REVIEW

Community-acquired pneumonia in children: an updated perspectives on its etiology, diagnosis, and treatment

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ABSTRACT

Pneumonia is a common pediatric infectious disease that is very familiar to pediatricians and is a major reason for hospitalization worldwide. Recent well-designed epidemiologic studies in the developed country indicated that respiratory viruses were detected in 30-70%, atypical bacteria in 7-17%, and pyogenic bacteria in 2-8% in children hospitalized with community-acquired pneumonia (CAP). The etiological distribution of CAP vary widely in according to the age of child and the epidemiologic season of the respiratory pathogen. Moreover, diagnostic test particularly for detection of *Streptococcus pneumoniae* and *Mycoplasma pneumoniae*, which are the two major bacterial pathogens involved in pediatric CAP, have several limitations. Therefore, the management and empirical antimicrobial therapy for children with CAP should be applied with stepwise manner based on the recent epidemiologic, etiologic, and microbiologic evidences.
INTRODUCTION

Pneumonia is a common infectious disease among children that is very familiar to pediatricians and is a major reason for hospitalization worldwide. Moreover, considering the fact that most of the novel infectious diseases that cause pandemics, including the ongoing coronavirus disease 2019 (COVID-19), were caused by respiratory pathogen, the clinical significance of pneumonia is even greater. Despite such an important disease, particularly in children, its diagnosis, treatment, and prevention have been implemented based on the studies conducted on adults. Recently, clinical studies have been conducted in some developing and developed countries to better diagnose and treat pneumonia in children. This review summarizes the results of major international and Korean studies conducted so far and proposes the most appropriate diagnosis and treatment policy based on the evidences.

EPIDEMIOLOGY

Pneumonia is the leading cause of death in children <5 years of age worldwide. Estimated numbers of global deaths by pneumonia were 0.76 million and the cause-specific mortality rate was 5.5 cases per 1,000 livebirths in 2015.\(^1\) Although mortality rates do not reach the levels observed in low- and middle-income countries, the morbidity and financial burden associated with pneumonia remain significant also in developed countries. In a recent large epidemiologic study in the United States (US), the annual incidence of community-acquired pneumonia (CAP) requiring hospitalization was 15.7 cases per 10,000 children, with the highest rate among children younger than 2 years of age.\(^2\)

During the last 20 years, the incidence of lower respiratory tract infection (LRTI) declined globally. A total number of episodes of clinical pneumonia in young children (<5 years of age) in 132 developing countries decreased by 22% from 178 x 10\(^6\) in 2000 to 138 x 10\(^6\) in 2015.\(^3\) Also, there has been a substantial decrease in the number of deaths and in mortality rate, which reflects not only economic development, improved nutrition, and reduced household crowding, but also the use of pneumonia-specific interventions such as improved case management—including empirical antibiotic treatment—and effective vaccines against leading causes of pneumonia in children.\(^4\)
While the number of pneumonia cases and death rates have significantly decreased, hospital visits and hospitalization rates are rising in both developing and developed countries, and the situation here in South Korea is no exception.\textsuperscript{3,5} According to the National Health Insurance Corporation database, the number of hospital visits increased from 9,509 to 12,833 per 100,000 population during 2004-2014, especially for those under 10 years of age.\textsuperscript{5} In an Asian multinational study, a total of 3,151 CAPs under the age of 5 were hospitalized in 2011 at three Korean hospitals, which accounted for 22.4% of all hospitalizations during that period. It was the highest level compared to Vietnam (5.4%), Malaysia (2.8%) and Indonesia (18.2%).\textsuperscript{6} In another study using the National Emergency Department Information System, a total of 329,380 children were diagnosed with pneumonia by visiting emergency departments (EDs) nationwide during 2007-2014.

In the last 5 years (2015.03-2020.02) before the COVID-19 pandemic, the number of CAPs in children in 4 referring hospitals in the Korean metropolitan area was 1.0 per 100 inpatients in department of pediatrics. It showed the most prevalent incidence in the winter season, when respiratory syncytial virus (RSV) and *Mycoplasma pneumoniae* were prevalent, and another increasing trends in March and September with the opening of school. However, the COVID-19 pandemic had a significant impact on the epidemiology of other respiratory viruses, showing a different epidemiology of pneumonia from the pre-pandemic.\textsuperscript{7} Nevertheless, the incidence of CAP increased significantly due to the circulation of RSV-B in the winter season of 2021 and human metapneumovirus (HMPV) and RSV-A in the fall-winter seasons of 2022 (unpublished data).

