

# Antibiotic treatment of pneumonia and bronchiolitis

## A prospective randomised study

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**SUMMARY** Routine administration of antibiotics in the treatment of pneumonia and bronchiolitis in infants and small children was evaluated in an open randomised prospective trial. From 1979–82 136 children between the age of 1 month and 6 years were allocated to one of two treatment groups shortly after their admission to a paediatric ward. Group A patients were to be given antibiotics but those in group B were not. None of the children had received antibiotics before hospital admission. A viral infection was diagnosed in 38 of the 72 patients from group A and in 34 of the 64 patients from group B. Respiratory syncytial virus was detected in 84% of these patients. Samples of tracheal secretions showed no differences between the groups in respect of cytology and bacterial flora. Nor were there any significant differences in the course of acute disease, the frequency of fever relapse and pulmonary complications. Fifteen patients from group B were subsequently treated with antibiotics: two of these developed secondary purulent infections of the middle ear and one showed a slight pleural effusion. These results do not support the routine use of antibiotics in infants and small children admitted to hospital with pneumonia and bronchiolitis.

Antibiotic treatment of lower respiratory tract infections may be curtailed now that more rapid techniques for detecting viruses have been developed.<sup>1</sup> In infants and small children immunofluorescent antibody test is especially useful in the acute stages of bronchiolitis and pneumonia often caused by infections with respiratory syncytial virus during epidemic occurrence of this agent. A single controlled trial has shown that antibiotic treatment of acute bronchiolitis is of no benefit,<sup>2</sup> but there is still uncertainty over the usefulness of antibiotics in viral pneumonia with radiological consolidation.<sup>1 3</sup> The presence of potentially pathogenic bacteria in the respiratory tract and suppression of local macrophage function in lung tissue during viral infections<sup>4</sup> may enhance the susceptibility to secondary bacterial infections.

We carried out an open randomised prospective trial to evaluate the benefit of antibiotic treatment in children with pneumonia. One group of children (group A) was allocated to standard antibiotic

treatment and the other (group B) was to receive no antibiotics. The course of acute disease and the frequency of fever relapse were determined, together with pulmonary complications, secondary bacterial infections, and subsequent indications for antibiotic treatment. Results of virological and bacteriological investigations performed on samples of respiratory secretions obtained shortly after admission to hospital and results of viral antibody studies on paired serum samples were used to compare the possible effect of antibiotic treatment on viral pneumonia in children.

### Patients and methods

**Patients investigated and study design.** A total of 150 children (53 girls and 97 boys) with pneumonia, admitted to two paediatric wards between December 1979 and November 1982, were initially included in the investigations. These patients had all been ill for less than one week and had not received

antibiotics before hospital admission. The diagnosis of pneumonia was based on either fine crepitating rales at auscultation or pulmonary consolidation on chest radiograph. The children were allocated to group A (antibiotic treatment) or group B (no antibiotic treatment) immediately after hospital admission. This allocation was done as a block randomisation for each group of 20 consecutive patients to obtain an equal representation of respiratory syncytial virus infections in the two groups. Children with chronic pulmonary or cardiac disease, mental retardation, or oncologic diseases were not included; nor were children with severe breathing difficulties or cyanosis, who needed oxygen treatment or artificial ventilation, and those with suspected septicaemia. It was decided that children allocated to group B should receive antibiotics where they developed cyanosis, bacterial complications, or fever lasting more than four days after admission in the absence of viral infection diagnosed by immunofluorescent antibody test.

Seventy two patients (25 girls and 47 boys) were allocated to group A and 66 (20 girls and 46 boys) to group B. Two boys from group B were later excluded as they did not conform to the inclusion criterion. Therefore, the eventual number of patients allocated to group B was 64. Twelve children with severe breathing difficulties were considered to be too ill to be included in the study. They underwent the same diagnostic investigations and a viral disease was diagnosed in seven of them. Fifteen children from group B received antibiotics later on during their stay in hospital, eight of them within the first three days. These 15 patients are referred to as group B<sup>a</sup> and the 49 patients who did not receive antibiotics as group B<sup>o</sup>.

The median age in group A was 18 months (range 1 to 61 months) and in group B 17.5 months (range 1 to 62 months). Twenty eight children from group A, 18 from group B<sup>o</sup>, and two from group B<sup>a</sup> were under 12 months of age.

