



## BTS Guidelines for the Management of Community Acquired Pneumonia in Childhood

British Thoracic Society of Standards of Care Committee

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# 1 Introduction

Community acquired pneumonia (CAP) can be defined clinically as the presence of signs and symptoms of pneumonia in a previously healthy child due to an infection which has been acquired outside hospital. In developed countries this can be verified by the radiological finding of consolidation. In the developing world a more practical term—acute lower respiratory infection—is preferred, reflecting the difficulties in obtaining a chest radiograph.

Ideally, the definition would include the isolation of a responsible organism. However, it is apparent from many studies that a pathogen is not identified in a significant proportion of cases that otherwise meet the clinical definition (see Section 3 on Aetiology). As it is assumed that CAP is caused by infection, the presumption is that current techniques have insufficient sensitivity to detect all relevant pathogens. Treatment guidelines therefore have to assume that, where pathogens are isolated, they represent all likely pathogens. There is a clear need for better diagnostic methods.

In creating guidelines it is necessary to assess all available evidence with consideration of the quality of that evidence. This we have endeavoured to do. We have then produced key points and management guidelines based on the available evidence supplemented by consensus clinical opinion where no relevant evidence was found. A summary of the key points and a further summary prepared specifically for use in primary care are also available on the *Thorax* website ([www.thoraxjnl.com](http://www.thoraxjnl.com)) and the British Thoracic Society website ([www.brit-thoracic.org.uk](http://www.brit-thoracic.org.uk)).

## METHODS OF GUIDELINE DEVELOPMENT

### Scope of guidelines

These guidelines address the management of CAP in infants and children in the United Kingdom. They do not include neonates or infants with respiratory syncytial virus bronchiolitis. The specific management of children with pre-existing respiratory disease or that of opportunistic pneumonias in immunosuppressed children is not addressed.

### Guideline development group

The guideline development group was set up by the BTS Standards of Care Committee to produce guidelines for children in parallel with those being produced for adults. It comprised three paediatricians with a special interest in respiratory disease, a paediatrician with special interest

in paediatric infectious diseases, a specialist registrar in paediatrics, a paediatric nurse, a general practitioner, and a guidelines methodologist. No external funding was obtained to support the development of the guidelines. Because of the breadth of scope of the topic, the guideline development was divided up into 12 sections and members were allocated to each. Eight of the 12 sections had at least two members allocated.

### Identification of evidence

Search strategies were developed for each of the 12 sections (excluding guideline methodology) with the assistance of an information scientist. These search strategies (see Appendix 1) included MeSH and free text terms and had no language restrictions. They were run on Medline (Winspurs, Silverplatter) and the Cochrane Library (Issue 3, 1999). Where searches yielded more than 1000 citations, these were limited to English.

### Assessing the literature

The sets of references generated by researchers were sifted for relevance to the clinical topic of the guidelines. Where two or more members were working on a section this was done independently. Initial sifting was on the basis of the title and abstract (as obtained from the specialist resource). Where there was doubt about whether a reference was relevant, the full publication was obtained. Studies from countries where the populations or clinical practices were very different from the UK were excluded unless they addressed questions which could be generalised to the UK (such as clinical assessment). The methodological quality of the publication was assessed using a checklist adapted from one previously developed for this purpose.<sup>1</sup>

### Synthesising the evidence

Once individual papers were checked for methodological rigour and clinical relevance they were categorised according to study design.<sup>1</sup> The evidence was synthesised by qualitative methods. The content of the identified papers was summarised into brief statements that were thought accurately to reflect the relevant evidence and the category of that evidence was indicated after each citation. The recommendations resulting from the evidence were graded according to the strength of that evidence (table 1). The strength of each recommendation ([A], [B], [C], or [D]) was indicated after each recommendation. Where

**Table 1** Grading of levels of evidence and guideline recommendations

Study design	Evidence level	Recommendation grade
Good recent systematic review of studies	Ia	A+
One or more rigorous studies, not combined	Ib	A-
One or more prospective studies	II	B+
One or more retrospective studies	III	B-
Formal combination of expert opinion	IVa	C
Informal expert opinion, other information	IVb	D

there was no identifiable evidence, and it was felt important to provide a recommendation within the guidelines, the lack of evidence was clearly stated and a recommendation based on a consensus from the group was provided (grade [D]).

#### **External review of guidelines**

Independent peer review of the guidelines was provided by three groups: potential users of the guidelines in primary and secondary care settings (including members of the British Paediatric Respiratory Society), content topic experts, and guideline methodologists. Although their comments influenced the style and content of the guidelines, these remained the responsibility of the guideline development group.

#### **Updating of guidelines**

It was agreed that the guidelines should be reviewed for the content and evidence base no later than 3 years after completion.

#### **Acknowledgements**

The British Thoracic Society provided support for travel and telephone conference costs of the Working Group.

#### **Conflicts of interest**

PH is a consultant to Wyeth Vaccines on pneumococcal conjugate vaccines.

## Synopsis of main recommendations

### Aetiology and epidemiology

- *Streptococcus pneumoniae* is the most common bacterial cause of pneumonia in childhood [II].
- Age is a good predictor of the likely pathogens:
  - Viruses are most commonly found as a cause in younger children.
  - In older children, when a bacterial cause is found, it is most commonly *S pneumoniae* followed by mycoplasma and chlamydial pneumonia [II].
- A significant proportion of cases of CAP (8–40%) represent a mixed infection [II].
- Viruses alone appear to account for 14–35% of CAP in childhood [II].
- In 20–60% of cases a pathogen is not identified [II].
- The mortality from CAP in children in developed countries is low [Ib].

### Clinical features

- Bacterial pneumonia should be considered in children aged up to 3 years when there is fever of  $>38.5^{\circ}\text{C}$  together with chest recession and a respiratory rate of  $>50/\text{min}$  [B]. For older children a history of difficulty in breathing is more helpful than clinical signs.
- If wheeze is present in a preschool child, primary bacterial pneumonia is unlikely [B].

### Radiological investigations

- Chest radiography should not be performed routinely in children with mild uncomplicated acute lower respiratory tract infection [A].
- Radiographic findings are poor indicators of aetiology.
- Follow up chest radiography should only be performed after lobar collapse, an apparent round pneumonia, or for continuing symptoms [C].

### General investigations

- Pulse oximetry should be performed in every child admitted to hospital with pneumonia [A].
- Acute phase reactants do not distinguish between bacterial and viral infections in children and should not be measured routinely [A].

### Microbiological investigations

- There is no indication for microbiological investigation of the child with pneumonia in the community.
- Blood cultures should be performed in all children suspected of having bacterial pneumonia [B].
- Acute serum samples should be saved and a convalescent sample taken in cases where a microbiological diagnosis was not reached during the acute illness [B].
- Nasopharyngeal aspirates from all children under the age of 18 months should be sent for viral antigen detection (such as immunofluorescence) with or without viral culture [B].
- When significant pleural fluid is present, it should be aspirated for diagnostic purposes, sent for microscopic examination and culture, and a specimen saved for bacterial antigen detection [B].

### Severity assessment

- Indicators for admission to hospital in infants:
  - oxygen saturation  $\leq 92\%$ , cyanosis;
  - respiratory rate  $>70$  beats/min;
  - difficulty in breathing;
  - intermittent apnoea, grunting;
  - not feeding;
  - family not able to provide appropriate observation or supervision.

## Synopsis of main recommendations (continued)

- Indicators for admission to hospital in older children:
  - oxygen saturation  $\leq 92\%$ , cyanosis;
  - respiratory rate  $>50$  breaths/min;
  - difficulty in breathing;
  - grunting;
  - signs of dehydration;
  - family not able to provide appropriate observation or supervision.

### General management

- The child cared for at home should be reviewed by a general practitioner if deteriorating, or if not improving after 48 hours on treatment [D].
- Families of children who are well enough to be cared for at home need information on managing pyrexia, preventing dehydration, and identifying any deterioration [D].
- Patients whose oxygen saturation is 92% or less while breathing air should be treated with oxygen given by nasal cannulae, head box, or face mask to maintain oxygen saturation above 92% [A].
- Agitation may be an indication that the child is hypoxic.
- Nasogastric tubes may compromise breathing and should therefore be avoided in severely ill children and especially in infants with small nasal passages. If used, the smallest tube should be passed down the smallest nostril [D].
- Intravenous fluids, if needed, should be given at 80% basal levels and serum electrolytes monitored [C].
- Chest physiotherapy is not beneficial and should not be performed in children with pneumonia [B].
- Antipyretics and analgesics can be used to keep the child comfortable and to help coughing.
- In the ill child, minimal handling may reduce metabolic and oxygen requirements.
- Patients on oxygen therapy should have at least 4 hourly observations including oxygen saturation [D].

