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Lung function impairment following mycoplasmal and other acute pneumonias

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Lung function impairment following mycoplasmal and other acute pneumonias. L.A. Laitinen, A.K. Miettinen, E. Kuosma, L. Huhtala, K. Lehtomäki.
ABSTRACT: We prospectively studied the lung function of 106 consecutive young patients with pneumonia.

At the time of hospital admission we observed impaired spirometric function in 48% of the patients. During and following treatment, the frequency of abnormalities in pulmonary function tests decreased rapidly. However, at the 15th day of hospitalization, abnormal ventilatory function was still demonstrated in 21% of the patients. Such prolonged impairment of ventilatory function was significantly more likely to result from pneumonia caused by *Mycoplasma pneumoniae* than from forms caused by adenovirus or *Streptococcus pneumoniae*. *Eur Respir J., 1992, 5, 670–674.*

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Pneumonia is generally considered to be a lung parenchymal disease. In pneumonia, typical changes in lung function include a restrictive ventilatory defect, and reduction in static lung volumes and lung diffusing capacity [1]. However, data on functional changes in the airways are scarce and conflicting.

The relative importance of different respiratory pathogens in causing impairment of lung function is also insufficiently understood. There is evidence that implicates *M. pneumoniae* as a cause of chronic sequelae following pneumonia. Tracheobronchial clearance is impaired for months after mycoplasmal infection [2]; and in children recovering from mycoplasmal pneumonia ventilatory abnormalities can persist for several months [3]. The association between respiratory infections with *M. pneumoniae* and exacerbation of asthma is well-established [4, 5]. Moreover, development of interstitial fibrosis [6, 7] and farmer's lung [8] as sequelae to mycoplasmal pneumonia have also been reported. Impairment in spirometric values and diffusing capacity has also been reported in association with pneumococcal [9] and various other types of pneumonia [10].

In the present study, we prospectively investigated lung function in 106 patients with pneumonia. The study was designed to assess the frequency and duration of lung function abnormalities occurring in pneumonia of various aetiologies, and to characterize the alterations specifically related to the commonest aetiological agents of pneumonia, *i.e. Streptococcus pneumoniae, Mycoplasma pneumoniae* and adenovirus.

Methods

Patients

The subjects were 106 consecutive military conscripts admitted to the Central Military Hospital, Finland, with symptoms and signs of respiratory infection and a pneumonic infiltrate on chest X-ray, diagnosed by two radiologists. The patients had a mean±SD age of 21±1.7 yrs. They had been found healthy in at least three medical examinations shortly before and during their service. Smoking habits and medical history, with special emphasis on asthma, were recorded by questionnaire. None of the patients had received antibiotics during their current illness. All were hospitalized and treated orally with phenoxymethylpenicillin, doxycycline or erythromycin, changed as indicated by clinical response and microbiological findings.

Tests for lung function

Lung function tests were performed on the day after admission (acute phase), and on the 8th and 15th day of hospitalization (convalescent phase). In addition, patients showing abnormal findings in measurements on the 15th day were tested repeatedly up to six months or until the findings normalized. The following spirometric values were recorded

(Pneumoscope II; Jäger, West Germany): forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), peak expiratory flow (PEF), maximal expiratory flow at 50% of FVC (MEF_{50}), maximal expiratory flow at 25% of FVC (MEF_{25}), and the ratio of FEV_1/FVC (FEV%) calculated. The patient repeated at least two flow volume curves and the values were taken from the envelope curve with the highest FEV_1 value. The results are expressed as a percentage of the reference values published by VILJANEN *et al.* [11]. FVC, FEV_1 and PEF values <80% of predicted, MEF_{50} values <52% of predicted, and MEF_{25} values <62% of predicted were considered abnormal.

designated as "other pneumonias". The clinical characteristics of the patients with pneumonia of different aetiologies are presented in table 1.

Altogether 51 (48%) out of 106 patients showed FVC, FEV_1 and/or PEF values below normal (*i.e.* <80% of predicted) on admittance. The mean±SD value for FVC was 91±15% of predicted; for FEV_1, 83±13% of predicted; and for PEF, 84±19 of predicted, indicating a mild to moderate impairment of the ventilatory function. A purely obstructive pattern in spirometry (FEV% <88% of predicted) was rare, occurring in only 6% of the patients. In 22 (21%) of the patients, the impairment was still demonstrated at the 15th day of hospitalization.