The duration of fever before admission, estimated on the basis of rectal temperature measurements,

was mean (SD) 1.7 days (1.7 days) for group A and 1.8 days (1.5 days) for group B.

**Virus detection.** Samples of nasopharyngeal secretions were obtained within 24 hours of hospital admission by suction through a nasal catheter. These samples, supplemented with transport medium, were taken to the laboratory in a cooling container within three hours. The indirect immunofluorescent antibody test was applied to spots of nasopharyngeal secretion cells which had been dried and fixed to slides. This method has been described.<sup>5</sup> The following antisera were used: influenza A virus, influenza B virus, parainfluenza 1 virus, parainfluenza 3 virus, and respiratory syncytial virus.

Fresh unfrozen samples of nasopharyngeal secretions were inoculated immediately into tissue cultures of HEP 2 cells to isolate respiratory syncytial virus or adenovirus, or into tissue cultures of primary monkey kidney cells with the purpose of isolating influenza virus. The identification of isolated viruses has been described.<sup>5</sup> About 60% of the nasopharyngeal secretion samples investigated by immunofluorescent antibodies were tested by tissue culture (Table 1).

Almost 80% of the nasopharyngeal secretion samples were also tested by the double antibody sandwich ELISA for respiratory syncytial virus antigen as described previously (Table 1).<sup>6</sup> This ELISA was performed on microtitre plates by use of an antiserum to respiratory syncytial virus polypeptides both as 'capture' antibody and as conjugate.<sup>6,7</sup>

**Serum antibody determinations.** Paired serum samples were obtained from 114 of the 136 patients at an interval of three weeks. Complement fixing antibodies were determined in respect of the following viral antigens: influenza A, influenza B, parainfluenza 1, adenovirus, and respiratory syncytial virus. In addition, complement fixing antibodies were determined for *Mycoplasma pneumoniae* and

Table 1 Number of different virological examinations and frequency of positive results in 136 infants and children with pneumonia allocated to 2 treatment groups (group A + antibiotics and group B - antibiotics)

Virus detection method	Group A (n=72)		Group B (n=64)	
	No	Positive (%)	No	Positive (%)
Immunofluorescent antibody test (NPS)	72	26 (36)	64	20 (31)
Tissue culture (NPS)	42	14 (33)	41	10 (24)
Respiratory syncytial virus antigen ELISA (NPS)	51	22 (43)	51	14 (27)
Respiratory syncytial virus IgM antibody ELISA (serum)	60	16 (27)	54	12 (22)
Respiratory syncytial virus IgG antibody ELISA (serum)	54	22 (41)	53	23 (43)
Complement fixing antibodies (serum)	59	23 (39)	55	24 (44)

NPS=nasopharyngeal secretion.

chlamydia. A four fold or higher rise in complement fixing antibody titre was considered significant.

Respiratory syncytial virus IgG antibodies were determined by an ELISA method described previously (Table 1).<sup>7</sup> A definite increase in IgG antibody concentration between two samples represents more than a doubling of the originally derived values.<sup>7</sup> Respiratory syncytial virus IgM antibodies were also determined by ELISA as described recently (Table 1).<sup>8</sup> In this reverse ELISA technique, due consideration was taken of possible interference by rheumatoid factor.

**Bacteriological investigations.** Tracheal suction was performed within 12 hours of hospital admission and before antibiotics were given. A sterile Thieman catheter (size 8) was passed blindly into the laryngeal aditus, where suction was performed. The catheter was withdrawn without suction in the nasopharynx. Gram stained films were examined under microscope and epithelial cells, number of leucocytes, and predominant bacterial flora were described. A differentiation between secretions of pure pharyngeal origin and secretions containing bronchial epithelial cells was made. A drop of sediment was cultured by use of standard methods. The following were regarded as normal pharyngeal flora:  $\alpha$ -haemolytic streptococci, coagulase negative staphylococci, *Bacillus species*, coryneforme rods, *Candida species*, and Gram negative diplococci (not *Neisseria meningitidis*). Other organisms were considered to be potentially pathogenic in the respiratory passages. They were roughly quantified as a few, several, or many according to the outmost strike in which they grew. These organisms were isolated, identified, and sensitivity tested. The organisms looked for especially were *Streptococcus pneumoniae*, *Haemophilus influenzae*,  $\beta$ -haemolytic streptococci, *Staphylococcus aureus*, enteric Gram negative rods, *Pseudomonas aeruginosa*, and *Neisseria meningitidis*. Findings of potentially pathogenic bacteria in group B patients did not necessarily indicate antibiotic treatment.