### Antibiotic management

- Young children presenting with mild symptoms of lower respiratory tract infection need not be treated with antibiotics [B].
- Amoxicillin is first choice for oral antibiotic therapy in children under the age of 5 years because it is effective against the majority of pathogens which cause CAP in this group, is well tolerated, and cheap. Alternatives are co-amoxiclav, cefaclor, erythromycin, clarithromycin and azithromycin [B].
- Because mycoplasma pneumonia is more prevalent in older children, macrolide antibiotics may be used as first line empirical treatment in children aged 5 and above [D].
- Macrolide antibiotics should be used if either mycoplasma or chlamydia pneumonia is suspected [D].
- Amoxicillin should be used as first line treatment at any age if *S pneumoniae* is thought to be the likely pathogen [B].
- If *Staphylococcus aureus* is thought the likely pathogen, a macrolide or combination of flucloxacillin with amoxicillin is appropriate [D].
- Although there appears to be no difference in response to conventional antibiotic treatment in children with penicillin resistant *S pneumoniae*, the data are limited and the majority of children in these studies were not treated with oral  $\beta$ -lactam agents alone.
- Antibiotics administered orally are safe and effective for children presenting with CAP [A].
- Intravenous antibiotics should be used in the treatment of pneumonia in children when the child is unable to absorb oral antibiotics (for example, because of vomiting) or presents with severe signs and symptoms [D].
- Appropriate intravenous antibiotics for severe pneumonia include co-amoxiclav, cefuroxime, and cefotaxime. If clinical or microbiological data suggest that *S pneumoniae* is the causative organism, amoxicillin, ampicillin, or penicillin alone may be used [D].
- In a patient who is receiving intravenous antibiotic therapy for the treatment of CAP, oral treatment should be considered if there is clear evidence of improvement [D].

### Complications

- If a child remains pyrexial or unwell 48 hours after admission with pneumonia, re-evaluation is necessary with consideration given to possible complications [D].

## 2 Incidence and mortality

### Age

There are no prospective studies on the incidence and mortality of CAP from the 1990s. The most recent estimates are derived from two studies performed in Finland between 1981 and 1982.<sup>2,3</sup> In the first study all cases of CAP (all radiologically confirmed) in four municipalities of a province in Finland were prospectively reported to a pneumonia register. The incidence for children less than 5 years of age was 36.0/1000/year (95% CI 29.2 to 42.8) and 16.2/1000/year (95% CI 13.0 to 19.4) for children aged 5–14 years. There was a strong male predominance in those aged under 5 years. One death was reported (0.1/1000/year, 95% CI 0 to 0.3)<sup>2</sup> [Ib]. In the second study only children who were admitted to hospital with CAP were included. The hospital provided care for all children within a geographically defined area and the incidence was calculated as 20/1000/year in those aged less than 2 years and 4/1000/year in children aged 1 month to 15 years<sup>3</sup> [Ib]. Estimates from a US population come from an 11 year study of children followed in a paediatric group practice in North Carolina between 1964 and 1975. Over this period 1483 episodes were classified as pneumonia (not radiologically confirmed): 40/1000/year in children aged 6 months to 5 years, 22/1000 in those aged 5–9 years, 11/1000 in those aged 9–12 years, and 7/1000 in 12–15 year old children<sup>4</sup> [Ib].

### Pathogen

Based on serological results, the authors of the first Finnish study were able to calculate the incidence of CAP by pathogen. For those less than

5 years of age, *Streptococcus pneumoniae* had an incidence of 8.6/1000/year, *Mycoplasma pneumoniae* 1.7/1000/year, and *Chlamydia* species 1.7/1000/year. For those aged 5–15 years the incidence figures were 5.4/1000, 6.6/1000, and 3.9/1000, respectively. The sex difference noted in those less than 5 years of age was mainly accounted for by *S pneumoniae* (11.2/1000 in boys and 5.7/1000 in girls). These figures include mixed infections<sup>2</sup> [Ib].

Another population based prospective surveillance study of invasive pneumococcal disease (based on culture positive cases only) was performed in Southern California between 1992 and 1995, yielding an incidence of pneumococcal pneumonia of 17/100 000/year in children aged 2 years or less. There were no deaths<sup>5</sup> [Ib].

### Risk factors

Only one case control study of risk factors for CAP in a developed country has been performed. The cases were those identified in the Finnish prospective study.<sup>2</sup> For children under 5 years of age, recurrent respiratory infections during the previous year, a history of wheezing episodes, and a history of acute otitis media treated by tympanocentesis before the age of 2 years were found to be significant in a multivariate model. For older children (5–15 years of age) a history of recurrent respiratory infections in the previous year and a history of wheezing episodes were found to be significant risk factors<sup>2</sup> [III].

### 3 Aetiology and epidemiology

Studies of the aetiology of CAP are complicated by the low yield of blood cultures,<sup>6–10</sup> the difficulty in obtaining adequate sputum specimens, and the reluctance to perform lung aspiration and bronchoalveolar lavage in children. All of the following also limit the ability to extrapolate the results of published studies to other populations: the season of the year in which the study was done, the age of those studied, the setting, whether or not children were admitted to hospital and the local criteria for admission, as well as whether or not the study period coincides with an epidemic of a certain pathogen. It is now further complicated by the increasing numbers of studies using specific serological or polymerase chain reaction (PCR) techniques that are not validated and include relatively small sample sizes.

Studies of specific pathogens are summarised in table 2. All of these are prospective studies in which pneumonia was community acquired and where the case definition includes clinical findings compatible with pneumonia together with radiological changes. All constitute levels of evidence of [Ib] or [II] (indicated). In the columns the percentage indicates the percentage of all CAP cases in which that organism was the only isolate detected. Where other isolates were also isolated it was classified as mixed and indicated in a separate column. In some studies it was not possible to determine whether infections were single or mixed (as indicated). Bacterial isolates are not included if isolated from a sputum or upper respiratory tract specimen in the absence of other evidence of significance—for example, a rise in antibody concentrations.

The studies span the 1980s and 1990s and only two come from a UK population. A number of different investigations have been used but certain general conclusions can be reached. The most obvious conclusion is that the pathogen is not identified in 20–60% of cases [II]. The two recent large studies incorporating the most comprehensive sets of investigations were able to establish an aetiology in 43%<sup>10</sup> and 85%<sup>8</sup> of cases, respectively. It is also apparent that a significant number of cases of CAP (8–40%) represent a mixed infection [II]. Juven *et al*<sup>8</sup> found a mixed viral-bacterial infection in 30%, a dual viral infection in 13%, and two bacteria in 7% of cases.

A number of viruses appear to be associated with CAP, the predominant one being respiratory syncytial virus (RSV). Others isolated include: parainfluenza, adenovirus, rhinovirus, varicella zoster virus, influenza, cytomegalovirus, herpes simplex virus, and enteroviruses. Overall, viruses appeared to account for 14–35% of CAP cases in childhood [II].

Quantifying the proportion of CAP caused by bacteria is more difficult. *Streptococcus pneumoniae* is assumed to be the most common bacterial cause of CAP but is infrequently found in blood cultures. It is commonly found in routine cultures of upper respiratory specimens, yet is known to be a commensal in this setting.

Antigen detection methods of urine are unreliable<sup>7</sup> [II]. Serological testing is a promising non-culture technique but responses will be age related. Overall, blood or pleural fluid culture of *S pneumoniae* is positive in 5–10% of cases of CAP [Ib]. The proportion of CAP due to *S pneumoniae* increases to 16–37% where serological testing is used [II]. Other bacterial pathogens appear to be less frequent causes of CAP. Claesson *et al*<sup>11</sup> assessed the antibody responses to non-capsulated *Haemophilus influenzae* and isolated it as the only pathogen from the nasopharynx of 43 of 336 children but a significant increase in IgG or IgM was shown in 16 (5% of all CAP) [II]. In the same study 3% also had a significant increase in antibodies to *Moraxella catarrhalis*, suggesting that it too is an uncommon cause of CAP in children.<sup>12</sup> This was supported by another study by Korppi *et al*<sup>13</sup> in which seroconversion to *M catarrhalis* was documented in only 1.5% of cases of CAP [II].

In these studies *Mycoplasma pneumoniae* accounted for 4–39% of isolates [II]. Where *Chlamydia pneumoniae* is sought, it appears to be a significant pathogen responsible for 0–20% of cases [II]. Biases which need to be considered in these reports include whether children with mycoplasmal (or chlamydial) pneumonia are over represented in hospital based studies because of failure of penicillin related antibiotic treatment in the community, or are over represented in community studies because they are less sick and therefore less likely to be referred to hospital.

#### Influence of age

Several generalisations are possible with respect to age. Evidence of specific aetiology tends to be more commonly found in older children<sup>14</sup> [II]; viral infections (especially RSV) are more commonly found in younger children<sup>3 6 8 10 14</sup> [II]; and *Chlamydia* and *Mycoplasma* species are more commonly found in older children<sup>6 10 14–16</sup> [II]. For example, Harris *et al*<sup>16</sup> found that patients over 5 years of age had a higher rate of *M pneumoniae* (42%) and *C pneumoniae* (20%) infections than those aged less than 5 years (15% and 9%, respectively) [II]. However, Block *et al*<sup>17</sup> found the incidence of *M pneumoniae* and *C pneumoniae* infections to be comparable in all age groups between 3 and 12 years of age. In particular, the finding of a 23% incidence of *M pneumoniae* infection and 23% of *C pneumoniae* infection in children aged 3–4 years is higher than others [II] and raises questions about appropriate treatment in this age group. In most studies the incidence of *S pneumoniae* is less influenced by age<sup>3 8 10</sup> [II].

#### Key points

- *Streptococcus pneumoniae* is the most common bacterial cause of pneumonia in childhood [II].

