Community-acquired pneumonia in children

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Community acquired pneumonia (CAP) is common in childhood. Viruses account for most cases of CAP during the first two years of life. After this period, bacteria such as *Streptococcus pneumoniae*, *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* become more frequent. CAP symptoms are nonspecific in younger infants, but cough and tachypnea are usually present in older children. Chest x-ray is useful for confirming the diagnosis. Most children can be managed empirically with oral antibiotics as outpatients without specific laboratory investigations. Those with severe infections or with persistent or worsening symptoms need more intensive investigations and may need admission to hospital. The choice and dosage of antibiotics should be based on the age of the patient, severity of the pneumonia and knowledge of local antimicrobial resistance patterns. The Canadian Paediatric Society recommends the use of the heptavalent conjugate pneumococcal vaccine, which is efficacious in reducing chest x-ray positive pneumonia by up to 20%.

Key Words: *Childhood; Community-acquired; Diagnosis; Pneumonia*

La pneumonie extra-hospitalière chez l'enfant

La pneumonie extra-hospitalière (PEH) est courante pendant l'enfance. Les virus sont responsables de la plupart des cas de PEH au cours des deux premières années de vie. Après cette période, des bactéries comme le *Streptococcus pneumoniae*, le *Mycoplasma pneumoniae* et le *Chlamydia pneumoniae* deviennent plus fréquentes. Les symptômes de PEH ne sont pas spécifiques chez les nourrissons, mais une toux et une tachypnée se manifestent généralement chez les enfants plus âgés. Une radiographie pulmonaire est utile pour confirmer le diagnostic. Il est possible de prendre en charge la plupart des enfants de manière empirique, au moyen d'antibiotiques oraux prescrits en clinique externe, sans explorations précises en laboratoire. Les enfants atteints d'une infection grave ou dont les symptômes persistent ou s'aggravent ont besoin de subir des explorations plus intensives, et il se peut qu'ils doivent être hospitalisés. Le choix et la posologie de l'antibiotique doivent dépendre de l'âge du patient, de la gravité de la pneumonie et de la connaissance des schèmes locaux de résistance antimicrobienne. La Société canadienne de pédiatrie recommande l'usage du vaccin anti-pneumococcique conjugué heptavalent, qui est efficace pour réduire jusqu'à 20 % des pneumonies confirmées par radiographie.

Community-acquired pneumonia (CAP) is a lower respiratory tract infection occurring in a child who has not resided in a hospital or health care facility in the preceding 14 days (1). In a recent study, the incidence of first episode pneumonia in unimmunized children younger than five years of age was 55.9 per 1000 person-years (2). It has been estimated that there are 41,000 Canadian children younger than five years of age with nonhospitalized CAP, while another 9600 are hospitalized annually (3). While the etiology of the pneumonia is not often easy to ascertain in the clinical setting, the greatest clue is the age of the child.

AGE-RELATED CAUSES OF PNEUMONIA

Vertical transmission of organisms from the maternal genital tract is the main route of entry of pathogens in the neonatal and early infancy period. The primary organisms responsible for pneumonia in the first three months of life are group B streptococci, gram-negative bacilli and occationally *Listeria monocytogenes* (4). Between three weeks and three months of life, infants may present with an insiduous afebrile pneumonitis syndrome caused by *Chlamydia trachomatis* (5-7). Overall, viruses are the most common causes of pneumonia in the first two years of life, accounting for up to 90% of pneumonias (8-11). The most commonly implicated viruses are respiratory syncytial virus, parainfluenza virus types 1, 2, and 3, influenza virus types A and B, adenovirus, rhinoviruses, and less commonly, herpes simplex virus and enteroviruses (12). With increasing age, the incidence of pneumonia decreases, but bacterial pathogens including *Streptococcus pneumoniae*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae* become more frequent. In children up to 15 years of age, *S pneumoniae* accounts for between 17% and 28% of all community-acquired pneumonia cases (13,14). The introduction of the pneumococcal protein-conjugate vaccines in the United States and some Canadian provinces has led to a substantial reduction in *S pneumoniae* as a cause of invasive diseases in these regions, including pneumonias (15). While the overall rates of invasive pneumococcal infections are decreasing, the proportion of isolates that are penicillin or ceftriaxone resistant is increasing (16,17). This development should lead to a change in the empiric antibiotic choices for children presenting with pneumonia in these regions.

