

Uncomplicated pneumonia in healthy Canadian children and youth: Practice points for management

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Although immunization has decreased the incidence of bacterial pneumonia in vaccinated children, pneumonia remains common in healthy children. Symptoms of bacterial pneumonia frequently overlap those present with viral infections or reactive airway disease. Optimally, the diagnosis of bacterial pneumonia should be supported by a chest radiograph before starting antimicrobials. Factors such as age, vital signs and other measures of illness severity are critical when deciding whether to admit a patient to hospital. Because *Streptococcus pneumoniae* continues to be the most common cause of bacterial pneumonia in children, prescribing amoxicillin or ampicillin for seven to 10 days remains the mainstay of empirical therapy for nonsevere pneumonia. If improvement does not occur, consideration should be given to searching for complications (empyema or lung abscess). Routine chest radiographs at the end of therapy are not recommended unless clinically indicated.

Key Words: Antimicrobial therapy; Bacterial pneumonia; Viral pneumonia

Most physicians who care for children and youth have had experience with managing acute pneumonia. The incidence of pneumonia due to any etiology is lower in the developed areas of the world compared with less developed areas because immunization coverage rates may be lower in developing areas.(1) Pneumococcal conjugate vaccines have been shown to decrease radiologically proven pneumonia admission rates in children younger than five years of age by an average of 27%.(2,3)

The present practice point focuses on the current diagnosis and management of uncomplicated, acute, community-acquired pneumonia in healthy immunized children with no underlying pulmonary pathology aside from mild reactive airways disease. The present practice point does not apply to persistent (chronic) pneumonia syndromes (with symptoms for >2 weeks), aspiration pneumonia or recurrent pneumonias, or to pneumonia associated with chronic medical problems such as immunodeficiency, because these pneumonias may be caused by different pathogens or require more extensive investigation. The present practice point replaces a previous document published in 2011.(4)

DEFINITION AND HOST RISK FACTORS

Pneumonia is an acute inflammation of the parenchyma of the lower respiratory tract caused by a microbial pathogen. Bacterial infections are usually primary but, occasionally, viral respiratory

La pneumonie non compliquée chez les enfants et les adolescents canadiens en santé : points de pratique sur la prise en charge

Même si la vaccination a réduit l'incidence de pneumonie bactérienne chez les enfants vaccinés, la pneumonie demeure courante chez les enfants en santé. Les symptômes de pneumonie bactérienne sont souvent similaires à ceux des infections virales ou d'une maladie réactive des voies respiratoires. Dans l'idéal, il faut confirmer le diagnostic de pneumonie bactérienne par une radiographie pulmonaire avant de prescrire des antimicrobiens. Il est essentiel de tenir compte de facteurs comme l'âge, les signes vitaux et d'autres mesures de gravité de la maladie pour décider ou non d'hospitaliser un patient. Puisque le *Streptococcus pneumoniae* continue d'être la principale cause de pneumonie bactérienne chez les enfants, le pilier du traitement empirique de la pneumonie bénigne demeure la prescription d'amoxicilline ou d'ampicilline sur une période de sept à dix jours. En l'absence d'amélioration, il faut envisager des complications (empyème ou abcès du poumon). La radiographie pulmonaire systématique n'est pas recommandée à la fin du traitement, à moins d'une indication clinique.

tract infections such as influenza are followed by bacterial pneumonias.(5) Uncomplicated pneumonias may be accompanied by small parapneumonic effusions. Evidence of empyema (pus in the pleural space), a lung abscess or a necrotic portion of lung parenchyma implies the development of a complicated pneumonia.

ETIOLOGY

The most common causes of pneumonia in infants and preschool children are viruses that usually, but not exclusively, circulate in winter (eg, respiratory syncytial virus, influenza, parainfluenza virus and human metapneumovirus). Viruses as a sole cause of pneumonia are less common in older children, with the exception of influenza.

