TREATING INFECTIONS

Outpatient treatment of pneumonia

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Abstract

In children, pneumonia must be differentiated from bronchiolitis and asthma. Pneumonia is the only one of these three conditions for which antibiotics are indicated. Clinical signs are more useful than radiological or laboratory investigations for differentiating pneumonia from bronchiolitis and asthma. A child has pneumonia if s/he has tachypnoea or indrawing and is not wheezing. The child's age and the severity of the illness episode predict the aetiology of the pneumonia. The majority of children with community-acquired pneumonia can be managed in primary care. The antibiotic of choice for children ≤ 5 years of age is oral amoxycillin and for older children and adolescents is oral erythromycin. Antibiotics will not prevent pneumonia in a child with an upper respiratory tract infection.

Up to 80% of adults with pneumonia can be managed as outpatients. Indicators of morbidity and mortality from pneumonia are well described. Clinical features and radiology do not reliably predict the causative agent in adults with pneumonia, thus initial treatment is empirical. *Streptococcus pneumoniae* is the most common cause of pneumonia in all studies. The initial antibiotic treatment should be active against this organism. Penicillin or

amoxycillin or erythromycin are all suitable. Erythromycin has the advantage of being active against *Mycoplasma pneumoniae* and Legionella species. Follow-up of patients is important to decide whether they are responding to the empirical treatment.

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Pneumonia is a common and serious problem. It is the fourth leading cause of death and the most common cause of death due to infection in New Zealand.[1] It is a major reason for antibiotic use and broad-spectrum agents are often prescribed for pneumonia when narrower-spectrum agents would be as effective. In a study of over 2000 adult patients with pneumonia treated at five centres in North America significant variation in antibiotic prescribing practices occurred between the centres. These variations lead to significant differences in antimicrobial costs but no differences in outcomes.[2]

Pneumonia is a disease that is concentrated at the extremes of age, with prevalence and severity being greatest for the youngest children and the oldest adults. This article will therefore discuss separately the diagnosis and management of pneumonia in children and adults.

Most patients with community-acquired pneumonia can be treated as outpatients. This is the group we will address in this article. The management of pneumonia in those who are immunosuppressed or in those requiring hospitalisation will not be discussed.

Pneumonia in children

Pneumonia is one of the diagnoses for which a significant proportion of hospitalisations are avoidable by the use of good primary or ambulatory care.[3] The paediatric pneumonia hospitalisation rate in Auckland is between three and ten times higher than reported from other Pacific and other Anglo-American nations.[4] It is not known whether this is due to pneumonia being more prevalent and severe or due to a greater proportion of our paediatric hospitalisations for pneumonia being avoidable by better primary and ambulatory care.

In children, pneumonia, bronchiolitis and asthma are the three lower respiratory tract illnesses that result in the greatest morbidity. Antibiotics should be given to children with pneumonia but not to children with bronchiolitis or asthma. Therefore it is important to differentiate pneumonia from these and other acute respiratory illnesses before making treatment decisions.

Age predicts the frequency and severity of pneumonia. Pneumonia is more common and more severe in younger than in older children. Based on data from Auckland, the pneumonia hospitalisation rate for children aged < 2 years is 11 times higher than for children aged 4 years or older.[4]

Unfortunately, as well as being more common and more severe in young children, pneumonia is also more difficult to diagnose. Most of the published literature on the diagnosis of pneumonia in children is from the developing world. The epidemiology of pneumonia in New Zealand children is dissimilar to that of other Anglo-American nations and shares some similarities with descriptions of pneumonia hospitalisations in developing countries.[4]

Therefore it is appropriate to refer to the published literature from developing and developed nations when trying to define how best to diagnose and treat pneumonia.

Most children with pneumonia present with cough or difficulty breathing, but only the minority of children with these symptoms have pneumonia.[5] In preschool-aged children, who have cough or difficulty breathing, the World Health Organization (WHO) have defined three key clinical signs that should be used when deciding whether or not a child has pneumonia. These clinical signs are tachypnoea, chest indrawing and absence of wheezing.[6] Based on these three clinical signs, the WHO has developed algorithms for deciding whether or not a child has severe pneumonia, pneumonia or no pneumonia. The algorithm is summarised in Figure 1.

