



An overview on paediatric community-acquired pneumonia

Ping LAM 林萍

Department of Paediatrics, Caritas Medical Center, Hong Kong

Introduction

Community-acquired pneumonia (CAP) refers to pneumonia that is acquired outside hospital in a previously healthy person. CAP is one of the most common and potentially serious infections in childhood. The annual incidence of CAP in children varies in different countries and it is much higher in developing countries. According to World Health Organization (WHO) estimation, the annual incidence of community-acquired pneumonia in developing countries is 290/1000/year in less than 5-year-old, with more than 95% of all worldwide episodes of pneumonia in young children occurring in developing countries.¹ In United States and Europe, the annual incidence was reported to be 36 to 40 cases per 1000.² One study done in a regional hospital in Hong Kong showed that the incidence of pneumonia requiring hospital admission was 6.4 episodes per 1000 children per year for children less than 5-year-old.³

Aetiology

The cause of CAP can be divided into viral, bacterial or mixed infection. A large variety of organisms can cause CAP in children and determining the cause in individual patients is often difficult. Problems involved in identifying pathogens include difficulty in obtaining good sputum samples in young children while other methods like direct culture of lung tissue is too invasive for children. Even with extensive investigations, in 20-60% of cases a specific pathogen is not identified.²

The commonest pathogen involved in bacterial pneumonia in childhood CAP after neonatal period is *Streptococcus pneumoniae*. Less common bacteria include *Haemophilus influenzae*, *Moraxella catarrhalis*,

Group A Streptococcus and *Staphylococcus aureus*. Co-infection with two or more organisms, viral and/or bacterial, was shown to be quite common, between 30% to 50% of cases in some studies.⁴

The patient's age is one of the most important clues to the aetiology of pneumonia.⁵ For neonates, Group B *Streptococcus* and gram-negative enteric bacteria acquired via vertical transmission from the mother are the most common organisms causing pneumonia. For infants aged three weeks to three months bacterial pneumonia is most common and *Streptococcus pneumoniae* is the most common bacteria involved. If the patient is afebrile and has conjunctivitis, *Chlamydia trachomatis* is a likely cause in this age group. Viruses are the most frequent cause of pneumonia in pre-school children and infants between 3-month and 5-year-old. The common viruses include *Respiratory Syncytial Virus* (RSV), *adenovirus*, *influenza virus* and *parainfluenza virus*. For children more than 5-year-old, *Mycoplasma pneumoniae* and *Chlamydial pneumoniae* become more common. Some studies have shown that there is increasing prevalence of *Mycoplasma pneumoniae* and *Chlamydial pneumoniae* in preschool children as well. Pertussis should be considered in the differential diagnosis of childhood community-acquired pneumonia especially when there is incomplete immunisation. In area of high prevalence like Hong Kong, *Mycobacterium tuberculosis* infection should also be considered.

Clinical Assessment

Important information in the initial history taking include the patient's age, immunisation status, travel history, recent antibiotic use, recent exposure to infections like tuberculosis, and any local epidemic at the time. We should also review the patient's past medical history to identify any underlying cardiac, pulmonary or immunological problems.

Email: lamp1@ha.org.hk



Common clinical features of pneumonia include cough, fever, tachypnoea and difficulty of breathing. WHO defined tachypnoea (Table 1) was shown to be the most specific and sensitive sign in diagnosing pneumonia in children less than 5-year-old.⁶ Bacterial pneumonia is more likely if the patient presents with fever $>38.5^{\circ}\text{C}$, chest recession, tachypnoea and dyspnoea. Features of viral pneumonia include presence of fever $<38.5^{\circ}\text{C}$ and wheeze. However, wheeze can also occur in *Mycoplasma pneumoniae* in older children.

A small proportion of pneumonia patients under 5-year-old may not present with respiratory signs. In an acutely ill and febrile child less than 5-year-old with no obvious source of infection, we should also consider the diagnosis of CAP.²

Radiological Assessment

Chest X-ray is generally regarded as the gold standard for diagnosing pneumonia. It has long been recognised that alveolar infiltrates are more common in bacterial pneumonia while interstitial infiltrates, atelectasis and hyperinflation are more common in viral pneumonia. However, studies have shown that CXR findings are too insensitive to be useful in differentiating between viral and bacterial pneumonia. Also, CXR have not consistently been shown to improve clinical outcomes.⁷ The British Thoracic Society (BTS) guideline on management of childhood CAP recommended CXR not to be performed routinely in children with mild uncomplicated acute lower respiratory tract infection.² CXR should only be ordered if clinical findings are ambiguous, there is suspicion of complication like pleural effusion or there is severe pneumonia or prolonged pneumonia not responsive to treatment. However, young children <5 -year-old with pneumonia may not present with

respiratory symptoms. One study⁸ showed that in children <5 -year-old with fever $>39^{\circ}\text{C}$ and white blood cell count $>20,000/\text{mm}^3$ with no additional clinical signs of pneumonia, 25% had radiographic signs of pneumonia. So CXR should be considered in children <5 years old with fever $>39^{\circ}\text{C}$ with no source of infection. Follow up CXR should only be performed after lobar collapse, round pneumonia, or when there is continuing symptoms.