Among bacteria, *Streptococcus pneumoniae* continues to be the most common bacterial pathogen causing pneumonia in children of all ages. Group A streptococcal pneumonia is much less common. Although *Staphylococcus aureus* is not a common cause of paediatric pneumonia, it has been increasingly encountered in communities where methicillin-resistant *S aureus* (MRSA) is prevalent. *Haemophilus influenzae* type b has almost disappeared because of vaccination. *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* are more common causes of pneumonia among school-age children, but they occasionally cause pneumonia in younger children.(6)

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TABLE 1
Age-specific criteria for tachypnea

Age	Approximate normal respiratory rates	Upper limit that should be used to define tachypnea
<2 months	34–50	60
2–12 months	25–40	50
1–5 years	20–30	40
>5 years	15–25	30

Data presented as breaths/min

SYMPTOMS AND SIGNS OF ACUTE PNEUMONIA

The symptoms of pneumonia may be nonspecific, especially in infants and younger children. Acute onset of fever, cough, difficulty breathing, poor feeding or vomiting, and lack of interest in normal activities are common symptoms. Chest or abdominal pain may also be prominent features. Abrupt onset of rigors favours a bacterial cause. *M pneumoniae* is typically characterized by malaise and headache for seven to 10 days before the onset of fever and cough, which then predominate. During annual influenza season, influenza (with or without a secondary bacterial infection) as a cause of pneumonia should be strongly considered. Influenza infections may be heralded by the sudden onset of systemic symptoms such as diffuse myalgias and fever, which are then followed by cough, sore throat or other respiratory symptoms.

Children typically experience fever and tachypnea (determined by counting the respiratory rate for 60 s in a calm state) (Table 1). Indrawing, retractions and/or a tracheal tug indicate respiratory distress (dyspnea). Measurement of oxygen saturation with pulse oximetry is indicated in all patients presenting to a hospital or with significant illness because hypoxemia may not be clinically apparent and cyanosis is only associated with severe hypoxemia. However, a normal oxygen saturation does not exclude the possibility of pneumonia.

Physical signs suggesting pneumonic consolidation include dullness to percussion, increased tactile fremitus, reduced normal vesicular breath sounds and increased bronchial breath sounds – all of which may be difficult to detect in young children. The predominance of wheezing and hypoxia should suggest the possibility of bronchiolitis or mucous plugging from asthma, rather than pneumonia. Signs of an effusion include dullness to percussion, decreased tactile fremitus, and decreased or absent breath sounds. There may be associated signs of dehydration and/or sepsis.

INVESTIGATIONS

Imaging

Radiographs are not indicated for children experiencing wheezing with a typical presentation of bronchiolitis or asthma because bacterial pneumonia is very unlikely. When bacterial pneumonia is suspected clinically (a febrile child with acute respiratory symptoms and physical findings compatible with consolidation or pleural effusion), a chest radiograph (both postero-anterior and lateral) should usually be obtained.

The reason for imaging is that the clinical features of other conditions overlap with bacterial pneumonia, and antibiotics may be avoided if the chest radiograph does not suggest bacterial pneumonia.(7) However, in cases where the diagnosis of bacterial pneumonia is highly suspected from history, combined with typical clinical and physical findings and the child is not sufficiently ill to require hospitalization, a chest radiograph is not essential. All hospitalized children should have a chest radiograph performed to assess the extent of pneumonia and determine the presence of pleural effusion or abscess.

The prominent radiographic pattern in bacterial pneumonia is alveolar/airspace disease that is seen as consolidations. Classically, these present as lobar consolidations with air bronchograms; however, airspace disease may also take the form of subsegmental or nodular opacities (eg, round pneumonia) or infiltrates. Clinical correlation is always important, especially when considering other, rarer causes of similar radiographic patterns.

Poorly defined patches of infiltrates or atelectasis are more indicative of a viral etiology.(8) The 'atypical' pathogens, *M pneumoniae* or *C pneumoniae*, classically produce bilateral focal or interstitial infiltrates that appear to be more extensive relative to the milder but persistent symptoms.

Ultrasound at the point of care appears to be sensitive and specific for detecting pneumonic infiltrates but requires further validation.(9) Ultrasound and computed tomography are also useful in the diagnosis of complicated pneumonia. Both will detect parapneumonic effusions, which often accompany uncomplicated pneumonia, as well as empyemas, where persistent fever is a predominant symptom. Culture and drainage of a pleural effusion is indicated if the effusion is large and/or is clinically important as a cause for respiratory compromise or when response to medical therapy alone is not satisfactory.(10)

DETECTING THE PATHOGEN

Determining the etiology of bacterial pneumonia is difficult in children. Most cases are not bacteremic at the time of diagnosis. If sputum is available (usually only in children >10 years of age), it should be sent for Gram staining and, if considered adequate, cultured.

Viral testing of nasopharyngeal secretions is usually not indicated for outpatients with suspected pneumonia. However, such testing should be strongly considered in children admitted during influenza season with possible viral pneumonia because antivirals are likely to be of benefit for influenza pneumonia, particularly in moderately to severely ill children.(11,12) Children (usually school age) with subacute, nonsevere pneumonia, presenting with features such as prominent cough, minimal leukocytosis and a nonlobar infiltrate, may have pneumonia caused by *M pneumoniae* or *C pneumoniae*. Nasopharyngeal specimens should be sent for molecular diagnostics if testing is available and the child is hospitalized, bearing in mind that the length of carriage is unknown; a positive result may indicate remote infection.

