

## Bacteremic Pneumococcal Pneumonia in Children

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We carried out a nationwide retrospective study on bacteremic pneumococcal pneumonia diagnosed from 1985 to 1994 in Finland. The records of 85 children were reviewed for symptoms, signs, laboratory data, and response to antibiotic therapy. The chest radiographs were reevaluated. Bacteremic pneumococcal pneumonia was characterized by high fever ( $\geq 39.0^{\circ}\text{C}$  in 93%), leukocytosis (WBC count on admission of  $\geq 15 \times 10^9/\text{L}$  in 84%), and ill appearance (in 79%). Lobar or segmental consolidation was found in 79% of the chest radiographs. Of the patients, 28% had no respiratory symptoms, 6% presented with only gastrointestinal symptoms in addition to fever, and 4% had fever only. Tachypnea was recorded in 19% and rales in 14% of the patients. After onset of antimicrobial treatment, children became afebrile within an average of 22 hours. One patient developed pleural empyema, and none of the patients died.

*Streptococcus pneumoniae* is the most common bacterial cause of community-acquired pneumonia in children [1–3]. The isolation of *S. pneumoniae* from blood remains the reference standard for the etiologic diagnosis of pneumococcal pneumonia, but diagnosis is based on blood culture for only 1%–3% of cases of pneumonia requiring hospitalization in developed countries [3–5]. In developing countries, an estimated 1 million deaths per year among children <5 years old are attributable to pneumococcal pneumonia [6]. Bacteremic pneumococcal infections are potentially life-threatening diseases also in developed countries, despite modern intensive care [7, 8]. Therefore, it is important to clarify clinical characteristics that may aid early diagnosis. Several studies of bacteremic pneumococcal infections have been conducted [7–12], but few data are available concerning the clinical and laboratory characteristics of bacteremic pneumococcal pneumonia in children.

We carried out a nationwide search in Finland for cases of pneumococcal pneumonia diagnosed by positive results of blood culture during a period of 10 years. The symptoms and signs, laboratory data, and radiographic findings of 85 cases are reported.

### Methods

**Subjects and study design.** In 1985, a nationwide surveillance system was set up to cover all serious bacterial infections

in children <16 years of age in pediatric hospitals ( $n = 36$ ) and microbiological laboratories ( $n = 25$ ). In addition to the intensified surveillance system, all laboratories report their positive results of culture of blood for bacteria to the National Board of Health. According to these records of the National Public Health Institute in Helsinki, 867 children had blood culture-confirmed pneumococcal bacteremia diagnosed in Finland during 1 January 1985 through 31 December 1994. Of these patients, 144 (16.6%) were reported to have had pneumonia. The chest radiographs were reevaluated by a pediatric radiologist unaware of the etiology. The diagnosis of pneumonia in this study was made if infiltrates compatible with pneumonia on the chest radiograph were found simultaneously with fever ( $>37.5^{\circ}\text{C}$ ). Forty patients were excluded because the radiographs were not available for the reevaluation, and 15 patients were excluded because infiltrates compatible with pneumonia were not found on the chest radiograph at the reevaluation. Four patients were excluded because their records were not available. Finally, the medical records and chest radiographs of the remaining 85 patients from 19 hospitals were reviewed.

**Statistical analysis.** The distributions of C-reactive protein (CRP) levels, WBC counts, duration of fever, and duration of all symptoms were skewed. Statistical analysis between two groups was conducted by use of the Mann-Whitney test and between three groups by the Kruskal-Wallis test.  $P < .05$  was considered statistically significant.

### Results

**Patient characteristics.** The mean age of the patients was 3.6 years (range, 0.4–15.8 years), and 65% of the 85 patients were boys. All patients were treated in the hospital. One child was African, and the rest were Caucasians. Twenty-three patients (26%) had a history of an underlying illness (table 1).