Among school-aged children, viruses only account for one-half of the pneumonia cases (11). *M pneumoniae* is the second most common agent after *S pneumoniae* and

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becomes the most common pathogen in young adolescents, identified in up to one-half of the cases (14). *C pneumoniae* is the second most common agent after *M pneumoniae* among young adolescents, accounting for up to one-third of all pneumonia cases (14).

CLINICAL FINDINGS

The symptoms of pneumonia in neonates are nonspecific and include poor feeding, hypotonia, floppiness, lethargy, apnea, temperature elevation or depression, and hypotension (4). In older children, presence of respiratory infection may be characterized by tachypnea and occasionally, hypoxia progressing to apnea and need for ventilatory support. The World Health Organization has defined clinical criteria for making the diagnosis of pneumonia (18). The criteria consist of presence of a cough associated with tachypnea. Tachypnea is defined as a respiratory rate over 40 breaths/min in children one to five years old, over 50 breaths/min in children two to 12 months old, and over 60 breaths/min in children under two months old. Use of the World Health Organization guidelines is associated with a sensitivity of about 70% to 74% and a specificity of 40% to 70% in correctly identifying pneumonia confirmed on the chest x-ray (19-20).

The chest x-ray may have discrete airspace or airway involvement, or a diffuse reticulonodular pattern indistinguishable from the picture seen with hyaline membrane disease. Patients with *C trachomatis* pneumonia usually present with an afebrile pneumonia associated with staccato cough, tachypnea, progressive difficulty breathing and chest x-ray findings of bilateral pulmonary infiltrates and air trapping (5-7). There is conjunctivitis in half of the cases. Chest examination may reveal diffuse crackles, but wheezing is not usually a feature. Laboratory examination may include an elevated total immunoglobulin M and eosinophilia.

Bacterial pneumonia is classically associated with the abrupt onset of chills and rigors, and a productive sounding cough (truly productive cough is very uncommon in children). The child more commonly appears toxic and physical examination reveals decreased breath sounds and crackles that are typically confined to one lobe. Chest x-ray usually confirms lobar involvement. In contrast, atypical pneumonia has an insidious onset and is associated with a nonproductive cough, low-grade fever, and generally the children are not as toxic as those with bacterial pneumonia. The chest x-ray shows more diffuse involvement. It should be noted that typical bacterial pathogens, such as *S pneumoniae* and *Haemophilus influenzae* are most commonly associated with the classic presentation, and atypical pneumonia is more commonly associated with *M pneumoniae* and *C pneumoniae*. However, all of these organisms may present in either fashion somewhere between the two extreme clinical pictures (21). *Legionella pneumophila* pneumonia is rare in children unless they are immunocompromised (22).

In any child, particularly adolescents who present with cough and fever, consideration should be given to tuberculosis. A proper history should always include whether the child has lived in a tuberculosis endemic area or has had contact with persons who are at high risk, such as First Nations people, immigrants from endemic areas, urban homeless, incarcerated individuals and persons with human immunodeficiency virus infection. Other clues to tuberculosis include a subacute presentation, anorexia, weight loss and night sweats (23). Production of sputum and hemoptysis should differentiate *C pneumoniae* or *M pneumoniae* infections from tuberculosis. Pertussis should be considered in the differential diagnosis of children presenting with symptoms and signs of CAP, particularly when cough and catarrh are prominent. However, pertussis rarely causes radiologically confirmed pneumonia.