ETIOLOGY

1. Results from the recent etiologic studies

As mentioned above, the use of effective vaccines such as pneumococcal conjugate vaccine (PCV), *Haemophilus influenza* type b (Hib) vaccine, and influenza vaccine, as well as the improvement of hygiene and living environment, and the efforts of World Health Organization (WHO) and each country to reduce pneumonia, have greatly reduced its global morbidity and mortality.\textsuperscript{3,4} At the same time, it is expected that the changes in the distribution
of causative pathogen of pneumonia have occurred. For more appropriate diagnosis, treatment, and prevention of pneumonia, it is important to know the distribution of pathogens that cause pneumonia in the present era. In terms of this urgent unmet need, large-scale epidemiologic and etiologic studies have recently been conducted.

The efforts for enhancing our understanding of recent pneumonia etiology were initiated in developing countries. Drakenstein study was conducted in 2012-2014 by Bill and Melinda Gates Foundation using the South African birth cohort.8 Also two large-scale multicenter prospective case-control cohort studies of pneumonia etiology in children have been conducted: Global Approach to Biological Research, Infectious disease and Epidemics in Low-income countries (GABRIEL) in 2010–20149 and the Pneumonia Etiology Research for Child Health (PERCH) study in 2011–2014.10 These two studies involved infants and toddlers under the age of 5 who were hospitalized for pneumonia (Table 1).

Among developed countries, the US first conducted a multicenter prospective case-control study for pneumonia etiology in children during 2010–2012, the well-known Etiology of Pneumonia in the Community (EPIC) study.2 A total of 2,638 children with CAP requiring hospitalization were enrolled in 3 hospitals for 2.5 years. In this study, 89% had radiographic evidence of pneumonia, and the pyogenic bacterial pathogen was detected only from blood, pleural effusion (PE), and bronchoalveolar lavage (BAL) fluid using both polymerase chain reaction (PCR) and conventional culture techniques. As a result of this comprehensive etiologic work-up for CAP in children, any pathogen was detected in 81%, viruses in 73%, pyogenic bacteria in 7%, and atypical bacteria like M. pneumoniae in 8%. Similarly, another US study was conducted to get data on the clinical characteristics and etiology of CAP in children in both inpatients and outpatients during 215-2018. In this study, except for S. pneumoniae, there were no significant differences between inpatients and outpatients in the proportions of children with specific pathogens detected.11 The main strengths of these studies include prospective collection of standardized data with advanced molecular diagnostic techniques.

The well-designed comprehensive etiologic studies on CAP in children, have rarely been conducted in Asia so far. A Japanese study in 2005-2006 investigated the detection frequency of pathogens from nasopharyngeal swab (NPS) in children with CAP using real-time PCR (rt-PCR) and bacterial culture. S. pneumoniae and M. pneumoniae were the most common
at 24% and 15%, respectively, and among viruses, rhinovirus was detected most commonly at
14.5%.\textsuperscript{12} This result showed that the \textit{S. pneumoniae} colonizing the nasopharynx of children
before the introduction of pneumococcal conjugate vaccine (PCV) in 2010 might be reflected.
However, in a Taiwan study conducted from 2010 to 2013 at eight participating medical centers,
the proportions of \textit{S. pneumoniae} was very high, even though the PCV was first introduced in
2005. In this study, respiratory specimens were excluded for detection of \textit{S. pneumoniae}; but,
they incorporated urinary antigen test results, which could not differentiate colonization and
true infection, particularly in children. As a result, the most common pathogen was \textit{S.
\textit{pneumoniae}} (31.6%), which were mostly detected by using the urinary antigen test only
(83.1%). In addition, they mainly used serologic tests, which had relatively low specificity, to
detect \textit{M. pneumoniae}, which were 2\textsuperscript{nd} most common pathogen identified (22.6%).\textsuperscript{13}

In China, a multicenter prospective study was conducted for the etiology of
radiologically confirmed CAP in the hospitalized children aged from 6 months to 14 years of
age in 2015. They tested for only eight respiratory viruses from oropharyngeal swab using the
direct fluorescent antibody (DFA) technique, used IgM serologic test for \textit{M. pneumoniae}
detection, and even did not report the test result for pyogenic bacteria. As a result, \textit{M.
\textit{pneumoniae}} was the most frequently detected pathogen (32.4%).\textsuperscript{14} In the major Asian studies
above, the rate of pyogenic bacteria and \textit{M. pneumoniae} was reported to be very high by
including culture and/or PCR results from upper respiratory tract specimens and incorporating
serologic test, respectively.

