NCC Pediatrics Continuity Clinic Curriculum: **Pneumonia** *Faculty Guide*

Goals & Objectives:

- To recognize the various etiologies of pneumonia (especially by age group)
- To recognize signs and symptoms of pneumonia
- To recognize when lab work and imaging might be helpful
- To know criteria for hospital admission and discharge
- To know complications from pneumonia

Pre-Meeting Preparation:

Please read the following enclosure:

- "Pneumonia" *(PIR, 2013)*

Conference Agenda:

- *Review* Pneumonia Quiz
- Complete Pneumonia Cases
- **Round-Table Activity:** Pneumonia X-Ray Quiz
  - **Go to www.cchs.net/pediatricradiology/imagegallery**
  - Under "Module Topic," select Childhood Pneumonia
  - Choose from 56 images. Click on "findings" and "diagnosis" for answer key.

Post-Conference: *Board Review Q&A*

Extra-Credit:

- www.cchs.net/pediatricradiology (Obtain Login; Complete "Childhood Pneumonia" module under Pediatric Radiology Curriculum, "Chest")
- Management of CAP in Infants & Children . . . *(PIDS & IDSA Guidelines, 2011)*

Edited by Maj(P) Matt Eberly, Capt Dan Adams, & MAJ Jennifer Hepps.

Pneumonia

Rani S. Gereige, MD, MPH,*
Pablo Marcelo Laufer, MD†

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.

Abbreviations

BAL:	bronchoalveolar lavage
CAP:	community-acquired pneumonia
CA-MRSA:	community-associated methicillin-resistant *Staphylococcus aureus*
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 *Staphylococcus aureus*
MSSA:	methicillin-sensitive *Staphylococcus aureus*
PCR:	polymerase chain reaction
RSV:	respiratory syncytial virus
VATS:	video-assisted thoracoscopic surgery
WHO:	World Health Organization

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

*Editorial Board. Department of Medical Education, Miami Children's Hospital, Miami, FL.
†Division of Pediatric Infectious Diseases, Miami Children's Hospital, Miami, FL.

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
• Sex: M:F = 1.25:1–2:1	Early-onset
• Socioeconomic/environmental factors: ◦ 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	• Prolonged rupture of the fetal membranes (>18 hours) • Maternal amnionitis • Premature delivery • Fetal tachycardia • Maternal intrapartum fever Late-onset • 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
• Underlying cardiopulmonary disorders and medical conditions: ◦ 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	

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 *Chlamydophila* (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	• Respiratory viruses • Rare causes of pneumonia: ○ Coronavirus ○ Varicella-zoster ○ Epstein-Barr virus ○ Mumps
Bacteria	Group B streptococci Gram-negative enteric bacteria *Ureaplasma urealyticum* *Listeria monocytogenes* *Chlamydia trachomatis* *Streptococcus pneumonia* Group D *Streptococcus* Anaerobes	*Streptococcus pneumoniae* *Haemophilus influenzae* *Mycoplasma pneumoniae* *Mycobacterium tuberculosis* *Chlamydia trachomatis*** *Mycoplasma hominis*** *Ureaplasma urealyticum*** *Bordetella pertussis*	*Streptococcus pneumoniae* *H influenzae* type b Nontypable *H influenzae* *Moraxella catarrhalis* *Staphylococcus aureus* (including CA-MRSA) *Streptococcus pyogenes* *Mycobacterium tuberculosis*	*Streptococcus pneumoniae* *Mycoplasma pneumoniae* *Chlamydia pneumoniae* *Mycobacterium tuberculosis* *Chlamydia psittaci* *Coxiella burnetti* *Klebsiella pneumoniae* *Legionella* *Streptococcus pyogenes* *Brucella abortus*
Fungi	Candida species • 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			*Coccidioides immitis* *Histoplasma capsulatum* *Blastomyces dermatitidis*
Other	Congenital toxoplasmosis Syphilis • Early-onset pneumonia			

Continued

Table 2. (Continued)

Pathogens	Neonates	Infants	Children <5 years	Children > 5 years
Comments	• Herpes simplex virus ○ 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	**Causes of "afebrile pneumonia of infancy" seen between age 2 weeks to 3–4 months. Symptoms include: • Insidious onset of rhinorrhea and tachypnea • Staccato cough • Diffuse inspiratory crackles • With or without conjunctivitis	Adenovirus serotypes 3, 7, and 21 have been associated with severe and complicated pneumonia Causes pneumonia complicated by necrosis and empyema. Frequently are seen after influenza and chickenpox	

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

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.

