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Hospital Medicine (CP Bonafide, Section Editor)

Management of Community-Acquired Pneumonia in Hospitalized Children

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Opinion statement

Community-acquired pneumonia (CAP) remains a leading cause of hospitalization in US children despite a decrease in the prevalence of disease resulting from widespread use of pneumococcal conjugate vaccines. Diagnostic testing should be limited to children hospitalized with moderate to severe disease, which is characterized by hypoxemia, respiratory distress, and/or sepsis. At a minimum, these children should have blood cultures and chest radiographs (CXRs) performed. Viral testing should also be performed during influenza season or in other scenarios where viral identification may reduce antibiotic use. Fully immunized children should be treated empirically with narrow-spectrum aminopenicillins, and amoxicillin is usually the best choice for empiric step-down oral therapy. The benefit of using macrolide antibiotics for suspected *Mycoplasma pneumoniae* remains unclear. These agents may be most beneficial for older children.

Pneumonia complication rates are increasing, and children who fail to improve after 48–72 h should be re-evaluated for treatment failure and complicated pneumonia, which may require further imaging, chest tube placement, or video-assisted thoracoscopic surgery (VATS). Children with complicated pneumonia require a prolonged duration of antibiotic therapy.

Introduction

Pneumonia is an acute infection of the lower airways with the potential to cause significant respiratory distress including tachypnea and increased work of breathing (see Table 1). Hospitalization is recommended for all young infants and those children with moderate to severe disease characterized by hypoxemia in the setting of respiratory distress. Community-acquired pneumonia (CAP) is a leading cause for pediatric hospitalization in the USA, with over 100,000 hospital admissions annually. Disease burden is highest among children under 5 years of age; this population accounts for two thirds of all pneumonia hospitalizations in children [1]. Prematurity and young age increase a child's risk of developing pneumonia. Modifiable risk factors for pediatric CAP include crowded living conditions, secondhand smoke exposure, and poor nutritional status [2–4].

Etiology of pediatric CAP

Pneumonia etiology varies by age, underlying conditions, geographic location, vaccine exposure, and seasonality. The introduction of pneumococcal conjugate vaccines (PCV) into childhood immunization schedules has changed the epidemiology of CAP in the USA and worldwide. Methods for identifying viral pathogens continue to improve, highlighting the enormous burden of viruses contributing to pneumonia in children. Several large-scale epidemiologic studies using comprehensive, modern diagnostic methods are currently underway, notably the Pneumonia Etiology Research for Child Health project (PERCH) focusing on the developing world and the Centers for Disease Control and Prevention Epidemiology of Pneumonia in the Community (EPIC) study in the USA [5].

Table 1. Signs of respiratory distress in pediatric CAP

Signs of respiratory distress	Accessory muscle use	Impending respiratory failure
• Age-based tachypnea (respiratory rate): - 0–2 months>60 - 2–12 months>50 - 1–5 years>40 ->5 years>20 • Dyspnea	• Grunting • Nasal flaring • Suprasternal retractions • Intercostal retractions • Subcostal retractions	• Apnea • Altered mental status • Grunting or head bobbing • Severe hypoxemia (requiring FiO2>50 % to maintain SaO2>92 %)

Adapted from PIDS/IDSA Guidelines

Bacterial causes of CAP

Common bacterial pathogens

Streptococcus pneumoniae remains the most common bacterial pathogen causing pneumonia in children. *Staphylococcus aureus* and *Streptococcus pyogenes* are much less common but frequently associated with severe disease. *Mycoplasma pneumoniae*, and to a lesser extent, *Chlamydophila pneumoniae*, are common in school-aged children, but also occasionally implicated in cases of pneumonia among younger children [6]. *Staphylococcus aureus* should be considered when pneumonia is complicated by pleural effusion, empyema, or necrotizing/cavitary lesions, and in children requiring intensive care unit (ICU) admission for respiratory failure or septic shock [7].

The role of pneumococcal conjugate vaccines

Streptococcus pneumoniae causes invasive disease in children ranging from lower respiratory tract infections to meningitis. A seven-valent pneumococcal polysaccharide conjugate vaccine (PCV-7) was licensed in 2000, providing protection from the most common virulent pneumococcal serotypes. PCV-7 has nearly eliminated invasive pneumococcal disease (IPD) due to vaccine serotypes, with disease rates in US children under 5 years old falling from 78.9 cases per 100,000 in the pre-vaccine years 1998–1999 to 2.7 cases per 100,000 in 2004 [8]. This translates into an estimated 47,000 fewer hospitalizations for pneumonia annually in children under 2 years old in 2007–2009 as compared to the pre-vaccine years 1997–1999 [9]. Analysis of data from the State Inpatient Databases in 10 states over a 10-year period following introduction of PCV-7 showed significant reductions in IPD and pneumonia in all age groups, suggesting the development of herd immunity from childhood PCV immunization programs [10]. The 13-valent pneumococcal conjugate vaccine (PCV-13) replaced PCV-7 in 2010, expanding coverage to include six additional virulent pneumococcal serotypes. Culture-proven IPD rates decreased 53 % among eight hospitals in children under 2 years old from 2000 to 2009 to 2011, with a 57 % decline in PCV-13 isolates during this time period [11]. Pneumonia hospitalization rates in Tennessee decreased an additional 27 % in children under 2 years old from PCV-7 years 2001–2010 compared to the post-PCV years 2010–2012 [12]. PCV-13 is predicted to prevent nearly 1 million pneumonia hospitalizations in US children over the next decade [13].

Viral causes of CAP

Viruses have been implicated in 45–77 % of cases of pediatric CAP in epidemiologic studies. Although viruses may be responsible for CAP as a single agent, multi-viral infections, or mixed viral-bacterial infections account for 10–20 % of cases [14]. Respiratory syncytial virus (RSV) is the most common virus detected in children with pneumonia (especially in young infants), followed closely by rhinovirus, which is common in children of all ages. Other viruses responsible for pediatric CAP include influenza, adenovirus, parainfluenza, and human metapneumovirus [6, 14–16].

Since viruses are usually isolated from the upper respiratory tract, it is often difficult to distinguish whether a particular virus is the primary or a contributing

cause of lower respiratory tract disease. Other considerations include asymptomatic viral infection or viral shedding following a recent infection. RSV is the only viral pathogen consistently associated with lower respiratory tract disease, whereas rhinovirus and bocavirus are common causes of upper respiratory infection and associated with prolonged viral shedding [14]. In the EPIC study, rhinovirus was detected in 31 % of children hospitalized with pneumonia and 22 % of asymptomatic children presenting for elective outpatient surgery [17]. A metareview reported that rhinovirus may be identified by PCR in up to 15 % of asymptomatic children [18].