2. Korean etiology studies

In South Korea, there has been no systematic analysis of the etiology of pneumonia in
children. However, the detection rates of the respiratory viruses for acute LRTIs were studied
by several researchers between 2000 and 2011, resulting from 10% to 73% (Table 2).\textsuperscript{15-20} The
most commonly detected viruses were RSV and parainfluenza virus (PIV), although
adenovirus and human rhinovirus (HRV) were the 2\textsuperscript{nd} most common viruses in some
studies.\textsuperscript{17,20} These studies are very limited because bronchiolitis was included and bacterial
pathogens were not investigated. On the other hand, in a study of 122 cases of empyema
diagnosed in 35 hospitals nationwide from 1999 to 2004, \textit{S. pneumoniae} was the most common
(36.9%), followed by *Streptococcus pyogenes* (6.6%) and *Staphylococcus aureus* (5.7%). In addition, in the analysis of 288 cases of lobar/lobular pneumonia diagnosed at a single institution from 2006 to 2008, pyogenic bacteria, which mostly comprised of *S. pneumoniae* (88.9%), was identified in 5.9% from blood and respiratory cultures and *M. pneumoniae* was identified in 50.7% by serologic tests.

A large-scale multicenter study for CAP etiology was recently conducted by a pediatric research network. This was a retrospective study in 30,994 hospitalized children with CAP between 2010 and 2015 at 23 hospitals. This study did not include data for pyogenic bacteria. The same group recently conducted a multicenter prospective study for CAP etiology in 1,023 children between 2018 and 2020 at 28 hospitals nationwide. *M. pneumoniae* (41.3%) and viruses (65.7%) with rhinovirus (30.5%) were commonly detected. A total of 264 bacteria (25.8%) were isolated by culture and/or PCR: *S. aureus* (13%), *S. pneumoniae* (9%), and *H. influenzae* (2%). The proportions of *M. pneumoniae* and pyogenic bacteria were much high as in the other Asian studies. These findings may indicate that colonized pyogenic bacteria might be misidentified as a pathogen and that the result of the serologic test with low specificity for *M. pneumoniae* was mainly used for the etiologic diagnosis.

To evaluate the etiologic distribution of CAP in Korean children with a different viewpoint, a retrospective multicenter study was recently conducted by another group. In this study, a rigorous case definition for CAP was applied with evident clinical symptoms, physical examination, and chest radiographic findings corresponding to pneumonia. In addition, researchers excluded upper respiratory tract specimens for detecting pyogenic bacteria to exclude colonization. Serologic test result for *M. pneumoniae* was regarded as positive only when a 4-fold increase between paired-blood samples or a much higher (usually 10 times) cut-off value with a single antibody titer was identified. Also, HRV, human bocavirus (HBoV), and human coronavirus (HCoV) were excluded as pathogens because they are often detected in the nasopharynx of asymptomatic children, and thus their etiologic role in CAP is not evident in children. As a result, in the last five years (from March 2015 to February 2020) before the COVID-19 pandemic, respiratory viruses were detected in 31.6%, atypical bacteria in 17.4%, and pyogenic bacteria only in 2.3% in children hospitalized with CAP. About half of the children had no pathogen detected. The most common pathogens were *M. pneumoniae* (16.8%) and RSV (13.7%), and among pyogenic bacteria, *S. pneumoniae* (0.6%) and *S. pyogenes* (0.6%).
DIAGNOSIS

1. Clinical diagnosis

Diagnosis of pneumonia is based on respiratory symptoms, physical examination, and/or chest radiograph findings. However, in the absence of clear alveolar consolidation and PE on chest X-ray (CXR), it may be difficult to distinguish other LRTIs – croup, bronchitis, and bronchiolitis from pneumonia. The case definitions for pneumonia by WHO are mainly used in developing countries, and the severity is classified by the degree of respiratory distress. Pneumonia is defined as cough/difficult breathing and age-adjusted tachypnea. In addition, the etiologic diagnosis of pneumonia is more complicated and difficult in the usual clinical situations.