**Clinical registration.** Consecutive clinical examinations were performed by one of the paediatricians responsible for the trial, except for the very first examination on admission to hospital. Respiratory rate, cyanosis, coughing, amount of secretion, chest retractions, wheezing, and pulmonary stethoscopic changes were recorded on the first, second, and third days, and either the seventh day or the day of discharge which ever was the earlier. The rectal body temperature was measured daily at 7 am and 4 pm.

The duration of fever after hospital admission was

measured as the time from admission to regaining normal temperature (37°C in the morning and 37.5°C in the afternoon). Before the study began it was decided that a difference of less than 48 hours in duration of fever was of no clinical importance. A child was regarded as 'pulmonarily healthy' when there were no clinical signs of pneumonia and normal findings at auscultation.

The children were examined again at a follow up visit three weeks after discharge from hospital. During the intervening period a questionnaire was filled in daily by the parents.

A blood sample, taken soon after admission, was used for white blood cell count and for serology. A second blood sample for serology was obtained at the follow up visit. A chest radiograph (front and side position) was taken early after admission and at follow up.

**Antibiotics.** Ampicillin, 100 mg/kg/24 hours orally in three doses for six days, was used for children under 2 years of age. In those aged over 2 years, V penicillin 300 000 IU three times a day was given for six days (that is 50 000 to 100 000 IU/kg/24 hours). In cases of penicillin allergy, erythromycin (Abbotin) 30 to 50 mg/kg/24 hours in three doses was given for six days. Where resistant strains were found the antibiotic treatment was changed in accordance with results of sensitivity tests.

**Ethical considerations.** As it is a well established practice in Denmark to treat pneumonia in small children with antibiotics, an open study was chosen for ethical reasons. The study was approved by the local ethical committee on human investigation. In all cases informed consent was obtained from the parents.

**Statistics.** The differences between the groups of patients investigated with respect to duration of fever were determined by rank sum test for unpaired data (Wilcoxon's test). The 95% confidence limits for the medians were taken from *Documenta Geigy* (Sixth edition, p 105). The  $\chi^2$  test, the medians, mean, standard deviation, standard error of mean, and range were determined for other observations. Level of significance: 5%.

## Results

**Virus infections detected.** An equal distribution of virus infections was detected in groups A and B (Tables 1 and 2). Fifty three per cent of the children had a viral infection diagnosed. This diagnosis was based on findings in nasopharyngeal secretions in 55 of the 72 virus infected patients. Respiratory syncy-

Table 2 Number of virus infections detected in 136 infants and children with pneumonia allocated to 2 treatment groups (group A + antibiotics and group B - antibiotics)

Virus infection detected	Group A (n=72)	Group B (n=64)
Respiratory syncytial virus	34 <sup>†</sup>	27 <sup>†</sup>
Influenza A	0	1
Influenza B	2	2
Parainfluenza	0	2
Adenovirus	2	2

<sup>†</sup> Respiratory syncytial virus infections: 23 in group A and 16 in group B based on immunofluorescent antibody technique. Five in group A and 8 in group B based on serology.

<sup>‡</sup> One of these patients also had influenza B.

tial virus was present in 84% of the virus infected children. In five patients from group A and in eight from group B the respiratory syncytial virus diagnosis was based on serological results alone. One patient from group A had a double infection with influenza B virus and respiratory syncytial virus. In three children an appreciable complement fixing antibody titre rise to *Mycoplasma pneumoniae* was found together with virus infections.

In only one of the 15 group B<sup>a</sup> patients (allocated to treatment without antibiotics but subsequently given these) was a viral infection (respiratory syncytial virus) detected by immunofluorescent antibody test on admission. Eight other patients from group B<sup>a</sup> had viral infections detected by antibody determination. The final diagnoses in these nine patients were: respiratory syncytial virus (6), influenza B virus (1), and adenovirus (2) infections.

Viral infection was diagnosed in 80% of the children aged under 1 year, in 55% of those between 1 and 2 years, and in only 33% of those aged over 2 years.

**Bacteriological findings.** There were no differences between groups A and B with regard to the cytology and the bacterial flora of the tracheal secretions. Forty four per cent of the tracheal secretions obtained contained bronchial epithelial cells. The rest were secretions from upper airways. Only 25% of the secretions contained large amounts of leucocytes and germs. Normal throat flora were obtained in all secretions. Most of the secretions grew either *S pneumoniae* or *H influenzae*, or both. No obvious difference was found in the growth of pathogens in secretion from patients with respiratory syncytial virus infections and patients without diagnosed viral infection (Fig. 1).