Other Laboratory Assessment

Acute phase reactants including white cell count, total neutrophil count, C reactive protein (CRP), and erythrocyte sedimentation rate (ESR) do not reliably distinguish between bacterial and viral infections according to recent prospective studies.⁹⁻¹¹ Acute phase reactants should not be measured as a routine.²

If the patient is severely ill or shows evidence of dehydration, urea and electrolytes should be checked. Inappropriate secretion of anti-diuretic hormone (ADH) is found to be associated with pneumonia.

Microbiological Investigations

Children with CAP managed in the community setting do not need microbiological investigations. However, the cause should be determined if there appears to be a community outbreak.

For patients with severe pneumonia admitted to hospital, microbiological investigations are important to find out the responsible pathogen. Direct lung aspiration and culture, which is considered to be gold standard in making microbiological diagnosis, was found to yield positive bacterial growth in 79% of children with pneumonia according to one African study.¹² However, this approach is obviously much too invasive to be considered in most children with pneumonia.

It is difficult to collect good sputum specimen in children. Good sputum specimen, defined as having less than 10 squamous epithelial cells and greater than 25 leukocytes per low power field, should be sent

Table 1. WHO defined tachypnoea

Age	Breaths/min
<2 months	>60
2-12 months	>50
1-5 years	>40
>5 years	>30



for gram stain and culture in children with more severe pneumonia. Nasopharyngeal aspirate is often taken in young children. However, bacterial growths in the nasopharynx frequently represent colonisation and do not indicate infection in the lower airways. On the other hand, viral antigen detection in nasopharyngeal aspirates is highly specific for viral infections including respiratory syncytial virus, parainfluenza virus, influenza virus and adenovirus infections. Blood cultures are positive in less than 10% of children and should be performed if bacterial pneumonia is suspected.

If pleural effusion is present, pleural fluid should be aspirated and sent for gram stain, cell count, glucose, biochemical study and culture. If available, antigen detection tests, like counter-immunoelectrophoresis (CIE) and latex agglutination (LA) can also be done. A positive serologic testing for IgM or a four-fold increase in IgG titers is diagnostic of Mycoplasma and Chlamydia infection. Cold agglutinins are often used as an acute test but the diagnostic value is limited. The positive predictive value of cold agglutinin for mycoplasma infection was shown to be 70% for 5-14 years old.¹³

General Management

Since cyanosis may be a late sign for hypoxic infants and children, oxygen saturation should be measured in children with pneumonia requiring hospital admission. Agitation may be an indication of hypoxia. It was reported that the risk of death was significantly increased when hypoxaemia was present in pneumonia patients admitted into hospital.¹⁴ Patients whose oxygen saturation is 92% or less should be treated with oxygen to maintain oxygen saturation above 92%.² Fluid therapy is needed if patient has persistent vomiting or is too breathless to eat or drink. Dehydration should be corrected first and intravenous fluids, if needed, should be given at 80% basal levels and serum electrolytes monitored as inappropriate ADH secretion is a recognised complication. Two randomised controlled studies and one observational study showed that physiotherapy did not have any effect on the length of hospital stay, pyrexia, or CXR findings in patients with pneumonia.¹⁵⁻¹⁷ BTS guideline suggests chest physiotherapy should not be performed in children with pneumonia.²

Antibiotics Treatment

The decisions about antibiotic treatment include whether or not to treat with antibiotics, which antibiotics to use, route of administration and the duration of treatment. Because aetiological organisms are seldom known at the start of treatment, choice of antibiotics is often empirical. Factors that can help us making decisions include the patient's age, severity of disease and epidemiologic factors. All neonates with pneumonia require hospital admission. Infants from one to three months of age with fever and all children who appear toxic should also be admitted to hospital for treatment.

Neonatal pneumonia should be assumed to be bacterial until proven otherwise. *Group B Streptococcus*, *E. coli* and *Listeria* are the common organisms causing neonatal pneumonia. Septic work up including blood culture, urine culture and lumbar puncture should be done on any neonate with fever and/or respiratory distress. Initial antibiotics of choice include intravenous ampicillin and gentamicin, with or without cefotaxime.

All febrile infants between 3 weeks to 3 months of age suspected of having bacterial pneumonia need hospital admission. Initial antibiotics can be cefuroxime or cefotaxime. If the infant is afebrile, nontoxic and has a dry cough or conjunctivitis, *Chlamydia trachomatis* infection is a likely diagnosis. In such case oral macrolide can be given in the outpatient setting but they should be followed up for any change in condition in 1 to 2 day's time. If the patient requires hospital admission, intravenous macrolide could be given.

