

Opinion

*Corresponding author

Larry B. Mellick, MD, MS, FAAP, FACEP
 Professor
 Department of Pediatrics and
 Emergency Medicine
 Georgia Regents University
 Augusta, GA 30912, USA
 E-mail: Lmellick@gru.edu

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Pediatric Pneumonia Guidelines: Inconsistencies between Guidelines, Scientific Evidence and Clinical Practice

Larry B. Mellick^{1*} and Dan McCollum²

¹Professor, Department of Pediatrics and Emergency Medicine, Georgia Regents University, Augusta, GA 30912, USA

²Assistant Residency Director, Department of Emergency Medicine, Georgia Regents University, Augusta, GA 30912, USA

In 2011 the Pediatric Infectious Diseases Society (PIDS) and the Infectious Diseases Society of America (IDSA) and the British Thoracic Society (BTS) created extensive guidelines with recommendations for the management of community acquired pneumonia in children.^{1,2}

There are a number of recommendations in these guidelines that seem to conflict with the evidence presented in the guidelines and elsewhere as well as clinical experience. The perceived disagreement between guidelines and clinical practice may be ours alone, but here are our thoughts and observations.

In order to accomplish this discussion, we have provided as succinctly as possible framed quotes from the guidelines that are well documented with references in the actual papers. Our response to and discussion of the conclusions made by the writers of the guidelines follow in subsequent paragraphs. Although, extensive references were not required as we are making the point that the guideline's recommendations seem to be odds with their own references, we hope our discussion will encourage the reader to review the actual guidelines to confirm for themselves whether or not our criticisms are valid.

ARE CHILDREN UNDER 2 YEARS OF AGE AT INCREASED RISK OR NOT?

A theme that is found in both guidelines is that the vast majority of infections in preschool children and especially under two years of age are viral infections. Both guidelines make recommendations that minimize investigations and interventions when viral infections are the suspected etiology. For the sake of brevity we will need to summarize the Pediatric Infectious Diseases Society (PIDS) and the Infectious Diseases Society of America (IDSA) and the British Thoracic Society (BTS) statements.

PIDS/IDSA

Antimicrobial therapy is not routinely required for preschool-aged children with CAP, because viral pathogens are responsible for the great majority of clinical disease. (strong recommendation; high-quality evidence)

BTS

*<All children with a clear clinical diagnosis of pneumonia should receive antibiotics as bacterial and viral pneumonia cannot be reliably distinguished from each other. [C]
 <Children aged <2 years presenting with mild symptoms of lower respiratory tract infection do not usually have pneumonia and need not be treated with antibiotics but should be reviewed if symptoms persist. A history of conjugate pneumococcal vaccination gives greater confidence to this decision [C]*

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However, the differentiation of viral versus bacterial pneumonia is often not easily accomplished. And, combined bacterial and viral pneumonias are actually quite common in these younger children.

PIDS/IDSA Guidelines

CAP in children in the United States, the focus of these guidelines, is defined simply as the presence of signs and symptoms of pneumonia in a previously healthy child caused by an infection that has been acquired outside of the hospital.

In many children with LRTI, diagnostic testing may identify 2 or 3 pathogens, including combinations of both viruses and bacteria, making it difficult to determine the significance of any single pathogen.

BTS

- One-third of cases of CAP (8-40%) represent a mixed infection.
- *Mycoplasma* is not unusual in children aged 1-5 years.

Additionally, the presented evidence would suggest that these younger CAP patients are actually at the highest risk for hospitalization and disease associated morbidity and mortality.

PIDS/IDSA

Pneumonia is the single greatest cause of death in children worldwide. Each year, >2 million children younger than 5 years die of pneumonia, representing ~20% of all deaths in children within this age group. Although difficult to quantify, it is believed that up to 155 million cases of pneumonia occur in children every year worldwide.

In the United States, outpatient visit rates for CAP between 1994-1995 and 2002-2003 were approximately 8% of US outpatient visits of 2 year olds were given the diagnosis of pneumonia while approximately 4% of US outpatient visits of 3-6 year olds were diagnosed with pneumonia.

The dramatic impact of pneumococcal vaccination on the incidence of community acquired pneumonia in children under two years of age is additional evidence that while viral infections are common, bacterial infections are also very common. The guidelines report that there has been a 20-30% decrease in the diagnosis of pneumonia in children in most areas. The guidelines also point out that a recent study of PCV11 showed a substantial reduction of 32% of pneumonias in those under one year but less than a 3% decrease in those that were 12-23 months old.¹ For children over the age of 2 they reported only a 9.1% reduction.¹ This evidence shows that the bulk of the benefit for the vaccine is to reduce pneumonia in those under 12 months.

The pneumococcal vaccine clearly does a great job in reducing the burden of illness in our most vulnerable patient population, young infants. However, there appears to be only a modest reduction in admissions for those over the age of 12 months. There is almost no change in the admission rate for those between 12 and 23 months.

