mg/kg per day in 4 divided doses for 10 days (maximum daily dose 1 to 2 g) • 2 to 4 mg/kg per day in 1 or 2 divided doses for 10 days (maximum daily dose 100 to 200 mg) • In children age ≥ 8 years • If macrolide resistance is suspected or documented, particularly if the child is severely ill
<i>Chlamydia pneumoniae</i>		
• Children age ≥ 8 years and adults	<ul style="list-style-type: none"> • Doxycycline 	<ul style="list-style-type: none"> • 2 to 4 mg/kg per day divided into 2 doses (maximum daily dose, 200 mg) for 10 to 14 days
• Children age < 8 years	<ul style="list-style-type: none"> • Erythromycin 	<ul style="list-style-type: none"> • 30 to 40 mg/kg per day divided into 4 doses for 10 to 14 days

S aureus and pneumococci. Pneumatocoles are frequently encountered, and radiologic cure lags behind clinical cure.

Lung abscess presents with nonspecific clinical signs and symptoms similar to those of pneumonia. It has an indolent course and is often associated with a parapneumonic effusion. Lung abscesses may occur in healthy children or may be secondary to a congenital (cystic malformation) or acquired (cystic fibrosis, immunodeficiency) lung anomaly. (25) Up to 90% of cases might be adequately treated with a prolonged course of intravenous antibiotics.

Parapneumonic effusion can be in the form of pleural effusion or empyema. The pleural fluid analysis allows differentiating one from the other (Table 5). Empyema is a pleural effusion that has become purulent or semipurulent.

Treatment of Complications

PARAPNEUMONIC EFFUSION. The effectiveness of treating pleural effusion and empyema in children and teens is unknown because there is a lack of well-designed controlled studies. Traditionally, pleural fluid is obtained by needle aspiration for culture, and antibiotic therapy is started. Further chest tube drainage is resorted to if there is no improvement or the patient's condition worsens. In severe cases, surgical intervention may be necessary. (4) The management of parapneumonic effusion depends on the size of the effusion and the child's degree of respiratory compromise. (16)

- A small, uncomplicated effusion (< 10 mm on lateral radiograph or opacification less than one-fourth of the hemithorax) can be empirically treated without

need for needle aspiration or chest tube drainage (with or without fibrinolysis) or VATS.

- A moderate-sized effusion (>10 mm rim of fluid with less than half the hemithorax opacified) in a child with respiratory compromise or empyema requires chest tube drainage with fibrinolytics or VATS (regardless of culture results).
- A large effusion (opacifies >50% of hemithorax) consistent with empyema (positive culture) requires chest tube drainage with fibrinolytics or VATS. (Both have been found to be equally effective and associated with decreased morbidity.) The choice of drainage procedure depends on local expertise. Either VATS or open chest debridement with decortication is indicated in a patient who continues to have moderate to large effusions and respiratory compromise despite 2 to 3 days of chest tube and fibrinolysis. Decortication is associated with higher morbidity rates. A chest tube that demonstrates lack of intrathoracic air leak and less than 1 ml/kg daily during the past 12 hour drainage can be clamped or removed.

Fibrinolytics are used along with chest tube placement for moderate to large effusions. The initial dose of fibrinolytics is administered at the time of chest tube placement with a “dwell” time, during which the chest tube is clamped, before applying suction to the tube. In various studies, the dwell time varied between 1 and 4 hours with a repeat administration of fibrinolytics anywhere from every 8, 12, or 24 hours later. On the basis of the currently available data, both chest tube with fibrinolysis and VATS are considered equally acceptable initial

