Lower respiratory tract infections in adults : a clinical diagnostic study in general practice

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Chapter IV

Chest radiography and relation to aetiology in patients with lower respiratory tract infections in general practice

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Submitted

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4.1 Abstract

Background: In patients with lower respiratory tract infection (LRTI) changes on the chest radiography are poorly characterised, especially in general practice. Our aim was to describe the range of findings on chest radiographs and the associations between these findings and the aetiology of LRTI.
Methods: From November 1998 until June 2001, patients aged ≥ 18 years were examined in a prospective observational study in general practices in the region of Leiden, The Netherlands. A standard medical history was taken and physical examination was performed. Sputum, blood and throat swabs were collected for diagnostic tests. Chest X-ray findings were assessed in relation to the pathogens causing LRTI.
Results: An abnormality on the chest X-ray was observed in 72 (55%) patients. Forty-five patients (35%) had changes due to infection and 26 (20%) due to pneumonia. Pathogens were detected in 84 patients (33 single bacterial, 43 single viral, 8 dual and 45 unknown aetiology). Twelve patients with bacterial infection (including dual infections), 4 patients with viral infection and 10 patients with infections of unknown origin had pneumonia. Twelve (29%) patients with a bacterial infection (including dual infections) compared to four (9%) patients with viral infection had pneumonia on the chest X-ray (OR 4.0, 95% confidence interval 1.2-13.8). When the chest X-ray was used as test to predict the presence of a bacterial infection, the positive predictive value was between 46% (minimal prevalence of bacterial infection 32%) and 85% (maximum prevalence of bacterial infection 67%). For the broader category of 'signs of infection' on the chest X-ray the positive predictive values were 42% and 80%, respectively.
Conclusions: Pneumonia on the chest X-ray was found more frequently in patients with a bacterial infection than in patients with a viral infection. However, the sensitivity and the specificity are such that pneumonia on the chest X-ray is not a reliable test to discriminate between bacterial and non-bacterial LRTI in general practice setting.

4.2 Introduction

Lower respiratory tract infections (LRTIs) are very common in general practice. A recent study in the UK showed an incidence of 44 per 1000 adult population per year.[1] The term LRTI is used for an inflammation of the respiratory tract from the larynx and bronchi down to the pulmonary parenchyma caused by

infectious agents, and includes bronchitis as well as pneumonia. Investigations into patients with LRTI in general practice showed radiographically confirmed pneumonia in 6% to 39% of these patients.[1,2,3,4,5] In patients with cough and sputum production, without abnormal findings on lung auscultation, changes on chest radiography are rare.[6] The radiological criteria for the diagnosis of pneumonia are well defined.[7]
In general practice the majority of the patients with LRTI is treated without further investigation other than physical examination. When further investigation is performed, chest radiography is the most commonly used technique. Chest radiography is performed in the presupposition that an infiltrate on the chest X-ray is basically of bacterial origin and therefore is considered as an indication for antibiotic treatment.
In a prospective study on the aetiology of LRTIs in general practice carried out by our study group, chest radiographs were performed.[8] This offered us the opportunity to describe the radiological abnormalities in those patients systematically. Our study questions were: What is the range of findings on chest radiographs and what are the associations between these findings and the aetiology of LRTI in patients in general practice?

4.3 Methods

Patients
Adult patients aged 18 and over, consulting their general practitioner (GP) for LRTI in the Leiden region, The Netherlands, were included between November 15, 1998 and June 1, 2001. The definition of LRTI used for the inclusion of patients is: (1) any abnormality on pulmonary auscultation and
(2) at least two of the following three signs and symptoms; (a) fever >38°C, or fever in the past 48 hours (reported by patient); (b) dyspnoea or cough (productive or non-productive); (c) tachypnoea, malaise or confusion. Patients who were pregnant or had diseases that could have obstructed completion of follow-up were excluded. A standard medical history and physical examination was done. Sputum samples, throat swabs and blood samples were collected for microbiological analysis. The characteristics of the patients are described in detail elsewhere.[8]
The Medical Ethics Committee of the Leiden University Medical Center approved the study.