No chlamydial infection was detected by the complement fixation method used.<sup>8</sup>

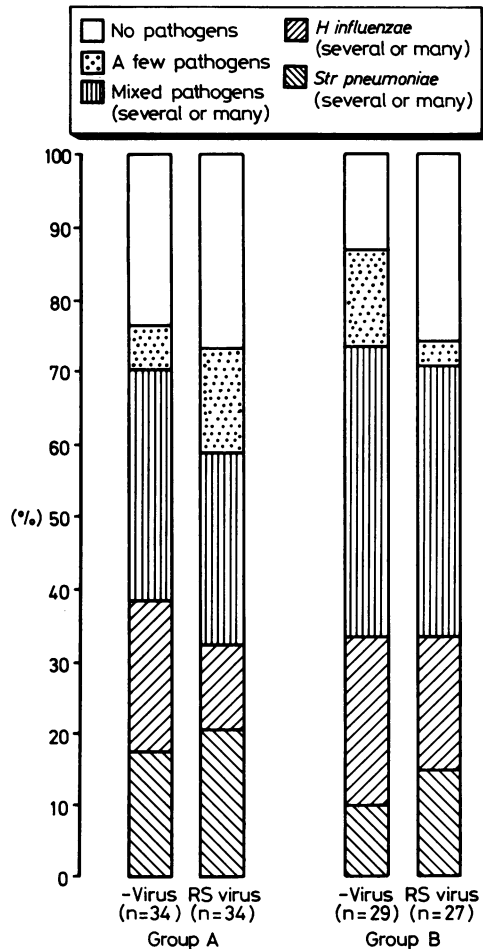


Fig. 1 Bacterial findings in tracheal secretions from 124 patients with pneumonia allocated to 2 treatment groups (group A + antibiotics and group B - antibiotics).

The percentage distribution quantified as a few, several, or many in patients with respiratory syncytial (RS) virus and those with no detectable virus is given.

**Clinical findings**

*Fever*

A difference of 18.5 hours between groups A and B was found in the median duration of fever after hospital admission (Fig. 2). Nearly the same differences were found when the medians of the respiratory syncytial virus subgroups of A and B and the subgroups of A and B in which no viral infection was found were compared (Fig. 2). The differences

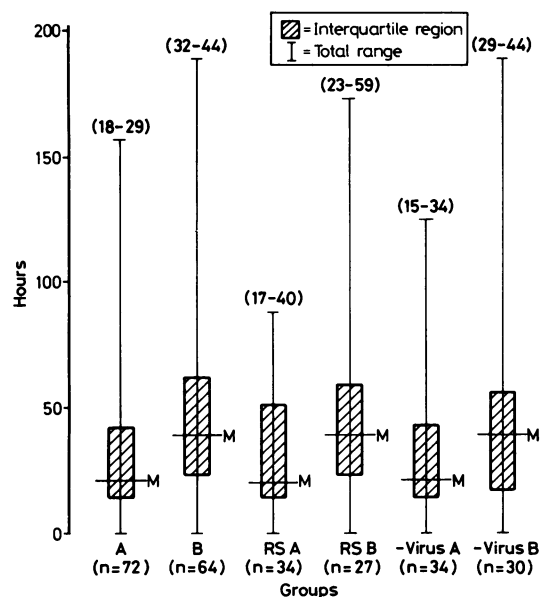


Fig. 2 Median duration of fever after hospital admission in various subgroups of children with pneumonia allocated to 2 treatment groups (group A + antibiotics and group B - antibiotics).

RS virus=respiratory syncytial virus; M=median. The 95% confidence limits for the different medians are given in the parentheses.

observed were not significant ( $P > 0.05$ ). The median duration of fever for the groups were: group A 20.5 hours (range 0 to 157 hours), group B 39 hours (range 0 to 189 hours) and group B<sup>a</sup> 38 hours (range 0 to 116 hours). In three children from group B with respiratory syncytial virus infections which had been diagnosed on the basis of serology alone, the duration of fever was prolonged. These children may have caught their respiratory syncytial virus infections during their stay in hospital, as no other reasons for the prolonged periods of fever were found.

