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REVIEW ARTICLE

Finnish guidelines for the treatment of community-acquired pneumonia and pertussis in children

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ABSTRACT

Evidence-based guidelines are needed to harmonise and improve the diagnostics and treatment of children's lower respiratory tract infections. Following a professional literature search, an interdisciplinary working group evaluated and graded the available evidence and constructed guidelines for the treatment of community-acquired pneumonia and pertussis. **Conclusion:** The clinical guidelines state that chest radiography is not needed if the child is diagnosed with pneumonia and treated at home. Complications should be considered if there is no improvement after antimicrobial therapy and a paroxysmal cough can indicate pertussis, which is life-threatening in unvaccinated infants and can lead to respiratory failure.

INTRODUCTION

Evidence-based clinical practice guidelines for the treatment of lower respiratory tract infections (LRTIs) in children were developed in Finland in 2013–2014. They were devised by an independent interdisciplinary working group, established by the Finnish Medical Society Duodecim and the Finnish Pediatric Society, that included paediatric infectious disease specialists, general paediatricians, a clinical microbiologist, a paediatric radiologist and a general practitioner. The scope of the guidelines was the treatment of acute paediatric LRTIs, excluding severe cases requiring admittance or intensive care.

Our professional librarian performed systematic literature searches using selected topics and questions and then the group reviewed the literature and evaluated the available evidence. The level of evidence was assessed and marked within guideline statements for the most critical decisions. The following category levels for the evidence were used: level A referred to strong evidence with at least two separate, high-quality studies, level B referred to moderate evidence with at least one high-quality study and level C referred to weak evidence with at least one satisfactory study. A high-quality study was defined as a study performed in an appropriate population with a strong study design, such as a randomised controlled trial with an appropriate outcome measure. The guideline document was peer-reviewed by 14 experts and clinicians before it was published in the Finnish Current Care Guidelines series in 2014. The process is described in detail on the Current Care Guideline web pages (www.kaypahoito.fi). The original document included approximately 200 references and more

Key notes

- Evidence-based guidelines are needed to harmonise and improve the diagnostics and treatment of children's lower respiratory tract infections.
- An interdisciplinary working group evaluated and graded the evidence and constructed guidelines for the treatment of community-acquired pneumonia and pertussis.
- The clinical guidelines cover areas such as when chest radiography is needed, the complications that can arise if antimicrobial therapy does not work and how a paroxysmal cough can indicate pertussis.

than 50 linked supplementary web pages presenting the systematic literature review for each statement. This formed the first part of the summary document. The second part presented other LRTIs, such as laryngitis, bronchiolitis and wheezing bronchitis in a separate document. The detailed search description by the professional librarian is presented (Tables S1–S2).

This paper presents the available evidence and the new guidelines for treating community-acquired pneumonia and pertussis in children in Finland. The *evidence-based statements*, which appear in italics in this paper, are presented and the reasoning behind the recommendations is discussed. Table 1 summarises the recommended antimicrobial treatment of LRTIs.

Pneumonia

Pneumonia is an infection of pulmonary alveoli or interstitial tissue and can be diagnosed either with chest radiography or indirectly based on clinical findings. Respiratory viruses on their own are responsible for one-third of childhood pneumonia cases, viruses combined with bacteria account for another third and bacteria alone accounts for the another third. *Streptococcus pneumoniae* were reported to have caused 37–44% of pneumonia cases in children treated in hospital and around 20% of pneumonia cases treated at home before the pneumococcal conjugated vaccine era (1,2). *Mycoplasma pneumoniae* has been estimated to cause 7–14% of pneumonia cases in hospital and 27% at home (1,3,4). Mycoplasma typically causes pneumonia in school-aged children (3). *Chlamydia pneumoniae* has been found in less than 10% of pneumonia cases in children (3). *Chlamydia trachomatis* is a rare cause of pneumonia in young infants, as it can be vertically transmitted to newborn infants from mothers during vaginal delivery. *Staphylococcus aureus* and *Streptococcus pyogenes* occasionally cause severe pneumonia in children.