- Age is a good predictor of the likely pathogens:
  - Viruses are most commonly found as a cause in younger children.
  - In older children, when a bacterial cause is found, it is most commonly *S pneumoniae* followed by *mycoplasma* and *chlamydial pneumonia* [II].
- A significant proportion of cases of CAP (8–40%) represent a mixed infection [II].
- Viruses alone appear to account for 14–35% of CAP in childhood [II].
- In 20–60% of cases a pathogen is not identified [II].
- The mortality from CAP in children in developed countries is low [Ib].

**Table 2** Published studies of specific pathogens associated with paediatric community acquired pneumonia

Reference [level of evidence]	Age (no)	Year and setting	Tests	Viral % (no)	Bacterial % (no)	Mycoplasma % (no)	Chlamydia % (no)	Mixed % (no)	Total % (no)
Korppi <sup>3</sup> [Ib]	0–15 y (195)	1981–2, Finland, community, IP	NPIA, serology (inc Spn)	18 (35) RSV (27)	Spn§, 3 Hi, 2 Mcat	0	1	§	§
Heiskanen-Kosma <sup>14</sup> [Ib]	3 m–14 y (201)	1981–2, Finland, community, IP† + OP	Serology (inc Spn)	14 (29) RSV (24)	11 (23) Spn, 2 Hi, 1 Mcat	10 (20)	5 (9)	25 (51)	66 (133)
Claesson <sup>6</sup> [II]	1 m–15 y (336: 167 IP, 169 OP)	1982–3, Sweden, hospital, IP + OP	BC, NPIA, NPC (Bact+), serology (inc Spn)	26 (87) RSV (55)	9 (29) Spn, 2 Hi	8 (26)	1*	9 (31)	55 (186)
Isaacs <sup>7</sup> [II]	1 m–14 y (57)	1985–6, Oxford, hospital, IP	BC, NPVC, NPIA (RSV), serology	35 (20) RSV (6)	4 (2) Spn, 1 Sa	0	*	1	42 (24)
Ruuskanen <sup>9</sup> [II]	6 m–15 y (50)	1989, Finland, hospital, IP	BC, NPVC, NPIA, serology (inc Spn)	28 (14) RSV (8)	8 (4) Spn, 1 Mcat	8 (6)	0*	30 (15)	80 (40)
Gendrel <sup>15</sup> [Ib]	18 m–13 y (104)	1992–4, Paris, hospital, IP + OP	BC, NPVC, NPIA, serology	23 (24) RSV (10)	10 (10) Spn, 1 (1) Sa	40 (42)	1 (1)*	9 (9)	84 (87)
Block <sup>17</sup> † [II]	3–12 y (260)	1992–3, USA, OP	BC, PC (My, Ch), PPCR (My), serology (My, Ch)	–	<1 (1) Spn,	19 (48)	20 (52)	8 (22)	47 (122)
Harris <sup>16</sup> † [II]	6 m–16 y (420)	1994–5, USA, OP	PC (My, Ch), PPCR (My), serology (My, Ch)	–	–	30 (124)	15 (63)	¶	45 (187)
Wubbel <sup>10</sup> † [II]	6 m–16 y (168)	1996–7, Texas, hospital, OP	BC, NPVC, NPIA, PC (My, Ch), PPCR (My, Ch), serology (inc Spn)	17 (26/157) RSV (13)	16 (21/129)	4 (7/168)	2 (4/168)	9 (15)	43 (73)
Clements <sup>42</sup> [II]	2 m–16 y (89)	1996–7, UK, hospital, IP	BC, NPIA, NPVC, PPCR (My, Ch, Pert), BPCR (Spn, My, Ch), serology (My, Ch, Leg, virus)	22 (20) RSV (12)	7 (6) Spn	13 (12)	2 (1)	6 (3)	54 (48)
Juven <sup>8</sup> [Ib]	1 m–17 y (254)	1993–5, Finland, hospital, IP	BC, NPVC, NPIA, PPCR (rhino), serology (inc Spn)	32 (81) RSV (40)	22 (56), Spn (42)	4 (10)	3 (7)	41 (105) Spn+ virus (46)	85 (216)

IP = inpatients; OP = outpatients; BC = blood culture; NPIA = nasopharyngeal immunoassay; NPVC = nasopharyngeal viral culture; PC = pharyngeal culture; PPCR = pharyngeal polymerase chain reaction; BPCR = blood polymerase chain reaction; RSV = respiratory syncytial virus; My = mycoplasma; Ch = chlamydia; Pert = pertussis; Leg = legionella; Spn = *Streptococcus pneumoniae*; Hi = *Haemophilus influenzae*; Mcat = *Moraxella catarrhalis*; Sa = *Staphylococcus aureus*; \*No serological tests for Cpn performed. †Studies designed as trials of antibiotic therapy. ‡Includes 43 children also reported in Korppi.<sup>35</sup> §Significant number of Spn cases identified by antigen detection assay therefore difficult to determine contribution of true Spn to total numbers. ¶Assumes no mixed infections.



## 4 Clinical features

Most of the recent work on the signs, symptoms, and severity of pneumonia has been provided by research in developing countries to help non-medical field workers in health care. In infants, chest indrawing and/or a respiratory rate over 50/min gave a positive predictive value of 45% of radiological evidence of consolidation and a negative predicative value of 83%<sup>18</sup> [II]. In children aged less than 5 years Palafox *et al*<sup>19</sup> found that, of all the clinical signs, WHO defined tachypnoea (respiratory rate >60 breaths/min in children aged <2 months, >50 breaths/min in children aged 2–12 months, and >40 breaths/min in children aged >12 months) had the highest sensitivity (74%) and specificity (67%) for radiologically defined pneumonia, but that it was both less sensitive and less specific early in the disease (<3 days' duration).

Respiratory rate is difficult to count in healthy restless children. In children with moderate to severe pneumonia it is probably easier because they are more sick and quieter. The respiratory rate appears to be helpful in determining severity in infants under 1 year where a rate of >70 breaths/min had a sensitivity of 63% and specificity of 89% for hypoxaemia<sup>20</sup> [II]. Between 12 and 36 months of age respiratory rates of >40 breaths/min were related to pneumonia, but in children aged >36 months tachypnoea and chest recession were not sensitive signs. Children can have pneumonia with respiratory rates of <40 breaths/min<sup>21</sup> [II], and crackles and bronchial breathing were reported to have a sensitivity of 75% and a specificity of 57%<sup>20</sup> [II]. High fever in both infants and children has been considered an important sign in the community, both in developed and developing countries<sup>22, 23</sup> [III] [II]. Because clinical symptoms together contributed more than signs, it has been suggested that the WHO guidelines for diagnosing pneumonia should include breathlessness—that is, difficulty in breathing—which was found to be more helpful than breath count<sup>24</sup> [II]. If all clinical signs (respiratory rate, auscultation, and work of breathing) are negative, the chest radiographic findings are unlikely to be positive.

A Medline search from 1982 to 1995 of studies which considered observer agreement of clinical examination suggested that observed signs (kappa 0.48–0.6) were better than auscultation signs (kappa 0.3)<sup>25</sup> [Ia]. Wheezing is not a useful

### Box 1 Features of bacterial lower respiratory tract infection (LRTI)

- Fever >38.5°C.
- Respiratory rate >50 breaths/min.
- Chest recession.
- Wheeze not a sign of primary bacterial LRTI (other than mycoplasma).
- Other viruses may be concurrent.
- Clinical and radiological signs of consolidation rather than collapse.

### Box 2 Features of viral lower respiratory tract infection (LRTI)

- Infants and young children.
- Wheeze.
- Fever <38.5°C.
- Marked recession.
- Hyperinflation.
- Respiratory rate normal or raised.
- Radiograph shows hyperinflation and, in 25%, patchy collapse.
- Lobar collapse when severe.

### Box 3 Features of mycoplasma lower respiratory tract infection (LRTI)

- Schoolchildren.
- Cough, wheeze, pneumonia.
- Interstitial infiltrates, lobar consolidation and hilar adenopathy.

sign for determining severity in infants and young children<sup>18</sup> [II]. Wheeze occurs in 30% of mycoplasma pneumonias and is more common in older children<sup>26</sup> [IVb]. Because of this, the clinical diagnosis of mycoplasma pneumonia without radiography can be confused with asthma. Symptoms in older children may include abdominal pain (reflecting referred pain from the diaphragmatic pleura) and chest pain. The signs of bronchial breathing and pleural effusion are not present at the onset of symptoms.

Serious consideration should therefore be given to bacterial infection when the presentation is a fever of >38.5°C, recession, and tachypnoea. If wheeze is present, a primary bacterial pneumonia is very unlikely. If present, a viral or mycoplasma infection should be considered or an underlying condition such as cystic fibrosis. Children with tuberculous pneumonia are severely ill and the radiographic appearances are suggestive. The features of bacterial, viral, and mycoplasma lower respiratory tract infection are shown in boxes 1, 2 and 3, respectively.

### Key points

- Bacterial pneumonia should be considered in children aged up to 3 years when there is fever of >38.5°C together with chest recession and a respiratory rate of >50/min [B]. For older children a history of difficulty in breathing is more helpful than clinical signs.
- If wheeze is present in a preschool child, primary bacterial pneumonia is unlikely [B].