Nine children from group A and six from group B had no fever after hospital admission. In 48 children (21 from group A, 18 from group B<sup>a</sup> and 9 from group B<sup>b</sup>) the temperature was raised to above 39°C. In 25 of these patients a viral infection was diagnosed.

Eight patients from group B<sup>a</sup> were given antibiotics before their temperature returned to normal. They continued to have fever for two to four days after starting antibiotics, except for one patient with otitis media and complicating mastoiditis, who responded well to antibiotics within 24 hours.

### Pulmonary symptoms

No difference was found between the groups with regard to the duration of pulmonary symptoms (Table 3). This also applies to the two groups of patients with respiratory syncytial virus infections (Table 4). Pulmonary symptoms in about 40% of the children resolved by day three. On the day of discharge and at the follow up visit, about 80% were without clinical symptoms or signs of pulmonary disease (Tables 3 and 4). The respiratory rate in all

Table 3 Clinical observations and duration of hospital stay in 136 children with pneumonia allocated to two treatment groups (group A + antibiotics and group B - antibiotics)

	Group A (n=72)	Group B (n=64)
<i>Duration of hospital stay (days)</i>		
Mean (SE) range	4.9(0.2)2-11	5.6(0.4)2-15
<i>Respiratory frequency (per min)</i>		
Mean (SE) and no observations		
Day 1	48(2.1)71	46(2.0)61
Day 2	38(1.9)62	39(2.0)58
Day 3	31(1.5)56	33(1.9)54
Discharge	29(1.5)60	28(1.1)53
<i>'Pulmonarily healthy'</i>		
No (%)		
Day 3	28(40)	27(43)
Discharge	55(76)	51(80)
After 3 weeks	54(76)	54(86)
<i>Radiological findings</i>		
No (%) with pulmonary consolidation		
On admission	58(81)	51(80)
After 3 weeks	17(26)	17(29)
<i>White blood cell count (<math>\times 10^9/l</math>)</i>		
Mean (SE) range	10.9(0.5)1.3-25.9	11.4(0.7)5.4-29.2

Table 4 Clinical observations and duration of hospital stay in 61 children with respiratory syncytial virus pneumonia, allocated to two treatment groups (group A + antibiotics and group B - antibiotics)

	Group A (n=34)	Group B (n=27)
<i>Duration of hospital stay (days)</i>		
Mean (SE) range	5.2(0.3)3-11	5.4(0.4)2-10
<i>Respiratory frequency (per min)</i>		
Mean (SE) range		
Day 1	49(2.4)24-70	48(3.6)24-80
Day 2	40(2.7)20-78	41(3.2)20-90
Day 3	33(2.0)18-48	39(3.3)16-84
Discharge	31(2.1)16-55	30(1.9)19-45
<i>'Pulmonarily healthy'</i>		
Day 3	11	9
Discharge	25	24
After 3 weeks	27	20
<i>Radiological findings</i>		
No with pulmonary consolidation		
On admission	25	22
After 3 weeks	7	6

the children was determined daily but in some patients the results were recorded as below or above 40 per minute. In 46 patients from group A and in 38 from group B the respiratory rate per minute was above 40 on admission. Seventy four per cent and 66% respectively of these patients had a respiratory rate below 40 per minute on day three. The mean respiratory rates per minute counted on different days during the stay in hospital are seen in Tables 3 and 4.

One patient from group B<sup>a</sup> was cyanotic within 24 hours of admission. An adenovirus infection was later diagnosed by antibody determination. One patient from group A was readmitted the day after discharge because of respiratory distress. She was treated with continuous positive air pressure, intermittently for two weeks, and her pulmonary symptoms continued for a longer period. No virus infection was diagnosed in this child.

#### *Radiological findings*

Eighty per cent of the children, equally distributed between groups A and B, had radiographic evidence of pulmonary consolidation (Tables 3 and 4). Fifteen per cent from group A and nine per cent from group B had only perihilar infiltrations, and in most of these patients a viral infection was diagnosed. There was no difference between the two groups in the number of children with persisting radiological changes at three weeks' follow up (Tables 3 and 4). In most children the persistent changes were slight, and all resolved eventually.

Two patients from group B<sup>a</sup> showed progressive radiological changes; in one a pleural effusion was observed during hospital stay. One child from group A developed an atelectasis which persisted for four months. In another group A patient radiological changes had not resolved after three weeks but these disappeared later.

