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Radiographic patterns and viral studies in childhood pneumonia at various ages

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Abstract. We aimed at evaluating the relationship between microbial etiology and chest radiograph appearance in various types of pneumonia. In a prospective study, the radiographic findings in 479 cases of acute pneumonia in children were compared with viral etiology and growth of potential bacterial pathogens in nasopharyngeal secretion. As the basis for viral etiology was most conclusive, the material was here classified according to the viral findings. The patients were divided into three age groups: 0–2, 3–5 and 6–15 years. The chest radiograms were analyzed blindly for the presence of hyperinflation and interstitial, alveolar and mixed interstitial-alveolar infiltrates. There was a statistically significant relationship between low age and occurrence of hyperinflation and interstitial infiltrates, and between high age and alveolar infiltrates. No unequivocal relationship was found between type of infiltrates or presence of atelectasis and proven viral etiology. We conclude that chest radiographs are not a useful indicator of microbial etiology in childhood pneumonia.

Respiratory tract infections constitute one of the world's greatest health problems in children [1]. Radiographic examination of the chest is often included in the care of patients to corroborate the clinical diagnosis of pneumonia and to check the resolution of parenchymal abnormalities after therapy. In addition, interest has been focused on whether chest radiography might provide a basis for differentiating between bacterial and viral etiology of the pneumonia, thereby guiding the initiation of treatment, but opinions differ on this question.

The aim of the present investigation was to assess the radiographic appearance of acute childhood pneumonia at different ages and with different origins of infection in order to elucidate the efficacy of chest radiography in determining etiological agents.

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Material and methods

This prospective study was performed at St. Göran's Children's Hospital, Stockholm, during the winter seasons of 1982–83 and 1983–84 and during the complete years of 1984 and 1985. Both inpatients and outpatients were included, based on the following criteria: maximum age 15 years, symptoms and signs of acute lower respiratory tract infection, and presence of acute pulmonary abnormalities on chest radiography.

Radiograms were taken in frontal and lateral view at the time of initial attendance at the hospital and judged for the presence of general hyperinflation (air trapping), alveolar, interstitial or mixed alveolar-interstitial infiltrates and atelectasis. Interstitial infiltrates included peribronchial infiltrates with or without bronchial wall thickening. Atelectasis was defined as diminished air within the lung or part of the lung associated with reduced lung volume [2]. Presence of local hyperinflation ($n = 3$) and enlarged hilum glands ($n = 16$) was also registered, but will not be included in the present study. The radiograms were reviewed jointly by two experienced pediatric radiologists with no knowledge of the findings of microbiological examinations.

Following preliminary radiographic diagnosis of pneumonia and after obtaining parental consent to enter patients in the study, samples were taken for microbiological investigation before treatment was initiated. The protocol required nasopharyngeal specimens for viral antigen detection and bacterial culture and blood samples for serological investigation. At check-up radiographic examination 4 or 6 weeks later, a second blood sample was taken for serological tests. Only the results of virological investigation will be reported here.

The attempt to reach a diagnosis of viral pneumonia was made on the demonstration of a respiratory virus by culture and/or antigen detection in nasopharyngeal secretion ($n = 11$), a significant increase in antibodies for major respiratory viral pathogens ($n = 309$), or both ($n = 159$). Serum was stored at – 20 °C at the laboratory until analyzed. Antibodies against common respiratory viruses (respiratory syncytial virus, adenovirus, parainfluenza 1, 2 and 3 and influenza A and B viruses) were determined by ELISA. Antibodies against Chlamydia antigen, common to all groups, and Mycoplasma pneumoniae were determined by complement fixation test. No positive reactions to Chlamydia antigen were obtained. A significant increase against Mycoplasma was recorded in 28 children. The results of etiological investigation will be presented in detail elsewhere (Forsgren M, Eriksson M, manuscript in preparation).

Complete protocols including clinical data and results of microbiological tests were available in 507 cases (484 patients) of acute

Table 1. Outcome of viral diagnosis in the different age groups

	Age group			Total
	I 0–2 years	II 3–5 years	III 6–15 years	
Positive virus tests	207 (64 %)	43 (43 %)	15 (27 %)	265
Negative virus tests	116 (36 %)	57 (57 %)	41 (73 %)	214
Total	323	100	56	479

Relative frequencies are given in parentheses
$P < 0.001$

Table 2. Frequency of hyperinflation at different ages in 479 children with acute pneumonia

	Age group			Total
	I 0–2 years	II 3–5 years	III 6–15 years	
Hyperinflation	166 (51 %)	22 (22 %)	13 (23 %)	201
n	323	100	56	479

$P < 0.001$

Table 3. Radiographic findings and age of 462 children with pneumonia

	Age group			Total
	I 0–2 years	II 3–5 years	III 6–15 years	
Interstitial infiltrates	135 (43 %)	37 (38 %)	15 (28 %)	187
Alveolar infiltrates	119 (38 %)	42 (43 %)	35 (65 %)	196
Mixed infiltrates	57 (18 %)	18 (19 %)	4 (7 %)	79
n	311	97	54	462

$P < 0.01$

lower respiratory tract infection with roentgenological signs of pneumonia. Twenty-eight children with Mycoplasma pneumoniae infection were not included, but will be presented separately. The final material thus comprised 479 cases of pneumonia (456 children), which for the sake of simplicity will be referred to here as patients or children.