BLOODWORK

Typical bacterial pneumonias usually present with higher peripheral white blood cell counts than 'atypical' bacterial or viral pneumonias (eg, *M pneumoniae*). A complete blood count with differential testing and blood cultures (before starting antimicrobial therapy, if possible) are indicated for children who are hospitalized. Even though the yield from blood cultures is low, a positive result is helpful, especially if the child subsequently experiences a complicated course. Furthermore, it is an important part of surveillance for invasive pneumococcal disease, especially in the post-13-valent conjugated pneumococcal vaccine era. As adequate volumes of blood are more likely to yield a pathogen, the minimum volume of blood cultured should be at least 1 mL to 2 mL in infants, 4 mL to 5 mL in children <10 years of age and 10 mL to 20 mL in older children.

GUIDELINES FOR REFERRAL TO HOSPITAL OR HOSPITAL ADMISSION

Most children with pneumonia can be managed as outpatients. Specific paediatric criteria for admission are not available. Hospitalization is generally indicated if a child has inadequate oral

TABLE 2
Doses of common antimicrobials recommended for suspected or proven bacterial pneumonia

Antibiotic	Route	Regimen
Amoxicillin, maximum 4000 mg/day	PO	40–90 mg/kg/day divided 3 times daily*
Ampicillin, maximum 12 g/day	IV	200 mg/kg/day divided every 6 h
Ceftriaxone, maximum 4 g/day	IV	50–100 mg/kg/day divided every 12 h or 24 h
Penicillin G (if confirmed to be due to <i>Streptococcus pneumoniae</i> that is penicillin-susceptible)	IV	200,000–250,000 U/day divided every 4 h to 6 h; maximum 24 million U/day
Azithromycin (for suspected or proven <i>Mycoplasma</i> or <i>Chlamydomphila pneumoniae</i>)	IV/PO	Given as a single daily dose; 10 mg/kg on day 1; 5 mg/kg on days 2 to 5; maximum 500 mg/day

*Although twice-daily dosing is adequate for otitis media, three times-daily dosing is recommended for pneumonia. IV Intravenously; PO Orally

intake, is intolerant of oral therapy, has severe illness or respiratory compromise (eg, grunting, nasal flaring, apnea, hypoxemia), or if the pneumonia is complicated. There should be a lower threshold for admitting infants younger than six months of age to hospital because they may need more supportive care and monitoring, and it can be difficult to recognize subtle deterioration clinically.

MANAGEMENT

If influenza is detected or suspected, strong consideration should be given to prompt treatment with neuraminidase inhibitors (oseltamivir, zanamivir). Treatment with antivirals has been shown to provide benefit and may prevent secondary bacterial infections, particularly in hospitalized or moderately to severely ill children.(12-14) When other viruses are detected in a nasopharyngeal sample and/or the chest radiograph is most compatible with viral pneumonia (ie, without consolidations), manage with supportive care (ie, oxygen and rehydration if required) without antibiotics, unless there is convincing evidence of a secondary bacterial pneumonia.

The primary goal of antimicrobial therapy, for the vast majority of uncomplicated community-acquired pneumonias, is to provide good coverage for *S pneumoniae*, because molecular-based techniques have shown this to be the predominant bacterial pathogen.(15-17) Therefore, outpatients with lobar or broncho-pneumonia should usually be treated with oral amoxicillin. Patients who require hospitalization but do not have a life-threatening illness should usually be started empirically on intravenous ampicillin. There is recent data demonstrating that ampicillin alone leads to a good clinical outcome in almost all cases of community-acquired pneumonia, including cases that require hospitalization.(18-20)

Children who experience respiratory failure or septic shock associated with pneumonia should receive empiric therapy with a third-generation cephalosporin because it offers broader coverage. Ceftriaxone or cefotaxime offer better coverage than amoxicillin or ampicillin for beta-lactamase-producing *H influenzae* and may be more efficacious against high-level penicillin-resistant pneumococcus – and possibly provide empirical coverage for the rare methicillin-susceptible *S aureus* (a rare cause of pneumonia).(21) However, when there is rapidly progressing multilobar disease or pneumatoceles, the addition of vancomycin is suggested empirically to provide extra coverage for MRSA until culture results are available. If results of microbiological investigations in these patients do not reveal a pathogen, transitioning to ampicillin with subsequent oral amoxicillin is reasonable.

