Eur Resp J
1990, 3, 1105–1113

Aetiology, outcome and prognostic factors in community-acquired pneumonia requiring hospitalization

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ABSTRACT: Outcome and prognostic factors were prospectively studied in 277 adult patients (average age 62 yrs) with community-acquired pneumonia requiring hospitalization. The aetiology was established in 68%, with *S. pneumoniae* as the predominating agent. Mortality was 4% (12 of 277), and all but one who died were ≥60 yrs of age. Features associated with high mortality included greater age, absence of chills and chest pain, high respiratory rate (>30 breaths·min^{-1}) and low serum albumin on admission, and the occurrence of airway colonization and secondary infection during hospital stay. Multivariate analysis showed that low serum albumin and the occurrence of secondary infection, but also absence of chills and airway colonization, were correlated to a higher mortality. In patients who survived, the median length of hospital stay was seven days, and at follow-up, about eight weeks after admission, 81% had recovered and chest X-ray was normal in 84%. In conclusion, we believe that the outcome of community-acquired pneumonia can be influenced by prophylactic measures against pneumococcal infection, and an increased surveillance of risk patients.

Eur Respir J., 1990, 3, 1105–1113.

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Keywords: Aetiology; community-acquired pneumonia; hospital treatment; outcome; prognostic factors.

Received: January 1990; accepted after revision June 21, 1990.

Community-acquired pneumonia (CAP) remains an important cause of morbidity and mortality even in highly developed countries. It has been estimated that, annually, about 0.4–4 persons per thousand require hospitalization because of pneumonia [1–4]. From the turn of the century to within a few years after the introduction of antibiotics, pneumonia mortality decreased from about 200 to 70 persons per 100,000 per year [5]. During the last few decades, however, the mortality rate from CAP has decreased but slowly, if at all [6], and pneumonia is still the fifth to sixth leading cause of death in the UK and the USA [1, 2, 7], as well as in Sweden [8]. The mortality rate from pneumonia in Sweden in 1986 was nearly 60 persons per 100,000 [8].

During the last 25 yrs mortality has ranged from 4–24% in adult patients hospitalized because of CAP, and many factors have been associated with high mortality [2, 9–18]. However, to our knowledge, there are only two studies in which the importance of different prognostic factors has been investigated with multivariate statistical methods, a British multi-centre study [2] and a Canadian study [18]. In the British study [2], mortality and outcome of the survivors were investigated, but patients >74 yrs of age were excluded. In Swedish hospitals this age group constitutes a substantial part of all admissions and deaths due to CAP [15]. Although MARRIE *et al.* [18], included patients of all ages in the Canadian study, 18% of their patients were admitted directly from nursing homes and their pneumonia cannot be considered as community-acquired.

The principal aim of the present prospective study was to determine the prognostic factors for mortality and for the outcome of the survivors, in adults requiring hospitalization because of CAP. We also wanted to correlate mortality to different aetiological agents.

Materials and methods

Patients

During a 10 mth period in 1987 all patients ≥18 yrs of age (except for human immunodeficiency virus (HIV)-infected patients) with community-acquired pneumonia (CAP) admitted to the Department of Infectious Diseases at Danderyd Hospital (DIDD) were included in a prospective study. CAP was defined as an acute lower respiratory tract disease, and/or fever >38.5°C, with onset before admission to hospital, and radiological signs of acute pneumonia, *i.e.* pulmonary

infiltrates proved by previous and/or later X-ray to be new or to diminish with clinical improvement. However, six patients with a clinical course and X-ray findings on admission highly suggestive of acute pneumonia were accepted, although there were no previous or later X-rays. All except four patients consented to participate and a total of 277 patients were included for analysis.

Our department serves approximately 750,000 inhabitants in Stockholm county. Patients are transferred to DIDD mainly from the medical department emergency rooms of six hospitals, and from general practitioners. In general, all pneumonia patients coming to the emergency rooms of Danderyd Hospital are transferred to DIDD. From the other five hospitals there is a tendency to transfer primarily the more severe cases, *i.e.* those with the most evident need for specialist care.

Protocol

Data were collected on specially-designed forms to record the history, physical examination, laboratory results, antimicrobial treatment, complications, outcome and follow-up. Outcome was assessed for mortality, length of hospital stay and, at follow-up, about eight weeks after admission to hospital, for return to normal daily activities ("delayed recovery") and resolution of the pulmonary X-ray ("delayed resolution").

Microbiology

Sputum samples were obtained from 256 patients, of whom 126 had not been treated with antibiotics (including therapy prior to admission). Sputum specimens were washed, Gram stained and cultured quantitatively [19]. Sputum was also cultured for *Legionella* spp. [20]. Bronchial secretions, obtained with fibreoptic bronchoscopy and a protected brush in 17 patients, were handled as described previously [21]. On average three blood samples for culture were obtained on admission from 237 patients, of whom 169 had not been treated with antibiotics.