Table 9. **Pneumonia Complications (2)(4)(13)(21)**

Complications	Comments
Respiratory complications	
Pleural effusion	<ul style="list-style-type: none"> • Associated with hypoalbuminemia
Empyema	<ul style="list-style-type: none"> • Affects 1:150 children with pneumonia • <i>Staphylococcus aureus</i>, <i>Streptococcus pneumoniae</i>, <i>Haemophilus influenzae</i> • 3 Stages: <ul style="list-style-type: none"> ◦ Exudative phase ◦ Fibrinopurulent phase ◦ Organizing phase • Associated with hypoalbuminemia • 3% of all pediatric hospitalizations • One-third of admissions for pneumococcal pneumonia
Pneumatocele	<ul style="list-style-type: none"> • Classically associated with <i>S aureus</i> • May occur with a variety of organisms • Frequently associated with empyema • Many involute spontaneously without treatment • Surgery for refractory cases • Occasionally lead to pneumothorax
Necrotizing pneumonia	<ul style="list-style-type: none"> • Seen in: <ul style="list-style-type: none"> ◦ <i>S pneumoniae</i> (especially serotype 3 and serogroup 19) ◦ <i>S aureus</i> ◦ Group A <i>Streptococcus</i> ◦ <i>Mycoplasma pneumoniae</i> ◦ <i>Legionella</i> ◦ <i>Aspergillus</i> • Prolonged fever • Septic appearance • Diagnosis: <ul style="list-style-type: none"> ◦ Chest radiography – radiolucent lesion ◦ Confirmed with contrast enhanced computed tomography • Rare
Lung abscess	<ul style="list-style-type: none"> • Predisposing factors: <ul style="list-style-type: none"> ◦ Aspiration (1–2 weeks after event) ◦ Airway obstruction ◦ Congenital lung anomaly ◦ Acquired lung anomaly • <i>S aureus</i> is the most frequently involved organism. Other organisms include anaerobes, <i>Klebsiella</i>, and streptococcal species • Should be suspected when: <ul style="list-style-type: none"> ◦ Unusually persistent consolidation ◦ Persistent round pneumonia ◦ Increased volume of involved lobe (bulging fissure) • Complications: <ul style="list-style-type: none"> ◦ Intracavitary hemorrhage ◦ Empyema ◦ Bronchopleural fistula ◦ Septicemia ◦ Cerebral abscess ◦ Inappropriate secretion of antidiuretic hormone

Continued

Table 9. (Continued)

Complications	Comments
Bronchopleural fistula Pneumothorax	
Other complications	
Hyponatremia	<ul style="list-style-type: none"> • 45% of children with community-acquired pneumonia • One-third of children hospitalized with community-acquired pneumonia • Increase length of stay, complications and mortality (in severe cases) • Secondary to syndrome of inappropriate antidiuretic hormone secretion
Sepsis or systemic inflammatory response system, meningitis, pericarditis, endocarditis, osteomyelitis, septic arthritis, central nervous system abscess, and atypical hemolytic-uremic syndrome	

- Stable and/or baseline mental and cardiorespiratory status.
- Ability to tolerate their home anti-infective regimen, and the caretaker at home has the ability to administer therapy.
- Ability to maintain adequate fluid and nutrition orally.

In addition, children hospitalized with pneumonia eligible for discharge:

- Who have had a chest tube and meet the requirements listed above, the chest tube must have been discontinued 12 to 24 hours before discharge with no clinical evidence of deterioration since chest tube removal
- Must have a follow-up plan prior to discharge.

drainage strategies, and either measure is found to be superior to chest tube alone. (16)

Additional imaging and further investigation to assess effusion progression are indicated for the child not responding to broad-spectrum therapy after 48 to 72 hours to assess progression of the effusion. For children receiving mechanical ventilatory support with no improvement, BAL or a percutaneous lung aspirate should be performed for culture to determine antibiotic resistance. An open lung biopsy for a Gram stain and culture should be obtained in the persistently and critically ill child receiving mechanical ventilatory support in whom previous investigations have not yielded a microbiologic diagnosis. (16)

Lung Abscess

Up to 90% of patients with a lung abscess may be adequately treated with intravenous antibiotics alone or with combination of intravenous antibiotics transitioning to oral antibiotics without requiring drainage of the abscess. (2)

Discharge Criteria

Children hospitalized with pneumonia are eligible for discharge when they demonstrate any of the following (Table 10) (15):

- Clinical improvement in level of activity and appetite, with a decreased fever for at least 12 to 24 hours.
- Sustained pulse oximetry measurements greater than 90% in room air for at least 12 to 24 hours.