#### *Duration of hospital stay*

The mean duration of hospital stay was the same for the two groups (Tables 3 and 4). Ten group A patients and 13 group B patients stayed for more than seven days because of continuous fever or pulmonary symptoms. Fourteen of these patients had a viral infection.

#### *Otitis media*

In 12.5% of the children, equally distributed between the two randomised groups, signs of acute otitis media were present during hospital stay, but in only two cases was a bacterial aetiology proved.

#### *White blood cell count*

The mean values (SD) and ranges of white blood cell counts obtained from 128 of the 136 patients are

seen in Table 3. Fifteen patients, six from group A and nine from group B, had white blood cell counts greater than  $15 \times 10^9/l$  ( $15 \times 10^3/mm^3$ ). There was no difference between the two randomised groups or between the groups with or without viruses in respect of the absolute numbers of neutrophils and band forms.

#### *Prolonged and complicating course of disease*

Two children from group A had prolonged fever despite antibiotic treatment (125 and 157 hours). The first grew *H influenzae* and *S pneumoniae* in the tracheal secretion and was treated with penicillin. The second had an adenovirus infection and a tonsillitis, and  $\beta$  haemolytic streptococci were cultured in the throat swab. He received penicillin. His radiological changes were persistent at the three week follow up but later resolved. A 9 month old child from group A developed an atelectasis, and another child of 6 months from group A was readmitted with persistent pulmonary symptoms of long duration.

Two children from group B succumbed to complicating purulent infections and were treated with antibiotics after one week. Pulmonary symptoms in one of these—a girl aged 20 months—resolved by day three, with declining fever. Later she got high fever again. After one week a mastoiditis was diagnosed. *Fusobacterium naviforme* was cultured from the mastoid bone by anaerobic culture. Blood culture grew anaerobic Gram negative rods (bacteroides). The initial examination of tracheal secretion showed no pathogenic bacteria. No virus infection was diagnosed. The other child, a 7 month old girl, had a purulent otitis media on day six. Respiratory syncytial virus was diagnosed in nasopharyngeal secretions by fluorescent antibodies on admission. From the middle ear secretion  $\beta$  haemolytic streptococci were cultured. Four children from group B stayed in hospital for more than 10 days because of respiratory symptoms or progressive radiological changes, one with a slight pleural effusion. All except one patient with influenza A had adequate antibiotic treatment which was begun on days three, four, or five. This obviously did not favour the course of disease.

#### *Readmissions*

A total of five patients were readmitted during the three week period of observation. Four of them, two from each randomised group, because of pulmonary symptoms. One patient was readmitted with a rotavirus gastroenteritis.

#### *Follow up visit*

All except two children attended the follow up visit

Table 5 Occurrence of clinical symptoms and treatment given during the period between discharge and the follow up visit 3 weeks later in group A (+ antibiotics) and groups B and B<sup>a</sup> (- antibiotics)

	Group A (n=71) (%)	Group B (n=63) (%)	Group B <sup>a</sup> (n=48) (%)
Fever	28	32	29
Respiratory distress	25	35	35
Coughing	59	57	63
Otalgia	6	6	6
Skin eruptions	14	0	0
Gastrointestinal symptoms	31	24	21
Medical attention	30	24	23
Antibiotic treatment after day 10	9	8	8

and questionnaires were answered for all the children (Table 5). As can be seen from the table, there is no difference between the groups when the frequency of respiratory symptoms, gastrointestinal symptoms, medical attention, and antibiotic treatment after discharge are compared. Ten children from group A had skin eruptions. In connection with a new febrile episode, one of them had urticaria five days after the antibiotic treatment was stopped. Seven eruptions were diagnosed as drug rashes, while two children had a candida diaper dermatitis.

## Discussion

In the present study we found no clinically important differences between the group of children who received antibiotics early in the course of disease and the group of children who were not given antibiotics during their hospital stay. This relates to the course of acute disease as well as the symptoms during the period of observation after discharge. Only one child had a severe complicating infection of the middle ear with mastoiditis which might have been avoided if antibiotics had been given earlier. On the other hand, the initial bacterial cultures gave no guidance with regard to antibiotic treatment in this child.