Table 1. – Clinical characteristics of 106 patients with pneumonia, stratified by the aetiological group

Symptom/finding on admittance	Mycoplasmal pneumonia (n=15)	Adenoviral pneumonia (n=11)	Pneumococcal pneumonia (n=29)	Other pneumonia (n=51)
Fever mean °C	38.8°	38.4°	38.9°	38.5°
Duration of fever days	3	4	3	3
Cough n	14	9	29	48
Productive cough n	6	4	22	34
Duration of cough days	5	5	8	7
Chest pain aggravated by breathing n	1	-	14	4
CRP* $mg \cdot l^{-1}$	59±53	50±52	116±82	76±58
ESR* $mm \cdot h^{-1}$	30±8	38±28	42±27	45±28
WBC* $\times 10^9 \cdot l^{-1}$	6.5±1.6	6.9±3.1	13.8±7.9	9.8±6.0
Chest X-ray findings n				
Alveolar pneumonia	10	4	18	21
Interstitial pneumonia	1	2	4	2
Mixed	4	5	7	28
≥2 lobes affected	2	-	3	8
Bilateral pneumonia	2	3	5	9
Atelectasis	2	-	3	1
Pleural fluid	-	-	1	5

*: mean±SD; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; WBC: white blood cells.

Other methods

The extensive microbiological techniques and studies have been described in detail previously [12]. Two-tailed Fisher's exact test, Chi-squared test and Student's t-test, when appropriate, were used for statistical comparisons.

Results

A microbiological diagnosis was established in 91 (86%) of the 106 patients. Clear-cut indications to consider *M. pneumoniae,* adenovirus or *S. pneumoniae* as the only aetiological agent were obtained in 55 (52%) of the patients. The remaining 51 patients showing either multiple positive microbiological findings or insufficient findings to allow definite aetiological diagnosis, along with sporadic cases caused by rare aetiological agents, were

Lung function in pneumonia was further analysed in 55 patients comprising the three major aetiological groups, namely mycoplasmal, adenoviral or pneumococcal pneumonias (tables 2 and 3). Abnormal spirometric findings in the acute phase were significantly more frequent among patients with mycoplasmal pneumonia than in those with adenoviral or pneumococcal pneumonia (table 2). In the acute phase, the most pronounced difference was seen in the frequency of abnormal FVC, PEF, MEF_{50} and MEF_{25} values.

Prolonged impairment in ventilatory function was also more frequent among patients with mycoplasmal than among those with adenoviral or pneumococcal pneumonia (table 3). Thus, on the 15th day, eight (53%) out of 15 patients with mycoplasmal pneumonia still showed some impairment in spirometric measurements, and in six (40%) of them the ventilatory defect persisted for one to six months.

Table 2. – Acute phase (day after admittance) abnormal findings in pulmonary function among 55 patients with pneumonia, stratified by the aetiological group

	Mycoplasmal pneumonia (n=15)	Adenoviral pneumonia (n=11)	Pneumococcal pneumonia (n=29)
Patients with abnormal findings in indicated measurement n			
FVC	5*	2	1
FEV_1	6	1	6
PEF	8*†	4	4
Any of the three	8	4	8
MEF_{50}	8	1	11
MEF_{25}	6**	0	6
Either of the two	10**†	1	12
Any spirometric measurement	10	4	14

Significance of differences; *: $p<0.05$ compared with pneumococcal pneumonia group; **: $p<0.05$ compared with adenoviral pneumonia group; †: $p<0.05$ compared with pneumococcal and adenoviral groups combined. FVC: forced vital capacity; FEV_1: forced expiratory volume in one second; PEF: peak expiratory flow; MEF_{50} and MEF_{25}: maximal expiratory flow at 50% and 25% FVC, respectively.

Table 3. – Convalescent phase (15th day of hospitalization) abnormal findings in pulmonary function among 55 patients with pneumonia, stratified by the aetiological group

	Mycoplasmal pneumonia (n=15)	Adenoviral pneumonia (n=11)	Pneumococcal pneumonia (n=29)
Patients with abnormal findings in indicated measurement n			
FVC	3	1	1
FEV_1	5	2	2
PEF	3	1	1
Any of the three	6*	2	3
MEF_{50}	6	1	5
MEF_{25}	6**	1	2
Either of the two	8+	1	5
Any spirometric measurement	8++	2	7

Significance of differences; *: $p=0.07$; and **: $p<0.05$ compared with both pneumococcal pneumonia group and pneumococcal and adenoviral pneumonia groups combined; +: $p<0.05$ compared with pneumococcal and/or adenoviral pneumonia groups; ++: $p=0.07$ compared with pneumococcal and adenoviral pneumonia groups combined. For abbreviations see legend to table 2.