The antimicrobial management of patients with suspected empyema is similar to that of patients without empyema because there is a predominance of *S pneumoniae* being the etiological agent, with some cases being due to Group A streptococcal or *S aureus*.(10,22) If the empyema is due to *S aureus*, pleural fluid cultures are usually positive if they were obtained within a day or two after start of antimicrobials. If vancomycin was started

empirically in such cases, it can usually be discontinued when cultures are negative if there is no other evidence of MRSA colonization or infection. If *S pneumoniae* is detected in blood or respiratory secretions and is penicillin-susceptible, treatment with either intravenous ampicillin or penicillin is recommended, followed by oral therapy with amoxicillin. If another pathogen is detected in pleural fluid or blood, modifications to the antimicrobial regimen should be made based on antimicrobial susceptibility.

The role of antimicrobials in treating both *M pneumoniae* and *C pneumoniae* is unknown because most children resolve infection without macrolides. However, treatment may be appropriate to hasten recovery in children who are more seriously ill or have persistent cough. The usual treatment is azithromycin for five days. However, macrolide resistance is now very common in *M pneumoniae* in Asia and sometimes occurs in Canada.(23,24) In children ≥ 8 years of age (minimum), doxycycline is likely to be effective against such strains.

If patients with suspected bacterial pneumonia do not respond to therapy within 48 h to 72 h, a chest radiograph should be obtained and a further clinical evaluation carried out. This reassessment should indicate whether an empyema or other complication has developed in the interim. Further history or imaging may also suggest a less common cause (eg, tuberculosis) or a non-infectious etiology (eg, a collagen vascular disease).

In Canada, it is still standard to treat uncomplicated presumed bacterial pneumonia in children who have been hospitalized for a total of seven to 10 days. In one recent study, five days appeared to be adequate for outpatient pneumonia.(13) Pneumonia complicated by empyema or abscess formation requires a longer duration of therapy, as determined by the clinical course (usually two to four weeks). Oral step-down therapy is usually appropriate once patients are improved, afebrile and otherwise ready for hospital discharge.

Suggested doses for the more commonly used antibiotics are listed in Table 2. In all situations, if a bacterial pathogen known to cause pneumonia is detected in blood or pleural fluid, it is almost certainly the sole pathogen and antimicrobial therapy should be modified to the narrowest spectrum agent based on susceptibility results of the pathogen isolated.

PREVIOUS ADVERSE EVENTS WITH PENICILLIN OR OTHER ANTIBIOTIC THERAPY

If a patient experienced a nonurticarial rash after previous use of a penicillin or amoxicillin, they can safely be started on ampicillin or amoxicillin therapy.

It is now recognized that the cross-reactivity rate between penicillins and second- or third-generation cephalosporins (apart from cefoxitin) is extremely low. Therefore, cefuroxime, cefprozil or ceftriaxone can be prescribed for penicillin-allergic patients. However, if the reaction to a penicillin included rapid onset of urticaria, angioedema, hypotension or bronchospasm following the dose of penicillin, the patient should be observed for 30 min following

the first dose of cephalosporin in a setting where epinephrine is available.⁽²⁵⁾ Clarithromycin or azithromycin may also be used, but pneumococcal resistance to these antimicrobials is increasingly common and careful follow-up must be ensured. Although rare, a history of a serious nonimmunoglobulin E-mediated reactions (eg, Stevens-Johnson syndrome or toxic epidermal necrolysis) attributed to an antibiotic is also a contraindication to using related antibiotics. In such cases, a different class of drug should be selected.

EXPECTED CLINICAL COURSE AND FOLLOW-UP FOR UNCOMPLICATED PNEUMONIA

Clinical improvement (improved appetite, decreasing fever, resolution of tachypnea and decreasing oxygen requirements) should be evident within 48 h of starting antibiotic therapy with bacterial pneumonia. However, improvement may be slower with viral pneumonia. If the patient does not show clinical improvement

or worsens within the expected time frame, a chest radiograph or ultrasound should be repeated to look for evidence of a complication (eg, empyema or abscess). Other reasons for lack of clinical resolution may include a foreign body aspiration, reactive airways disease with atelectasis, a congenital pulmonary anomaly, tuberculosis or unrecognized immunodeficiency with an opportunistic infection.

Radiographic resolution in most uncomplicated pneumonia cases may take up to four to six weeks. Repeat radiographs when children are otherwise well are not indicated to document improvement.⁽²⁶⁾

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