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)

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):

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 (×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 pneumonia*
- 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 *Chlamydophila* 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 jirovecci* 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 nondiagnostic 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 influenza 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.

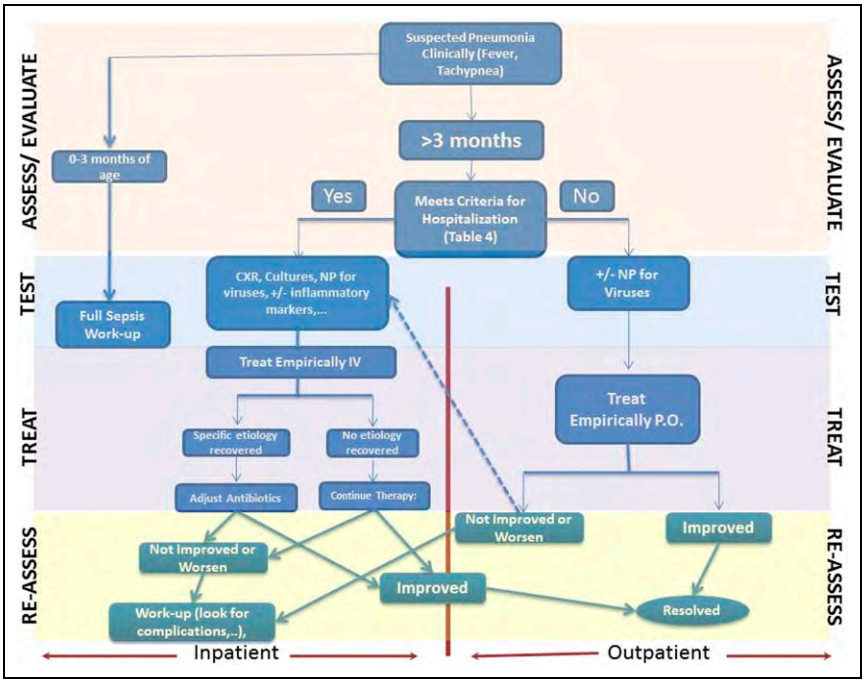

Figure. General approach to childhood pneumonia.

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 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 pneumoniae in pediatrics are caused by

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

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

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

Pathogen	Antibiotic(s)	Comments
Streptococcus pneumoniae		
• Penicillin susceptible	• Penicillin or ampicillin (drug of choice)	50–90 mg/kg daily
	• Cefuroxime • Cefotaxime • Ceftriaxone • Clindamycin (oral or intravenous)	For patients allergic to β-lactam antibiotics
• Intermediate and resistant strains	• Cefotaxime • Ceftriaxone • Linezolid and • Clindamycin • Cefdinir	Most active oral cephalosporin in vitro against penicillin-resistant strains
○ Pneumococcal serotype 19A	• Vancomycin, linezolid, or levofloxacin	Multidrug resistant to penicillin, macrolides, clindamycin, and trimethoprim-sulfamethoxazole
Mycoplasma pneumoniae	• Azithromycin	• 10 mg/kg in 1 dose on the first day and 5 mg/kg in 1 dose for 4 days
	• Clarithromycin	• 15 mg/kg per day in 2 divided doses for 10 days
	• Erythromycin	• 30 to 40 mg/kg per day in 4 divided doses for 10 days
	• Tetracycline	• 20 to 50 mg/kg per day in 4 divided doses for 10 days (maximum daily dose 1 to 2 g)
	• Doxycycline	• 2 to 4 mg/kg per day in 1 or 2 divided doses for 10 days (maximum daily dose 100 to 200 mg)
	• Doxycycline or a fluoroquinolone	• In children age ≥8 years
		• If macrolide resistance is suspected or documented, particularly if the child is severely ill
Chlamydia pneumoniae		
• Children age ≥8 years and adults	• Doxycycline	• 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	• Erythromycin	• 30 to 40 mg/kg per day divided into 4 doses for 10 to 14 days