Severe acute respiratory syndrome (SARS)-associated coronavirus has recently been added to the list of pathogens causing pneumonia (24,25). This disease is characterized by temperature of over 38°C and one or more clinical findings of respiratory illness (eg, cough, shortness of breath, difficulty breathing or hypoxia), and in severe cases, radiographic evidence of pneumonia or respiratory distress syndrome, or autopsy findings consistent with pneumonia or respiratory distress syndrome without an identifiable cause (26). In addition, there is need to have traveled to an endemic area within 10 days of symptom onset or to have had close contact with a person known or suspected to have SARS. It is unclear whether this condition will remain a major problem during the coming years. Other important clues to etiology of pneumonia include exposure to parrots or other psittacine birds (*Chlamydia psittaci* infection); exposure to farm animals such as sheep, goats, cattle and cats (*Coxiella burnetti*); travel to southwestern United States, northern Mexico and parts of Central and South America (*Coccidioides immitis*); and travel to or residence in eastern and central United States and Canada (*Histoplasma capsulatum*).

DIAGNOSIS

Chest x-ray

Suspicion of diagnosis on clinical grounds should be followed by chest x-ray confirmation due to the lack of agreement between clinical pneumonia and radiologically-confirmed pneumonia, and to prevent unnecessary antibiotic use when a more likely diagnosis is viral bronchitis (27,28).

Follow-up chest x-ray is not indicated except for a child who is presenting with recurrent pneumonias. Follow-up films are useful to determine whether there has been resolution between episodes in the latter scenario (29).

Other tests

Children who are only mildly or moderately ill (no respiratory distress, able to eat and drink, alert and cooperative) can be managed expectantly without specific tests because empiric treatment is usually effective. Children with persistent or worsening symptoms, those who have underlying illness or those who have severe disease need more intensive investigations and management. The priority of investigations

TABLE 1
Empiric antimicrobial therapy for paediatric pneumonia, by age group

Age group	Outpatients	Patients in hospital	Patients in intensive care unit
1 to 3 months			
Afebrile pneumonitis	Initial outpatient management not recommended	Erythromycin 40 mg/kg/d in 4 doses or other macrolide for 10 to 14 days	Erythromycin 40 mg/kg/d in 4 doses or other macrolide for 10 to 14 days
Other	Initial outpatient management not recommended	Cefuroxime 150 mg/kg/d in 3 doses for 10 to 14 days	Cefuroxime 150 mg/kg/d in 3 doses or cefotaxime 200 mg/kg/d in 3 doses plus cloxacillin 100-200 mg/kg/d in 4 doses for 10 to 14 days
3 months to 5 years	Amoxicillin 40 mg/kg/d or 80 mg/kg/d to 90 mg/kg/d* in 3 doses or erythromycin 40 mg/kg/d in 4 doses or other macrolide for 7-10 days	Ampicillin 150 mg/kg/d in 4 doses or cefuroxime 150 mg/kg/d in 3 doses for 7 to 10 days	Cefuroxime 150 mg/kg/d in 3 doses plus erythromcyin 40 mg/kg/d in 4 doses or other macrolide for 7 to 10 days
5 to 18 years	Erythromycin 40 mg/kg/d in 4 doses or other macrolide for 7 days	Erythromycin 40 mg/kg/d in 4 doses or other macrolide with or without cefuroxime 150 mg/kg/d in 3 doses or ampicillin 150 mg/kg/d in 4 doses for 7 to 10 days	Cefuroxime 150 mg/kg/d in 3 doses for 7 to 10 days, plus erythromycin 40 mg/kg/d in 4 doses or other macrolide for 7 days

*Data from Jadavji et al (41) and Bartlett et al (42). *In areas with significant (>10%) rates of intermediate or high level penicillin resistant* Streptococcus pneumoniae*, a daily dosage of 80 mg/kg to 90 mg/kg is recommended (42). In younger infants (3 months to 2 years), the higher dose is recommended*

should be to confirm the common causes and to quickly diagnose causes that would not respond to treatment with the empiric antibiotics. Bacteria identified from nasal and throat cultures have no predictive value in identifying the organisms causing pneumonia. There are few tests that are currently useful in rapid viral diagnoses. While elevated white cell counts and a left shift increase the likelihood of a bacterial infection, they are not predictive enough in distinguishing between viral and bacterial pneumonias. C-reactive protein is also more likely to be elevated in patients with bacterial than viral pneumonia, but there is too much overlap for the test to be clinically useful (30).