Co-infection with viruses and bacteria

Viruses facilitate bacterial infection through direct damage to the respiratory tract and indirect modulation of inflammatory pathways [19]. Analysis of bacteriologic and histopathologic data from the 1918–1919 influenza pandemic indicates that the majority of influenza-related deaths from that period resulted from secondary bacterial pneumonia [20•]. Although mortality was much lower, the 2009 H1N1 influenza pandemic also demonstrated a high number of children with confirmed or suspected secondary bacterial pneumonia. Retrospective studies reported radiologic pneumonia in 34–57 % of children hospitalized with influenza and laboratory confirmed bacterial pneumonia in up to 15 % of hospitalized infants [21, 22].

Diagnosis of CAP

A retrospective cohort study of children evaluated for pneumonia at 36 emergency departments across the USA between 2007 and 2010 reported a wide range in the use of diagnostic testing including chest x-rays (CXRs) (39–76 %),complete blood counts (CBC) (11–29 %) and blood cultures (11–28 %). Children seen at high test-utilizing hospitals had increased odds of hospitalization for CAP (OR 1.86), but no difference in the rate of return visits to the ED [23••]. These results highlighted the need for evidence-based guidelines to standardize diagnostic testing in CAP. In 2011, the Pediatric Infectious Disease Society (PIDS) and the Infectious Disease Society of America (IDSA) released joint guidelines for the management of CAP in children. The PIDS/IDSA guidelines describe the quality of evidence and strength for each recommendation (see Table 2).

Imaging modalities

CXR

The PIDS/IDSA guideline recommends the performance of a chest x-ray (CXR) for all children hospitalized with CAP. CXRs help clinicians to assess the extent of disease in children requiring hospitalization, and may reveal complications such as pleural effusion and empyema. While the guideline definition does not require a radiographic diagnosis of pneumonia, studies from developed nations tend to use radiographic pneumonia as the criterion gold standard for diagnosis. CXR may not be reliable early in the course of pneumonia, as radiographic infiltrates may lag behind clinical findings of pneumonia, and CXR findings

Table 2. Summary of PIDS/IDSA guidelines for diagnosis in children hospitalized with CAP [24]

Diagnostic modality	Indication	Strength of recommendations	Quality of evidence
Diagnostic guidelines for uncomplicated CAP			
Initial CXR	• Children with moderate to severe disease (all children who meet criteria for hospitalization)	Strong	High
Follow-up CXR (after 48–72 h of antibiotics)	• Failure to improve • Persistent fever • Worsening disease	Strong	Moderate
Lung ultrasound	• Not addressed in guidelines	N/A	N/A
Blood cultures before antibiotics	• Hospitalized children with moderate to severe disease	Strong	Low
Blood cultures following antibiotics	• Only in children who fail to improve or worsen on antibiotics	Strong	Moderate
Mycoplasma PCR	• Children with signs/symptoms of atypical pneumonia	Weak	Moderate
Sputum culture	• Any child who can produce sputum	Weak	Low
Pneumococcal urinary antigen	• Not recommended	Strong	High
Rapid influenza antigen	• During influenza season	Strong	High
	• When clinical suspicion is high	Weak	Low
Other viral antigen	• If the test is sensitive/specific • If result would change management	Weak	Low
CBC	• Reserve for severe disease		
Acute phase reactants (ESR, CRP, PCT)	• May be useful in severe disease • Must be interpreted in context of other data	Weak	Low
Other bacterial PCR in uncomplicated PNA	• Not addressed in guidelines	N/A	N/A
Diagnostic guidelines for complicated CAP			
Pleural gram stain and culture	• On any pleural specimen obtained	Strong	High
Pleural cell count	• Differentiate bacterial infection from mycobacteria and malignancy	Weak	Moderate
Antigen testing and bacterial PCR	• Useful for pathogen identification	Strong	Moderate
Other pleural testing (pH, glucose, protein, LDH)	• Not recommended	Weak	Very low
CXR	• Confirmatory when pleural effusion is suspected	Strong	High
Ultrasound or Chest CT	• If CXR does not conclusively diagnose effusion	Strong	High

The strength of the recommendation indicates the balance between desirable and undesirable effects of the intervention. The quality of the evidence depends upon the study design, power of the study, and the limitations of the results. Recommendations that are considered "weak" or based on "low" quality evidence are likely to change as new evidence is generated

should not supplant clinical judgment for the diagnosis of childhood CAP. CXR also does not reliably differentiate between viral or bacterial etiologies [14, 25,

26]. While the dose exposure from CXR is much less than for chest CT, cumulative films may contribute to measurable radiation exposure in young children. Thus, follow-up CXRs should be limited to children who fail to improve or worsen after 48–72 h of antibiotic therapy.

Lung ultrasound—an emerging technology

Current use of point-of-care lung ultrasound for the diagnosis of pneumonia is largely limited to the identification of pleural effusion and other local complications. Recent data from Italy suggest that lung ultrasound performed by expert technicians is as accurate as CXR for the diagnosis of pediatric CAP, and outperforms CXR in the diagnosis of complicated pneumonia [27, 28]. A 2013 USA study evaluating point-of-care lung ultrasound performed by emergency medicine clinicians who completed a brief training found that this modality had a sensitivity of 86 % and a specificity of 89 % for the detection of CAP [29]. Lung ultrasound can also be used for follow-up imaging without a risk of cumulative radiation exposure [30]. Lung ultrasound is a promising non-invasive technique for the diagnosis of pneumonia, but both point-of-care testing and expert performance require further evaluation before lung ultrasound can replace CXR for the diagnosis or serial imaging of pneumonia.

Bacterial testing

Blood cultures

There is weak evidence supporting the PIDS/IDSA recommendation for routine use of blood cultures in children hospitalized for CAP. Culture results may guide appropriate treatment and provide important data about the changing etiology of CAP in a post-vaccine era. However, there are drawbacks to the routine use of blood cultures, including a high rate of contamination resulting in false positive culture results. Furthermore, less than 10 % of children hospitalized for uncomplicated CAP have documented bacteremia [33, 34••]. When a pathogen is isolated, culture results may not change antibiotic selection [35, 32]. Others have suggested a strategy that limits blood cultures to children at risk for severe or complicated bacterial disease [31••, 32]. However, until diagnostics are available to consistently distinguish viral from bacterial disease, accurately identifying this population may prove problematic.