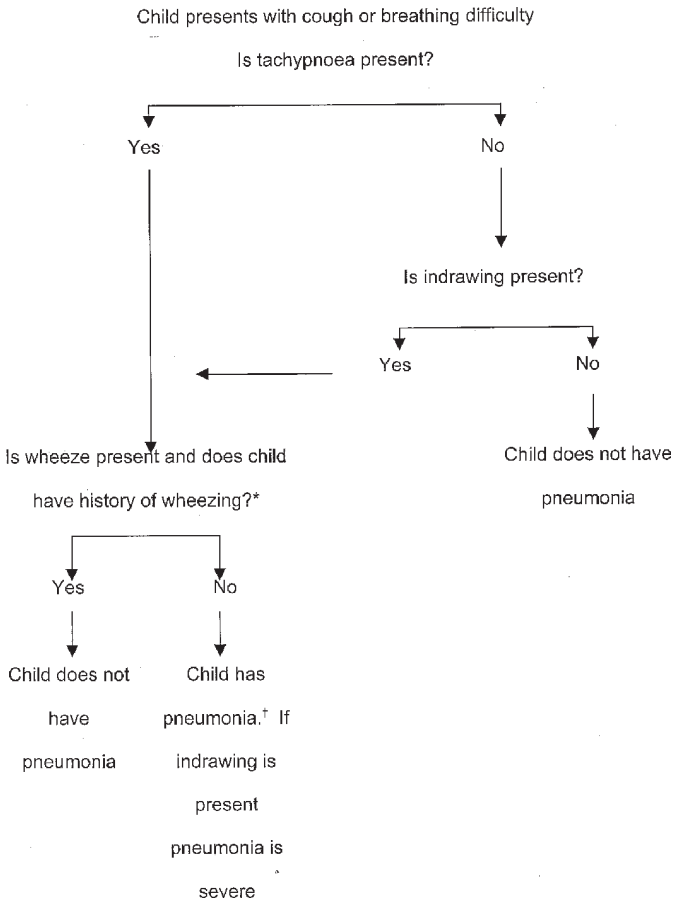

Figure 1. WHO algorithm for diagnosing pneumonia. *A child with indrawing with a first episode of wheezing should be treated as if this illness is severe pneumonia even though that diagnosis may be proved incorrect in the subsequent 24 to 48 hours. †The WHO recommends that antibiotics only be given to those children with pneumonia or severe pneumonia.

Tachypnoea is defined by the WHO as a respiratory rate > 60 breaths per minute if < 2 months of age; > 50 breaths per minute if aged 2 to 12 months and > 40 breaths per minute if aged 12 months to 5 years.[6] The respiratory rate should be counted over 60 seconds. Respiratory rates counted over 30 seconds are two to four breaths per minute higher than respiratory rates counted over 60 seconds.[7] Chest indrawing is defined as retraction of the lower chest wall on inspiration.[5]

Tachypnoea increases the probability that a child has pneumonia and the absence of tachypnoea reduces the probability. Chest indrawing increases the probability of pneumonia but the absence of chest indrawing does not result in a significant reduction in the probability that a child has pneumonia. Children with nasal flaring or grunting have a threefold increased probability and children with crepitations a two- to threefold increased probability, of

having pneumonia. The absence of these clinical signs reduces the probability of pneumonia by approximately 25%. The presence of wheeze decreases the likelihood of pneumonia in children aged > 2 months but increases the likelihood in children aged < 2 months. The absence of wheeze neither increases nor decreases the probability of pneumonia. The presence or absence of fever neither increases nor decreases the probability of pneumonia.[8]

Clinicians invariably use a combination of clinical signs when deciding whether or not a child has pneumonia. Unfortunately the probability of pneumonia based upon the presence or absence of combinations of different clinical signs has not as yet been adequately evaluated.

A reasonable conclusion from the literature is that tachypnoea is the key clinical sign in determining whether or not a child has pneumonia. If chest indrawing, nasal flaring, grunting or crepitations are also present, then the probability of pneumonia is increased further. A child with wheeze who has a past history of wheeze is unlikely to have pneumonia. If there is no respiratory distress, tachypnoea, crackles or decreased breath sounds then pneumonia is ruled out of the differential diagnosis.[9]

Aetiology. Pneumonia in children is caused by a number of viruses and bacteria, with the proportion that is viral or bacterial being different in different countries. There is minimal published data on the aetiology of paediatric pneumonia in New Zealand. In developing countries, a larger proportion of pneumonia is due to bacterial infections than in developed countries, however, it should be noted that viral studies are less extensive in reports from developing countries.[10] In both developed and developing countries the clinical severity of pneumonia is the best predictor of aetiology. The probability that pneumonia is due to bacterial infection increases with increasing severity of the episode of pneumonia. In developed countries the aetiology of community-acquired pneumonia has been defined by the child's age as well as by the severity of the episode of illness. A summary of the results from studies performed is contained in Table 1.[9]

Table 1. Aetiology of pneumonia by age group in developed countries*.