Chest radiographs
Chest radiographs of patients consulting their general practitioner for LRTI were collected. In accordance with the study protocol the chest radiographs (postero-anterior and lateral) were performed 5 to 7 days after inclusion in the study. They were performed in one of 3 hospitals, close to where the patient

lived. Local radiologists made the first assessment during routine daily practice. A radiologist (FEJAW), who was not informed about the results of the first assessment, re-examined the radiographs systematically afterwards. In case of a discrepancy between the two assessments, a third radiologist (HMZ) was asked to judge. The aim was to reach consensus. If previous X-rays were available, they were used for comparison.

Radiographic findings

The presence of alveolar or non-alveolar (i.e. interstitial or combined alveolar and interstitial) consolidation, cavitation, pleural effusion, air bronchogram, loss of volume and peri-bronchial wall thickening was noted.[7,9,10] The extent of involvement, lobar or non-lobar was noted down and also if one or both lungs were involved. Any abnormalities not due to infection, i.e. signs of a chronic obstructive pulmonary disease (COPD), cardiomegaly, etc. were registered as well.

Based on the description of the radiographic findings five groups of radiographic diagnoses were evaluated: (1) Pneumonia, (2) Airways disease (peri-bronchial wall thickening without a consolidation), (3) Non-infectious pulmonary features (abnormality on pulmonary parenchyma not due to infection), (4) Non-pulmonary features (cardiomegaly and others) and (5) Normal (none of the above mentioned findings present).

Four types of pneumonia were distinguished:

- Bronchopneumonia (patchy consolidation, loss of volume, without air bronchogram).
- Segmental pneumonia (consolidation with air bronchogram, localised predominantly in one segment).
- Multi-focal pneumonia (consolidation with air bronchogram, in two or more lobes).
- Interstitial pneumonia (peri-bronchial thickening and ill-defined reticulonodulair shadowing).

Aetiological classification

The aetiological diagnosis of LRTI was based on microbiological assays including bacterial and viral cultures, serological techniques and a polymerase chain reaction for specific targets; details have been described elsewhere.[8] The aetiologies were classified as bacterial, viral or dual infections (if both a bacterium and a virus was found) according to the microbiological findings. When no pathogen was found the aetiology was classified as being unknown.

Statistical analysis

Data were analysed using Statistical Package for the Social Sciences (SPSS) version 11.0 for Windows. Mean values were calculated for the numerical

variables. The chi-square test was used to compare percentages between groups. Significance level was set at 0.05.
For the presence of pneumonia (infiltrate on the chest X-ray) and for the presence of signs of infection (pneumonia on the chest X-ray or airways disease (peri-bronchial wall thickening without a consolidation) as predictor of bacterial infection odds ratio's (ORs), sensitivities (Se), specificities (Sp), positive predictive values (PPV) and negative predictive values (NPV) were calculated with 95% confidence intervasl (CI).

4.4 Results

Patients
A total of 145 patients with LRTI were included in the study. In 137 of these patients a chest radiograph was performed. Two patients considered themselves too ill, four patients refused, one was recovered and one had forgotten to visit the hospital for chest radiography. From these chest radiographs 129 could be reviewed in detail, eight went missing. The mean age of the patients was 50 (SD14), 86 patients (53%) were female and 76 (59%) were ex-or current smokers. Ex-smokers had higher mean pack-years of smoking (24 years) than current smokers (20 years). Half the patients (n=63) had co-morbidity (from medical records GP), predominantly cardiovascular (23%) and/or pulmonary (19%) diseases; six patients had both. The mean length of time between the onset of symptoms and inclusion in the study and the chest X-ray was 9 and 14 days, respectively.

Radiographic findings
In the routine assessment 29 patients were diagnosed with pneumonia, of which 4 were regarded as doubtful, 7 as possible and 18 as confirmed pneumonia (descriptions by radiologists in local hospitals). In the re-examination (by FEJAW) 23 patients were considered to have pneumonia. A third opinion to reach consensus was necessary in 20 patients. Finally 26 patients (20%) were diagnosed to have pneumonia based on the chest X-ray. An abnormal chest radiograph was observed in 72 patients (55%). The chest radiographic features of patients with LRTI are shown in Table 4.1. Pulmonary findings consistent with an infection were seen in 45 (35%) patients (including airways disease and pneumonia). The most common type of pneumonia was segmental pneumonia seen in 11 (42%) patients. Pneumonia was predominantly seen in the left lower lobe (in 15 patients, 58%). Three patients had pneumonia in both lungs. In patients with non-infectious pulmonary findings signs of COPD were predominant and in patients with non-pulmonary findings signs of cardiomegaly were the most common feature. In 18 patients more than one chest radiographic abnormality was found.