Alternatives to blood culture for bacterial pathogen identification include sputum cultures, rapid antigen testing, and polymerase chain reaction (PCR). The pneumococcal urinary antigen test has excellent reported sensitivity, but suffers from a 15 % false positive rate, likely due to upper respiratory tract colonization with *Streptococcus pneumoniae* [36, 37]. Thus, the urinary antigen test is not recommended for use in children [38]. Whole-blood PCR is more sensitive than culture and targets are available for several bacteria, including *Streptococcus pneumoniae*, although commercially available tests are lacking. PCR testing of upper respiratory tract samples is not recommended for bacterial pathogens owing to frequent colonization. Testing for *M. pneumoniae* is the one exception as it is not thought to colonize the upper respiratory epithelium. Sputum cultures are a non-invasive method available for older children who can produce sputum. High quality

samples are difficult to obtain from young children and infants who cannot reliably expectorate; however, inducing sputum with inhaled hypertonic saline has been used in research studies with variable results [39].

Viral testing

Rapid testing for influenza is important when influenza is prevalent in the local community. Testing for other viruses may be warranted, particularly if pathogen identification leads to a reduction in unnecessary antibiotic use. Older methods such as viral culture and direct fluorescent antibody (DFA) testing have largely been supplanted by viral PCR testing of upper respiratory tract samples. .

Serology and acute phase reactants

Serologic testing is not recommended in children with uncomplicated CAP as its clinical utility is very low. A complete blood count (CBC) should be performed in children with severe and complicated disease. Although leukocytosis is often associated with bacterial infection, white blood cell count does not easily distinguish between viral and bacterial disease. Anemia and/or thrombocytopenia may signal marrow suppression or platelet dysfunction seen in systemic complications such as sepsis. Acute phase reactants (e.g., C-reactive protein [CRP]) are often elevated in CAP. CRP levels >100 had a positive predictive value of 88 % in predicting radiographic pneumonia in one study, but one thirds of children with pneumonia had normal CRP levels <20 [40]. Furthermore, CRP does not reliably distinguish between viral and bacterial pathogens in CAP. A meta-analysis of eight studies and 1320 children concluded that a CRP level >40 only weakly predicts a bacterial etiology [41]. Serial measurements of CRP may have a role in assessing response to therapy, but further research is needed in this area.

Procalcitonin (PCT) may have more value than CRP as a marker for serious bacterial infections (SBI) in children. Using multiple diagnostic modalities to detect *Streptococcus pneumoniae*, one study reported that a procalcitonin level <0.5 ruled out pneumococcal pneumonia in over 90 % of cases [42]. Proposed PCT cutoff values indicative of bacterial disease range from 0.25 to 2.5 ng/mL in recently published studies [43–45, 40]. PCT levels may also be used to guide antibiotic therapy. A randomized control trial found no increase in rates of treatment failure when antibiotics were restricted to hospitalized children with PCT levels >0.25. This strategy translated into a 15 % reduction in antibiotic use for those with CAP in the PCT arm and shortened antibiotic duration by 50 % [46••]. Additional research into the clinical utility of PCT and other possible markers of bacterial infection are very much needed.

Diagnosis of complicated CAP

Epidemiology and etiology of complicated CAP

CAP may have local, systemic, or metastatic complications. Parapneumonic effusions have been reported in up to 25 % of children with CAP [24, 47]. Empyema occurs in up to 5 % of children hospitalized with CAP and may be further complicated by the development of necrosis, cavitation, or bronchopleural fistulas. Metastatic complications of CAP (osteomyelitis, meningitis, endocarditis, pericarditis, septic arthritis) are rare.

Although rates of pneumonia declined with PCV introduction, rates of local complications increased by 78 % between 1997 and 2006 [48]. National hospitalization rates for empyema in US children increased from 3 to 6 per 100,000 following the release of PCV-7 [49]. Experts posit that increased rates of complicated pneumonia result from more accurate diagnostic techniques and changes to the spectrum of pathogens responsible for pediatric CAP, as non-vaccine pneumococcal serotypes replace the conjugate vaccine serotypes and virulent strains of *Staphylococcus aureus* become more prevalent [50, 51].

As with uncomplicated CAP, *Streptococcus pneumoniae* remains the most common pathogen isolated by pleural fluid cultures, with identification of this pathogen in up to 71 % of empyemas [52•]. Other *Streptococcus* species and *Staphylococcus aureus* are less frequently identified. Pleural fluid culture is more likely to identify a pathogen when compared to blood culture [53–55]. Bacterial PCR increases pathogen identification when compared to culture-based methods, improving etiologic yield from 25–35 to 85–88 % in children with empyema [52•, 56].

Diagnosis of parapneumonic effusion and empyema

Parapneumonic complications progress along a continuum from small effusions containing free-flowing fluid to large and often complex infections within the pleural space. A clear transudate often develops in the pleural space in response to local inflammation and pleuritis. When bacteria are present, this fluid is often quickly replaced by purulent material and progressive infection [57, 58]. An initial CXR may show blunting of the costophrenic angle or a peripheral rim of pleural fluid indicative of effusion. A decubitus or lateral CXR may help to determine whether an effusion is free flowing or loculated, but large effusions are nearly impossible to differentiate from other causes of opacification seen on CXR [59]. Lung ultrasound is a superior tool for detecting loculations, septations, and fronds associated with empyema, and can differentiate pleural fluid from consolidated lung tissue [60, 61]. Neither CXR nor ultrasound can definitively diagnose empyema, but children with high grade findings on ultrasound such as organization, septation, and fronds within the pleural fluid have improved outcomes when treated with operative drainage procedures [60].

Diagnosis and treatment of the child with a parapneumonic effusion depends on the size of the fluid collection and the degree of respiratory compromise [24]. Small effusions (<10 mm on lateral CXR or <1/4 of the hemi-thorax on CXR) usually resolve with empiric antibiotic therapy and may be monitored clinically if the child appears well. Repeat imaging should be performed if the child fails to improve. Large (>1/2 hemithorax) and/or more complicated parapneumonic effusions and empyemas are less likely to resolve without a pleural drainage procedure. Pleural fluid specimens should be sent for cell count, gram stain, culture and bacterial PCR (if available) to guide treatment. An elevated pleural leukocyte count may indicate bacterial etiology in cases where a pathogen is not identified by culture or PCR.

Diagnosis of necrotizing pneumonia

Necrotizing pneumonia with abscess and cavity formation is a rare but increasing complication of pediatric CAP [50]. This complication should be suspected

in an ill-appearing child with high fever, tachypnea, and tachycardia, or in a child who fails to respond to empiric therapy. CT scans may help to distinguish necrotic cavities and air–fluid levels from abscess formation, but these images may not necessarily change the management of necrotizing disease.

Streptococcus species, *Staphylococcus aureus*, and *Klebsiella pneumoniae* are common causes of necrotizing pneumonia in children [62]. Lung abscesses are often polymicrobial in nature, and may involve *Staphylococcus aureus*, *Streptococcus* species, gram-negative organisms, and anaerobes. Neurocognitively impaired children may be at increased risk for aspiration of these pathogens from the upper respiratory or GI tracts. *Staphylococcus aureus* is well described as a cause of severe necrotizing pneumonia in the literature, and is associated with leukopenia, erythroderma, purulent cough, and pulmonary hemorrhage [51, 63].