S aureus and pneumococci. Pneumatoceles 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	• Associated with hypoalbuminemia
Empyema	• Affects 1:150 children with pneumonia • *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae* • 3 Stages: ◦ Exudative phase ◦ Fibrinopurulent phase ◦ Organizing phase • Associated with hypoalbuminemia • 3% of all pediatric hospitalizations • One-third of admissions for pneumococcal pneumonia
Pneumatocele	• Classically associated with *S aureus* • 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	• Seen in: ◦ *S pneumonia* (especially serotype 3 and serogroup 19) ◦ *S aureus* ◦ Group A *Streptococcus* ◦ *Mycoplasma pneumoniae* ◦ *Legionella* ◦ *Aspergillus* • Prolonged fever • Septic appearance • Diagnosis: ◦ Chest radiography – radiolucent lesion ◦ Confirmed with contrast enhanced computed tomography • Rare
Lung abscess	• Predisposing factors: ◦ Aspiration (1-2 weeks after event) ◦ Airway obstruction ◦ Congenital lung anomaly ◦ Acquired lung anomaly • *S aureus* is the most frequently involved organism. Other organisms include anaerobes, *Klebsiella*, and streptococcal species • Should be suspected when: ◦ Unusually persistent consolidation ◦ Persistent round pneumonia ◦ Increased volume of involved lobe (bulging fissure) • Complications: ◦ 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	• 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	

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.
- Stable and/or baseline mental and cardiorespiratory status.
- Ability to tolerate their home antiinfective 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.

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.)

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Pneumonia Quiz

1. In the US, pneumonia is estimated to occur in **2.6%** of children younger than 17 years old.

2. The mortality rate from pneumonia in developed countries is less than **1** per 1,000 per year.

3. Name 3 reasons why it is presumed that pneumonia infections peak in the winter months.
   a. indoor crowding leading to enhanced droplet transmission
   b. impaired mucociliary clearance
   c. peak of viral infections

4. Define pneumonia:

Lower respiratory tract infection typically associated with fever, respiratory symptoms, and evidence of parenchymal involvement by either physical exam or the presence of infiltrates* on chest radiography.

5. Complete the following table:

AGE GROUP	MOST LIKELY BUGS
0-3 months	Group B streptococcus, Gram negative bacteria, *Streptococcus pneumoniae*, viruses, *Chlamydia trachomatis*
3 months - 5 years	Viruses (50-60%); *Streptococcus pneumoniae*
> 5 years	Atypical organisms (*Mycoplasma pneumoniae* and *Chlamydophila pneumoniae)*

6. List 3 possible complications from pneumonia:

Pleural effusion, empyema, pneumatocele, necrotizing pneumonia, lung abscess

* "Consolidation", if Dr. Patterson is your attending physician.

Pneumonia Cases

Case 1: Mom brings 4 year old Timmy into your office for his annual well-child check. During the visit, she also mentions that Timmy has had a runny nose and cough for the past few days. She noticed last night and this morning that he seemed warm to the touch, but she didn't take his temperature. You look at his vital signs and note a respiratory rate of 26 with a pulse oximetry reading of 96% and a temperature of 100.9.

What else do you want to know?

- PMHx: Born at term, no chronic medical problems. Not on any medications. No prior hospitalizations; no prior ER visits for wheezing or respiratory distress.
- Immunzations: up to date, including recent flu shot
- SocHx: In daycare, older siblings at home with upper respiratory infections

Timmy is non-toxic appearing, but doesn't appear as active as you've seen him in other visits. You note some mild rhinorrhea, an intermittent cough, and diffuse faint end-expiratory wheezing.

What do you think is going on with Timmy? What are the signs/symptoms of pneumonia?

Most likely viral pneumonia

Signs & Symptoms: Fever, cough, tachypnea, increased work of breathing, hypoxia, crackles, retractions, rhonchi, nasal flaring, wheezing. Upper lobe pneumonias may present with radiating neck pain, while lower lobe pneumonias may present as vague abdominal pain.

You explain to Mom that you think Timmy likely has pneumonia. She asks you whether or not he needs a chest x-ray, and if Timmy has to be admitted to the hospital.

What do you tell her?

Pneumonia can be diagnosed with history and physical exam alone in this case. Due to the diffuse wheezing and low-grade fever and non-abrupt onset, it's likely that he has viral pneumonia. He doesn't need a chest x-ray, nor does he need to be admitted to the hospital.

What kind of "return to care" precautions do you give Mom?