Follow-up

Children hospitalized with pneumonia must follow up with their primary care physician soon after discharge to ensure continued improvement and adherence with the antibiotic regimen prescribed. It is important to discuss with caretakers that cough may persist for several weeks to 4 months after a CAP and 3 to 4 months after viral pneumonia or pertussis. Recovering children may continue to have moderate dyspnea on exertion for 2 to 3 months.

Special Considerations

Immunodeficiency

Children and young adults who are immunocompromised secondary to congenital or acquired immunodeficiency require special considerations in their treatment regimen in addition to coverage for the typical pathogens discussed in the normal host (2):

- Gram-negative bacilli (including *Pseudomonas aeruginosa*) and *S aureus* are common causes in neutropenic patients or in patients with white blood cell defects.
- History of exposure to an aquatic reservoir of *Legionella pneumophila*, such as a river, lake, air-conditioning tower, or water distribution system, places the patient at risk for legionellosis.
- Opportunistic fungi, such as *Aspergillus* and *Candida*, are the most common fungal pathogens in immunocompromised patients. *Aspergillus* affects the lungs through spore inhalation.

Table 10. Pneumonia Discharge Criteria (15)

- Clinical improvement (activity level, appetite)
- Afebrile for 12–24 hours
- Sustained pulse oximetry >90% on room air for 12–24 hours
- Baseline and stable cardiorespiratory and mental status
- Ability to tolerate oral anti-infective therapy and ability of caretaker to administer it
- Ability to tolerate oral intake of food and fluids
- For children who had a chest tube, the tube must have been discontinued 12–24 hours before discharge with no clinical signs of deterioration
- Availability of a follow-up plan before discharge

- Other opportunistic pathogens include *Fusarium* species and *Pneumocystis jirovecii* (formerly known as *Pneumocystis carinii*).
- Viral pathogens to be considered include rubeola, cytomegalovirus, varicella zoster virus, and Epstein-Barr virus.
- Atypical mycobacteria are a significant pathogen in children infected with human immunodeficiency virus (HIV).
- HIV-positive patients or patients receiving immunosuppressive or chronic steroid therapy must be treated for latent tuberculosis. (21)

The treatment of HIV-infected children depends on their CD4 cell count. Most children in the United States benefit now from antiretrovirals and have normal immune status so their treatment parallels those without HIV infection. Those children whose CD4 cell count is low are at risk of unusual pathogens, such as *Pneumocystis jirovecii* or cryptococcus; consulting with an infectious disease specialist is recommended. (28)

Cystic Fibrosis

Pneumonia in patients with cystic fibrosis is caused by infection by *S aureus*, *P aeruginosa*, and *H influenzae* (mostly nontypable strains) early in their disease. Older children with cystic fibrosis have multiple drug-resistant gram-negative organisms, such as *Burkholderia cepacia*, *Stenotrophomonas maltophilia*, and *Achromobacter xylosoxidans*. *Aspergillus* species and nontuberculous mycobacteria also may also cause disease in this population. These patients rarely get rid of their bacteria, so reviewing previous cultures is very important.

Sickle Cell

In patients with sickle cell anemia who present with fever, hypoxia, and respiratory distress due to acute chest syndrome, atypical bacterial pathogens are primarily the culprits. Other causes include *S pneumoniae*, *S aureus*, and *H influenzae*.

Other special considerations for therapy include the following:

- Residence or travel to certain geographic areas that are endemic for specific pathogens, such as tuberculosis (Asia, Africa, Latin America, and Eastern Europe), or exposure to individuals at high risk for tuberculosis, including homeless, incarcerated individuals, and HIV-infected patients.
- Exposure to certain animals such as the deer mouse (hantavirus), bird droppings (Histoplasmosis), birds (*Chlamydophila psittaci*), sheep, goats, or cattle (*Coxiella burnetii* – Q fever)