### CLASSICAL CLINICAL FEATURES

#### Pneumococcal pneumonia

Pneumococcal pneumonia starts with fever and tachypnoea. Since alveoli are poorly endowed

with cough receptors, cough only occurs when lysis is present and debris is swept into the airways where cough receptors are plentiful. This accords with the many studies which emphasise the history of fever and breathlessness together with signs of tachypnoea, indrawing and unwell appearance ("toxaemia", "looks sick")<sup>18 21 24-27</sup> [II]. This illness should therefore be considered in febrile tachypnoeic infants.

#### **Staphylococcal pneumonia**

Staphylococcal pneumonia is now rare in developed countries and, at the onset, is indistinguishable from pneumococcal pneumonia<sup>23</sup> [IVb]. It is almost exclusively a disease of infants but can complicate influenza in older children.

#### **Mycoplasma disease**

Fever, arthralgia, headache, cough and crackles in a school-child would suggest mycoplasma infection<sup>26</sup> [IVb], but again this can resemble pneumococcal and staphylococcal pneumonias as well as adenoviral illness if wheezing is prominent.

#### **Others**

*Chlamydia trachomatis* pneumonia is apparently not a fatal illness. The "staccato" cough is not specific, and crackles are described more frequently than wheeze. The only really significant clinical feature is a history of sticky eye in 50% of cases in the neonatal period.

It is unclear whether pertussis pneumonia is a primary pneumonia or is the result of aspiration<sup>28</sup> [IVa]. It may co-exist with other pneumonias<sup>29</sup> [III].

## 5 Radiological, general and microbiological investigations

### RADIOLOGICAL INVESTIGATIONS

#### When to do a chest radiograph?

Published studies which examine the relationship between respiratory signs and pneumonia on the chest radiograph give contradictory results. In a study of the value of chest radiography in children <5 years old with a temperature of  $\geq 39^{\circ}\text{C}$  and white blood cell count of 20 000/mm<sup>3</sup> or greater without an alternative major source of infection and with no additional clinical signs of pneumonia, radiographic signs of pneumonia were detected in about 25%<sup>30</sup> [II]. This suggests that a chest radiograph should be undertaken in young children with a pyrexia of unknown origin. In a different study Heullitt *et al*<sup>31</sup> reported a sensitivity and specificity for detecting radiographic pneumonia of 45% and 92%, respectively, for the presence of fever and tachypnoea in infants under 3 months. Only 6% of febrile infants had an abnormal chest radiograph in the absence of respiratory signs. The authors recommend that a chest radiograph should be obtained in febrile infants only when signs of respiratory distress are present<sup>31</sup> [III]. However, the radiological features of segmental consolidation are not always easy to distinguish from those of segmental collapse, apparent in about 25% of children with bronchiolitis<sup>32 33</sup> [II] [II]. Taking these studies together, it would seem advisable to *consider* a chest radiograph in a child aged <5 years with a fever of  $>39^{\circ}\text{C}$  of unknown origin unless classical features of bronchiolitis are present.

One of the largest studies of the value of chest radiography was undertaken in children aged between 2 months and 5 years managed as outpatients with time to recovery as the main outcome<sup>34</sup> [Ib]. Chest radiography did not affect the clinical outcome in these children with acute lower respiratory infection. This lack of effect was independent of clinicians' experience. There are no clinically identifiable subgroups of children within the WHO case definition of pneumonia who are likely to benefit from a chest radiograph. The authors concluded that routine use of chest radiography was not beneficial in ambulatory children aged over 2 months with acute LRTI. Antibiotic prescription was more frequent in those who underwent radiography (61% *v* 53%). This was the only trial identified in a recent Cochrane review.<sup>35</sup>

In a review of the value of chest radiography in infants with a clinical diagnosis of acute bronchiolitis, treatment was not altered by the radiographic signs (patchy collapse was evident in 25%). The authors concluded that the request for a chest radiograph in acute bronchiolitis should be made only when the need for intubation is being considered, where there has been an unexpected deterioration in the child's condition, or the child has an underlying cardiac or pulmonary disorder<sup>32</sup> [II]. Lobar or segmental consolidation was observed more often in children aged <6 months infected with respiratory syncytial virus (RSV) than in older children with RSV infection<sup>36</sup> [Ib].

#### Observer agreement on radiographic signs of pneumonia

Clinicians basing the diagnosis of lower respiratory infections in young infants on radiographic diagnosis should be aware that there is variation in intraobserver and interobserver agreement among radiologists on the radiographic features used for diagnosis. There is also variation in how specific radiological features are used in interpreting the radiograph. However, the cardinal finding of consolidation for the diagnosis of pneumonia appears to be highly reliable<sup>37</sup> [II] and reasonably specific for bacterial pneumonia (74% of 27 patients with alveolar shadowing had bacterial proven pneumonia)<sup>38</sup> [III]. Lateral radiographs are unhelpful<sup>39</sup> [II].

#### Agreement between radiographic findings and clinical diagnosis

The evidence for having pneumonia without an abnormal chest radiograph is anecdotal. Anecdote suggests that fever and tachypnoea are present before classical consolidation is present. There is some evidence for an abnormal chest radiographic appearance without either fever or tachypnoea<sup>40</sup> [III]. How this is managed depends on whether the patient is thought to have a developing illness or one which is resolving, as doubtless happened in the days before antibiotics.

#### Which pathogen?

Chest radiography is too insensitive to be useful in differentiating between patients with *bacterial pneumonia* and those whose pneumonia is non-bacterial<sup>41 42</sup> [II]. There is no radiological pattern pathognomonic for *mycoplasma pneumoniae*. Interstitial infiltrates, lobar consolidation, and hilar adenopathy have all been described. Pleural effusions are rare<sup>43</sup> [III].

Because of poor observer agreement and appreciable false negative errors when viral and bacterial readings were compared with titre increases and positive bacterial cultures, respectively, radiographic findings are poor indicators of an aetiological diagnosis in ambulatory children with pneumonia and, of themselves, are an insufficient database for making therapeutic decisions<sup>44</sup> [II]. There is no evidence that an experienced clinician would be more confident diagnosing non-bacterial pneumonia from the clinical features, age of the child, and the chest radiograph.

#### Follow up radiographs

Children with lobar collapse should probably all be followed up and reviewed with a radiograph. A follow up radiograph is also sensible for children with apparent round pneumonia to ensure tumour masses are not missed. Follow up radiographs after acute uncomplicated pneumonia are of no value where the patient is asymptomatic<sup>45 46</sup> [II] [III].

### Key points

- Chest radiography should not be performed routinely in children with mild uncomplicated acute lower respiratory tract infection [A].
- Radiographic findings are poor indicators of aetiology.
- Follow up chest radiography should only be performed after lobar collapse, an apparent round pneumonia, or for continuing symptoms [C].

## GENERAL INVESTIGATIONS

### Community

There is no indication for any tests in a child with suspected pneumonia in the community.

### In hospital

#### Pulse oximetry

Oxygen saturation (Sao<sub>2</sub>) measurements provide a non-invasive estimate of arterial oxygenation. The oximeter is easy to use and requires no calibration. However, it requires a pulsatile signal from the patient. When using paediatric wrap around probes, the emitting and receiving diodes need to be carefully opposed. It is also highly subject to motion artefacts. To obtain a reliable reading, (1) the child should be still and quiet; (2) a good pulse signal (plethysmograph) should be obtained; and (3) once a signal is obtained, the saturation reading should be watched over at least 30 seconds and a value recorded once an adequate stable trace is obtained.

In a prospective study from Zambia the risk of death from pneumonia was significantly increased when hypoxaemia was present<sup>20</sup> [Ib].

#### Key point

- Pulse oximetry should be performed in every child admitted to hospital with pneumonia [A].

### Acute phase reactants

White cell count, total neutrophil count, C reactive protein (CRP), and erythrocyte sedimentation rate (ESR) are generally performed in the belief that they help distinguish bacterial from viral infections and the clinician will therefore find them helpful in deciding whether or not to prescribe antibiotics.

Recent prospective studies have examined the usefulness of acute reactants in distinguishing bacterial from viral pneumonia.<sup>47–48</sup> Nohynek *et al*<sup>48</sup> studied 121 children admitted to hospital with acute lower respiratory infection. Using culture and serological techniques, they divided the children into four groups: those with a bacterial infection (n=30), those with a viral infection (n=30), those with mixed infections (n=24), and those of unknown aetiology (n=37). The distribution of ESR, full blood count, and CRP values was wide within each group and they could not identify cut off points that would reliably distinguish bacterial from viral infections or bacterial and mixed infections from viral infections [Ib]. Korppi *et al*,<sup>47</sup> in a similar prospective study examined whether pneumococcal infection (n=29), could be distinguished from pneumococcal and viral infection (n=17) or viral infection alone (n=23). There was a statistically significant difference in the CRP level, ESR, and absolute neutrophil count between pneumococcal infection alone and viral infection alone, but specificity and sensitivity remained poor (white cell count >15 000: sensitivity 33%, specificity 60%; neutrophil count >10 000: sensitivity 28%, specificity 63%; CRP >60 mg/l: sensitivity 26%, specificity 83% for *S pneumoniae* versus a viral infection) [Ib].