**Epidemiology and serogroups.** There was a seasonal variation in the number of cases of bacteremic pneumococcal pneumonia, with the peaks during May and December. The

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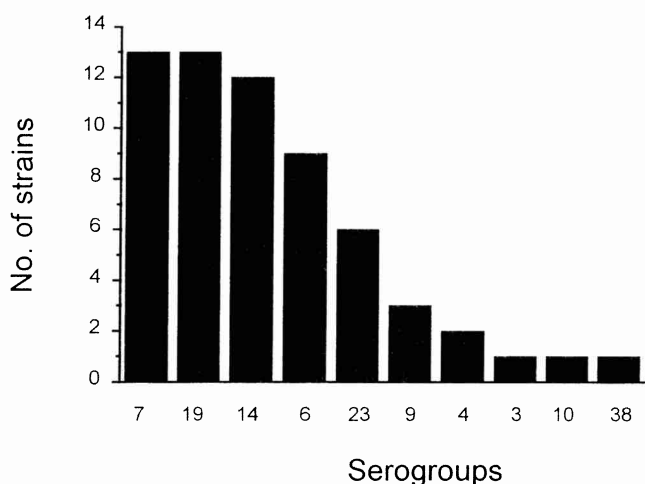
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**Table 1.** Underlying illnesses in 85 Finnish children with bacteremic pneumococcal pneumonia during 1985–1994.

Underlying illness	No. (%)
None	62 (73)
Recurrent respiratory infections	8 (9)
Asthma	3 (4)
Down syndrome	3 (4)
Severe heart disease	1 (1)
Hydronephrosis	1 (1)
Lipoid nephrosis	1 (1)
Chromosomal abnormality	1 (1)
Bronchopulmonary dysplasia	1 (1)
Ectodermal dysplasia	1 (1)
Hemiplegia	1 (1)
Congenital hydrocephalus	1 (1)
Encephalopathy	1 (1)

**Figure 1.** Serogroup distribution of 61 pneumococcal strains causing pneumonia in children in Finland between 1985 and 1994.

serogroups of 61 strains are presented in figure 1. Of the 53 *S. pneumoniae* isolates with antibiotic susceptibility data available, all were susceptible to penicillin.

**Presenting symptoms.** The most common symptoms (according to parental reporting) before admission are presented in table 2. Respiratory symptoms (cough and/or nasal symptoms) were recorded for 72% of the patients; 38% had gastrointestinal symptoms (vomiting, diarrhea, or abdominal pain). Five patients (6%) had only gastrointestinal symptoms in addition to fever. Fever as the only symptom was recorded in 4% of the patients. The duration of symptoms before admission was on average 5.0 days (median, 3.0 days; range, 0.5–30.0 days). Fever had lasted an average of 2.4 days (median, 2.0 days; range, 0–14 days) before admission. The mean of the highest body temperature before or on admission was 39.7°C (median, 40.0°C; range, 38.3–41.2°C), and 93% of the patients had a body temperature of  $\geq 39.0^\circ\text{C}$  before or on admission (data available from 67 patients).

**Clinical signs.** The most common sign was ill appearance (table 2). Results of lung auscultation were recorded as normal for 29% of the patients. Nine patients had otitis media, and six patients had maxillary sinusitis. Meningitis was suspected in 14 children (16%), but for all of them, culture of CSF was negative.

**Radiological findings.** Alveolar infiltrations were observed in most cases (table 3). Patients with lobar pneumonia had been febrile longer than were patients with nonlobar pneumonia (median, 2.5 days; range, 0.5–14 days; vs. median, 1 day; range, 0–14 days;  $P = .043$ , Mann-Whitney test). There was no difference in duration of illness before admission between these patient groups (median, 3 days; range, 0.5–30 days for each group;  $P = .090$ ).