Statistical analysis

Differences in proportions between groups were analyzed by means of chi-square test with a 0.05 level of significance. The prevalence of virus positivity was analyzed as a function of radiographic findings and age by fitting a logistic regression model.

Results

The age distribution is shown in Table 1. The majority of the patients were in the younger age groups.

The patients were divided into two groups according to the results of the virological tests: positive outcome (265 children, 55 %) and negative outcome (214 children, 45 %; Table 1). Demonstrable virus infection was more common in age group I than in age groups II and III ($P < 0.01$ and 0.001, respectively); the difference between the two higher age groups was not statistically significant.

Seventy-two children had atelectasis, distributed with similar incidence in the virus-positive and virus-negative group. Pleural reaction was found in 24 cases, predominantly in the virus-negative group ($P < 0.05$).

Hyperinflation with or without parenchymal infiltrates was more common in age group I than in groups II and III ($P < 0.001$; Table 2). There was no difference between groups II and III.

The age-related distribution of the parenchymal infiltrates is given in Table 3. Interstitial infiltrates were most common in group I and diminished with age; the difference between groups I and III was statistically significant ($P < 0.05$). The occurrence of alveolar infiltrates increased with age; the difference between groups I and III was significant ($P < 0.001$). Within the separate age groups the difference between the rates of interstitial and alveolar infiltrates was significant in group III only ($P < 0.01$). Mixed infiltrates were less frequent in all age groups, particularly among the older children. Their variation by age was not significant. Seventeen patients with isolated hyperinflation were not included.

The prevalence of demonstrable virus etiology as a function of age, hyperinflation and parenchymal infiltrates was studied for the total material by means of a logistic regression analysis (Table 4). Significant factors for the prevalence of demonstration of virus etiology were age ($P = 0.008$) and an interaction between age and infiltrates ($P = 0.02$). The latter was due to the mixed infiltrates; disregarding these, age remained as the only significant factor. No significant effect was caused by hyperinflation. In order to separate the effect of age from that of the infiltrate on the prevalence of virus positivity, it was necessary to evaluate each age group separately (Table 5).

Age group I: there was a statistically significant difference in the frequency of virus positivity for the various infiltrate groups ($P = 0.01$). This disparity was mainly due to a small difference between the groups of alveolar and mixed infiltrates ($P = 0.003$). No statistically significant difference was found between the groups with alveolar and interstitial infiltrates.

Age group II: no statistically significant difference in frequency of virus positivity was found between the different types of infiltrates.

Age group III: there was a statistically significant effect of infiltrates on the prevalence of virus positivity, partly due to the high prevalence of viral pneumonia in the group with mixed infiltrates. The result is, however, ambiguous because of the small number of cases in this group ($n = 4$). Anyhow, there was no statistically significant difference between the virus-positive and -negative groups for the distribution of alveolar and interstitial infiltrates.

Discussion

In this study we have tried to elucidate the radiographic appearance of acute childhood pneumonia at different ages, relating the findings to virological findings. The assessment of the microbial etiology of pneumonia is complicated. For diagnosis of viral pneumonia, the demonstration of viral antigen or virus in nasopharyngeal se-

Table 4. Prevalence (%) of infiltrates, with or without concomitant hyperinflation, and of isolated hyperinflation in relation to age and to the outcome of viral tests

	Infiltrates						Hyp + only
	Interstitial		Alveolar		Mixed		
	Hyp +	Hyp –	Hyp +	Hyp –	Hyp +	Hyp –	
Age group I							
Positive virus tests	67 (57)	54 (27)	29 (27)	73 (59)	52 (16)	46 (12)	75 (9)
Negative virus tests	33 (28)	46 (23)	71 (11)	29 (22)	27 (15)	54 (14)	25 (3)
Age group II							
Positive virus tests	55 (6)	46 (12)	75 (3)	37 (14)	50 (2)	43 (6)	0 (0)
Negative virus tests	45 (5)	54 (14)	25 (1)	63 (24)	50 (2)	57 (8)	100 (3)
Age group III							
Positive virus tests	38 (3)	29 (2)	0 (0)	19 (6)	0 (0)	75 (3)	50 (1)
Negative virus tests	62 (5)	71 (5)	100 (3)	81 (26)	0 (0)	25 (1)	50 (1)