Host response indices are best at detecting invasive infections. In children many acute lower respiratory infections may be less invasive and mucosal limited and cause less host

response. Some viral agents, particularly adenovirus or influenza virus, are capable of causing invasive infection and hence may induce a host response very similar to that seen in invasive bacterial infections. Acute phase reactants do not therefore usually distinguish between bacterial and viral infection in children [Ib].

Acute phase reactants can also be measured as a baseline and may then only be useful if the patient does not improve on treatment as expected.

#### Key point

- Acute phase reactants do not distinguish between bacterial and viral infections in children and should not be measured routinely [A].

### Urea and electrolytes

Investigation of urea and electrolytes to assess electrolyte imbalance is undertaken if the patient is severely ill or shows evidence of dehydration. Inappropriate secretion of anti-diuretic hormone (ADH) is recognised in both children and adults with pneumonia. In adults it has been shown that there is a latent vasopressin dependent impairment of renal water excretion in acute pneumonia.<sup>49</sup> A study of 264 children admitted to hospital with pneumonia in India showed hyponatraemia at admission in 27% and it was calculated that, in 68% of these children, the hyponatraemia was secondary to inappropriate ADH secretion.<sup>50</sup> Treatment is with fluid restriction.

## SPECIFIC MICROBIOLOGICAL INVESTIGATIONS

It can be difficult to determine the responsible pathogen in children with acute LRTI. The gold standard would be to take samples directly from the infected area of the lung, and the yield from bacterial growth from lung punctures in African children is high (79%).<sup>51</sup> Most often in western countries, however, less invasive sampling measures are used for diagnosis.

### Community

There is no indication for microbiological investigation of the child with pneumonia in the community.

### In hospital

For patients admitted to hospital with pneumonia, it is important to attempt a microbiological diagnosis. It is clear from a number of studies that 10–30% of infections will have a mixed viral and bacterial aetiology<sup>8, 23</sup> [II].

### Bacterial pneumonia

- Blood cultures: blood cultures should be performed in all children suspected of having bacterial pneumonia but are positive in less than 10%.
- Nasopharyngeal culture: bacterial growth in the nasopharynx does not indicate infection in the lower airways<sup>52</sup> [Ib].
- Pleural fluid: pleural fluid should be aspirated for diagnostic purposes where it is regarded as significant either on clinical examination or radiologically. In a large study of 840 pleural fluid samples from children aged 0–12 years with clinical symptoms of acute bacterial pneumonia, bacteria were cultured in 17.7% of cases (sensitivity 1; specificity 0.23).<sup>53</sup> In the same study, antigen detection tests, counter-immunoelectrophoresis (CIE), latex agglutination (LA), and dot enzyme linked immunoabsorbent assay (dot ELISA) were also performed for *S pneumoniae* and *H influenzae*. Culture, CIE, and LA were taken together as a gold standard for the evaluation of dot ELISA. Overall, dot ELISA was more sensitive but less specific (sensitivity 0.91, specificity 0.55) than CIE (sensitivity 0.47, specificity 1) or LA (sensitivity 0.77, specificity 0.85) [Ib].

**Table 3** Summary of the diagnostic value of specific microbiological investigations

Test	Diagnostic value	False positive rate	False negative rate
Blood culture	++++	–	+++
Viral antigen detection (nasopharyngeal aspirate)	+++	–	+
Viral culture	+++	–	++
Serum antigen	++	+	++
Urine antigen	+	++	++
Paired antibody titre	+++	+	++
Bacterial culture of nasopharyngeal secretions	–	+++	+
Lung puncture culture*	++++	–	+

\*The risk/benefit ratio of this test is too high in the developed world where antibiotics are readily available.

- Serological diagnosis:
  - Urine: in a 1996 study Ramsey *et al*<sup>54</sup> found that antigenuria was present in 4% of asymptomatic children and 16% of children with acute otitis media as well as 24% of children with acute LRTI. The specificity is therefore too poor for this to be a helpful test in diagnosis [III].
  - Serum: a number of antigen, antibody, and pneumococcal immune complex methods of serological diagnosis have become available.<sup>55, 56</sup> No single test has specificity and sensitivity sufficiently high to be diagnostic on its own. A range of assays therefore needs to be performed. Current tests are particularly poor in the very young<sup>55</sup> [II].

#### Mycoplasma pneumoniae

Complement fixation tests: a rise in paired titre is regarded as the gold standard for the diagnosis of *M pneumoniae*. IgM ELISA has been shown to reach a diagnostic level during the second week of the disease.<sup>57</sup> Cold agglutinins are often used as an acute test but their value is limited. In children aged 5–14 years the positive predictive value for mycoplasma of a rapid cold agglutinin test was 70%.<sup>58</sup>

#### Viral pneumonia

Viral antigen detection in nasopharyngeal aspirates is highly specific for respiratory syncytial virus, parainfluenza virus, influenza virus, and adenovirus. Sensitivities of this test

approach 80%, particularly in infants.<sup>55</sup> Nasopharyngeal aspirates should also be cultured for viruses, although infections are also diagnosed by rises in titre in paired serum samples [II]. Nasal lavage can be substituted for nasopharyngeal aspirates.<sup>59</sup>

The results of viral detection tests are particularly useful for cohorting infected children during outbreaks and for epidemiological purposes.

A summary of the diagnostic value of specific microbiological investigations is shown in table 3.

#### Key points

- There is no indication for microbiological investigation of the child with pneumonia in the community.
- Blood cultures should be performed in all children suspected of having bacterial pneumonia [B].
- Acute serum samples should be saved and a convalescent sample taken in cases where a microbiological diagnosis was not reached during the acute illness [B].
- Nasopharyngeal aspirates from all children under the age of 18 months should be sent for viral antigen detection (such as immunofluorescence) with or without viral culture [B].
- When significant pleural fluid is present, it should be aspirated for diagnostic purposes, sent for microscopic examination and culture, and a specimen saved for bacterial antigen detection [B].

## 6 Severity assessment

Children with CAP may present with fever, tachypnoea, breathlessness, difficulty in breathing, cough, wheeze, headache, abdominal pain, or chest pain (see clinical features) and the severity of the condition can range from mild to life threatening (see table 4).

Infants and children with mild to moderate respiratory symptoms can be managed safely at home. Those with signs of severe disease should be admitted to hospital.

### INDICATIONS FOR ADMISSION TO HOSPITAL

A key indication for admission to hospital is hypoxaemia. In a study carried out in the developing world, children with low oxygen saturations were shown to be at greater risk of death than adequately oxygenated children.<sup>20</sup> The same study showed that a respiratory rate of 70 breaths/min or more in infants aged <1 year was a significant predictor of hypoxaemia. Oxygen saturation levels ( $Sa_{o_2}$ ) below 92%, other clinical signs of severe disease, and a family incapable of appropriate observation and supervision of the child are all indicators for admission to hospital.

Indicators for admission to hospital in infants:

- $Sa_{o_2} \leq 92\%$ , cyanosis;
- respiratory rate >70 beats/min;
- difficulty in breathing;
- intermittent apnoea, grunting;
- not feeding;

- family not able to provide appropriate observation or supervision.

Indicators for admission to hospital in older children:

- $Sa_{o_2} \leq 92\%$ , cyanosis;
- respiratory rate >50 breaths/min;
- difficulty in breathing;
- grunting;
- signs of dehydration;
- family not able to provide appropriate observation or supervision.

### INDICATIONS FOR TRANSFER TO INTENSIVE CARE

Transfer to intensive care should be considered when:

- the patient is failing to maintain an  $Sa_{o_2}$  of >92% in  $Fi_{o_2}$  of >0.6;
- the patient is shocked;
- there is a rising respiratory rate and rising pulse rate with clinical evidence of severe respiratory distress and exhaustion, with or without a raised arterial carbon dioxide tension ( $Paco_2$ );
- there is recurrent apnoea or slow irregular breathing.

**Table 4** Severity assessment

	Mild	Severe
Infants	Temperature <38.5°C RR <50 breaths/min Mild recession Taking full feeds	Temperature >38.5°C RR >70 breaths/min Moderate to severe recession Nasal flaring Cyanosis Intermittent apnoea Grunting respiration Not feeding
Older children	Temperature <38.5°C RR <50 breaths/min Mild breathlessness No vomiting	Temperature >38.5°C RR >50 breaths/min Severe difficulty in breathing Nasal flaring Cyanosis Grunting respiration Signs of dehydration

## 7 General management (other than antibiotics)

### GENERAL MANAGEMENT IN THE COMMUNITY

#### Key points

- *The child cared for at home should be reviewed by a general practitioner if deteriorating, or if not improving after 48 hours on treatment [D].*
- *Families of children who are well enough to be cared for at home need information on managing pyrexia, preventing dehydration, and identifying any deterioration [D].*

### GENERAL MANAGEMENT IN HOSPITAL

#### Oxygen therapy

Hypoxic infants and children may not appear cyanosed. Agitation may be an indication of hypoxia.