**Laboratory data.** WBC counts, CRP levels, platelet counts, and sodium values on admission are listed in table 3. On admission, 4% of the patients had both WBC counts of  $4\text{--}15 \times 10^9/\text{L}$  and CRP levels of  $<20 \text{ mg/L}$ . Of 12 patients who had a WBC count of  $<15 \times 10^9/\text{L}$  on admission, 7 (58%) had a CRP level of  $>60 \text{ mg/L}$  (suggested screening value for pneumococcal pneumonia [13]). Patients with CRP levels of  $>60 \text{ mg/L}$  had been febrile longer (median, 2 days) than were patients with CRP levels of  $<20 \text{ mg/L}$  (median, 1 day;  $P < .001$ , Mann-Whitney test). The median WBC counts and CRP levels from day 0 (on admission) to day 4 are shown in figure 2. Patients with lobar pneumonia had significantly higher CRP levels than did patients with segmental or other pneumonias from day 0 to day 3 (data not shown). No differences were found in WBC counts between groups. Among all patients who had WBC counts of  $<15 \times 10^9/\text{L}$  on admission, WBC counts

**Table 2.** Symptoms and clinical signs on admission among 85 children with bacteremic pneumococcal pneumonia.

Symptom or sign	No. (%)
Fever ( $>37.5^\circ\text{C}$ )	84 (99)*
Cough	47 (55)
Nasal symptoms	42 (49)
Lethargy or irritability	33 (39)
Vomiting	27 (32)
Abdominal pain	10 (12)
Poor eating or poor drinking	18 (21)
Dyspnea	9 (11)
Chest pain	7 (8)
Febrile seizures	6 (7)
Headache	6 (7)
Diarrhea	2 (2)
Ill appearance	67 (79)
Rhonchi	36 (42)
Tachypnea	16 (19)
Tachycardia	13 (15)
Rales/crackles	12 (14)
Dehydration	11 (13)
Decreased breath sounds	9 (11)
Cyanosis	5 (6)

\* One patient became febrile in hospital.

**Table 3.** Radiological and laboratory findings on admission among children with bacteremic pneumococcal pneumonia.

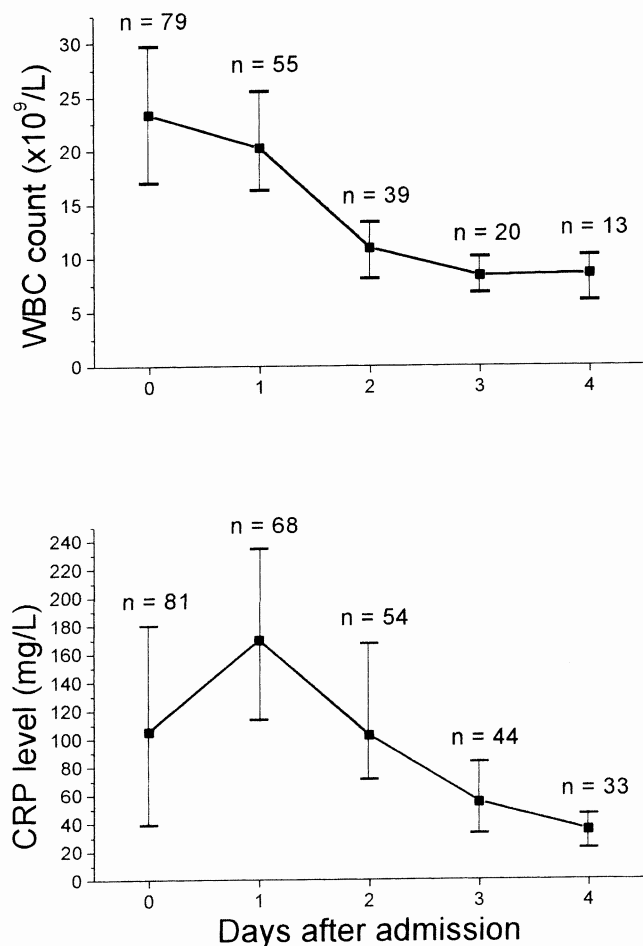
Finding	No. (%)
Chest radiographic finding (n = 85)	
Infiltrations	
Alveolar	71 (84)
Interstitial	8 (9)
Alveolar and interstitial	6 (7)
Localization	
Right lung	45 (53)
Left lung	28 (33)
Bilateral	12 (14)
Segmental consolidation	35 (41)
Lobar consolidation	32 (38)
Pleural fluid	17 (20)
Atelectasis	13 (15)
Enlarged lymph nodes	6 (7)
Hyperaeration	1 (1)
Pneumothorax	1 (1)
Laboratory parameter	
WBC count ( $\times 10^9/L$ ) (n = 79)	
<4.0	0
4.0–9.9	4 (5)
10.0–14.9	8 (10)
15.0–19.9	19 (24)
20.0–29.9	30 (38)
$\geq 30.0$	18 (23)
Neutrophils (%) (n = 27)	
<60.0	2 (7)
60.0–69.9	5 (19)
70.0–79.9	9 (33)
80.0–89.9	8 (30)
$\geq 90.0$	3 (11)
C-reactive protein level (mg/L) (n = 81)	
<20	12 (15)
20–59	14 (17)
60–179	34 (42)
$\geq 180$	21 (26)
Sodium level (mmol/L) (n = 52)	
<130	5 (10)
130–134	19 (37)
$\geq 135$	28 (54)
Platelet count ( $\times 10^9/L$ ) (n = 44)	
<150	0 (0)
150–400	30 (68)
>400	14 (32)