Only two of the eight group B<sup>a</sup> patients, initially randomised not to receive antibiotics but still treated with antibiotics before day four, had symptoms that conformed to the conditions prescribed for starting antibiotic treatment before day four. Fever and bacterial findings in the tracheal secretions were more often determinants than pulmonary symptoms in the decision to begin antibiotic treatment. But the bacterial findings in tracheal secretions were of no value in predicting which of the children might develop complicating bacterial infections. The bacterial flora observed is comparable with the flora of throat and nasophary-

ngeal swabs described earlier.<sup>9</sup> The results of the microscopic examinations of tracheal secretions emphasise the difficulties of avoiding mixture of throat secretions when obtaining these for bacterial diagnostic research. We did not, however, find it justified to make transtracheal puncture in these children.

Blood culture might have showed a bacteraemia in some of the children.<sup>10</sup> Unsuspected bacteraemia has been described in children with high fever and pneumonia or other localised infections.<sup>11</sup> But the risk of bacteraemia was not described to be higher in connection with pneumonia than in children with upper respiratory infections or otitis media. In the present study, a blood culture was used only when septicaemia or bacteraemia were suspected clinically, according to the normal procedure in children with fever.

A viral infection was diagnosed in 53% of the children and among these 84% were caused by respiratory syncytial virus. They occurred mainly during epidemic outbreaks in winter, and mainly in children under 2 years of age. This is in accordance with earlier reports.<sup>9, 12</sup> In the present study, it was expected that the children in whom no virus infection was diagnosed would be those with bacterial pneumonias, but neither the course of disease, the secretory bacterial findings, nor the white blood cell counts helped in distinguishing the bacterial pneumonias from the pure viral infections. Some of the children, however, with no proved virus infection may have had other virus infections which were not investigated.

In accordance with our results, a number of other authors did not find any association between white blood cell counts and the bacterial/virus genesis of respiratory infections.<sup>3, 13-15</sup> White blood cell counts, however, greater than  $15 \times 10^9/l$  ( $15 \times 10^3/mm^3$ ) have been described as predictive of bacteraemia.<sup>10, 16</sup>

The clinical differentiation between the diagnoses bronchiolitis and pneumonia has been discussed earlier by several authors.<sup>1, 12</sup> The diagnosis pneumonia, based on stethoscopic and radiological observations, was generally an indication for antibiotic treatment in our wards. Children in whom no radiological changes were later discovered were not, therefore, excluded. According to the categories stated earlier, some of the children in this study had the diagnosis acute bronchiolitis.<sup>12</sup> The proportion of children with peribronchial thickenings as the only radiological changes in pneumonia is comparable with earlier descriptions.<sup>12</sup> As stated earlier, it is important to realise that radiological and stethoscopic findings cannot distinguish primary bacterial pneumonia from pneumonia of viral origin.<sup>17</sup> Only one child in this study had a pleural effusion, and

none had pneumothorax, pneumatocele, or lung abscess indicating a possible bacterial infection.<sup>17 18</sup>

The occurrence of clinical symptoms during the observation period is a reflection of the general tendency of infections in this age group of children rather than an indication of sequelae after the pulmonary infections we examined. A difference between the two randomised groups in frequency of skin eruptions, however, was noted.

In spite of the knowledge of the viral aetiology of most acute respiratory infections in infants and small children, antibiotics are still the initial treatment in many paediatric wards.<sup>19</sup> This also applies to Danish paediatric wards. Ampicillin is the drug most commonly used.<sup>19</sup> The main reason for giving antibiotics is the fear of bacterial superinfection. A probable association between respiratory syncytial virus and *H influenzae* type b in throat cultures from children under 1 year of age has been described.<sup>13</sup> In an earlier study, however, of 781 children with respiratory infections, antimicrobial drugs administered prophylactically did not reduce the incidence of bacterial complications.<sup>15</sup> Also, uncritical use of ampicillin increases the rate of resistant organisms in the upper respiratory tract<sup>20</sup> and the rate of allergic skin eruptions.

The conclusion of the present study is that routine antibiotic treatment of acute lower respiratory infections in infants and small children admitted to hospital is not indicated, even if pulmonary consolidations are present. In case of a secondary rise of temperature or prolonged fever lasting more than one week, a bacterial superinfection should be suspected. Respiratory signs alone are not an indication for antibiotic treatment.

The study was supported by Statens Lægevidenskabelige Forskningsfond (J no 552-1070), Dronning Louises Børnehospitals Forskningsfond (J no 4/80), and Nationalforeningen til Tuberculøsens Bekæmpelse. Peter Kirkegård Hansen assisted at the statistical investigations.

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Received 18 June 1984