Treatment of CAP

Empiric antibiotic therapy

Therapy with intravenous (IV) ampicillin or penicillin G should be administered to previously healthy and fully immunized children who are hospitalized for pneumonia. Use of these agents is endorsed by the PIDS/IDSA guidelines as well as other national and international health organizations, and is supported by a strong body of evidence [26, 24, 64, 65]. In the post-PIDS/IDSA guidelines era, first-line use of aminopenicillins has increased significantly, but early studies indicate that physicians continue to treat up to 90 % of hospitalized children with broad spectrum cephalosporins [66]. There is good evidence that treatment with appropriately dosed aminopenicillin therapy overcomes most B-lactam resistance, without impairing readmission rates, length of stay (LOS), or costs of hospitalization [48, 67, 68].

A third-generation cephalosporin (e.g., ceftriaxone) should be administered if the child is not fully immunized, has a life-threatening infection, complications such as empyema, or resides in a region with high rates of pneumococcal resistance to penicillin. When *Staphylococcus aureus* is suspected, such as in complicated pneumonia and severe disease with systemic manifestations, anti-staphylococcal therapy (including vancomycin or clindamycin in MRSA-prevalent areas) should be added.

Macrolide antibiotics

Macrolides alone do not provide adequate empiric coverage for CAP due to high rates of macrolide resistance among serotypes of *Streptococcus pneumoniae* [69]. However, macrolides are the preferred therapy for pneumonia due to atypical pathogens. Although the PIDS/IDSA guidelines recommend consideration of macrolide therapy when atypical pathogens are a significant concern, it is impossible to reliably discern atypical CAP from that caused by viruses or other bacteria on clinical grounds alone (Table 3). PCR testing may help to better inform treatment decisions at the point of care. However, even when an atypical pathogen is diagnosed, the utility of treating these infections in children remains unclear [70, 71•]. The answer may depend on the age of the child. In a multicenter retrospective cohort study of over 20,000 children hospitalized with pneumonia, Beta-lactam–macrolide combination therapy decreased LOS by 31 % in children 12–18 years old compared to Beta-lactam monotherapy,

Table 3. Empiric antibiotic regimens for pediatric inpatients with CAP adapted from IDSA guidelines

	Initial IV Therapy	IV Alternative	Oral "Step Down"	Oral Alternative
Typical Organisms (*Streptococcus pneumoniae, Group A Streptococcus *)*	Ampicillin (150–200 mg/kg/day every 6 h) OR Penicillin G (200,000-250,000 U/kg/day every 4–6 h) *Prefer Ceftriaxone/cefotaxime if not fully immunized for Hib or S. Pneumoniae**	Ceftriaxone (50–100 mg/kg/day) OR Cefotaxime (50 mg/kg/dose every 8 h) Others: clindamycin, vancomycin,	Amoxicillin (80–90 mg/kg divided BID-TID daily) OR Levofloxacin for resistant streptococcus pneumoniae with MIC >4	2nd or 3rd generation cephalosporin Levofloxacin
"Atypical" Organisms (*Mycoplasma pneumoniae, Chlamydophila Pneumoniae **)*	Azithromycin (10 mg/kg/day on day 1, 5 mg/kg/day on days 2–5) *Transition to oral azithromycin on day 2 is preferred*	Erythromycin (5 mg/kg every 6 h) Levofloxacin	Azithromycin (5 mg/kg/day)	Clarithromycin Erythromycin Levofloxacin Moxifloxacin Doxycycline
*Staphylooccus Aureus****	Empiric coverage for typical organism AND: Vancomycin (40–60 mg/kg/day every 6–8 h OR Clindamycin (40 mg/kg/day every 6–8 h	Linezolid (10 mg/kg/dose, <12 years old: every 8 h, ≥12 years old: every 12 h)	Clindamycin (30–40 mg/kg/day divided 3 or 4 times a day)	Linezolid
Organisms Causing Empyema	Ceftriaxone (50–100 mg/kg/day) OR Cefotaxime (50 mg/kg/dose every 8 h) Strongly consider adding staphylococcal coverage****	Levofloxacin + MRSA coverage if suspected	Amoxicillin OR Amoxicillin-clavulonate (Both dosed 80–90 mg/kg amox divided BID-TID daily) +MRSA coverage if suspected	Levofloxacin Clindamycin Linezolid

* There is increased risk of B-lactam resistant strains of S pneumoniae in children who are not fully immunized. 2nd/3rd generation cephalosporins cover resistant streptococcus pneumoniae and Hemophilus Influenza B

**Add empiric "typical" bacterial coverage if diagnosis of atypical pneumonia is uncertain

*** Empiric therapy for Staphylococcus aureus should always cover MRSA. If MSSA is isolated, a B-lactam or cephalosporin may be sufficient

**** Many clinicians add empiric anti-staphylococcal coverage for empyema, starting with clindamycin and progressing to vancomycin in the child who is severely ill or fails to improve

but had no effect on children less than 6 years old [72]. Macrolides prove more effective in school-aged children presumably because atypical pathogens are more common in this age group. Macrolides may also be important for those with very severe pneumonia through both immune-modulating and antimicrobial effects [73] [74]. Macrolide therapy is associated with improved outcomes among critically ill adults hospitalized for pneumonia, even when they are infected by macrolide-resistant organisms [55].

Treatment of complicated disease

Children with pneumonia complicated by pleural effusion should receive empiric coverage for *Streptococcus pneumoniae* and other common pathogens. Small parapneumonic effusions may resolve with empiric aminopenicillin antibiotics alone. A third-generation cephalosporin plus anti-staphylococcal coverage is recommended for children with complicated effusions and empyema. For anti-staphylococcal coverage, vancomycin is preferred for life-threatening infections and/or documented MRSA bacteremia. Depending on local resistance profiles, clindamycin may be sufficient for less severe disease or as step-down therapy.

Antibiotic management of lung abscess and necrotizing pneumonia should always include staphylococcal and streptococcal coverage; anaerobic coverage should be strongly considered, especially in cases where aspiration pneumonia is suspected. Children with necrotizing pneumonia require prolonged antibiotic therapy [50].

A 2005 meta-analysis comparing primary medical versus operative management of empyema reported superiority of operative interventions over conservative medical management. This study demonstrated decreased re-intervention rates and time with chest tube in place, shorter duration of antibiotic therapy, shorter length of stay, and decreased in-hospital mortality rates with initial operative management [75]. One multicenter study of US children's hospitals compared outcomes for patients treated with a variety of drainage procedures including thoracotomy, chest tube placement with and without fibrinolytics, and video-assisted thoracoscopic surgery (VATS). They reported similar outcomes for chest tube placement regardless of whether fibrinolytics were used. There were no significant differences in LOS, but children who received initial VATS were less likely to require additional drainage procedures [76••].