were higher on the following day. WBC counts and CRP levels increased after admission for 34% and 74% of the patients, respectively. High body temperature ( $\geq 39.0^\circ\text{C}$ ) with leukocytosis (WBC count of  $\geq 15 \times 10^9/L$ ) and lobar or segmental consolidation on the chest radiograph was found among 70% of the patients (all of these data available from 63 patients). A WBC count of  $\geq 15 \times 10^9/L$  and/or CRP level of  $>60$  mg/L with high body temperature ( $\geq 39.0^\circ\text{C}$ ) and lobar or segmental consolidation on the chest radiograph were found among 76% of the patients (data available from 63 patients).

**Antibiotic treatment.** One child was receiving antibiotic treatment at admission (oral trimethoprim-sulfamethoxazole).

In hospital, all patients received antibiotic treatment. Initially, 73 patients received iv antibiotic therapy (penicillin, 48; cefuroxime, 24; ceftriaxone, 1), 5 patients received im antibiotic therapy (penicillin, 4; cefuroxime, 1), and 7 patients received oral antibiotic therapy (erythromycin, 3; penicillin, 2; amoxicillin, 1; and trimethoprim-sulfamethoxazole, 1). Four children were treated with oral antibiotics only. *S. pneumoniae* was susceptible in vitro to the antibiotics used.

**Outcome.** The records of body temperatures (measured about four times a day) were available from 77 patients. On average, fever lasted for 22 hours (median, 12 hours; range, 2–192 hours) after initiation of antibiotic treatment. Duration of fever of  $>48$  hours was documented for 5 (6%) of 77 patients. One of these patients had pleural empyema, one had pleural fluid, one had encephalopathy, one had hydrocephalus, and one had a history of recurrent respiratory infections. The mean duration of hospitalization was 5.5 days (median, 5 days; range, 1–21 days). None of the patients died. Six percent of the patients developed a new episode of pneumonia during the



**Figure 2.** WBC counts and C-reactive protein (CRP) levels among children with bacteremic pneumococcal pneumonia. Data are medians with 25th and 75th percentiles. Values from day 0 (on admission) to day 4 and number of measurements (n) each day are shown.

following month (follow-up records were available from 48 patients). One patient had blood culture–confirmed pneumococemia without infection focus four weeks after discharge.

## Discussion

Our observations confirm that most children with bacteremic pneumococcal pneumonia have a typical illness with high body temperature ( $\geq 39.0^{\circ}\text{C}$ ), leukocytosis (WBC count of  $\geq 15 \times 10^9/\text{L}$ ), and lobar or segmental consolidation on the chest radiograph [9, 10, 14, 15]. However, as many as 30% of the patients had an atypical illness (8% having only one and 22% having two of the three characteristics), which demonstrates the clinical variability of bacteremic pneumococcal pneumonia.