Assays based on the polymerase chain reaction have been used in recent studies for diagnosing *M pneumoniae*, *C pneumoniae* and *C trachomatis*, but are not yet routinely available to most practicing physicians (31). Febrile children should have blood specimens obtained for bacterial cultures. Such cultures will yield an organism in 10% to 30% of cases.

MANAGEMENT

Decisions about which child needs hospital admission have to be made on a case-by-case basis using factors such as hydration status, oxygenation status, toxic appearance, lack of response to oral therapy and recurrence or underlying disease. If the patient has inadequate oral intake or diarrhea, intravenous hydration and antibiotics should be given. Children who are hypoxic or in respiratory distress should receive oxygen and may need positive end-expiratory airway pressure or ventilation. The choice of antibiotics for suspected bacterial pneumonia should be based on the age group of the child. Empiric treatment for neonates should reflect the recommendations for treatment of neonatal sepsis. For children who are between three weeks and three months of age with afebrile pneumonia syndrome of infancy, a macrolide such as erythromycin should be given (32). Infants with severe pneumonia who are admitted to the intensive care unit should also receive coverage against *Staphylococcus aureus* and *H influenzae* (33,34) (Table 1). Management of a child with suspected SARS infection should be done in consultation with an infectious diseases consultant.

For children aged three months to five years, *S pneumoniae* has been the most frequent bacterial organism. Penicillins and first- and second-generation cephalosporins remain effective, even in children with pneumonia due to penicillin-resistant *S pneumoniae* (35,36). For this reason, ampicillin is the drug of choice, but some experts recommend increasing the dose to ensure adequate serum and lung levels. Macrolides should also be added for empiric treatment in this age group to cover *M pneumoniae* and *C pneumoniae*, particularly in those who are outpatients. Randomized clinical trials comparing erythromycin with either clarithromycin or azithromycin have shown the newer agents to be equally effective, but with many fewer side effects (31,37-39). Table 1 summarizes the Canadian consensus guidelines for empiric management of pneumonia in children with modification of the ampicilin recommendation to take into consideration the possibility of penicillin-resistant *S pneumoniae*.

PREVENTION

It has been estimated that about 9000 and 2118 cases of nonhospitalized and hospitalized CAP cases, respectively, in Canadian children less than five years of age are due to *S pneumoniae* (3). A heptavalent pneumococcal vaccine (Prevnar, Wyeth-Ayest, Canada) has been licensed in Canada since June 2001 and in the United States since February 2000. When four doses of this vaccine were given to infants at two months, four months, six months and 12 to 15 months of age, all cases of pneumonia were reduced by 4.3%, but episodes of pneumonia associated with a positive

chest x-ray were reduced by 20.5% among confirmed cases and by 17.5% on the intention to treat analysis (2). The vaccine works best in children younger than one year of age (32.2% reduction in pneumonias associated with abnormal chest x-ray, compared with 23.3% in infants during the first two years, and 9.1% after two years of age). Based on these data and the impact on other invasive pneumococcal diseases, the Canadian Paediatric Society and the National Advisory Committee on Immunization recommend routine immunization of all Canadian children aged two months to two years, and of older children in high-risk groups (eg, patients with sickle cell anemia, asplenic patients, those with human immunodeficiency virus infection, the immunocompromised and those with certain chronic diseases) with the pneumococcal heptavalent vaccine (3,40).

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