Patients whose oxygen saturation is less than 92% while breathing air should be treated with oxygen given by nasal cannulae, head box, or face mask to maintain oxygen saturation above 92%. There is no strong evidence to indicate that any one of these methods is more effective than any other. A study comparing the different methods in children under 5 years of age concluded that the head box and nasal cannulae are equally effective,<sup>60</sup> but the numbers studied were small and definitive recommendations cannot be drawn from this study. It is easier to feed with nasal cannulae, but the maximum flow rate of oxygen recommended by the manufacturer by this method is 2 l/min. Alternative methods of delivering higher concentrations of humidified oxygen such as face mask or head box may be necessary.

Where the child's nose is blocked with secretions, gentle suctioning of the nostrils may help [D]. No studies assessing the effectiveness of nasopharyngeal suction were identified.

#### Key points

- *Patients whose oxygen saturation is 92% or less while breathing air should be treated with oxygen given by nasal cannulae, head box, or face mask to maintain oxygen saturation above 92% [A].*
- *Agitation may be an indication that the child is hypoxic.*

#### Fluid therapy

Children who are unable to maintain their fluid intake due to breathlessness or fatigue need fluid therapy. Studies on preterm infants or infants weighing <2000 g have shown that the presence of a nasogastric tube compromises respiratory status<sup>61 62</sup> [II]. Older children may be similarly affected, although potentially to a lesser extent because of their larger nasal passages, so although tube feeds offer nutritional benefits over intravenous fluids, they should be avoided in severely ill children. Where nasogastric tube feeds are used, the smallest tube should be passed down the smallest nostril.<sup>63</sup> There is no evidence that nasogastric feeds given continuously are any better tolerated than bolus feeds (no studies were identified); however, in theory, smaller more frequent feeds are less likely to cause stress to the respiratory system.

Patients who are vomiting or who are severely ill may require intravenous fluids. These should be given at 80% of basal levels (once hypovolaemia has been corrected) and serum electrolytes should be monitored in the severely ill as inappropriate ADH secretion is a recognised complication.<sup>50 64</sup>

#### Key points

- *Nasogastric tubes may compromise breathing and should therefore be avoided in severely ill children and especially in infants with small nasal passages. If used, the smallest tube should be passed down the smallest nostril [D].*
- *Intravenous fluids, if needed, should be given at 80% basal levels and serum electrolytes monitored [C].*

#### Physiotherapy

Two randomised controlled trials<sup>65 66</sup> and an observational study<sup>67</sup> conducted on adults and children showed that physiotherapy did not have any effect on the length of hospital stay, pyrexia, or chest radiographic findings in patients with pneumonia. There is no evidence to support the use of physiotherapy including postural drainage, percussion of the chest, or deep breathing exercises<sup>66</sup> [Ib], <sup>65 67</sup> [III]. There is a suggestion that physiotherapy is counterproductive, with patients who receive chest physiotherapy being at risk of having a longer duration of fever than the control group.<sup>65</sup> In addition, there is no evidence to show that physiotherapy is beneficial in the resolving stage of pneumonia.<sup>68</sup>

A supported sitting position may help to expand lungs and improve respiratory symptoms in children with respiratory distress.

#### Key point

- *Chest physiotherapy is not beneficial and should not be performed in children with pneumonia [B].*

#### Management of fever and pain

Children with acute LRTI are generally pyrexial and may have some pain, including headache, chest pain, arthralgia (in the case of mycoplasma pneumonia), referred abdominal pain, and possibly earache from associated otitis media (see section on Clinical features). Pleural pain may interfere with depth of breathing and may impair the ability to cough. Antipyretics and analgesics can be used to keep the child comfortable and to help coughing. Minimal handling helps to reduce metabolic and oxygen requirements and this should be considered when planning and carrying out procedures, investigations, and treatments.

#### Key points

- *Antipyretics and analgesics can be used to keep the child comfortable and to help coughing.*
- *In the ill child, minimal handling may reduce metabolic and oxygen requirements.*

**Monitoring**

The frequency of monitoring—including heart rate, temperature, respiratory rate, oxygen saturation level, respiratory pattern including chest recession and use of accessory muscles—is determined by the child's condition. The sicker the child, the more likely that continuous oxygen saturation monitoring will be needed. Patients on oxygen therapy should

have at least 4 hourly observations including oxygen saturation.

**Key point**

- *Patients on oxygen therapy should have at least 4 hourly observations including oxygen saturation [D].*



## 8 Antibiotic management

### INTRODUCTION

The management of a child with CAP involves a number of decisions regarding treatment with antibiotics:

- whether to treat with antibiotics;
- which antibiotic and by which route;
- when to change to oral treatment;
- duration of treatment.

There is a clear dearth of large pragmatic randomised controlled trials to provide the evidence necessary to make these decisions. Many of the studies identified by the searches were designed to support the licensing of new treatments which were compared with a “standard” antibiotic regimen. Although designed as randomised controlled trials, they frequently involved small numbers of patients and both the “new antibiotic” group and the “standard therapy” comparison group had a very high rate of complete recovery from pneumonia. These studies did not appear to be powered to show a difference in efficacy between the two regimes and certainly were not powered to demonstrate equivalence. Likewise, it was not possible to assess the differential safety of the various regimens which have been compared in these trials. The lack of evidence for treatment with antibiotics which has been identified in this review highlights the need for well designed randomised controlled trials to address the key questions concerning the management of CAP in children.

### WHETHER TO TREAT WITH ANTIBIOTICS

One of the major problems in deciding whether to treat a child with CAP with antibiotics is the difficulty in distinguishing bacterial pneumonia (which would benefit from antibiotics) from non-bacterial pneumonia (which would not). This difficulty has been described in Section 3 on Aetiology. Resistance to antibiotics among bacterial pathogens is increasing and is of concern; an important factor in this increase is the overuse of antibiotics. Only one study was identified in which children with diagnosed pneumonia treated with antibiotics were compared with a group not treated with antibiotics<sup>69</sup> [II]. This study was a randomised controlled trial of 136 young Danish children aged 1 month to 6 years. The diagnosis of pneumonia was based on the auscultatory findings of fine crepitations or radiographic appearances of pulmonary consolidation. Over half the children were diagnosed as having viral pneumonia on the basis of laboratory evidence, caused by RSV in most cases. The children had relatively mild signs and symptoms and those with severe breathing difficulty, cyanosis, suspected septicaemia, and pre-existing pulmonary or cardiac disease were excluded. The treatment group received either ampicillin or penicillin V, depending on their age. There were no differences in the course of the illness between the two groups but 15 of the 64 in the placebo group did eventually receive antibiotics. There are

concerns about the generalisability of this study to a UK setting of children admitted to hospital with CAP as, in the UK, in about half the patients entered into the study bronchiolitis would have been the clinical diagnosis.

There is increasing concern about the inappropriate use of oral antibiotics and a recent commentary<sup>70</sup> [IV] suggested that, by educating parents about the drawbacks of oral antibiotics, they may be empowered to question their doctors about antibiotic use.

### Key point

- *Young children presenting with mild symptoms of lower respiratory tract infection need not be treated with antibiotics [B].*

### CHOICE OF ANTIBIOTIC

It is clear that there is variation in medical prescribing which largely reflects custom and local practice. We have reviewed the relevant scientific evidence and provide recommendations based, where possible, on that evidence, but more frequently recommendations are based on judgements about what constitutes safe and effective treatment. In pneumonia in children the nature of the infecting organism is almost never known at the initiation of treatment and the choice of antibiotic is therefore determined by the reported prevalence of different pathogens at different ages and the associations between specific pathogens and certain clinical features.

### Macrolides compared with other groups of antibiotics

In adults macrolide antibiotics have been shown to reduce the length and severity of pneumonia caused by *Mycoplasma pneumoniae* compared with penicillin or no antibiotic treatment.<sup>71</sup> There are no similar studies in children. This class of antibiotics is also effective against a wide range of bacterial pathogens and thus has a number of advantages. Three randomised controlled trials which compared macrolides with other groups of antibiotics were identified<sup>10 16 72</sup> [Ib]. Harris *et al*<sup>16</sup> found no difference between treatment with a macrolide antibiotic and a penicillin based antibiotic [Ib]. Langtry and Balfour<sup>73</sup> showed that azithromycin was slightly more efficacious than ceftibuten, but this was a small study and a review of azithromycin treatment of paediatric pneumonia showed that azithromycin was similar to all comparator antibiotics (co-amoxiclav, cefaclor, erythromycin or josamycin) [II]. There were no clinical significant differences in efficacy between azithromycin and these comparator agents at the end of treatment.

### Macrolides compared with other macrolide antibiotics

Manfredi *et al*<sup>74</sup> compared azithromycin for 3–5 days with erythromycin for 7 days and found no difference in efficacy [Ib]. Block *et al*<sup>77</sup> compared erythromycin with clarithromycin, each given for 10 days, and also found no differences in efficacy

[II], and Ficnar *et al*<sup>75</sup> compared a 3 day course of azithromycin with a 5 day course and showed no difference between the two treatment groups [II].

### Cephalosporins compared with non-cephalosporins

Two randomised controlled trials were identified in this group<sup>76-77</sup> [II]. In a study by Amir *et al*<sup>76</sup> parenteral treatment with ceftriaxone for 2 days was followed by either 8 days of treatment with co-amoxiclav or 8 days of treatment with cefixime. There were no differences between the groups. Klein<sup>77</sup> compared cefpodoxime proxetil with amoxicillin clavulanate and also found no difference between the treatment groups.