If Timmy starts having trouble breathing, looks like he's working hard to breathe or breathing too fast, isn't able to stay hydrated, starts running high fevers, or isn't improving over the next few days, bring him back to clinic (or the ER if it's after hours).

Mom thanks you for your advice. On the way out the door, she asks if Timmy can still receive his 4 year old immunizations today in light of his pneumonia.

What do you tell her?

There is good evidence that all immunizations are safe in children with mild acute illness and low grade fever. However, if significant lower respiratory tract disease is present, most would hold off on the immunizations...just because you don't want immunization adverse effects (rare, but severe allergic rxn for example) to cloud or worsen the clinical picture. In this case, immunize.

Case 2: Dad brings 2 year old Rebecca for an acute visit today because she's had a cough and runny nose for the past few days, but now has developed a fever and seems to be breathing faster than normal. She has an unremarkable past medical history: born at term, no hospitalizations, and takes no routine medications. Her vital signs are as follows: T 102.6, RR 38, HR 135, BP 92/64, SpO2 90% on room air. Physical exam is remarkable for a fussy-appearing toddler with increased work of breathing, tachypnea, suprasternal and supraclavicular retractions, and crackles at the left lower lung base.

What else would you like to know?

-Immunization status
-Ability to take PO (vomiting?)
-Hydration status
-Any recent antibiotic usage?

Dad says that she just hasn't been herself the past couple of days. She's not really eating much, has vomited 3 times in the past 24hrs, and is drinking sips of water occasionally. She only had 2 wet diapers yesterday, and her diaper when she got up this morning was barely damp. Her immunizations are up to date for her age, including the flu vaccine, and she hasn't ever had antibiotics before.

What do you do now?

Call the ward team for admission due to her increased work of breathing, tachypnea, hypoxia, likely inability to tolerate oral antibiotics, and IV fluids.

Lucky for you, you have ward call tonight, so a perfect opportunity for continuity of care with Rebecca! You decide to walk Rebecca and her Dad up to the ward to get settled and conduct the all-important IPASS handoff with the outgoing team.

What would you like to do with Rebecca on the ward? What kind of antibiotics are you going to start her on?

-IV fluids (bolus NS 20ml/kg due to dehydration, and then start maintenance fluids with D5NS)
-Cephalosporin (**Ceftriaxone 50-75 mg/kg/day**)
-Supplemental oxygen
-CXR
-Labs (CBC with differential, RFP, blood cultures, RSV/Flu)
    * *CRP/ESR can be obtained to judge the response to treatment if desired, but clinical improvement should suffice*

What do you expect to see on the chest x-ray?

-Can be anything from nothing to a consolidated infiltrate in the left lower lobe.
    * Possibly nothing on the CXR because radiographic findings can lag behind the clinical picture for up to 72hrs, and due to her dehydration, an infiltrate may not be present initially.

Rebecca is started on 2L via nasal cannula on admission to the ward. She is started on appropriate antibiotics and does well overnight. You find in her the play room the following morning. After 24 hours on antibiotics, she is afebrile with a normal respiratory rate. She is able to be weaned off IV fluids the following day, and manages to spend the next night off of supplemental oxygen, so is discharged home by noon on her third hospital day.

What antibiotic should she go home on?

High-dose Amoxicillin to complete a 10 day course

** This is likely Pneumococcal pneumonia. Classically, children have fever >101, tachypnea, appear ill, have a round opacity on CXR, and have WBC > 20,000.*

She follows up 2 days after discharge (currently on day 5 of antibiotics) with you in clinic. She's back to her normal self per Dad, eating/drinking well, no respiratory distress, and playing with her brothers. Dad asks you if she needs a repeat CXR at some point to make sure if the pneumonia is gone. He also wants to know if she needs to finish the last 5 days of antibiotics since she's back to her baseline.

What do you tell him?

Finish the antibiotics!

As this was her first pneumonia, and no significant PMHx to speak of, she doesn't require a film now (or in 6 weeks) to confirm resolution of the infiltrate. Follow-up films are done in kids with repeated bouts of pneumonia.

Pneumonia Board Review

1. During teaching rounds, the pediatric ward resident reports on a 4-month-old circumcised male infant who was admitted to the pediatric ward for fever that morning. The infant is now afebrile and has had respiratory rates of 40 breaths/min while sleeping and greater than 60 breaths/min when awake. The infant has a soft, flat fontanelle on physical examination and is not irritable. The only diagnostic studies obtained on admission were a urinalysis and complete blood count, the results of which were normal, except for a white blood cell count of 16.0.