Absolute numbers given in parentheses
Hyp +, Presence of hyperinflation; Hyp –, absence of hyperinflation

Table 5. Relation of the type of infiltrate in the different age groups to the demonstration of viral infection

	Infiltrates			Total
	Interstitial	Alveolar	Mixed	
Age group I				
Positive virus tests	84 (42 %)	86 (43 %)	28 (14 %)	198
Negative virus tests	51 (45 %)	33 (29 %)	29 (26 %)	113
				$P < 0.01$
Age group II				
Positive virus tests	18 (42 %)	17 (40 %)	8 (18 %)	43
Negative virus tests	19 (35 %)	25 (46 %)	10 (18 %)	54
				N.S.
Age group III				
Positive virus tests	5 (36 %)	6 (43 %)	3 (21 %)	14
Negative virus tests	10 (25 %)	29 (73 %)	1 (2 %)	40
				$P < 0.05$

cretion is relevant, as the viral infection is spread throughout the respiratory tract. This is the preferred method, especially in small children. Serodiagnosis, on the other hand, is a very powerful diagnostic tool in children over 6 months of age and has to be included in the older age groups to achieve maximum sensitivity [3]. The role of bacteria in pneumonia is more difficult to elucidate, a fact which restricts the present investigation. Bacteria in nasopharyngeal secretion are a less reliable indicator of the microbial flora of the lower respiratory tract. Definite diagnosis of bacterial infection has been considered to require the presence of bacteria in blood culture or in aspirates at direct lung puncture. In recent years, new serological approaches have been added to the diagnostic arsenal to facilitate diagnosis of bacterial pneumonia [3]. There are, however, obvious difficulties in evaluating the relevance of the different methods as no "gold standard" for bacterial etiology exists. In the present study, only results of viral tests have been considered, although we are well aware that the reported infections comprise a mixture of pure viral infection and viral infection with superimposed bacterial infection. Although the finding of potential bacterial pathogens in nasopharyngeal secretion is a poor indicator of bacterial infection in the lung, it has been used in several investigations. Our analysis has therefore also included the finding of potential bacterial pathogens in nasopharyngeal secretion; the material was thus classified into four etiological groups (viral, bacterial, mixed viral and bacterial, and indeterminate). The general conclusions were identical with those presented above.

Bacterial infection initially takes place in the alveoli, whereas a virus attacks the bronchial epithelium and spreads to the peribronchial tissue. These are the pathoanatomical correlates to the alveolar and interstitial infiltrates seen on the radiograms. The pathological process is not always that clear, and the pathological-roentgenological correlation is imperfect [4]. Alveolar or interstitial infiltrates are rarely found in isolation at chest radiographic examination of acute pneumonia in children. When one type of infiltrate was not predominating, we characterized them as mixed infiltrates. Hyperinflation is caused by structural conditions – the already narrow airways are partially obstructed by inflammatory changes in the bronchial wall and by mucus secretion and, in addition, by the liability to bronchial hyperresponsiveness, most marked in infants and small children [5, 6]. The present investigation showed that hyperinflation varied with age but not with the outcome of the virological tests. The preponderance of hyperinflation in younger children has been described earlier [7, 8].

It has been suggested that the radiographic appearance of pneumonia yields information on the etiologic agent with a varying degree of reliability and can therefore guide treatment [7, 9–14]. It has been proposed that virus infections cause mainly interstitial infiltrates and hyperinflation and bacterial infections mainly alveolar infiltrates, but these reports have generally been devoid of statistical support. Furthermore, some studies either presented no microbiological analyses or the etiologic pathogen was surmised on clinical grounds. Like some other investigators [15–20], we could not confirm a relationship between the demonstration of viral pathogens and the type of infiltrates at chest radiographic examination. We did find, however, that the patient's age was a major factor for the type of radiographic appearance; interstitial infiltrates were most

common in younger and alveolar infiltrates in older children. The fact that virus infections, hyperinflation and interstitial infiltrates were all more common in younger children may explain the previous assumption that a relationship exists between viral pneumonia and the described radiological findings. We were also unable to confirm the assumption that the occurrence of atelectasis should be more common in case of viral infection. Pleural effusion was, however, found more often in the virus-negative group; unfortunately radiographic examination with the patient in lateral decubitus position had not been generally included.

The information provided by chest radiography has been considered essential for guiding the clinical decision-making process. In approximately 20 % of cases, the preradiography diagnosis and planned treatment were changed as a result of the radiographic findings, mostly by withholding or instituting antibiotics and spasmolytic agents [12, 21]. These studies were not designed to evaluate whether the changes in treatment plans were correct or not. The fact that the type of infiltrate was related to the patients' age and not to the etiological agent does not support the idea that radiography is a solid basis for guiding the treatment.

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