We found that bacteremic pneumococcal pneumonia usually began with prodromal symptoms, such as cough, rhinitis, or vomiting, which developed during one to several days, and were later followed by high fever. It should be noted, however, that one-fourth of the patients presented without any respiratory symptoms, and 9% of the children had neither symptoms nor signs of respiratory tract infection. In a recent study by Totapally and Walsh [8], 18% of children with bacteremic pneumococcal pneumonia had no respiratory symptoms or signs. Our finding that 38% of the patients presented with gastrointestinal symptoms is consistent with previous reports [8, 16]. Gastrointestinal symptoms, especially in the absence of any indication of respiratory infection, may be misleading in the diagnostic workup of a child with pneumonia, which supports the view that a chest radiograph should be obtained from children with high fever ( $\geq 39.0^{\circ}\text{C}$ ) and ill appearance, these being the most common findings in the children in the present study.

Seventy-nine percent of the children with bacteremic pneumococcal pneumonia appeared ill. In a study of hospitalized children with nonbacteremic community-acquired pneumonia in Finland, only 32% of the children were considered to be moderately to severely ill [3]. In the present study, tachypnea was uncommon, but the respiratory rate was not counted systematically. Usually when marked tachypnea is present, its clinical appearance is evident and it is recorded. Many studies have suggested that tachypnea is the best clinical sign distinguishing children with pneumonia from children with uncomplicated upper respiratory tract infection [17–19]. In this study rales (crackles) were present in 14% of the patients. Earlier it has been shown that rales are usually present on auscultation in 30%–46% of children with pneumonia [17, 20–23]. Finally, rales on auscultation and/or tachypnea—the two suggested signs of pneumonia—were documented in only 26% of the patients. Eleven percent of the children in the present study had decreased breath sounds, whereas in a recent, retrospective study, Tan et al. [23] documented them in 55% of children with pneumococcal pneumonia. However, all the findings should be considered with care because of the retrospective nature of these studies.

Laboratory findings were normal for some patients with

bacteremic pneumococcal pneumonia on admission. Of note, WBC counts seemed to increase more rapidly than did CRP levels. The highest WBC counts were usually detected on admission, whereas the highest CRP values were detected not until the day after admission (figure 2). The WBC counts also decreased more rapidly than did CRP levels in response to antibiotic therapy. A CRP level of  $>60$  mg/L has been suggested to be a screening value for pneumococcal pneumonia [13]. In our study, 58% of the patients with WBC counts of  $<15 \times 10^9/\text{L}$  had CRP levels of  $>60$  mg/L on admission, suggesting that it is practical to use both WBC count and CRP level in screening for pneumococcal pneumonia.

Several studies have shown that bacterial pneumonia cannot be differentiated from nonbacterial pneumonia on the basis of the chest radiograph [24–26], but lobar or segmental consolidation in the chest radiograph has been associated with pneumococcal pneumonia both in children and in adults [10, 14]. We found that bacteremic pneumococcal pneumonia in children sometimes presented as interstitial infiltrations, and one-fifth of the patients did not have lobar or segmental consolidation in their chest radiograph at the time of diagnosis. Infiltrations in the chest radiograph change during the course of an illness, and whether the consolidation in the chest radiograph is classified as lobar may, thus, depend on the stage of the infection. Higher CRP levels in patients with lobar pneumonia compared with those in patients with segmental or other pneumonia may reflect relatively greater tissue destruction. Although *S. pneumoniae* was the etiologic agent for the pneumonia found, we cannot exclude the possibility of other microbial involvement, because etiologic tests, except culture of blood, were rarely performed. Mixed viral-bacterial infections are common in childhood pneumonia [27–29], but bacterial-bacterial infections have also been detected [28, 30, 31]. Consequently, other microbes may have had an impact on findings on chest radiography.

Most patients became afebrile within 24 hours, indicating a rapid response to antibiotics. In our study, the incidence of complications was low; only one patient who had fever during antibiotic treatment for 8 days developed an empyema. None of the children died. In pneumococcal bacteremia, the mortality rate in children has varied from 1% to 7% in developed countries [10, 16, 32–36].

In conclusion, although the majority of children with bacteremic pneumococcal pneumonia have typical illness, the diagnosis may be difficult because many patients in developed countries may not have tachypnea and rales. Additionally, some patients appear well, present without respiratory symptoms, and have normal laboratory findings in the early phase of the infection.

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