2. Pneumococcal pneumonia

Particularly bacterial pneumonia, such as S. pneumoniae, which is the most important pathogen in CAP because it should be treated with an antibiotics, is difficult to be accurately identified in children. A small proportion of cases are detected by blood and/or PE culture even under ideal conditions. Sputum could not be adequately produced by young children and can be easily contaminated by organisms carried in the nasopharynx. Also, detection of pneumococcus in the nasopharynx or positivity on the urinary antigen test may represent asymptomatic carriage, which is prevalent even in healthy young children. When pneumococci are present in the nasopharynx, genomic fragments of the bacteria can be detected in the blood through PCR, so blood PCR for pneumococcus has low specificity in children with CAP. Moreover, diagnostic serology is insensitive in children, and paired samples are difficult to obtain. The BAL or lung biopsy performed to avoid contamination with upper respiratory secretions are the gold standard of diagnostic technique in pneumonia, but these procedures are rarely performed in children with CAP due to their invasiveness. Thus, even with sufficient etiologic work-up, there is a possibility that the diagnosis of some bacterial pneumonias may be missed even in cases of pneumonia for which the causative bacteria have not been identified, or pneumonia in which respiratory viruses have been detected.
Therefore, it is common to use empirical antibiotics according to the clinical findings suggesting the possibility of pyogenic bacterial pneumonia – lobar/lobular consolidation, empyema/PE, and high inflammatory markers (C-reactive protein [CRP] and procalcitonin [PCT]), etc. In particular, if these findings occur outside of the *M. pneumoniae* epidemic period (which may have similar clinical manifestations) or in children who have not completed the immunization with PCV, the probability of pneumococcal etiology of this pneumonia might be high. Recent studies have additionally suggested that the nasopharyngeal (NP) carriage load of pneumococcus is higher in pneumococcal CAP than in other etiologic CAPs, and thus can be used to diagnose pneumococcal CAP.27-29

3. *Mycoplasma pneumonia*

Atypical pneumonia pathogens include *M. pneumoniae, Chlamydophila pneumoniae, Chlamydia trachomatis*, and *Legionella pneumophila*, but *M. pneumoniae* accounts for most of the causes of atypical CAP in children. However in neonates and infants less than 3 months of age, *C. trachomatis* can sometimes manifest in a pattern similar to viral pneumonia such as RSV. A repetitive staccato cough, tachypnea, and rales are characteristic but wheezing is uncommon.30 All atypical bacteria are usually detected by PCR in respiratory samples because culture is difficult and takes a long time. Recently, multiplex PCR kits containing major respiratory viruses along with these atypical bacteria have been commercialized and frequently used in clinical settings.31

However, caution is required in interpretation as *M. pneumoniae* may be detected in NP in asymptomatic healthy children depending on the time of prevalence, region, target age, and race.32 Mycoplasma PCR in sputum samples show widely distributed sensitivity as 9%–100%, has poor concordance with paired serology, and does not reliably differentiate infection from colonization.33 On the other hand, one of the most widely used method for the diagnosis of *M. pneumoniae* is serology. A 4-fold or higher rise in antibody levels in the acute-convalescent serum is considered a diagnosis, but it is difficult to apply in the clinical settings. Therefore, a single titer of IgM is usually measured, but it can remain high for months or possibly years, may not appear in very young children or during re-infection, and positive predictive value can be as low as 15%.32-34 However, a single antibody titer of 1:640 or higher
in an antibody test including both IgG and IgM was highly concordant to the positive results of Mycoplasma PCR test from NPA in Korean children. Thus we may use a high single titer of serologic (IgG + IgM) test for *M. pneumonia* to enhance the specificity, although the sensitivity is probably reduced, particularly in school-aged children and adolescent with CAP during the *M. pneumoniae* epidemic season.

As mentioned above, atypical bacterial pneumonia, particularly *M. pneumoniae* pneumonia has limitations in clinical diagnosis because it can show various symptoms, severity, laboratory findings, and CXR findings. However, if a school-aged child who has received all PCVs develops a CAP accompanied by lobar/lobular consolidation or PE during the *M. pneumoniae* epidemic, the possibility of *M. pneumoniae* pneumonia might be high.