Prevention and/or Control

The most effective prevention method based on strong evidence is active immunization of children against *H influenzae* type b, *S pneumoniae*, influenza, and pertussis. Influenza virus vaccine should be administered annually to all infants 6 months or older and to adult caretakers of infants younger than 6 months. The latter should also receive the pertussis vaccine. High-risk infants should receive the RSV-specific monoclonal antibody-based on the American Academy of Pediatrics recommendation. (4)(16) Several measures can be adopted to prevent or decrease transmission. Because transmission occurs by droplet or contact, good hand washing and good personal hygiene are the most important measures. Standard isolation precaution is required in hospitalized patients with pneumococcal pneumonia and negative isolation in patients with TB. Other measures include limiting exposure to infected individuals and to cigarette smoke. Additional infection control measures based on cause include the following:

- Respiratory syncytial and parainfluenza viruses – gown and gloves (ie, contact precautions).
- Influenza virus, group A *Streptococcus* (for the first 24 hours of treatment), MSSA, *Bordetella pertussis* (until patient has received 5 days of effective therapy), and *M pneumoniae* – mask within 3 ft (ie, droplet precautions).
- Adenovirus – contact and droplet precautions.
- Methicillin-resistant *S aureus* – special organism precautions; contact and droplet precautions and dedicated patient equipment.

Summary Points and Practice Changes

- On the basis of strong evidence, chest radiographs are not routinely needed to make the diagnosis of pneumonia, particularly in suspected CAP in a child with mild lower respiratory symptoms who is a candidate for outpatient management. (16)
- On the basis of strong evidence, infants younger than 3 months with suspected bacterial pneumonia will likely benefit from hospitalization.
- Moderate evidence indicates that blood cultures should not be routinely performed in a child older than 3 to 6 months with suspected CAP who is fully immunized, who has nontoxic effects, and who is a candidate for outpatient management.
- On the basis of moderate evidence, blood cultures may recover the causative organism in children hospitalized with severe pneumonia, in those who do not demonstrate clinical response despite adequate antibiotic coverage, or in children with complicated pneumonia.
- On the basis of moderate evidence, fever and tachypnea are the most sensitive clinical signs of pneumonia, particularly after the first 3 days of illness
- On the basis of strong evidence, oral antibiotics are as effective as intravenous antibiotics in the treatment of mild-moderate CAP. (5)

(The evidence-based practice guidelines for the management of CAP in children older than 3 months (16) serves as a resource for the clinician desiring more details related to decisions surrounding diagnosis and management.)