Adjuncts to antimicrobial therapy

Supportive care

Children who are hospitalized for pneumonia should be monitored for hypoxemia and dehydration. Supportive care may include intravenous or oral rehydration, nutritional support, supplemental oxygen, and frequent respiratory monitoring. Patients with acute wheezing and a history of asthma may benefit from bronchodilators and corticosteroids. Cough suppressant therapies

are not recommended. In particular, clinicians should be aware of the theoretical risk of respiratory depression from codeine-containing cough syrup [77]. There is similarly insufficient evidence for the use of chest physical therapy or zinc supplementation [78, 79].

Corticosteroid therapy

Recent evidence suggests that corticosteroids only benefit the subpopulation of children with pneumonia who present with wheezing. A study evaluating the use of corticosteroids in children treated for CAP in the emergency department found that children with wheezing benefited from corticosteroids in conjunction with bronchodilator therapy, whereas those without wheezing had a prolonged length of stay and increased risk of readmission when treated with corticosteroids [80]. Corticosteroid therapy was also associated with antibiotic treatment failure when given to outpatients who did not have asthma [81].

Treatment failure and escalation of care

A child that fails to improve after 48–72 h of IV antibiotic therapy should be re-evaluated for inadequate antibiotic coverage and/or complicated pneumonia. Children with worsening clinical status should have a repeat blood culture performed to assess for bacteremia, repeat imaging to assess for the development of local complications, and broadening of their antimicrobial coverage. Transfer to an ICU should be considered for a child with impending respiratory failure or signs of shock (see Table 4).

Table 4. Selected indications for ICU admission in CAP

Indications for ICU admission
• Failure to improve with supplemental oxygen therapy
• Pulse oximetry level <92 % on Fi02>50 %
Acute need for positive pressure ventilation
• Acute initiation of BIPAP or CPAP
• Acute increase in positive pressure ventilation settings
Signs of sepsis
• Sustained tachycardia
• Hypotension
• Need for pharmacologic support to maintain blood pressure or perfusion
Altered mental status
• May be associated with hypoxia or hypercarbia
Impending respiratory failure
• Signs of severe respiratory distress on physical examination may include grunting, apnea, and head bobbing (see Table 1)
• A team-based assessment should be made with input from respiratory therapy, bedside clinicians and intensivists
• Severity of illness scoring may help to alert clinicians respiratory failure in the context of a team-based assessment and other available data

PIDS/IDSA guidelines make a strong recommendation for all of the parameters listed in Table 4, although the quality of evidence varies

Response to therapy and discharge criteria

Children should be considered eligible for discharge on oral antibiotics when they defervesce, their work of breathing improves, and when they no longer require supplemental oxygen or intravenous fluids. Most children hospitalized with uncomplicated pneumonia are discharged within 2–3 days. National and international guidelines recommend a short course of IV antibiotics before transitioning to oral therapy, but the evidence for this recommendation is scant. Emerging research from the developing world suggests a role for initial empiric oral therapy in severe disease, but more studies are needed [82]. In practice, most children receive IV therapy while hospitalized, with transition to oral therapy shortly before discharge.

Oral amoxicillin is preferred over both second- and third-generation oral cephalosporins and macrolides for pneumococcal coverage. Oral cephalosporins cover only 60–70 % of prevalent pneumococcal strains [69]. Oral alternatives useful in cases of penicillin or cephalosporin allergy include amoxicillin-clavulanate, clindamycin, fluoroquinolones, clindamycin, and linezolid (see Table 3). Intramuscular ceftriaxone administered once daily by the pediatrician or home nursing agency is a reasonable alternative to oral amoxicillin that covers >95 % of virulent pneumococcal serotypes. Intramuscular ceftriaxone should be considered for the outpatient treatment of children who no longer require skilled nursing but still need parenteral antibiotics, children who cannot tolerate oral antibiotics, and in cases where outpatient adherence is a concern [69].

The optimal treatment duration is not well defined in the literature. Most guidelines recommend antibiotic treatment for 7–10 days, with the addition of a macrolide for 5 days duration if there is concern for atypical infection. A longer duration of treatment is recommended if *Staphylococcus aureus* is suspected and in cases of complicated pneumonia.

Conclusions

The worldwide burden of CAP has decreased over the past decade, largely due to widespread pneumococcal immunization. However, CAP remains a leading cause of pediatric hospitalizations, with increasing rates of complicated disease in the post-conjugate vaccine era. Viruses are most common in younger children, while *M. pneumoniae* is commonly found in school-aged children. *Streptococcus pneumoniae* and other bacteria remain as important causes of CAP in all age groups and are increasingly associated with local complications. Although recent guidelines suggest limiting diagnostic testing for children with CAP, when managing patients with severe or complicated disease, a CXR and blood culture should be considered to help guide treatment. The role of other testing is less clear. Narrow-spectrum antibiotics, including ampicillin for hospitalized children and amoxicillin for outpatients are first-line therapy for the treatment of most children hospitalized with uncomplicated CAP. Combination therapy with a macrolide may be considered for school-aged children. Critical areas for

future research include enhanced diagnostics (rapid, sensitive, cost-effective) for discerning viral from bacterial CAP; a better understanding of determinants of disease severity; and effective prevention and treatment strategies, particularly for viral pathogens.

Compliance with Ethics Guidelines

Conflict of Interest

Laura H. Simon declares that she has no conflict of interest. Kavita Parikh declares that she has no conflict of interest. Derek J. Williams declares that he has no conflict of interest. Mark I. Neuman declares that he has no conflict of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- • Of importance
- •• Of major importance