There was no significant relationship found between sex, old age, smoking and radiographic pneumonia. Co-morbidity, particularly pulmonary diseases, was found in one patient with pneumonia and in 40 patients without pneumonia on the chest X-ray.

Table 4.1 Distribution of radiographic and aetiological findings in 129 patients with lower respiratory tract infection

Radiographic findings	Aetiology				
	Bacterial N = 33	Viral N = 43	Dual N = 8	Unknown N = 45	Total N = 129
Pneumonia	10	4	2	10	26
Segmental pneumonia	(3)	(1)	(1)	(6)	(11)
Bronchopneumonia	(3)	(2)	(1)	(3)	(9)
Interstitial pneumonia	(1)			(1)	(2)
Multi focal pneumonia	(3)	(1)			(4)
Airways disease	5	5	2	7	19
Non-infectious pulmonary features	7	8	1	10	26
Non-pulmonary features	5	5	2	7	19
Normal chest X-ray	11	25	2	19	57

Values are number of cases. Eighteen patients had more than one radiographic finding.

Aetiological findings

Pathogens were identified in 84 patients (65%), 33 had a single bacterial infection, 43 a single viral infection and 8 had a dual infection. In total a bacterial micro-organism was found in 41 patients (single bacterial and dual infection). The most common bacterial pathogens found were *Mycoplasma pneumoniae* and *Haemophilus influenzae* and the most common virus was Influenza virus type A. In the 129 patients studied the distribution of bacterial pathogens was *Mycoplasma pneumoniae* 10%, *Haemophilus influenzae* 9%, *Streptococcus pneumoniae* 7% and other bacterial pathogens 5% and the distribution of viral pathogens was Influenza virus (A and B) 28%, others 9%.

Relationship between aetiology and chest radiographic findings

Pneumonia on the chest X-ray was found in 12 (29%) out of 41 patients with a bacterial infection (including the dual infections), in 4 (9%) out of 43 patients with a viral infection and in 10 (22%) out of 45 patients with an unknown aetiology. The distribution of radiographic findings and aetiology is shown in Table 4.1. The difference between the proportions of pneumonia on the chest X-

ray in patients with bacterial infections (n=41) compared to patients with viral infections (n=43) was significant (P-value 0.02), with OR 4.0 (95% CI, 1.2-13.8). Findings on the chest X-ray related to infection (pneumonia and airways disease) were found in 19 (46%) of the patients in whom a bacteria, in nine (21%) patients with a virus and in 17 (38%) patients in whom no pathogen was detected. The difference between the proportions of signs of infection on the chest X-ray in patients with bacterial infections (n=41) compared to patients with viral infections (n=43) was significant (P-value 0.01), with OR 3.3 (95% CI, 1.3-8.5). The proportions of non-infectious pulmonary findings and non-pulmonary findings were similar in patients with bacterial infections, viral infections or infections of unknown aetiology.
The chest X-ray was examined as test for the prediction of bacterial infections. This examination was performed with the 84 patients in whom pathogens were detected. The test characteristics are shown in table 4.2.

Table 4.2 Characteristics of the chest X-ray as test for identification of patients with a bacterial infection

	Radiographic findings	
	Pneumonia	Signs of infection
At observed prevalence (41/84)		
Sensitivity (95% CI)	29% (16-46%)	46% (31-63%)
Specificity (95% CI)	91% (75-97%)	79% (64-90%)
Positive predictive value (95% CI)	75% (48-93%)	68% (48-84%)
Negative predictive value (95% CI)	57% (45-69%)	61% (47-74%)
At maximum prevalence (86/129)		
Positive predictive value (95% CI)	85% (65-96%)	80% (65-90%)
Negative predictive value (95% CI)	38% (29-47%)	41% (30-52%)
At minimal prevalence (41/129)		
Positive predictive value (95% CI)	46% (27-65%)	42% (28-58%)
Negative predictive value (95% CI)	72% (63-81%)	74% (63-83%)

CI = 95% confidence interval.