References

1. Ebell MH. Clinical diagnosis of pneumonia in children. *Am Fam Physician*. 2010;82(2):192–193
2. Puligandla PS, Laberge JM. Respiratory infections: pneumonia, lung abscess, and empyema. *Semin Pediatr Surg*. 2008;17(1):42–52
3. Browne LR, Gorelick MH. Asthma and pneumonia. *Pediatr Clin North Am*. 2010;57(6):1347–1356
4. Schlaudecker EP, Frenck RW Jr. Adolescent pneumonia. *Adolesc Med State Art Rev*. 2010;21(2):202–219, vii–viii
5. Wilder RA. Question 1: are oral antibiotics as efficacious as intravenous antibiotics for the treatment of community acquired pneumonia? *Arch Dis Child*. 2011;96(1):103–104
6. World Health Organization. Pneumonia. Fact sheet No. 331. April 2013. <http://www.who.int/mediacentre/factsheets/fs331/en/>
7. Shah S, Sharieff GQ. Pediatric respiratory infections. *Emerg Med Clin North Am*. 2007;25(4):961–979, vi
8. Esposito S, Principi N. Unsolved problems in the approach to pediatric community-acquired pneumonia. *Curr Opin Infect Dis*. 2012;25(3):286–291
9. Scott JA, Wonodi C, Moisi JC, et al; Pneumonia Methods Working Group. The Definition of pneumonia, the assessment of severity, and clinical standardization in the Pneumonia Etiology Research for Child Health study. *Clin Infect Dis*. 2012;54(Suppl 2):S109–S116.
10. Lynch JP III, Zhanel GG. Streptococcus pneumoniae: epidemiology and risk factors, evolution of antimicrobial resistance, and impact of vaccines. *Curr Opin Pulm Med*. 2010;16(3):217–225
11. Virkki R, Juven T, Rikalainen H, Svedström E, Mertsola J, Ruuskanen O. Differentiation of bacterial and viral pneumonia in children. *Thorax*. 2002;57(5):438–441
12. Nohynek H, Madhi S, Grijalva CG. Childhood bacterial respiratory diseases: past, present, and future. *Pediatr Infect Dis J*. 2009;28(10 Suppl):S127–S132
13. Prayle A, Atkinson M, Smyth A. Pneumonia in the developed world. *Paediatr Respir Rev*. 2011;12(1):60–69
14. Don M, Canciani M, Korppi M. Community-acquired pneumonia in children: what's old? What's new? *Acta Paediatr*. 2010;99(11):1602–1608
15. Mulholland S, Gavranich JB, Gillies MB, Chang AB. Antibiotics for community-acquired lower respiratory tract infections secondary to *Mycoplasma pneumoniae* in children. *Cochrane Database Syst Rev*. 2012;9(Issue 9):CD004875 10.1002/14651858.CD004875.pub4
16. Bradley JS, Byington CL, Shah SS, et al; Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Executive summary: the management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. *Clin Infect Dis*. 2011;53(7):617–630
17. Shah VP, Tunik MG, Tsung JW. Prospective evaluation of point-of-care ultrasonography for the diagnosis of pneumonia in children and young adults. *JAMA Pediatr*. 2013;167(2):119–125
18. Mularoni A, Furfaro E, Faraci M, et al. High Levels of β -D-glucan in immunocompromised children with proven invasive fungal disease. *Clin Vaccine Immunol*. 2010;17(5):882–883
19. Hage CA, Knox KS, Davis TE, Wheat LJ. Antigen detection in bronchoalveolar lavage fluid for diagnosis of fungal pneumonia. *Curr Opin Pulm Med*. 2011;17(3):167–171
20. Boonsangskul V, Niyompattama A, Teosirimongkol C, Sriwanichrak K. False-positive serum and bronchoalveolar lavage Aspergillus galactomannan assays caused by different antibiotics. *Scand J Infect Dis*. 2010;42(6-7):461–468
21. Ranganathan SC, Sonnappa S. Pneumonia and other respiratory infections. *Pediatr Clin North Am*. 2009;56(1):135–156, xi
22. Chang CC, Cheng AC, Chang AB. Over-the-counter (OTC) medications to reduce cough as an adjunct to antibiotics for acute pneumonia in children and adults. *Cochrane Database Syst Rev*. 2012; 2(Issue 2):CD006088 10.1002/14651858.CD006088.pub3
23. Lassi ZS, Haider BA, Bhutta ZA. Zinc supplementation for the prevention of pneumonia in children aged 2 months to 59 months. *Cochrane Database Syst Rev*. 2010; (12, Issue 12):CD005978 10.1002/14651858.CD005978.pub2
24. Yakoob MY, Theodoratou E, Jabeen A, et al. Preventive zinc supplementation in developing countries: impact on mortality and morbidity due to diarrhea, pneumonia and malaria. *BMC Public Health*. 2011;11(Suppl 3):S23 <http://www.biomedcentral.com/1471-2458/11/S3/S23>
25. Clifford V, Tebruegge M, Vandeleur M, Curtis N. Question 3: can pneumonia caused by penicillin-resistant Streptococcus pneumoniae be treated with penicillin? *Arch Dis Child*. 2010;95(1):73–77