Table 1 Antimicrobial treatment of lower respiratory tract infections in children

Clinical condition	Recommended treatment
Pneumonia	
Treatment at home (good general condition)	Amoxicillin 50–80 mg/kg/day*: three orally for seven days
	Add macrolide if mycoplasma suspected
	Penicillin allergy: cephalosporins†, clindamycin, macrolides or doxicyclin (>8 year) *per os*
Treatment in hospital	G-penicillin 200 000 IU/kg/day: four doses intravenously
	Add oral macrolide if mycoplasma suspected
	Penicillin allergy: cephalosporins† or clindamycin intravenously
Influenza	Oseltamivir orally‡
Pertussis	Azithromycin orally 10 mg/kg/day: one dose for five days or
	Clarithromycin orally 15 mg/kg/day: two doses for seven days

*Amoxicillin dose 80 mg/kg/days, if penicillin resistance of pneumococcal strains is common in the area.
†Approximately 5% of children with severe penicillin allergy may experience allergic symptom after exposed to cephalosporins, but severe allergic reactions are very rare.
‡Oseltamivir dosing: <1 year 6 mg/kg/day, <15 kg 30 mg × 2, 16–23 kg 45 mg × 2, 24–40 kg 60 mg × 2 and >40 kg 75 mg × 2.

Both 10-valent and 13-valent pneumococcal conjugate vaccines are currently available for children. In Finland, the 10-valent pneumococcal conjugate vaccine was introduced to the national immunisation programme for infants in 2010 and its effectiveness has been 100%, with a 95% confidence interval (CI) of 83–100% against invasive pneumococcal diseases after three doses and 92% (95% CI 58–100%) after two doses in a clinical trial (5). After the introduction of pneumococcal immunisations with conjugate vaccines, the incidence of blood culture-confirmed pneumococcal infections decreased significantly in children of less than five years of age in Finland (6). At the same time, both macrolide and penicillin resistance decreased among pneumococcal isolates obtained from children (6). The reported annual incidence of pneumonia in children of less than five years of age has been reported to range from 0.2–0.33% to 3.5–4%. Approximately half of the young children with pneumonia are treated in hospital, compared to 20% of 5- to 10-year old children and <10% of children over the age of 10 years (3,7). Mortality due to pneumonia is rare among previously healthy children without underlying conditions.

Treatment of pneumonia

The most common symptoms of pneumonia are fever, cough and dyspnoea, even though the most common reason for an acute cough in children is acute viral bronchitis. Typical auscultatory findings of pneumonia are crepitations (fine crackles) or silenced breath sounds. Chest radiography is not needed if a child is treated for pneumonia at home and the pneumonia can be clinically diagnosed (8–10). In a randomised controlled trial in children with LRTI, chest radiography did not affect the overall outcome, but those allocated to the chest radiography group received more antimicrobials than controls (11). Thus, chest radiography should not be obtained in children with other LRTIs, such as wheezing bronchitis or bronchiolitis, to exclude pneumonic changes in radiography. In many countries, chest radiography is still frequently used despite recommendations that it should not be (12). However, chest radiography is still useful for severely ill hospitalised children and in complicated pneumonia. It should also be performed for all children with silenced breath sounds, a poor response to antimicrobial treatment of pneumonia after 48 hours or a poor general condition (8,9). The interpretation of a chest radiograph requires expertise and inter-rater agreement tends to be rather poor. *Alveolar pneumonia is reliably detected in chest radiography, but interstitial changes are not so reliably diagnosed* (level B) (8,13,14). *Obtaining both antero-posterior/postero-anterior (AP/PA) and lateral images does not add to the sensitivity or specificity of radiological diagnosis of pneumonia in children when compared to just the AP/PA image* (level A) (15,16).

Alveolar infiltrates suggest bacterial pneumonia (level B) (17–20).

Elevated C-reactive protein concentrations or leucocyte counts increase the possibility of bacterial pneumonia, but low C-reactive protein concentrations or leucocytes do not exclude bacterial pneumonia (level A) (8,21–25). In particular, C-reactive protein values can still be normal during the first hours of bacterial disease. *Laboratory tests for detecting pneumococcal antigens in urine samples are not useful for children* (level B) (8,9,26–29). Even though urine antigen tests are used in adult patients, pneumococcal nasopharyngeal carriage is common in children, which increases the proportion of false-positive cases. Laboratory tests for mycoplasma infections, including antibody and polymerase chain reaction (PCR) based assays, are not generally useful in clinical settings (8,9). The outcome of most respiratory tract infections caused by *M. pneumoniae* in children is good without antimicrobial treatment. Immunoglobulin (Ig) M-class antibodies remain positive for long time after acute infection. Therefore, reliable serological diagnosis usually requires the results of paired serum samples, which are not available for acute treatment. In addition, asymptomatic children or children with improved clinical conditions do not require antimicrobial treatment for antibody-positivity for *M. pneumoniae*.