For preschool children between 3 months to 5 years of age, viral pneumonia are most common. If viral infection is suspected because of associated viral symptoms like pharyngitis and rhinorrhoea, antibiotics can be withheld with close follow up of the patient. Pneumococcal infection is the most common cause of bacterial pneumonia in this age group. In Hong Kong, studies have shown that about 32% and 16-26% of *S. pneumoniae* in children are penicillin intermediate and penicillin resistant respectively.^{18, 19} Erythromycin and septrin resistance is even higher



at 77% and 80% respectively. Because of the high level of antibiotic resistance, first line treatment of suspected pneumococcal pneumonia should be high dose amoxicillin (80-90 mg/kg/day). Studies have shown that penicillin intermediate pneumococcal pneumonia can be successfully treated with high dose penicillin while penicillin resistant pneumococcal pneumonia can be successfully treated with third generation cephalosporins like cefotaxime and ceftriaxone.²⁰ Alternatively, vancomycin can be used in critically ill patient with high level penicillin resistant pneumococcal pneumonia. If a beta-lactamase-producing organism such as *H. influenzae*, *M. cararrhalis* or *Methicillin-sensitive S. aureus* is suspected, penicillin combined with beta-lactamase inhibitors can be used. Some combination preparations provide high dose amoxicillin while others only provide standard dose amoxicillin. Amoxicillin could be given in addition to combination drug to give high dose amoxicillin if necessary. For children admitted to hospital, intravenous cefuroxime or cefotaxime are drugs of choice.

M. pneumoniae and *C. pneumoniae* infections are more common in older children between 5 to 18 years of age. However, *S. pneumoniae* is still a significant pathogen in school-aged children and adolescents. Pneumococcal pneumonia usually presents with abrupt onset of high fever and sputum-producing cough while Mycoplasma pneumonia and Chlamydial pneumonia often begin with headache, gastrointestinal symptoms or pharyngitis. If Mycoplasma or Chlamydial pneumonia is suspected, a macrolide such as azithromycin or clarithromycin is the drug of choice. If pneumococcal pneumonia is suspected, high-dose amoxicillin is the drug of choice. For patients with more severe pneumonia requiring hospitalisation, cefuroxime or cefotaxime should be used in combination with a macrolide.

Based on custom and common practice, BTS guideline on management of childhood CAP suggests 5-7 days of antibiotic treatment for mild pneumonia and 10 days for more severe pneumonia.² Two recent double-blind, randomised controlled studies^{21,22} examined whether a 3-day course of oral amoxicillin was as effective as a 5-day course for treatment of non-severe pneumonia in young children. Both studies demonstrated 3-day treatment was as effective as 5-day treatment. These studies were done in less

developed countries where the standard of treatment for pneumonia is 5 days antibiotics instead of 7-10 days. Also the failure rates of 15-20% from these studies are quite high. Both studies emphasised the need for more trials to determine the optimum dose of the antibiotic and the duration of treatment.

For patients with severe pneumonia requiring hospital admission initial treatment is usually intravenous antibiotics. Antibiotics can be changed to oral form once patient has stabilised.² In a recent study on treatment of severe pneumonia in hospitalised patients, oral amoxicillin was found to be equivalent to intravenous penicillin.²³

If fever or symptoms persist after 48 hours of treatment, detailed re-evaluation is necessary. Some of the possible causes include inappropriate antibiotics or inadequate dose because of drug resistance or rare organisms, lung complication such as pleural effusion, empyema or lung abscess, and host immunosuppression or coexistent disease like bronchiectasis.

Prevention

Annual influenza vaccine is recommended for all high-risk children older than six months of age. The American Academy of Pediatrics also recommends vaccination of all children between six months and 23 months of age to protect against complications of influenza, including pneumonia.²⁴

Recently, a new heptavalent pneumococcal conjugate vaccine covering serotypes 4, 6B, 9V, 14, 18C, 19F and 23F was licensed. This vaccine produces immunity for the seven most common disease-producing serotypes of *S. pneumoniae* in children. Ho et al¹⁹ showed that serotypes in the 7-valent formulation accounted for approximately 90% of all invasive pneumococci isolates and also accounted for the majority of penicillin-resistant and multi-drug resistant pneumococci among young children in Hong Kong. Initial trials have shown the vaccine to be safe and effective in preventing invasive disease, pneumonia as well as nasopharyngeal carriage state.²⁵⁻²⁷ There is also reduction in vaccine-type disease in unvaccinated children and adults because of herd immunity. The vaccine is especially important



in the fight against drug resistant *Strep. pneumoniae* and it was shown that there is significant drop in the frequency of drug resistant infections with vaccine use. The heptavalent vaccine is now recommended for routine use in the United States and some European countries.²⁸ However there is concern that the vaccine may increase carriage of noninvasive serotypes and patients may be more likely to develop infection with serotypes not covered by the heptavalent vaccination. The long-term benefits of this heptavalent pneumococcal vaccine are promising and should be continually monitored.

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