### Comparison of two cephalosporins

Three studies<sup>78-80</sup> compared two cephalosporins, two of which were randomised controlled trials<sup>78, 80</sup> [II]. No differences were detected between the groups in any of the three studies. In all the studies a third generation cephalosporin was evaluated against cefaclor.

### Antibiotic resistance

Antibiotic resistance among pneumococci is increasing and is of concern because pneumococcus is an important cause of severe CAP in children and because penicillin and macrolide resistance are increasingly linked. Two studies addressed the response to antibiotic treatment of children with pneumonia caused by penicillin resistant *S pneumoniae*. The United States Pediatric Multicenter Pneumococcal Surveillance Study Group (consisting of eight children's hospitals) prospectively identified children with *S pneumoniae*; 257 episodes were included. 8% of isolates were intermediate and 6% were resistant to penicillin, and 3% were intermediate and 2% were resistant to cefotaxime. There was no difference in outcome between susceptible and resistant cases. Note that a high proportion received parenteral antibiotics: 80% of outpatients had an intravenous dose of a cephalosporin followed by a course of oral antibiotics and 17% received an oral  $\beta$ -lactam course alone. 48% of inpatients had an intravenous course of a cephalosporin followed by a course of oral antibiotic, 20% had intravenous cephalosporin with intravenous penicillin, and 16% had intravenous cephalosporin and intravenous vancomycin. Of those with penicillin resistant organisms, all but one had at least one dose of an intravenous antibiotic<sup>81</sup> [III].

In another study Friedland<sup>82</sup> compared factors in 78 South African children admitted to hospital with pneumonia (25 intermediate resistance to penicillin, 53 penicillin susceptible) and found no difference in outcome. Treatment included oral amoxicillin in four and intravenous ampicillin or penicillin in 12 [III].

A recent report of a closed audit loop showed that prescribing can be rationalised to simple narrow spectrum antibiotics with the introduction of a local management protocol. This has the potential to reduce the likelihood of antibiotic resistance developing.<sup>42</sup>

Information on the antibiotics recommended for treatment of CAP in children is shown in the table in Appendix 2.

### Key points

- *Amoxicillin is first choice for oral antibiotic therapy in children under the age of 5 years because it is effective against the majority of pathogens which cause CAP in this group, is well tolerated, and cheap. Alternatives are co-amoxiclav, cefaclor, erythromycin, clarithromycin and azithromycin* [B].

- *Because mycoplasma pneumonia is more prevalent in older children, macrolide antibiotics may be used as first line empirical treatment in children aged 5 and above* [D].
- *Macrolide antibiotics should be used if either mycoplasma or chlamydia pneumonia is suspected* [D].
- *Amoxicillin should be used as first line treatment at any age if S pneumoniae is thought to be the likely pathogen* [B].
- *If Staph aureus is thought the likely pathogen, a macrolide or combination of flucloxacillin with amoxicillin is appropriate* [D].
- *Although there appears to be no difference in response to conventional antibiotic treatment in children with penicillin resistant S pneumoniae, the data are limited and the majority of children in these studies were not treated with oral  $\beta$ -lactam agents alone.*

### ROUTE OF ADMINISTRATION

One large adequately powered trial<sup>83</sup> compared the efficacy of treatment with intramuscular penicillin (one dose) and oral amoxicillin given for 24–36 hours to children with pneumonia treated in the Accident & Emergency Department [Ib]. Evaluation at 24–36 hours did not show any differences in outcome between the groups. Parenteral administration of antibiotics in children (which, in the UK, is generally intravenous) is traumatic as it requires the insertion of a cannula, drug costs are much greater than with oral regimens, and admission to hospital is generally required. However, in the severely ill child, parenteral administration ensures that high concentrations are achieved rapidly in the lung. The parenteral route should also be used if there are concerns about oral absorption.

### Key points

- *Antibiotics administered orally are safe and effective for children presenting with CAP* [A].
- *Intravenous antibiotics should be used in the treatment of pneumonia in children when the child is unable to absorb oral antibiotics (for example, because of vomiting) or presents with severe signs and symptoms* [D].
- *Appropriate intravenous antibiotics for severe pneumonia include co-amoxiclav, cefuroxime, and cefotaxime. If clinical or microbiological data suggest that S pneumoniae is the causative organism, amoxicillin, ampicillin, or penicillin alone may be used* [D].

### SWITCHING FROM PARENTERAL TO ORAL ANTIBIOTICS

No randomised controlled trials which addressed the issue of when it is safe and effective to transfer from intravenous to oral antibiotic therapy were identified. There can thus be no rigid statement about the timing of transfer to oral treatment and this is an area for further investigation.

### Key point

- *In a patient who is receiving intravenous antibiotic therapy for the treatment of CAP, oral treatment should be considered if there is clear evidence of improvement* [D].

### DURATION OF ANTIBIOTIC TREATMENT

This is another area where there is no evidence from randomised controlled trials and is a priority for further research. Only one trial was identified which compared two different treatment durations of the same antibiotic in children with CAP—and this was a new macrolide, azithromycin. The treatment durations described in Appendix 2 are thus based on custom and practice.

## 9 Complications and failure to improve

If a child remains pyrexial or unwell 48 hours after admission, re-evaluation is necessary. Answers to the following questions should be sought:

- Is the patient having appropriate drug treatment at an adequate dosage?
- Is there a lung complication of pneumonia such as a collection of pleural fluid with the development of an empyema or evidence of a lung abscess?
- Is the patient not responding because of a complication in the host such as immunosuppression or coexistent disease such as cystic fibrosis?

### TREATMENT FAILURE

There has been concern that the increased incidence of penicillin resistant *S pneumoniae* would lead to failure of treatment. However, a recent study<sup>84</sup> has shown that there is no difference in the percentage of children in hospital treated successfully with penicillin or ampicillin when the organism was penicillin susceptible or penicillin resistant [III]. The authors noted that the serum concentration of penicillin or ampicillin achieved with standard intravenous dosages was much greater than the MIC for most penicillin resistant strains.

### PLEURAL EFFUSION AND EMPYEMA

Parapneumonic effusions develop in approximately 40% of bacterial pneumonias admitted to hospital. A persisting pyrexia despite adequate antibiotic treatment should always lead the clinician to be suspicious of the development of an empyema. Fluid in the pleural space is revealed on the chest radiograph and the amount of fluid is best estimated by ultrasound examination. There is much current debate on the best management

of parapneumonic effusion and empyema. Where an effusion is present and the patient is persistently pyrexial, the pleural space should be drained.

Lung abscess is a rare complication of CAP in children and suspicion is often raised on the chest radiograph. Diagnosis can be confirmed by CT scanning.<sup>85</sup> Prolonged intravenous antibiotic courses may be required until the fever settles, but it is extremely rare for other interventions to be necessary. Cysts may be present for many months in a well child.

Metastatic infection can rarely occur as a result of the septicaemia associated with pneumonia. Osteomyelitis or septic arthritis should be considered, particularly with *S aureus* infections.

### COMPLICATIONS OF SPECIFIC INFECTIONS

#### *S aureus* pneumonia

Pneumatoceles occasionally leading to pneumothorax are commonly seen with *S aureus* pneumonia. The long term outlook is good with normal lung function.<sup>86 87</sup>

#### *Mycoplasma pneumoniae*

Complications in almost every body system have been reported in association with *M pneumoniae*. Rashes are common; the Stevens-Johnson syndrome occurs rarely; haemolytic anaemia, polyarthritis, pancreatitis, hepatitis, pericarditis, myocarditis and neurological complications including encephalitis, aseptic meningitis, transverse myelitis and acute psychosis have all been reported.

#### Key point

- If a child remains pyrexial or unwell 48 hours after admission with pneumonia, re-evaluation is necessary with consideration given to possible complications [D].

# 10 Prevention and primary care issues

## PREVENTION

Undoubtedly, the general improvements in public health over the last century have contributed greatly to the prevention of CAP. However, there is still more to be done in improving housing, reducing crowding, reducing smoking, and improving the uptake of routine vaccines against *Haemophilus influenzae* type b (Hib) and *Bordatella pertussis*. New acellular pertussis vaccines may also help to reduce the incidence of pertussis by improving primary vaccine coverage and allowing the possibility of booster doses to be given to older children. There are also exciting new vaccines on the horizon which have the possibility of reducing pneumonia due to influenza and *S pneumoniae*.

Although Hib is an uncommon cause of pneumonia, a study of the impact of a Hib conjugate vaccine (albeit in the developing world) indicated that it is probably more common than had been believed.<sup>88</sup> The impact of Hib conjugate vaccine on pneumonia in the UK is not known, but it has presumably declined since Hib vaccination began.

Whooping cough (*Bordatella pertussis*) continues to be seen in the UK with some evidence that increasing numbers are being seen in younger children.<sup>89</sup> Improved uptake of primary pertussis vaccination would help to prevent cases, but another important factor may be an increasing pool of susceptible older children and adults. Booster doses of the current whole cell pertussis vaccine are not an option for this group because of reactogenicity.<sup>90</sup> However, the new less reactogenic acellular pertussis vaccines may become an alternative<sup>91</sup> and might help to reduce cases of pertussis overall.