BTS

The incidence of all-cause and pneumococcal pneumonia in children aged <2 years and pneumococcal pneumonia in children aged 2-4 years decreased in the USA after pneumococcal vaccination (PCV) became universal. In the UK, admission rates for childhood pneumonia decreased by 19% between 2006 and 2008 to 10.79/10,000 following the introduction of conjugate pneumococcal vaccine (PCV7) to the national childhood immunisation programme.

The effect is most striking in the first year with a 32.2% reduction, and a 23.4% reduction in the first 2 years. A recent study of PCV11 found that, although 34% of radiologically-confirmed pneumonias were prevented in children under 1 year, there was only a 2.7% decrease in those aged 12-23 months. In children aged >2 years there was only a 9.1% reduction. A Cochrane systematic review found a pooled vaccine efficacy for PCV11 of 27% for reduction of radiographically-confirmed pneumonia in children <2 years and 6% for clinical pneumonia.

Evidence statements

- *S pneumoniae* is the most common bacterial cause of pneumonia in childhood.
- *S pneumoniae* causes about one-third of radiologically confirmed pneumonia in children aged <2 years.
- The introduction of PCV7 has dramatically decreased IPD due to vaccine serotypes in the UK, but a steady increase in vaccine serotype replacement is evident in the UK.

Inconsistencies

Both the PIDS/IDSA and BTS guidelines seem to emphasize the role of viral infections in children under two years of age. The PIDS/IDSA guidelines even state that antimicrobial therapy is not routinely required for preschool-aged children with CAP, because viral pathogens are responsible for the great majority of clinical disease. However, the overwhelming evidence is that even though viral infections are common, bacterial infections are also common as are viral and bacterial co-infections. Additionally, atypical pneumonias are not rare and the population at most risk of morbidity and mortality from CAP are less than two years of age.

The existence of common bacterial co-infection with children with viral pneumonia complicates their treatment. In recent years there has been an increasing availability of rapid viral panels. Some of these panels focus only on a single virus such as influenza but many test for a wide variety of viral pathogens. The common co-existence of bacterial co-infection should cause a provider to pause prior to withholding antibiotics in a child with a positive viral panel, especially if that child appears ill.

DOWNPLAYING CHEST RADIOGRAPHS IN THE FACE OF EVIDENCE

Both guidelines recommend against obtaining chest radiographs for the confirmation of suspected CAP.

However, both guidelines also clearly presented evidence that the clinical diagnosis of pneumonia without a radiograph is very difficult. While there are clinical clues suggestive of pneumonia such as increased respiratory rate and cough, these

are very nonspecific and insensitive. The British Thoracic Society (BTS) guidelines reported that 82% of 1848 chest radiographs obtained in a Pakistani study that was based on the WHO criteria of tachypnea without 'danger symptoms' were classified as normal and commented that "Other studies have drawn similar conclusions."²

PIDS/IDSA

Routine chest radiographs are not necessary for the confirmation of suspected CAP in patients well enough to be treated in the outpatient setting (after evaluation in the office, clinic, or emergency department setting). (strong recommendation; high-quality evidence)

Chest radiographs, posteroanterior and lateral, should be obtained in patients with suspected or documented hypoxemia or significant respiratory distress (Table 3) and in those with failed initial antibiotic therapy to verify the presence or absence of complications of pneumonia, including parapneumonic effusions, necrotizing pneumonia, and pneumothorax. (strong recommendation; moderate-quality evidence)

BTS

- Chest radiography should not be considered a routine investigation in children thought to have community acquired pneumonia (CAP). [A-]
- Children with signs and symptoms of pneumonia who are not admitted to hospital should not have a chest x-ray. [A-]

PIDS/IDSA

Tachypnea is a nonspecific clinical sign, but may represent a marker for respiratory distress and/or hypoxemia. "Rapid breathing as perceived by the mother" was statistically associated with hypoxemia in a study of children with pneumonia. An increase in the age-specific respiratory rate or tachypnea has been linked to treatment failure in children with severe pneumonia in the developing world. Although tachypnea in infants with pneumonia may correlate with presence of hypoxemia, tachypnea may also be caused by fever, dehydration, or a concurrent metabolic acidosis. In a study from a pediatric emergency department in Boston of children <5 years old undergoing chest radiography for possible pneumonia, the respiratory rates for those with documented pneumonia did not differ significantly from those for children without pneumonia. However, of children with WHO-defined tachypnea, 20% had confirmed pneumonia, compared with 12% without tachypnea.