1. HCUP Nationwide Inpatient Sample (NIS). Healthcare Cost and Utilization Project (HCUP). 2011. Agency for Healthcare Research and Quality, Rockville, MD. www.hcup-us.ahrq.gov/nisoverview.jsp.
2. Grant CC, Emery D, Milne T, Coster G, Forrest CB, Wall CR, et al. Risk factors for community-acquired pneumonia in pre-school-aged children: risk factors for pneumonia. J Paediatr Child Health. 2012;48(5):402–12.
3. Heiskanen-Kosma T, Korppi M, Jokinen C, Heinonen K. Risk factors for community-acquired pneumonia in children: a population-based case–control study. Scand J Infect Dis. 1997;29(3):281–5.
4. CLARK JE, HAMMAL D, HAMPTON F, SPENCER D, PARKER L. Epidemiology of community-acquired pneumonia in children seen in hospital. Epidemiol Infect. 2007;135(2):262–9.
5. Murdoch DR, O'Brien KL, Driscoll AJ, Karron RA, Bhat N, Pneumonia Methods Working Group, et al. Laboratory methods for determining pneumonia etiology in children. Clin Infect Dis Off Publ Infect Dis Soc Am. 2012;54 Suppl 2:S146–52.
6. Michelow IC, Olsen K, Lozano J, Rollins NK, Duffy LB, Ziegler T, et al. Epidemiology and clinical characteristics of community-acquired pneumonia in hospitalized children. Pediatrics. 2004;113(4):701–7.
7. Montagnani C, Cocchi P, Bianchi L, Resti M, de Martino M, Galli L. Severe infections caused by Panton-Valentine leukocidin-positive *Staphylococcus aureus* in infants: report of three cases and review of literature. Acta Paediatr. 2013;102(6):e284–7.
8. Hicks LA, Harrison LH, Flannery B, Hadler JL, Schaffner W, Craig AS, et al. Incidence of pneumococcal disease due to non-pneumococcal conjugate vaccine (PCV7) serotypes in the United States during the era of widespread PCV7 vaccination, 1998–2004. J Infect Dis. 2007;196(9):1346–54.
9. Griffin MR, Zhu Y, Moore MR, Whitney CG, Grijalva CG. U.S. hospitalizations for pneumonia after a decade of pneumococcal vaccination. N Engl J Med. 2013;369(2):155–63.
10. Simonsen L, Taylor RJ, Young-Xu Y, Haber M, May L, Klugman KP. Impact of pneumococcal conjugate vaccination of infants on pneumonia and influenza hospitalization and mortality in all age groups in the United States. mBio. 2011 Jan 3;2(1):e00309–10 – e00309–10.
11. Kaplan SL, Barson WJ, Lin PL, Romero JR, Bradley JS, Tan TQ, et al. Early trends for invasive pneumococcal infections in children after the introduction of the 13-valent pneumococcal conjugate vaccine. J March 2013. 2013;32(3):203–7.
12. Griffin MR, Mitchel E, Moore MR, Whitney CG, Grijalva CG. Declines in pneumonia hospitalizations of children aged <2 years associated with the use of pneumococcal conjugate vaccines—Tennessee, 1998–2012. MMWR Morb Mortal Wkly Rep. 2014;63(44):995–8.

13. Rubin JL, McGarry LJ, Strutton DR, Klugman KP, Pelton SI, Gilmore KE, et al. Public health and economic impact of the 13-valent pneumococcal conjugate vaccine (PCV13) in the United States. Vaccine. 2010;28(48):7634–43.
14. Pavia AT. What is the role of respiratory viruses in community-acquired pneumonia?: What is the best therapy for influenza and other viral causes of community-acquired pneumonia? Infect Dis Clin North Am. 2013;27(1):157–75.
15. Cevey-Macherel M, Galetto-Lacour A, Gervaix A, Siegrist C-A, Bille J, Bescher-Ninet B, et al. Etiology of community-acquired pneumonia in hospitalized children based on WHO clinical guidelines. Eur J Pediatr. 2009;168(12):1429–36.
16. Tsolia MN, Psarras S, Bossios A, Audi H, Paldanius M, Gourgiotis D, et al. Etiology of community-acquired pneumonia in hospitalized school-age children: evidence for high prevalence of viral infections. Clin Infect Dis Off Publ Infect Dis Soc Am. 2004;39(5):681–6.
17. Jain S. Findings from the Etiology of Pneumonia in the Community (EPIC) Study. 2012 Apr 30
18. Jartti T, Jartti L, Peltola V, Waris M, Ruuskanen O. Identification of respiratory viruses in asymptomatic subjects: asymptomatic respiratory viral infections. Pediatr Infect Dis J. 2008;27(12):1103–7.
19. Beadling C, Slifka MK. How do viral infections predispose patients to bacterial infections? Curr Opin Infect Dis. 2004;17(3):185–91.
20.• Morens DM, Taubenberger JK, Fauci AS. Predominant role of bacterial pneumonia as a cause of death in pandemic influenza: implications for pandemic influenza preparedness. J Infect Dis. 2008;198(7):962–70.
The authors applied modern histopathologic and diagnostic techniques in the evaluation of autopsy samples from the 1918–1919 influenza pandemic, finding that the majority of pandemic deaths were due to secondary bacterial pneumonia.
21. Cox CM, D'Mello T, Perez A, Reingold A, Gershman K, Yousey-Hindes K, et al. Increase in rates of hospitalization due to laboratory-confirmed influenza among children and adults during the 2009–10 influenza pandemic. J Infect Dis. 2012;206(9):1350–8.
22. Blumental S, Huisman E, Cornet M-C, Ferreiro C, de Schutter I, Reynders M, et al. Pandemic A/H1N1v influenza 2009 in hospitalized children: a multicenter Belgian survey. BMC Infect Dis. 2011;11(1):313.
23.•• Florin TA, French B, Zorc JJ, Alpern ER, Shah SS. Variation in emergency department diagnostic testing and disposition outcomes in pneumonia. Pediatr. 2013;132(2):237–44.
This study reports large variations in diagnostic testing among several large children's hospitals prior to release of the PIDS/IDSA guidelines. Differences in testing did not affect patient outcomes.
24. Bradley JS, Byington CL, Shah SS, Alverson B, Carter ER, Harrison C, et al. 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 Off Publ Infect Dis Soc Am. 2011;53(7):e25–76.
25. Brogan TV, Hall M, Williams DJ, Neuman MI, Grijalva CG, Farris RWD, et al. Variability in processes of care and outcomes among children hospitalized with community-acquired pneumonia: Pediatr Infect Dis J. 2012 May;1.
26. Nascimento-Carvalho CM, Madhi SA, O'Brien KL. Review of guidelines for evidence-based management for childhood community-acquired pneumonia in under-5 years from developed and developing countries. Pediatr Infect Dis J. 2013;32(11):1281–2.
27. Copetti R, Cattarossi L. Ultrasound diagnosis of pneumonia in children. Radiol Med (Torino). 2008;113(2):190–8.
28. Don M, Barillari A, Cattarossi L, Copetti R. On behalf of the "Italian-Slovenian group on lung ultrasound for pediatric pneumonia". Lung ultrasound for paediatric pneumonia diagnosis: internationally officialized in a near future?: lung ultrasound for paediatric pneumonia diagnosis. Acta Paediatr. 2013;102(1):6–7.
29. 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.
30. Reissig A, Gramegna A, Aliberti S. The role of lung ultrasound in the diagnosis and follow-up of community-acquired pneumonia. Eur J Int Med. 2012;23(5):391–7.
31.•• Shah SS, Dugan MH, Bell LM, Grundmeier RW, Florin TA, Hines EM, et al. Blood cultures in the emergency department evaluation of childhood pneumonia: Pediatr Infect Dis J. 2011 Jan;1.
Clinicians completing a brief training are able to diagnose pneumonia using point of care ultrasound with high specificity as compared to CXR.
32. Myers AL, Hall M, Williams DJ, Auger K, Tieder JS, Statile A, et al. Prevalence of bacteremia in hospitalized pediatric patients with community-acquired pneumonia. Pediatr Infect Dis J. 2013;32(7):736–40.
33. Hickey RW, Bowman MJ, Smith GA. Utility of blood cultures in pediatric patients found to have pneumonia in the emergency department. Ann Emerg Med. 1996;27(6):721–5.
34.•• Heine D, Cochran C, Moore M, Titus MO, Andrews AL. The prevalence of bacteremia in pediatric patients with community-acquired pneumonia: guidelines to reduce the frequency of obtaining blood cultures. Hosp Pediatr. 2013;3(2):92–6.
Retrospective application of restricted institutional guidelines for use of blood cultures in CAP correctly identified all children with true bacteremia in one children's hospital. This suggests a role for further restriction of blood cultures in pediatric CAP.
35. Williams DJ. Do all children hospitalized with community-acquired pneumonia require blood cultures? Hosp Pediatr. 2013;3(2):177–9.