Influenza is a common cause of respiratory tract illnesses in children and a recognised cause of CAP. Children may also be important in the spread of influenza in the community. In a double blind, placebo controlled, randomised trial in healthy children a live attenuated cold adapted intranasal vaccine had high efficacy (93%) against culture positive influenza.<sup>92</sup> This vaccine was very well tolerated and has the advantage over the inactivated vaccine of not requiring an injection. This raises the possibility of widespread vaccination against influenza in healthy children, but more information is required on the burden of this disease in our community.

Finally, the pneumococcus is known to be the most common bacterium isolated from children with CAP. The pneumococcal polysaccharide vaccine is ineffective in young children but the new conjugate vaccines are immunogenic in infants from 2 months of age.<sup>93</sup> A recent double blind efficacy trial of a pneumococcal conjugate vaccine in the USA found 97.4% efficacy against invasive pneumococcal disease.<sup>94</sup> This raises the prospect of routine use of this vaccine in healthy children, but more data on the burden of pneumococcal disease in our population and the cost effectiveness of vaccination need to be gathered before this could be recommended.

## PRIMARY CARE ISSUES

### Definition

These guidelines refer to childhood pneumonia, a term which may be more helpful to hospital than to primary care physicians. The World Health Organisation term "acute respiratory infection" is regarded as synonymous in describing lower respiratory infections and may be more useful to general practitioners. It also recognises that there is a significant overlap in infants between the clinical pictures of bronchiolitis and viral pneumonia. The guidelines should help to inform primary care management of any child with signs of an acute lower respiratory infection.

### Incidence

Drawing on the Finnish and US data described elsewhere in these guidelines, the average UK general practitioner with a list size of 1700 patients is likely to encounter about 13 cases of childhood pneumonia each year. Most of these will be in children under the age of 5 years and most will be of viral origin.

### Role of the general practitioner

Most children with childhood pneumonia will present to general practitioners and will be managed in the community. The role of the general practitioner is to identify that the child has an acute respiratory infection; to assess severity; to provide information, management advice and medical treatment when necessary; and to monitor progress and recovery.

### Clinical features

The most useful signs are fever, tachypnoea, breathlessness, chest recession, crackles, and bronchial breathing. Headache, abdominal pain or chest pain may be present; cough and wheeze are often unhelpful.

### Severity assessment

Assessment is important both to identify severely ill children who should be referred to hospital and to prevent unnecessary admission of those who can be more effectively managed at home. Severe illness may be characterised by hypoxaemia if pulse oximetry is available and/or suggestive clinical signs such as infants aged <1 year with respiratory rates of 70 breaths/min or more, or tachypnoea and chest recession in older children. Other signs such as vomiting, failure to maintain fluid intake, and the presence of other illness or disability should be taken into account. Admission should be considered where there are concerns regarding the ability of a family to successfully manage an ill child at home. Failure to improve within 48 hours or a deteriorating clinical picture are additional indicators for hospital assessment.

### Investigations

With the exception of pulse oximetry which is useful in assessing severity, these are not helpful

in UK primary care settings. Radiography should be considered only when it assists exclusion of other diagnoses. Microbiological sampling is unhelpful because of the difficulty in obtaining useful samples and the fact that most infections are viral in origin.

**Management**

Community based management is described elsewhere in these guidelines.

**Prevention**

General practitioners should be proactive in trying to:

- reduce exposure to smoking;
- improve the uptake of routine vaccines against *H influenzae* type b (Hib) and *Bordatella pertussis*.

**Comment**

Since 1996 there have been important changes in out of hours provision of primary care in the UK; 80% of out of hours contacts are now provided by general practice cooperatives or deputising services, and most of England is now covered by "NHS Direct", a telephone help line for patients staffed by registered nurses. It is more likely that professionals who are unfamiliar with their medical history and family circumstances will manage patients, and this may make assessment and monitoring more difficult.

"NHS Direct" is algorithm driven; we recommend that the guidelines are used to inform these. The usefulness of pulse oximetry is emphasised in these guidelines, investment in such technology would help assessment and should be considered by out of hours organisations.

## Appendix 1: Search strategy

The search strategies used by the adult group were compiled by Richard Marriot, Senior Medical Librarian at Nottingham City Hospital.

They were revised for children and the subjects regrouped as:

- Incidence
- Aetiology
- Primary care
- Clinical features
- Diagnosis
- Radiology
- Complications
- Antibiotic therapy
- Drug therapy
- Other management
- Nursing
- Prognosis
- Prevention

The rewritten searches were reviewed by Olwen Beaven (Cochrane Cystic Fibrosis Group) in Liverpool who is an information specialist.

The searches were run on an online database (Medline) using Winspirs with Silverplatter as the interface. There were no language restrictions.

The titles and abstracts were screened by one reviewer. If the subject matter looked appropriate a paper was selected (including foreign language articles). Citations from countries where the populations or practice of medicine are very different from our own (for example, Far East, Russia) were excluded unless they focused on universally useful information such as clinical assessment.

Some of the wider searches initially yielded more than 1000 citations and these were limited to English.

Unlike Ovid, Silverplatter requires inputting "child", "infant", etc as thesaurus terms rather than limiting by age. "Adolescence" retrieves adult studies and therefore greatly expanded the hits, but more than half were unsuitable and hopefully covered by the adult guidelines. "Child", "pre-school child", and "infant" were therefore used.

Selected citations were sent to two reviewers per subject. Any disagreements were resolved by discussion.

## Appendix 2: Community acquired pneumonia pharmacopoeia

Drug	Age	Dose	Frequency (× daily)	Notes	Duration	Approx NHS cost price (exc VAT) per course†
<i>Oral treatments:</i>						
Amoxicillin	1 m–2 y	125 mg or 8 mg/kg	3	Dose may be doubled in severe infection	7–10 days*	£2.50
	2–12 y	125–250 mg or 8 mg/kg	3			
	12–18 y	500 mg	3			
Azithromycin	6 m–2 y	10 mg/kg	1		5 days	£13.50
	3–7 y	200 mg	1			
	8–11 y	300 mg	1			
	12–14 y	400 mg	1			
	≥14 y	500 mg	1			
Cefaclor	≤1 y	62.5 mg	3		7–10 days*	£12.00
	1–5 y	125 mg	3			
	6–12 y	250 mg	3			
	12–18 y	250 mg	3			
		375 mg (MR tablets)	2			
Clarithromycin	birth–1 y	7.5 mg/kg	2		7–10 days*	£17.00
	1–2 y	62.5 mg	2			
	3–6 y	125 mg/kg	2			
	7–9 y	187.5 mg	2			
	10–12 y	250 mg	2			
	12–18 y	250 mg	2			
Co-amoxiclav	birth–1 y	0.266 ml/kg (125/31 suspension)	3	Doses may be doubled in severe infections; Augmentin Duo is an alternative preparation given twice daily (see BNF)	7–10 days*	£9.00
	1–6 y	5 ml (125/31 suspension)	3			
	7–12 y	5 ml (250/62 suspension)	3			
	12–18 y	1 tablet (250/125)	3			
Erythromycin	birth–1 m	10–15 mg/kg	3	Doses may be doubled in severe infections	7–10 days*	£2.00
	1 m–2 y	125 mg	4			
	2–8 y	250 mg	4			
	9–18 y	500 mg	4			
<i>Intravenous treatments:</i>						
Amoxicillin	1 m–18 y	30 mg/kg	3	Dose may be doubled in severe infection (max daily dose 4 g)	Based on clinical response and ability to tolerate oral treatment	£20.00
Ampicillin	1 m–18 y	25 mg/kg	4	Max single dose 1 g (severe infection: max single dose 3 g)	Based on clinical response and ability to tolerate oral treatment	£22.00
	IV infusion	100 mg/kg	4			
Benzyl penicillin	1 m–12 y	25 mg/kg (50 mg/kg)	4	In severe infections doses of 50 mg/kg may be given 6 times daily (max 14.4 g/day)	Based on clinical response and ability to tolerate oral treatment	£17.50
		50 mg/kg	6			
	12–18 y	300–600 mg (2.4 g)	4			
			6			
Cefotaxime	1 m–12 y	50 mg/kg	2	The frequency may be increased to four times daily in severe infections	Based on clinical response and ability to tolerate oral treatment	£72.50
	12–18 y	1–3 g	2			
Cefuroxime	<7 days	30 mg/kg	2	20 mg/kg is appropriate for most infections	Based on clinical response and ability to tolerate oral treatment	£39.50
	>7 days	30 mg/kg	3			
	1 m–18 y	10–30 mg/kg	3			
Co-amoxiclav	1 m–12 y	30 mg/kg	3	Dosage based on co-amoxiclav content. Over 3 months of age dose frequency can be increased to 4 times daily in severe infections	Based on clinical response and ability to tolerate oral treatment	£44.50
	12–18 y	1.2 g	3			

\*May need up to 14 days depending on clinical response. †For 10 year old patient of weight 30 kg (approx). Doses are based on information contained in the following texts: BNF No 38; Data Sheet Compendium 1998/99; Alder Hey Book of Children's Doses (1996); Guy's, St Thomas' and Lewisham Paediatric Formulary 4th Edition; Medicines for Children 1999. The ages ranges used are those suggested by the British Paediatric Association and the Association of the British Pharmaceutical Industry. Information prepared by Paula Hayes MRPharms, RLC NHS Trust.

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