4. Respiratory viruses

Detection of respiratory viruses in patients with pneumonia is mainly performed on NPA or NP swab samples using a commercially available multiplex real-time RT-PCR. Unlike most bacteria, respiratory viruses have a low probability of asymptomatic colonization, so respiratory viruses detected in children and adolescents suffering from pneumonia are generally accepted as the causative agent of pneumonia. However, HRV, HBoV, and HCoV are exceptions. Because these viruses often cause asymptomatic infection or shedding for a long time after infection, it can be seen that they are detected at a similar rate in the asymptomatic control group as in the pneumonia patients. Serology can be a method to support the RT-PCR test, but it is also clinically limited because it has the possibility of false-positivity and false-negativity, and acute and convalescent serums should be obtained.

5. Novel etiologic diagnostics

Syndromic multiplex PCR panels have been developed. It enables the detection of viruses, atypical bacteria, pyogenic bacteria, and antimicrobial resistance marker genes from respiratory specimens. Semi-quantitative results are also provided for the bacterial targets. The panel showed a sensitivity of 100% and a specificity of 87.2%. Metagenomics and Pan-Viral Group PCR can detect additional viruses, some known to be pathogenic, in NP/oropharyngeal
specimens from one-third of children hospitalized with CAP without a previously identified etiology. Both broad-range methods could be useful tools in future epidemiologic and diagnostic studies.\(^{40}\) Cell-free plasma next-generation sequencing was available in 2017, to supplement standard of care diagnostic techniques. In a previous study in US, among 15 children hospitalized with CAP, a pathogen identified in 13 of 15 (86%) children with cell-free plasma sequencing compared with 47% for those using standard culture and PCR based methods alone.\(^{41}\) RNA sequencing profiles by transcriptional analysis of blood from infants with RSV LRTI allow specific diagnosis, better understanding of disease pathogenesis, and assessment of disease severity. This technique may open new era for identification of potential therapeutic or preventive targets, if applied to the appropriate clinical setting.\(^{42}\)

**TREATMENT**

1. Empirical antimicrobial therapy

   Among the children with CAP in the developed country, 60-90% might have viral etiology, thus they would need a conservative management with symptomatic care during the disease course. However, children with presumed bacterial and influenza viral pneumonia would need an empirical antimicrobial therapy in the initial presentation. The Pediatric Infectious Disease Society (PIDS) and Infectious Disease Society of America (IDSA) in the US recommended amoxicillin or ampicillin for children with presumed pyogenic bacterial pneumonia, azithromycin for children with presumed atypical pneumonia, and oseltamivir or zanamivir for children with presumed influenza pneumonia.\(^{43}\) Also the Korea Centers for Disease Control and Prevention (KCDC) similarly recommended at the 2017 guidelines for the antibiotic use in children with LRTIs.\(^{44}\)

   However, the clinical suspicion of etiology of CAP in children is not easy and inaccurate, so most clinicians usually prescribe antibiotics. Therefore, unless carefully selected pyogenic bacterial pneumonia, the effect of empirical amoxicillin is generally not significant. It was evidenced from several well-designed large-scale RCTs in developing country. In children aged 2 to 59 months in Malawi, placebo treatment of non-severe fast-breathing pneumonia was significantly inferior to treatment with amoxicillin in terms of overall treatment.
failure. However, by day 4, approximately 93% of children receiving placebo were without treatment failure, and there was no significant difference between groups in treatment failure or relapse by day 14. In Pakistan, among children younger than 5 years of age with non-severe pneumonia, the frequency of treatment failure was higher in the placebo group than in the amoxicillin group, but a difference that did not meet the non-inferiority margin for placebo. Also in the US, among children visited to ED with suspected CAP, the treatment failure or admission within 30 days were not statistically different between those who did and did not receive an antibiotic prescription.

In terms of antibiotic treatment duration, treatment courses of 10 days with amoxicillin have been best studied and recommended by both 2011 IDSA and 2017 KCDC guidelines. However, a 5-day course with high-dose oral amoxicillin was not inferior to a 10-day course in 6- to 59-month-old outpatients with community-acquired alveolar pneumonia, which is more likely to be pyogenic bacterial cause. In Malawian children, treatment with amoxicillin for chest-indrawing pneumonia for 3 days was non-inferior to treatment for 5 days. In the UK, among children with CAP discharged from an ED or hospital ward (within 48 hours), lower-dose outpatient oral amoxicillin was non-inferior to higher dose, and 3-day duration was non-inferior to 7 days, with regard to need for antibiotic re-treatment. In the SAFER (Short-Course Antimicrobial Therapy for Pediatric Respiratory Infections) trial in Canada, short-course (5d) antibiotic therapy appeared to be comparable to standard care (10d) for the treatment of previously healthy children with CAP not requiring hospitalization.