26. Sutijono D, Hom J, Zehtabchi S. Efficacy of 3-day versus 5-day antibiotic therapy for clinically diagnosed nonsevere pneumonia in children from developing countries. *Eur J Emerg Med.* 2011;18(5):244–250
27. Gilchrist FJ. Is the use of chest physiotherapy beneficial in children with community acquired pneumonia? *Arch Dis Child.* 2008;93(2):176–178
28. Punpanich W, Groome M, Muhe L, Qazi SA, Madhi SA. Systematic review on the etiology and antibiotic treatment of pneumonia in human immunodeficiency virus-infected children. *Pediatr Infect Dis J.* 2011;30(10):e192–e202
29. Wonodi CB, Deloria-Knoll M, Feikin DR, et al; Pneumonia Methods Working Group and PERCH Site Investigators. Evaluation of risk factors for severe pneumonia in children: the Pneumonia Etiology Research for Child Health study. *Clin Infect Dis.* 2012;54 (Suppl 2):S124–S131
30. Chang AB, Chang CC, O’Grady K, Torzillo PJ. Lower respiratory tract infections. *Pediatr Clin North Am.* 2009;56(6):1303–1321
31. Esposito S, Cohen R, Domingo JD, et al. Do we know when, what, and for how long to treat? antibiotic therapy for community-acquired pneumonia. *Pediatr Infect Dis J.* 2012;31(6):e78–e85

PIR Quiz

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- Anticipatory guidance to parents of children recovered from pneumonia includes discussion about the length of time that cough may persist. What is the length of time that cough may normally persist after a community-acquired pneumonia?
 - 2 weeks.
 - 4 weeks.
 - 2 months.
 - 3 months.
 - 4 months.
- Prevention of pneumonia in children includes active immunization of adult caretakers of infants younger than 6 months against which of the following pathogens?
 - Bordetella pertussis*.
 - Haemophilus influenzae* type b.
 - Neisseria meningitidis*.
 - Respiratory syncytial virus.
 - Tuberculosis.
- A 10-year-old boy presents with a history of fever, headache, malaise, mild sore throat, and worsening nonproductive cough. Lung examination reveals diffuse crackles. Chest radiographs reveal bilateral diffuse patchy infiltrates. The next step in management is to prescribe:
 - Amoxicillin.
 - Amoxicillin-clavulanate.
 - Azithromycin.
 - Cephalexin.
 - Penicillin.

4. A previously healthy, fully immunized 3-year-old girl presents with a 4-day history of gradual onset of runny nose, cough, fatigue, and slightly fast breathing. She continues to drink liquids but refuses solid foods. Temperature is 38.3°C. Physical examination reveals a tired-appearing child with mild tachypnea and subtle intercostal retractions. Lung examination reveals adequate aeration and crackles over all lung fields bilaterally. The next step in management is:
- Amoxicillin (50 mg/kg daily).
 - Blood culture.
 - Chest radiographs.
 - Close observation and follow-up.
 - Complete blood cell count.
5. One week ago, a previously healthy 6-year-old boy was seen in the outpatient clinic with a 5-day history of fever, chills, fatigue, muscle aches, and cough. Laboratory testing revealed a diagnosis of influenza A for which he was not treated because of delay in diagnosis. Today he returned to the clinic looking significantly worse, with tachypnea, dyspnea, and retractions. Chest radiography suggests a small empyema in the right lower lobe. The next step in management is to prescribe:
- Ampicillin.
 - Amoxicillin-clavulanate.
 - Azithromycin.
 - Ceftriaxone and clindamycin.
 - Penicillin.

Parent Resources from the AAP at HealthyChildren.org

- English only: <http://www.healthychildren.org/English/health-issues/conditions/chest-lungs/Pages/Pneumonia.aspx>

Corrections

In the April 2013 article "Pelvic Inflammatory Disease" (Trent M. *Pediatr Rev.* 2013;34(4):163–172), the video link at the end of the second-to-the-last paragraph in the section titled "Does Outpatient Treatment Work for Adolescents?" should read as follows: <http://www.youtube.com/watch?v=IGuXF8vpjQ>.

Readers can also search PID and Johns Hopkins on the general YouTube web page to locate the video.

Also, the beginning of the second sentence in the following paragraph should read, "One Brazilian trial has demonstrated that ceftriaxone 250 mg intramuscularly (IM) plus 1 g of azithromycin given orally at baseline each week for 2 weeks...". The journal regrets these errors.

Pneumonia

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Pediatrics in Review 2013;34;438

DOI: 10.1542/pir.34-10-438

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