Of the following, the MOST appropriate next step is
A. administration of 100 mL normal saline
B. chest radiography
C. lumbar puncture
D. reassurance of the resident that this represents normal respiratory variation
E. urine culture

Respiratory rates vary across a relatively wide range in pediatric patients, depending on factors such as age and activity status. Therefore, strict definitions of tachypnea and bradypnea are difficult to determine and always must be considered in association with other factors such as current clinical status and individual history. Because tachypnea is a sensitive indicator of lower airway disease, patients who have elevated respiratory rates deserve a clinical evaluation in the context of other associated symptoms.

The tachypnea, history of fever, and elevated white blood cell count described for the boy in the vignette warrant chest radiography. Although lumbar puncture and a urine culture often are indicated to evaluate infants who have fever, the elevated respiratory rate combined with reassuring neurologic examination results and normal urinalysis make pneumonia a more likely diagnosis. Administration of a normal saline bolus would not be expected to improve the abnormal respiratory rate.

2. A 16 year-old girl presents with a 4-day history of fever, chills, nonproductive cough, and sore throat and a maculopapular truncal rash. On physical examination, she is well appearing. Her temperature is 39.1, her respiratory rate is 24 breaths/min, and her pulse rate is 76/min. Examination of the girl's head, eyes, ears, nose, and throat reveals an erythematous pharynx without exudates. Her neck is supple without lymphadenopathy. Respiratory auscultation reveals scattered crackles in her lungs, and cardiac auscultation shows no murmur, rub, or gallop. Her abdomen is without organomegaly, her extremities are without lesions, and results of her neurologic examination are within reference range. There is a pink maculopapular rash primarily on her trunk. You obtain a chest radiograph.

Of the following, the BEST test for confirming the cause of this child's pneumonia is
A. blood culture
B. cold agglutins
C. nasopharyngeal aspirate for viral antigens
D. sputum Gram stain and culure
E. throat swab for mycoplasma polymerase chain reaction

The combination of pharyngitis, nonproductive cough, chills, scattered rales, and skin rash in conjunction with the girl's age and the presence of bilateral infiltrates on chest radiograph is typical of symptomatic Mycoplasma pneumonia infection. Detection of mycoplasma DNA by polymerase chain reaction on throat swab specimens has recently been demonstrated to be a sensitive and specific method for diagnosing M pneumonia respiratory infections. The test is becoming increasingly clinically available. If

not available, mycoplasma IgG and IgM serology can be obtained. Routine isolation of the organism is not readily available.

It is unlikely that the girl in the vignette has "typical" bacterial pneumonia, such as caused by Streptococcus pneumoniae. Additionally, bacteremia is unlikely with bacterial pneumonia at this age. Although cold agglutinins are frequently sent for the diagnosis of Mycoplasma infection, they are neither sensitive nor specific. Therefore, cold agglutinins are of no value and should not be ordered. Nasopharyngeal aspirate for viral antigens would be an appropriate test for detecting respiratory viruses. Although viral infections may cause many of the same symptoms as described in the vignette, the chills, the high fever, and the radiographic findings of bilateral patchy infiltrates are consistent with Mycoplasma infection at this age.

3. A 6-year-old boy presents to the emergency department in February with a 6-day history of febrile illness that was initially characterized by the abrupt onset of elevated temperature (38.9), cough, coryza, sore throat, headaches, and malaise. The boy was evaluated by his pediatrician for those symptoms 5 days ago and tested positive on a rapid influenza diagnostic test. He seemed to be improving until 24 hours ago, when he had an increase in temperature to 39.9 and complained of shortness of breath. The boy has not received influenza immunization in the past year. A review of his symptoms reveals that he has had 3 episodes of boils on his buttocks that ruptured spontaneously over the past 6 months. On physical examination, he is sleepy and coughing with perioral cyanosis. The boy's temperature is 39.7, his respiratory rate is 36 breaths/min with intercostals retractions and grunting, and his oxygen saturation is 89% on room air.

Physical examination of his head, eyes, ears, nose, and throat does not show any abnormalities. Respiratory auscultation reveals diffuse crackles bilaterally with decreased breath sounds, and cardiac auscultation reveals no murmur, rub, or gallop. There are no lesions on the boy's extremities and his abdomen is benign and without organomegaly. Neurologically, he is sleepy but arousable and the remainder of the results from this examination are within normal limits.