36. Neuman MI, Harper MB. Rapid antigen assay for the diagnosis of pneumococcal bacteremia in children: a preliminary study. Ann Emerg Med. 2002;40(4):399–404.
37. Neuman MI, Harper MB. Evaluation of a rapid urine antigen assay for the detection of invasive pneumococcal disease in children. Pediatrics. 2003;112(6):1279–82.
38. Esposito S, Bosis S, Colombo R, Carlucci P, Faelli N, Fossali E, et al. Evaluation of rapid assay for detection of streptococcus pneumoniae urinary antigen among infants and young children with possible invasive pneumococcal disease. Pediatr Infect Dis J. 2004;23(4):365–7.
39. Lahti E, Peltola V, Waris M, Virkki R, Rantakokko-Jalava K, Jalava J, et al. Induced sputum in the diagnosis of childhood community-acquired pneumonia. Thorax. 2009;64(3):252–7.
40. Florin TA, Ambroggio L. Biomarkers for community-acquired pneumonia in the emergency department. Curr Infect Dis Rep [Internet]. 2014 Dec;16(12).
41. Flood RG, Badik J, Aronoff SC. The utility of serum C-reactive protein in differentiating bacterial from non-bacterial pneumonia in children: A Meta-Analysis of 1230 Children. Pediatr Infect Dis J [Internet]. 2008 Jan [cited 2014 Nov 4];PAP.
42. Galetto-Lacour A, Alcoba G, Posfay-Barbe KM, Cevey-Macherel M, Gehri M, Ochs MM, et al. Elevated inflammatory markers combined with positive pneumococcal urinary antigen are a good predictor of pneumococcal community-acquired pneumonia in children. Pediatr Infect Dis J. 2013;32(11):1175–9.
43. Toikka P, Irjala K, Juven T, Virkki R, Mertsola J, Leinonen M, et al. Serum procalcitonin, C-reactive protein and interleukin-6 for distinguishing bacterial and viral pneumonia in children. J July 2000. 2000;19(7):598–602.
44. Nascimento-Carvalho CM, Cardoso M-RA, Barral A, Araújo-Neto CA, Guerin S, Saukkoriipi A, et al. Procalcitonin is useful in identifying bacteraemia among children with pneumonia. Scand J Infect Dis. 2010;42(9):644–9.
45. Cohen JF, Leis A, Lecarpentier T, Raymond J, Gendrel D, Chalumeau M. Procalcitonin predicts response to beta-lactam treatment in hospitalized children with community-acquired pneumonia. Hartl D, editor. PLoS ONE. 2012 May 17;7(5):e36927.
46.•• Esposito S, Tagliabue C, Picciolli I, Semino M, Sabatini C, Consolo S, et al. Procalcitonin measurements for guiding antibiotic treatment in pediatric pneumonia. Respir Med. 2011;105(12):1939–45.
This randomized control trial reported that procalcitonin levels can guide the use and duration of antibiotic therapy in hospitalized children without increased risk of treatment failure.
47. Williams DJ, Shah SS. Community-acquired pneumonia in the conjugate vaccine era. J Pediatr Infect Dis Soc. 2012;1(4):314–28.
48. Lee GE, Lorch SA, Sheffler-Collins S, Kronman MP, Shah SS. National hospitalization trends for pediatric pneumonia and associated complications. Pediatr. 2010;126(2):204–13.
49. Li STT, Tancredi DJ. Empyema hospitalizations increased in US children despite pneumococcal conjugate vaccine. Pediatr. 2010;125(1):26–33.
50. Spencer DA, Thomas MF. Necrotising pneumonia in children. Paediatr Respir Rev. 2014;15(3):240–5.
51. Gillet Y, Vanhems P, Lina G, Bes M, Vandenesch F, Floret D, et al. Factors predicting mortality in necrotizing community-acquired pneumonia caused by Staphylococcus aureus containing Panton-Valentine leukocidin. Clin Infect Dis. 2007;45(3):315–21.
52.• Blaschke AJ, Heyrend C, Byington CL, Obando I, Vazquez-Barba I, Doby EH, et al. Molecular analysis improves pathogen identification and epidemiologic study of pediatric parapneumonic empyema. Pediatr Infect Dis J. 2011;30(4):289–94.
Species-specific bacterial PCR increases pathogenic yield of pleural samples when compared to pleural culture alone, and demonstrates improvements over broad-based PCR methods.
53. Gollomp K, Rankin SC, White C, Mattei P, Harris MC, Kilpatrick LE, et al. Broad-range bacterial polymerase chain reaction in the microbiologic diagnosis of complicated pneumonia. J Hosp Med. 2012;7(1):8–13.
54. Pernica JM, Moldovan I, Chan F, Slinger R. Real-time polymerase chain reaction for microbiological diagnosis of parapneumonic effusions in Canadian children. Can J Infect Dis Med Microbiol J Can Mal Infect Microbiol Med AMMI Can. 2014;25(3):151–4.
55. Slinger R, Hyde L, Moldovan I, Chan F, Pernica JM. Direct Streptococcus pneumoniae real-time PCR serotyping from pediatric parapneumonic effusions. BMC Pediatr. 2014;14(1):189.
56. Blaschke AJ, Byington CL, Ampofo K, Pavia AT, Heyrend C, Rankin SC, et al. Species-specific PCR improves detection of bacterial pathogens in parapneumonic empyema compared with 16S PCR and culture. Pediatr Infect Dis J. 2013;32(3):302–3.
57. Hamm H, Light RW. Parapneumonic effusion and empyema. Eur Respir J. 1997;10(5):1150–6.
58. Islam S, Calkins CM, Goldin AB, Chen C, Downard CD, Huang EY, et al. The diagnosis and management of empyema in children: a comprehensive review from the APSA outcomes and clinical trials committee. J Pediatr Surg. 2012;47(11):2101–10.
59. Balfour-Lynn IM, Abrahamson E, Cohen G, Hartley J, King S, Parikh D, et al. BTS guidelines for the management of pleural infection in children. Thorax. 2005;60 suppl 1:i1–21.
60. Ramnath RR, Heller RM, Ben-Ami T, Miller MA, Campbell P, Neblett WW, et al. Implications of early sonographic evaluation of parapneumonic effusions in children with pneumonia. Pediatrics. 1998;101(1):68–71.
61. Calder A, Owens CM. Imaging of parapneumonic pleural effusions and empyema in children. Pediatr Radiol. 2009;39(6):527–37.
62. Patradoon-Ho P, Fitzgerald DA. Lung abscess in children. Paediatr Respir Rev. 2007;8(1):77–84.