2. Antimicrobial therapy for *M. pneumoniae*

Macrolides are recommended as the first-line therapy however, macrolide resistance rates in *M. pneumoniae* among children have been increasing substantially. Macrolide resistance did not contribute to the clinical severity of *M. pneumoniae* pneumonia, but resistance may be an aggravating factor. Antibiotics may not be required for treatment in mild cases due to the self-resolving nature of *M. pneumonia* infection, regardless of macrolide resistance. The clinical benefit of tetracyclines and fluoroquinolones has been shown in terms of shortening duration of symptoms and rapid defervescence in some reports. However, due to safety concerns regarding these two alternative antibiotics, clinicians should weigh the risks
and benefits when choosing treatment options. Alternative antibiotics may be considered when patients remain febrile or when chest x-rays show deterioration at least 48-72 hours after macrolide treatment. The detailed recommendations for the treatment of macrolide-resistant *M. pneumoniae* pneumonia can be found in the 2019 guideline co-developed by the Korean Society of Pediatric Infectious Disease and the Korean Academy of Pediatric Allergy and Respiratory Disease, and would not be covered here as it is beyond the scope of this review.

3. Antiviral therapy

Among the viral pathogen causing CAP in children, influenza virus and SARS-CoV-2 are currently recommended for the treatment with antiviral agent. Early treatment with oseltamivir reduce the duration of illness and hospitalization for patients with serious illness or those with ongoing clinical deterioration. Zanamivir (in ≥7 years-old) and peramivir (in ≥6 months-old) could also be administered by inhalation and parenterally, respectively, for the treatment of influenza pneumonia. Remdesivir is suggested for children (≥3.5 kg) with severe COVID-19 including pneumonia who need supplemental oxygen without mechanical ventilation. Nirmatrelvir/ritonavir is considered for adolescents (≥12 years-old and ≥40 kg) at high risk of progression to severe disease, who do not require supplemental oxygen and are within 5 days of symptom onset and. High risk factors are obesity, diabetes, heart disease, chronic lung diseases, seizure disorders, and an immunocompromised status. Otherwise for the treatment of other common respiratory viruses causing CAP in children, specific antiviral therapy including ribavirin for RSV and cidofovir for adenovirus are not usually recommended.

4. Steroids

Clinical trials yielded conflicting data about the benefit of adding systemic corticosteroids for treatment of CAP. Recent RCTs conducted in adults indicated that short-term corticosteroid treatment reduces time to clinical stability in patients admitted to hospital for CAP or reduces the risk of treatment failure among patients with severe CAP and high initial inflammatory response, but these effects were not significant in the clinical standpoints.
To evaluate the strength and weakness of steroid therapy in children with CAP, pediatric researches should be performed. However, for some particular pathogens, the effectiveness of corticosteroids have been relatively well evaluated and recommended for the treatment in some situations. First of all, early corticosteroid therapy reduce disease morbidity in children with CAP by *M. pneumoniae*, particularly macrolide-resistant *M. pneumoniae*, without increasing the incidence of adverse reactions.\(^{62,63}\) Also, corticosteroids are recommended in children and adolescents with severe to critical COVID-19. It might reduce an excessive immune and inflammatory responses in the severe course of COVID-19 pneumonia.\(^{58}\)

5. Recommendation for management of CAP in children

With regard to the recent epidemiology and advances in diagnostics and therapeutics, we recommend the management strategy of CAP in otherwise healthy children as shown in the Fig.1.