For resource-poor regions of the world, the World Health Organization (WHO) defines pneumonia primarily as cough or difficult breathing and age-adjusted tachypnea: (age 2–11 months, >50/min; 1–5 years, >40/min; >5 years, >20 breaths/min). Furthermore, severe pneumonia is defined as "cough or difficulty breathing plus one of the following: lower chest in drawing, nasal flaring, or grunting." Very severe pneumonia is defined as "cough or difficulty breathing plus one of the following: cyanosis, severe respiratory distress, inability to drink or vomiting everything, or lethargy/unconsciousness/convulsions." Such definitions of various levels of severity and studies to validate interventions for each level of severity

Inconsistencies

The diagnosis of pneumonia without a chest radiograph in children is a foreign concept to most clinicians. Experienced clinicians might willingly diagnose pneumonia without a radiograph in the presence of rales or crackles on auscultation. However, the diagnosis of pneumonia based on respiratory rate and cough as described in the guidelines is a clinical guess at best. It is very common for a child with a viral upper respiratory infection to have tachypnea recorded on triage vital signs, especially if the child is crying or febrile. Intuitively, it would appear that over diagnosis and over treatment of simple respiratory tract infections misdiagnosed as pneumonia would be the natural outcome of this approach.

It is also unclear if data and guidelines for resource poor countries should be applied in areas where radiographs are easily obtainable. The minimal radiation exposure of a chest radiograph should be considered but is unlikely to prevent a clinician from getting a radiograph. The need for good antibiotic stewardship and risks of overuse of antibiotics by clinicians rarely obtaining radiographs seems to be of much more concern.

ATYPICAL PNEUMONIAS AND PRESCHOOL CHILDREN

Both PIDS/IDSA and BTS guidelines acknowledge that contrary to past teachings preschool children actually are infected relatively commonly with the pathogens responsible for atypical pneumonias. However, while the guidelines recognize these infections as being substantial, their recommendations do not seem to adequately address the management of these infections.

PIDS/IDSA

"The age at which one should begin to strongly consider *M. pneumoniae* as the cause of CAP is not well defined. *M. pneumoniae* is increasingly being diagnosed serologically as a cause of LRTI in young children.

BTS

"*Mycoplasma* is not unusual in children aged 1–5 years."

A study of 154 children by Michelow et al. found that, as has been proposed more recently, preschool children are just as likely as those of school age to have atypical pneumonia. There are likely to be geographical variations in these findings."

"Improved short- and long-term outcomes have been described in children with respiratory tract infections (a mixture of upper and lower by clinical diagnosis) treated with macrolides compared with those not treated. Of those children with lower respiratory tract infections due to *M pneumoniae* and/or *C pneumoniae* assessed as 'clinical failures', 83% had not been treated with macrolides.

"< Macrolide antibiotics may be added at any age if there is no response to first-line empirical therapy. [D]

< Macrolide antibiotics should be used if either *mycoplasma* or *chlamydia pneumoniae* is suspected or in very severe disease. [D]"

Inconsistencies

While both groups acknowledge that there is growing evidence that *M. pneumoniae* and *Chlamydial pneumoniae* infect a substantial number of preschool children, both guidelines had difficulty giving clear recommendations on how to address this very real possibility. For years the teaching has been that these infectious agents were rarely found in infants and young children. The recognition that *M. pneumoniae* and *Chlamydial pneumoniae* infections are relatively common infectious agents in preschool children and infants is relatively recent knowledge. Unfortunately, it seems that the greater abundance of evidence for these infections in older children and adolescence continues to dominate these guidelines. The lack of strong evidence for treatment effectiveness and diagnostic tools for differentiating the infection from other lower respiratory tract infections in younger children results in guidelines that do not seem to fully

address or acknowledge these infectious organisms that may be responsible for nearly a quarter of the community acquired pneumonias.

CONCLUSION

- While the guidelines emphasize viral infections in the youngest patients and withholding antibiotics, the evidence shows that bacterial infections are also very common and that the morbidity and mortality of pneumonia are greatest for children under two years of age.
- Strong evidence exists that confirm combined bacterial and viral infections are common. And, the greatest benefit from the pneumococcal vaccine occurred with children under two years of age. These observations would strongly suggest that withholding antibiotics should only be performed when the clinician can be confident that the condition is most consistent with a solitary viral infection. Unfortunately, it is unclear at this time how to establish this diagnosis.
- Existence of a viral infection does not rule out co-existent bacterial infection. Cessation of antibiotics should not be based solely on a positive viral panel, especially if the child appears ill.
- It is very challenging to accurately make the diagnosis without a chest radiograph. While it may be very appropriate to not obtain a chest radiograph in resource poor settings, we fear that the diagnosis of pneumonia with only the presence of cough and tachypnea will lead to an increasing overuse of antibiotics. Due to chest radiographs not being perfectly sensitive for pneumonia, clinicians may still consider the diagnosis of pneumonia based on physical examination findings alone. This seems very reasonable in ill appearing children, but should be done rarely in well appearing children to avoid the overuse of antibiotics.
- The prevalence of atypical causes of pneumonia is higher than once thought in young children. A Cochrane review revealed uncertainty about whether antibiotics should be routinely used in children with mycoplasma pneumonia. It seems reasonable to consider the use of antibiotics in patients with suspected or confirmed *M. pneumoniae* or *C. pneumoniae* pneumonia but more evidence is definitely needed.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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