Because in 35% of the patients the aetiology is unknown we calculated the predictive values for the outside limits of the prevalence of bacterial infection. When we assume that all patients, in whom no pathogen was found, have a viral infection (minimal bacterial prevalence of 32%), the positive predictive value for a patient with pneumonia on the chest X-ray to have bacterial infection was 46%. Assuming all unknown cases were of bacterial origin (maximal bacterial prevalence 67%), the positive predictive value to have bacterial infection when an infiltrate on the chest X-ray is present was 85%. When the same is done for the broader category of ‘signs of infection’ on the chest X-ray the positive

predictive values at minimal and maximal prevalence of bacterial infection are 42% and 80%, respectively.

4.5 Discussion

Patients who consulted their general practitioner with symptoms of a lower respiratory tract infection and who had abnormalities on auscultation of the chest, showed a variety of chest radiographic abnormalities. Most common were the changes that were attributed to pneumonia and to non-infectious pulmonary features. Patients with a radiographically confirmed pneumonia had a four times higher chance to have a bacterial infection than a viral infection compared to patients without pneumonia on the chest X-ray.

In patients with bacterial infection, including dual infection, we found 46% 'signs of infection' on the chest X-ray and in patients with viral or unknown infections this was 30%. Macfarlane et al.[1] , who studied the aetiology in 289 patients of whom 17% showed chest radiographic changes due to infection and 6% pneumonia, found chest radiographic changes consistent with infection in 25% of the patients with bacterial/atypical pathogens and in 16% of the patients with viral infection or no pathogens identified.

When the chest X-ray was used as test to predict a bacterial infection, the positive predictive value was 75% (range 46% to 85% dependant on the outside limits of the prevalence of 32% to 67%) in patients with pneumonia on the chest X-ray and in the broader category of 'signs of infection' the positive predictive value was 68% (range 42% to 80%). In the present study 54% of the patients with a bacterial or dual infection had no signs of infection (pneumonia or airways disease) on the chest X-ray, for which several reasons can be postulated. The infection may have been minor and may not have affected the lung tissue. It is also possible that the sensitivity of the chest X-ray was too low to detect the infection.

Chest radiography was used as the standard reference to identify pneumonia, because of its low cost and general accessibility. Both the low sensitivity and the inter-observer variability, play a role in its reliability. Because of the low sensitivity we could have missed some of the infiltrates. To reduce the possibility of false-positive or false-negative test results, we re-examined the chest X-rays. The chest X-rays were taken about five to seven days after inclusion in the study. Another study by Macfarlane et al.[11] showed that abnormalities generally persist for a fairly long time, one week after the diagnosis of pneumonia only 5% to 10% of the abnormalities had resolved. Nevertheless, we may have missed the diagnosis pneumonia in a few patients.

When pneumonia on the chest X-ray would have been used as diagnostic test for the presence of bacterial infection, i.e. as indication for the start of antibiotic treatment, in the observed population with known aetiology (n=84), the

following would have happened. Sixteen patients would have been treated with antibiotics. Of them 12 indeed had bacterial infection and would have been treated correctly. Of the 68 patients who would not have received an antibiotic, 29 had bacterial infection and were treated incorrectly, considering bacterial LRTI an indication for antibiotic therapy. When 'signs of infection' on the chest X-ray would have been the criterion, the following would have happened. Twenty-eight patients would have been treated with antibiotics. Of them 19 indeed had bacterial infection and would have been treated correctly. Of the 56 patients who would not have received an antibiotic, 22 had bacterial infection and were treated incorrectly.

Although the reduction of antibiotic use that can be achieved by using the chest X-ray as criterion for antibiotic treatment is high (80% and 66% using pneumonia or signs of infection as indication, respectively) compared with the antibiotic treatment of 128 of the 129 patients with LRTI as the case in our study population, the proportions of untreated patients with bacterial infection are unacceptable in this population of severely ill patients.

In conclusion, the present study shows that although pneumonia or signs of infection on the chest X-ray was found more frequently in patients with bacterial infections than in patients with viral infections the chest X-ray is of limited value for the decision to treat a patient with clinical signs of LRTI in general practice with antibiotics or not.

4.6 References

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