**Conclusions**

Community-acquired pneumonia is a common infectious disease that can be easily diagnosed and treated by all pediatricians, but it is a disease that requires unnecessary waste of medical resources, excessive antibiotic administration, and hospitalization because accurate diagnosis and appropriate treatment are not frequently performed. Just as evidence-based scientific diagnosis and treatment policies have become the basis for wisely overcoming emerging infectious diseases such as COVID-19, multidisciplinary clinical studies are needed to better understand CAP in children and appropriately diagnose, treat, and prevent it.
REFERENCES


7. Suh JH, Yun KW, Han MS, Choi SJ, Lee H, Park JY, et al. Etiology and clinical characteristics of community-acquired pneumonia in Korean children during pre-


<table>
<thead>
<tr>
<th>Region/center</th>
<th>GABRIEL&lt;sup&gt;9&lt;/sup&gt;</th>
<th>PERCH&lt;sup&gt;10&lt;/sup&gt;</th>
<th>EPIC&lt;sup&gt;2&lt;/sup&gt;</th>
<th>CHIRP&lt;sup&gt;11&lt;/sup&gt;</th>
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<td><strong>Multi-national (n=8)</strong>*</td>
<td>Multi-national (n=7)**</td>
<td>US (3 hospitals)</td>
<td>US (6 hospitals)</td>
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<tr>
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<td>2010-2014</td>
<td>2011-2014</td>
<td>2010-2012</td>
<td>2015-2018</td>
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<td>Hospitalized and outpatient clinic</td>
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<td><strong>Age</strong></td>
<td>2-60 months</td>
<td>1-59 months</td>
<td>&lt;18 years</td>
<td>2 mo-18 yo</td>
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<td><strong>CAP category included</strong></td>
<td>Radiologically confirmed, primary end-point pneumonia (WHO&lt;sup&gt;64&lt;/sup&gt;)***</td>
<td>WHO-defined severe or very severe pneumonia&lt;sup&gt;65&lt;/sup&gt; with a positive x-ray</td>
<td>Radiologically confirmed</td>
<td>Radiologically confirmed</td>
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<td><strong>Cases (n)</strong></td>
<td>888</td>
<td>1,769</td>
<td>2,222</td>
<td>441</td>
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<td><strong>Controls (n)</strong></td>
<td>870</td>
<td>5,102</td>
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<tr>
<td><strong>Pathogen detected</strong></td>
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<td>81%</td>
<td>64.6%</td>
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<td><strong>Virus m/c</strong></td>
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<td>61.4%</td>
<td>73%</td>
<td>55.6%</td>
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<td><strong>Pyogenic bacteria</strong></td>
<td>HRV (24.9%), RSV (20.0%), Bocavirus (9.2%)</td>
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<td><strong>Atypical bacteria</strong></td>
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<td>Spn (9.9), Hib (2.7), SA (2.0)</td>
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<td>Mpn (1.5%), Cpn (0.4%)</td>
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* Cambodia, China, Haiti, India, Madagascar, Mali, Mongolia, Paraguay
** Bangladesh, The Gambia, Kenya, Mali, South Africa, Thailand, Zambia

*** The presence of end-point consolidation (as defined above) or pleural effusion that is in the lateral pleural space (and not just in the minor or oblique fissure) and was spatially associated with a pulmonary parenchymal infiltrate (including other infiltrate)
Table 2. Proportion of viral etiology among acute lower respiratory tract infection in Korean children from previous studies

<table>
<thead>
<tr>
<th>Ref</th>
<th>Period</th>
<th>N</th>
<th>Viral testing</th>
<th>Total% (Viral)</th>
<th>RSV</th>
<th>PIV</th>
<th>ADV</th>
<th>IFZ</th>
<th>HRV</th>
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<td>26.1</td>
<td>56.3</td>
<td>20.2</td>
<td>10.0</td>
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<td>2002-2006</td>
<td>3854</td>
<td>culture</td>
<td>9.8</td>
<td>29.6</td>
<td>32.3</td>
<td>14.0</td>
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<td>17</td>
<td>2005</td>
<td>654</td>
<td>multiplex RT-PCR</td>
<td>35.8</td>
<td>34.2</td>
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<td>60.6</td>
<td>23.7</td>
<td>7.9</td>
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N, number; RSV, respiratory syncytial virus; PIV, parainfluenza virus; ADV, adenovirus; IFZ influenza virus; HRV, human rhinovirus; RT-PCR, reverse transcription-polymerase chain reaction
Key messages

1. Most common confirmed cause of CAP in children are *M. pneumoniae* (8-40%) and RSV (15-20%).

2. Pyogenic bacteria are detected in 2-5% from children hospitalized with CAP.

3. Most common pyogenic bacteria isolated are *S. pneumoniae* (40-50%) and *S. pyogenes* (10-25%).

4. Diagnosis of CAP should be conservatively made by both evident clinical and radiological criteria for the proper management.

5. Etiologic diagnosis of CAP should also be made on the appropriate interpretation of the test results.