Age group	Predominant organisms from most to least frequent in each age group.
0 to 1 months	Group B streptococcus Gram negative organisms
1 to 3 months	*Chlamydia trachomatis* Respiratory syncytial virus (RSV) *Bordetella pertussis*
1 to 24 months	RSV, other respiratory viruses† Mixed viral or viral/bacterial infections Bacterial infections: Mostly *Streptococcus pneumoniae* and less frequent haemophilus species (both typable and non-typable) and *Mycoplasma pneumoniae*
2 to 5 years	Respiratory viruses *Streptococcus pneumoniae* Haemophilus species *Mycoplasma pneumoniae* *Clamydia pneumoniae*
6 to 18 years	*M. pneumoniae* and *S. pneumoniae* are the predominant pathogens. Respiratory viruses account for <15% of episodes of pneumonia in children >5 years of age.

*The proportion of pneumonia in each age group which is bacterial increases with increasing severity of the pneumonia. †Other respiratory viruses = parainfluenza, influenza and adenoviruses.

Investigations. Having decided, based on clinical examination, that a child has pneumonia and requires antibiotics, there is minimal information other than the child's age and the illness severity that is useful for deciding which antibiotic to use. Investigations that are readily available are infrequently helpful in determining whether or not to prescribe antibiotics and which antibiotic to prescribe.

Sputum and throat swabs do not help determine whom should receive antibiotics. Sputum production is a non-specific response to airway inflammation, produced by viral and bacterial infections and by non-infectious processes such as asthma. Trying to obtain a sputum sample from a preschool-aged child is usually unrewarding. Leucocytes are found as frequently in sputum from which a virus is subsequently isolated as from sputum from which a bacterial culture is positive.[11] Where nasopharyngeal and percutaneous lung aspiration samples have been obtained simultaneously from children with pneumonia, bacterial culture of the nasopharyngeal sample has been poorly predictive of the culture results from lung aspirates.[12] A blood culture is a relatively insensitive test for bacterial pneumonia in children. In a recent study of children hospitalised with pneumonia in Auckland, blood cultures were positive in 3% (10/389) with four of these ten positive cultures revealing a skin contaminant, (Grant CC, Pati A, Tan D, Vogel S, Aicken R, Scragg R; unpublished observations).

Neither the presence nor height of fever, nor the total or differential white cell count nor the serum C-reactive protein are helpful in differentiating viral from bacterial pneumonia.[13,14] Inter-observer agreement between radiologists has been shown to be poor when categorising children's chest radiographs as normal, equivocal or indicative of pneumonia or when differentiating children who have a proven viral or bacterial aetiology for their pneumonia.[15,16]

Treatment. Antibiotics should be prescribed for children in whom pneumonia has been diagnosed. Given the dearth of randomised controlled trials on antibiotic use, the choice of antibiotics should be based on aetiology as defined by the severity of the episode of illness and the age of the child. Oral antibiotics will provide adequate coverage for most mild to moderate episodes of pneumonia. Parenteral antibiotics should be used for neonates or those requiring hospitalisation because of the severity of the pneumonia or other contributing factors (Table 2). For children aged 3 months to 5 years with pneumonia, amoxicillin 40 mg/kg/day given in three divided doses for seven to ten days is the treatment of choice. For children aged > 5 years and adolescents with pneumonia, erythromycin 40 mg/kg/day in four divided doses for seven days is the treatment of choice.

Antibiotics should not be prescribed to try to prevent a child developing pneumonia. Antibiotics do not prevent the development of pneumonia in children with upper respiratory tract infections.[17]

Pneumonia in adults

The diagnosis of pneumonia in adults may be straightforward, with the patient complaining of a productive cough, associated with fever and shortness of breath. The examination will suggest focal consolidation and chest radiography will confirm the diagnosis. However, pneumonia may present in a more subtle way, with non-pulmonary symptoms such as myalgias, malaise and headache predominating, especially early in the illness. A standard posterior-anterior and lateral chest radiograph should be performed in those with respiratory symptoms and other suggestive findings such as fever > 37.8°C, pulse rate > 100 beats per minute or an abnormal lung examination.[18]

After a thorough history and examination the decision to send the patient to hospital or treat as an outpatient can be made. Up to 80% of adults with pneumonia can be managed as outpatients. Factors listed in Table 2 increase the risk of

Table 2. Indications for admission in children and adults with pneumonia.

	Children[9]	Adult[22,30]
Age	<6 months	>65 years
Primary care management	No response to appropriate oral antibiotics	No response to appropriate oral antibiotics
Comorbidity	Preexisting medical illness, dehydration, vomiting	Preexisting medical illness
Clinical signs	Toxic appearance or severe respiratory distress or oxygen requirement	Clinical signs: respiratory rate >30 breaths/min, diastolic blood pressure <60mmHg, temp. >38.3°C, confusion, extrapulmonary disease
Social	Social stress, no car, no phone, language or communication barriers	Unable to comply with therapy or follow-up
Laboratory		WBC* ≤ 4000 or ≥ 20,000 10^9/L, pO2 ≤ 8KPa (60mmHg), urea ≥ 7 mmol/L
Microbiology		Aetiology: Staphylococcal, Gram negative rod, aspiration or post obstructive pneumonia
Radiology		CXR: multilobar involvement, cavity or effusion

* WBC: White cell count.

death or a complicated course. When these factors are present, especially if multiple risk factors coexist, admission, should be considered. In addition, the home situation of the patient is important and should be taken into account.