63. Gillet Y, Etienne J, Lina G, Vandenesch F. Association of necrotizing pneumonia with panton-valentine leukocidin–producing staphylococcus aureus, regardless of methicillin resistance. Clin Infect Dis. 2008;47(7):985–6.
64. Lodha R, Kabra SK, Pandey RM. Antibiotics for community-acquired pneumonia in children. In: The Cochrane Collaboration, editor. Cochrane Database of Systematic Reviews [Internet]. Chichester, UK: John Wiley & Sons, Ltd; 2013.
65. Williams DJ, Hall M, Shah SS, Parikh K, Tyler A, Neuman MI, et al. Narrow vs broad-spectrum antimicrobial therapy for children hospitalized with pneumonia. Pediatr. 2013;132(5):e1141–8.
66. Ross RK, Hersh AL, Kronman MP, Newland JG, Metjian TA, Localio AR, et al. Impact of infectious diseases society of America/pediatric infectious diseases society guidelines on treatment of community-acquired pneumonia in hospitalized children. Clin Infect Dis. 2014;58(6):834–8.
67. Leyenaar JK, Shieh M-S, Lagu T, Pekow PS, Lindenauer PK. Comparative effectiveness of ceftriaxone in combination with a macrolide compared with ceftriaxone alone for pediatric patients hospitalized with community-acquired pneumonia. Pediatr Infect Dis J. 2014;33(4):387–92.
68. Galli L, Montagnani C, Chiappini E, de Martino M. Treating paediatric community-acquired pneumonia in the era of antimicrobial resistance. Acta Paediatr. 2013;102:25–33.
69. Harrison CJ, Woods C, Stout G, Martin B, Selvarangan R. Susceptibilities of Haemophilus influenzae, streptococcus pneumoniae, including serotype 19A, and Moraxella catarrhalis paediatric isolates from 2005 to 2007 to commonly used antibiotics. J Antimicrob Chemother. 2009;63(3):511–9.
70. Biondi E, McCulloh R, Alverson B, Klein A, Dixon A, Ralston S. Treatment of mycoplasma pneumonia: a systematic review. Pediatr. 2014;133(6):1081–90.
71.• Mulholland S, Gavranich JB, Gillies MB, Chang AB. Antibiotics for community-acquired lower respiratory tract infections secondary to *Mycoplasma pneumoniae* in children. In: The Cochrane Collaboration, editor. Cochrane Database of Systematic Reviews [Internet]. Chichester, UK: John Wiley & Sons, Ltd; 2012.

A recent Cochrane review found insufficient evidence from the literature to recommend the use of macrolide antibiotics in pediatric lower respiratory tract infection.

72. Ambroggio L, Taylor JA, Tabb LP, Newschaffer CJ, Evans AA, Shah SS. Comparative effectiveness of empiric β-lactam monotherapy and β-lactam–macrolide combination therapy in children hospitalized with community-acquired pneumonia. J Pediatr. 2012;161(6):1097–103.
73. Kovaleva A, Remmelts HHF, Rijkers GT, Hoepelman AIM, Biesma DH, Oosterheert JJ. Immunomodulatory effects of macrolides during community-acquired pneumonia: a literature review. J Antimicrob Chemother. 2012;67(3):530–40.
74. Steel HC, Theron AJ, Cockeran R, Anderson R, Feldman C. Pathogen- and host-directed anti-inflammatory activities of macrolide antibiotics. Mediat Inflamm. 2012;2012:1–17.
75. Avansino JR, Goldman B, Sawin RS, Flum DR. Primary operative versus nonoperative therapy for pediatric empyema: a meta-analysis. Pediatrics. 2005;115(6):1652–9.
76.•• Shah SS, Hall M, Newland JG, Brogan TV, Farris RWD, Williams DJ, et al. Comparative effectiveness of pleural drainage procedures for the treatment of complicated pneumonia in childhood. J Hosp Med. 2011;6(5):256–63.

This study compared a variety of pleural drainage techniques, reporting decreased need for additional drainage procedures with initial VATS, but no differences in outcomes compared to chest tube placement.

77. 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. In: The Cochrane Collaboration, editor. Cochrane Database of Systematic Reviews [Internet]. Chichester: Wiley; 2014.
78. Chaves GS, Fregonezi GA, Dias FA, Ribeiro CT, Guerra RO, Freitas DA, et al. Chest physiotherapy for pneumonia in children. In: The Cochrane Collaboration, editor. Cochrane Database of Systematic Reviews [Internet]. Chichester: Wiley; 2013.
79. Haider BA, Lassi ZS, Ahmed A, Bhutta ZA. Zinc supplementation as an adjunct to antibiotics in the treatment of pneumonia in children 2 to 59 months of age. In: The Cochrane Collaboration, editor. Cochrane Database of Systematic Reviews [Internet]. Chichester: Wiley; 2011.
80. Weiss AK, Hall M, Lee GE, Kronman MP, Sheffler-Collins S, Shah SS. Adjunct corticosteroids in children hospitalized with community-acquired pneumonia. Pediatr. 2011;127(2):e255–63.
81. Ambroggio L, Test M, Metlay JP, Graf TR, Blosky MA, Macaluso M, et al. Adjunct systemic corticosteroid therapy in children with community-acquired pneumonia in the outpatient setting. J Pediatr Infect Dis Soc. 2014 Mar 27;piu017.
82. Rojas-Reyes MX, Granados Rugeles C. Oral antibiotics versus parenteral antibiotics for severe pneumonia in children. In: The Cochrane Collaboration, editor. Cochrane Database of Systematic Reviews [Internet]. Chichester: Wiley; 2006.