Neuraminidase inhibitors are effective for treating symptoms of influenza in children, if the treatment begins within 48 hours of the start of symptoms (level A) (30–33). Neuraminidase treatment can be used after 48 hours in severely ill children or hospitalised children with influenza pneumonia (34). *Orally administered amoxicillin is probably effective in treating pneumonia in previously healthy children whose clinical condition does not require hospitalisation* (level C) (35) (Table 1). The proportion of penicillin resistant pneumococci was low in Finland in 2010 (3–4%), but the susceptibility to penicillin was decreased (intermediate) in 20–22% of the clinical strains. Almost one-third of paediatric pneumococcal isolates are resistant to macrolides in Finland. *Macrolides may be beneficial in treating pneumonia caused by M. pneumonia* (level C) (36).

In clinical practice, complications such as empyema, lung abscess or necrotising pneumonia should be considered if the fever continues and the general condition of a child with pneumonia is not improving within 48 hours of starting antimicrobial therapy (level C) (8,9,37). Children with suspected complications of pneumonia should be sent to a hospital where it is possible to carry out further imaging, such as ultrasound, CT or MRI. Chest radiography should not be routinely repeated after pneumonia is treated (38). However, in cases of recurrent pneumonia, pleural effusion or major atelectasis, control radiography should be considered (8,9). If tuberculosis or a tumour is suspected, the child should be referred to hospital for further evaluation.

Pertussis

Pertussis should be suspected if an infant has a paroxysmal cough (level B) (39–42). A confirmed respiratory syncytial virus infection does not exclude the possibility of pertussis (42), which can be a life-threatening disease in unvaccinated infants. In addition to a paroxysmal cough, infants with pertussis often present with apnoeas and the risk of death is increased in the presence of a high lymphocyte count, seizures and shock (43). Th incidence of pertussis is low in vaccinated preschool children, but has recently been increasing worldwide in school children and adolescents and this may increase the risk of pertussis transmission to infants. In the United States, the incidence of pertussis per 100 000 per year was one to two in the 1980s, two to three in the 1990s and nine in the 2010s (44), and in Europe, it was 4.1 in 2003–2007 and 4.9 in 2009 (45). Even though pertussis is vaccine-preventable disease, acellular pertussis vaccines are less potent than whole cell pertussis vaccines and, in addition, the genetic changes in circulating *Bordetella pertussis* strains may increase vaccine failures (44). One-third of pertussis cases are diagnosed among adults (46). Introducing pertussis immunisation for young adults has been considered in many countries, and pregnant women are currently vaccinated against pertussis in the United Kingdom (45).

In Finland, the occurrence of pertussis was at its highest in 2003–2007 but has been decreasing during recent years. The acellular pertussis vaccine has been used in Finland since 2003 and is given as a part of national immunisation programme at the ages of three months, five months, 12 months, four years and 13–14 years. Currently, 10–20 cases of pertussis are diagnosed among unvaccinated infants in Finland each year.

Treatment of pertussis

The diagnosis of pertussis should be carried out by PCR for B. pertussis bacteria (level A) (47,48). The National Institute for Health and Welfare recommends that the *B. pertussis* culture should be obtained simultaneously and sent to their reference laboratory for epidemiological surveillance of circulating strains in Finland.

Azithromycin and clarithromycin are effective in eradicating B. pertussis bacteria (level A) (49–53). Erythromycin is no longer recommended because of the potential gastrointestinal side effects (53). *Symptomatic treatment of pertussis-related cough is generally ineffective* (level B) (54–59). *Exposed family members of a confirmed pertussis case can be treated with macrolide prophylaxis, which effectively prevents new pertussis cases within families* (level B) (60,61).

CONCLUSION

Evidence-based guidelines have been developed to harmonise and improve the diagnosis and treatment of children's LRTIs. The Finnish clinical guidelines state that chest radiography is not needed if the child is diagnosed with pneumonia and treated at home. They also state that complications should be considered if there is no improvement after antimicrobial therapy and that a paroxysmal cough can indicate pertussis, which is life-threatening in unvaccinated infants and can lead to respiratory failure.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1 The databases and terminology used in the systematic literature search.
Table S2 Detailed description of search strategies.