In four of these patients a mild to moderate obstruction was observed, whereas in two patients a restrictive pattern predominated. Impairment in ventilatory function persisting for more than one month occurred in only two out of 29 patients with pneumococcal and in none of the 11 patients with adenoviral pneumonia.

Of all patients, 62% were regular smokers. No significant difference could be demonstrated in the distribution of smokers and nonsmokers in the aetiological categories. Nor was any significant association found between smoking and impairment of ventilation. Also, the recovery of ventilatory function in smokers followed the same pattern as that in nonsmokers (data not shown).

Discussion

Approximately half of the pneumonia patients in this study showed impaired ventilatory function in the acute phase of the illness as demonstrated by

spirometric measurements. Following treatment, ventilatory function improved rapidly in most cases and only 22 (21%) of the 106 patients had abnormal FVC, FEV_1 and PEF values at the 15th day of hospitalization.

Especially in the acute phase, pleural pain may have caused some restrictive spirometric impairment. Chest pain was, however, frequently reported only among the patients with pneumococcal pneumonia, of whom 48% complained of chest pain aggravated by breathing; this is in concordance with earlier reports [13]. Excessive mucus production may have caused some of the obstructive spirometric impairment in the acute phase. A significant decrease in FEV% was only occasionally found, suggesting that bronchial obstruction was uncommon. Because of the coexisting restrictive impairment, however, it is possible that the frequency of obstruction was underestimated. During the follow-up of patients with prolonged ventilatory impairment, an obstructive pattern was found in the majority of cases.

Strict microbiological and/or serological criteria were employed in establishing the aetiological categories. Since the relatively large number of patients made it possible to exclude all cases with vague or rare aetiological diagnosis, we confined the comparison of lung function to those pneumonia cases with definite mycoplasmal, adenoviral or pneumococcal aetiology. As already demonstrated in earlier studies [3, 10], we found wide variety in the patterns of functional impairment in each aetiological group. Thus, no particular type of functional abnormality could be related to any of the three agents studied.

Abnormalities in spirometric measurements were, however, significantly more frequent and persistent among patients with mycoplasmal than among those with adenoviral or pneumococcal pneumonia. In the acute phase of mycoplasmal pneumonia, a coexisting obstructive and restrictive failure was the most characteristic abnormality. In six out of 15 patients with mycoplasmal pneumonia such a syndrome persisted for more than one month and in two patients for more than five months.

It has been demonstrated that viable *M. pneumoniae* cells can persist in the respiratory tract long after administration of effective antimicrobials [14, 15], which might result in prolonged irritation and, thereby, airways obstruction. As *M. pneumoniae* invades the bronchioles and alveoli, causing low-grade inflammation and fibrinous exudation, it is also possible to postulate subsequent sensitization of airways to other irritants causing the obstructive syndrome.

One can also hypothesize an allergic reaction to *M. pneumoniae* as the pathogenic mechanism behind the airways obstruction, similar to that assumed to take place in respiratory syncytial virus infections in children [16]. Immunoglobulin E (IgE) specific for *M. pneumoniae* has been demonstrated in sera of atopic individuals [17]. However, history suggesting type I allergy was not related to prolonged functional impairment in this study, and none of the patients who were included in the aetiological comparison had a history of asthma.

Contrary to many previous reports [18, 19], smoking did not predispose to any functional impairment in pneumonia. The very short smoking history of the young patients in the present study, however, probably accounts for this discrepancy.

In conclusion, the present study among young, otherwise healthy, men demonstrates that pneumonia frequently causes transient impairment in ventilatory function even in the absence of any identifiable pre-existing abnormalities. Prolonged airways involvement extending to the peripheral airways was especially likely to occur in patients with a *M. pneumoniae* aetiology. As mycoplasmal infection can be successfully treated and the course of the clinical infection shortened by prompt administration of appropriate antibiotics, *e.g.* erythromycin or tetracyclines, one can also expect to lessen the probabilty of long-term sequelae if the specific aetiological diagnosis can be reached in the early phase of the infection. When confronted with a patient with pneumonia showing prolonged impairment of ventilatory function, the possibilty of mycoplasmal infection should be considered.

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