Chest radiography shows diffuse interstitial infiltrates with right pleural effusion. The following are the results of the boy's laboratory tests: WBC 28.4 (75% N, 10% B, 10% L, 5% M); H/H 11.2/32.3; platelet count 353.

Of the following, the MOST likely pathogen responsible for this boy's acute deterioration is
A. group A B-hemolytic Streptoccocus
B. Haemophilus influenza
C. Mycoplasma pneumonia
D. Staphylococcus aureus
E. Streptococcus pneumoniae

Lower respiratory tract infection is the second most common complication of influenza after otitis media. The development of increasing respiratory distress 5 days into the course of influenza with marked toxicity and the increased white blood cell count with left shift in the boy in the vignette suggests secondary bacterial pneumonia. Staphylococcus aureus (including community-acquired methicillin-resistant S aureus), Streptococcus pneumonia, and group A Streptococcus are the leading organisms to consider in this setting. Bacterial coninfection with influenza, especially with S aureus, increases the risk of fatality. The recent history of recurrent boils reported in the child in this vignette suggests potential methicillin-resistant S aureus (MRSA colonization).

Group A Streptoccus is also associated with severe interstitial pneumonia that complicates influenza but is less common than S aureus. S pneumonia can complicate influenza infections as well but typically produces more focal consolidation in the lungs. Haemophilus influenza and Mycoplasma pneumonia do not typically cause illness as severe as described in this case and are not reported as common complications of influenza infection.

Other complications of influenza infection include neurologic syndromes that range from febrile seizures to encephalitis with status epilepticus or severe encephalopathy. Reye syndrome has been reported aspirin use during an influenza infection. Severe myositis (more common with influenza B infection) may occur. Myocarditis, pericarditis, and toxic shock syndrome (in association with S aureus or group A Streptococcus) are other rare complications of influenza infection.

4. A 17-year-old boy is applying for entry into military service and a complete history and physical examination. During the interview, he states that he is healthy, although he admits to being treated for three cases of pneumonia over the past 10 years. A chest radiograph performed during the last infection showed a left lower lobe pneumonia, and the patient states that the infection is "always on that side." The only finding of note on the physical examination today is slightly diminished breath sounds over the left lower lobe.

Of the following, the MOST likely cause for this boy's recurrent pneumonias is
A. bronchogenic cyst
B. congenital cystic adenomatoid malformation
C. congenital lobar emphysema
D. extrapulmonary sequestration
E. intrapulmonary sequestration

The presentation of recurrent unilateral pneumonias should prompt the clinician to consider congenital malformations of the lung, specifically pulmonary sequestration. Pulmonary sequestrations can be classified as intrapulmonary or extrapulmonary. Intrapulmonary sequestrations account for 75% to 90% of all sequestrations. Patients usually present in adolescence or adulthood with cough, wheezing, fever, and recurrent pulmonary infections. Surgical lobectomy generally is curative. Although also located on the left side in most cases, extrapulmonary sequestrations usually present prior to 6 months of age and often occur in conjunction with other congenital anomalies such as colonic duplication, pulmonary hypoplasia, or vertebral anomalies. Extrapulmonary sequestration can present similarly to intrapulmonary sequestrations, with cough, dyspnea, and infection, but also can result in feeding difficulty and, in rare cases, congestive heart failure due to increased shunting.

Bronchogenic cysts are the most common cause of a cyst in the lung. Most commonly located near central airway structures, bronchogenic cysts may present with symptoms of airway compression or infection, but they frequently are asymptomatic and discovered incidentally on chest radiography.

Congenital cystic adenomatoid malformation (CCAM) is another common congenital lung anomaly that typically is identified on prenatal ultrasonography. Most CCAMs present in the newborn period with respiratory distress and, depending on the type, may involve an entire lung, be associated with congenital anomalies, or result in fetal hydrops and pulmonary hypoplasia. Affected patients can present during childhood with recurrent pneumonia, but CCAM is less common than intrapulmonary sequestration at the age of the boy in the vignette.

Congenital lobar emphysema (CLE) is the most common neonatal cause of cystic malformation of the lung, and similar to CCAM, typically presents in the neonatal period with respiratory distress and airway obstruction.