Investigations. For adult patients with a productive cough, sputum should be collected before the patient starts antibiotics as yield of fastidious bacteria such as *S pneumoniae* and *Haemophilus influenzae* is zero if collected after antibiotics have been taken. Gram stain of sputum may suggest the causative agent and culture allows sensitivity testing as well as identification. Special stains for mycobacteria, *Pneumocystis carinii* and Legionella may be indicated. The IgM titre for Mycoplasma is usually positive within seven days of symptoms beginning and may thus be helpful clinically.

Aetiology. The causes of pneumonia in patients treated as outpatients are not well known. Table 3 shows the aetiology of pneumonia in adult patients admitted to Waikato and Christchurch hospitals.[19,20]

Table 3. Causes of community acquired pneumonia in adults requiring admission in New Zealand.

Organism	% in Waikato (n = 92)*	% in Christchurch (n = 255)*
Streptococcus pneumoniae	33	39
Mycoplasma pneumoniae	18	16
Influenza A virus	8	5
Legionella species	4	11
Staphylococcus aureus	3	3
Haemophilus influenzae	5	11
Others	11	14
No cause found	28	29

* In 10 Waikato and 60 Christchurch patients more than one organism was identified

Treatment. Antibiotics should be started as soon as possible. Thus initial treatment is usually empirical, and may often remain so, because the causative agent is only identified in approximately 70% of patients in prospective studies and in considerably fewer in clinical practice. In addition clinical features and radiology do not reliably predict a causative agent.[21,22]

The two recent studies performed in New Zealand identified *S pneumoniae* as the most common cause of pneumonia in adults requiring admission. It has been suggested that the true prevalence of *S pneumoniae* is underestimated by our current tests and that it probably accounts for most episodes of pneumonia where no cause is found.[23] Thus outpatients with uncomplicated pneumonia of unknown aetiology should receive treatment active against *S pneumoniae*. Amoxycillin or penicillin or erythromycin are all suitable. Erythromycin has the advantage of being active against mycoplasma and legionella species. However, patient tolerance may not be as high. It is interesting to note that for uncomplicated pneumonia the British Thoracic Society recommends amoxycillin or benzyl penicillin while the American Thoracic Society recommends a macrolide such as erythromycin.[22,24] There are very few prospective trials that have compared different antibiotic regimes for pneumonia. For uncomplicated pneumonia, seven to ten days' therapy is usually given. For pneumonia due to mycoplasma 10 to 14 days is recommended.

If an elderly patient, or one with other medical problems, is being treated as an outpatient amoxycillin/clavulinic acid or cefuroxime should be given to provide cover against *H influenzae*. Patients with severe pneumonia need even broader-spectrum therapy, including coverage for legionella but they also need aggressive inpatient supportive care.

Pneumococcal resistance to penicillin is increasing globally. However, in-vitro resistance to penicillin does not preclude successful treatment of pneumonia with penicillin. Penicillin levels achieved in blood or respiratory secretions are many times higher than the minimum inhibitory concentration of intermediate resistant and most highly resistant pneumococcal isolates. No difference in clinical response has been found in pneumonia due to intermediate resistant compared with that due to fully sensitive pneumococci.[25] As the incidence of high-grade, penicillin resistance rises it may be necessary to modify treatment but we are not yet at this stage in New Zealand.

Follow-up. It is important to arrange definite follow-up to assess a patient's response to treatment. With effective antibiotic therapy some improvement should be seen in 48 to 72 hours. If not, or if the patient is deteriorating, a change in antibiotic may be necessary or admission to hospital considered. In a study of non-hospitalised patients with pneumonia in France, 22% of the patients had failed to improve two to four days after starting treatment. One half of the non-responders were then hospitalised and the other half were switched to second-line therapy such as a macrolide.[26] Similarly, in a British study 26% returned for a second consultation and three quarters of these had their

antibiotic changed. Eight percent returned for a third consultation.[27] These studies show that initial empiric therapy will not always be correct.

The need for a follow-up chest radiograph is a matter of debate. Follow-up chest radiographs are most justified for patients with a delayed response, an uncertain cause of pneumonia, recurrent pneumonia or for those who may have lung neoplasms.[23]

Prevention. Annual influenza vaccination and a pneumococcal vaccination (repeated once after five years) should be given to those likely to suffer severe pneumonia, for example, those over 65 years of age or with medical problems.[28,29]

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