Pneumococcal antigen detection, using a coagglutination test (Phadebact Pneumococcus test, Pharmacia Diagnostics AB, Sweden [22]) was performed on all sputum specimens, as well as on urine samples obtained from 266 patients on admission. Antibodies to pneumococcal haemolysin (pneumolysin) were measured with an enzyme immunoassay (EIA) on paired sera from 202 patients [23]. Paired sera from 211 patients were examined for antibodies to *Legionella* spp. (12 antigens) with indirect immunofluorescent antibody test (IFA) [24], to *Chlamydia pneumoniae* (TWAR strain) with microimmunofluorescence [25], and from 214 patients for antibodies to *Mycoplasma pneumoniae*, *Chlamydia psittaci/trachomatis* and respiratory tract viruses (respiratory syncytial virus, parainfluenza 1–3 virus, influenza A and B virus, and adenovirus) with enzyme immunoassays [26]. A lymphogranuloma venereum 2 (LGV2) strain was used as antigen for the diagnosis of *C. psittaci/trachomatis*.

Nasopharyngeal secretion was obtained from 244 patients on admission. The supernatant was inoculated into Helen Lake (HeLa), green monkey tree kidney (GMK) and Madin-Darby canine kidney (MDCK) cell culture tubes for isolation of viruses. The cell suspension was, after washing, placed on glass slides and fixed in acetone. Immunofluorescence was performed using monoclonal antibodies against influenza A and B.

During hospitalization, colonization of the respiratory tract with pathogens capable of causing a secondary pneumonia, was followed with repeated cultures from oropharynx and sputum, as described elsewhere [27].

Colonization was evaluated in 245 of 277 patients, and of these 93 became colonized. Nosocomial infection was defined in accordance with the Center for Disease Control (CDC) criteria [28].

Diagnostic definitions

The following diagnostic criteria were used for the respective pathogens: *Streptococcus pneumoniae:* 1) positive cultures from blood, pleural fluid, bronchial secretion, or sputum ($\geq 10^5$ colony-forming units (cfu)·ml^{-1}; irrespective of Gram stain result); or 2) detection of pneumococcal antigen in sputum or urine; or 3) a twofold or greater rise of antibody titre to pneumolysin, or a single titre in either sample above the 99th percentile upper limits for healthy adults [23].

Other bacteria: positive cultures from blood, pleural fluid, or sputum ($\geq 10^5$ cfu·ml^{-1}; with a corresponding Gram stain).

Legionella spp: growth in cultures from sputum or bronchial secretion; or a fourfold or greater rise of indirect immunofluorescent antibody (IFA) titres against *Legionella pneumophila* serogroup 1 (CDC-criteria, [29]). A presumptive legionella infection was diagnosed by a single titre ≥256, or a fourfold or greater rise of IFA titres against any one of the other 11 antigens used.

M. Pneumoniae, *C. psittaci*, *C. pneumoniae* and respiratory viruses: a significant rise of antibody titres [25, 26], or detection/isolation of virus from nasopharyngeal secretions. For adenovirus, a significant titre rise only was taken as a criterion for an aetiological diagnosis.

Statistical analysis

Based on clinical experience and earlier studies 24 variables (table 1) from the recorded data were examined for association with the four outcome variables; death, duration of hospital stay, delayed recovery and delayed resolution. Mean values will be given in the text with the standard deviation in brackets.

For univariate analysis of categorical variables the Chi-squared test with Yates' correction was used. For variables with small expected values the exact test of Fisher (two-tailed) was employed. Continuous variables

Table 1. – Risk factors for death according to the univariate analysis, in 277 patients hospitalized because of CAP

Variable	No.* (%) of patients		p	Odds ratio with 95% confidence interval		
	Died	Survived				
History						
Age**	74±13	61±21	0.05			
Chronic respiratory disease	1/11 (9)	46/245 (17)	>0.2			
Chronic cardiac or hepatic disease, or diabetes mellitus	5/12 (42)	57/264 (22)	0.14	2.6	{0.79,	8.5}
Malignancy	1/12 (8)	15/265 (6)	>0.2			
Any chronic dis.	5/12 (42)	103/265 (39)	>0.2			
Immunosuppression†	2/12 (17)	30/265 (11)	>0.2			
Alcoholism	1/10 (10)	18/252 (7)	>0.2			
Hospitalized during last 5 yrs	6/12 (50)	154/265 (58)	>0.2			
Hospitalized with pneumonia last 5 yrs	2/12 (17)	34/264 (13)	>0.2			
Chills	2/12 (17)	112/265 (42)	0.06	3.7††	{0.79,	17.2}
Chest pain	2/12 (17)	123/264 (47)	0.05	4.4††	{0.95,	20.4}
On admission						
Patients delay§	4.4±2.8	4.6±1.9	>0.2			
On antibiotics	2/12 (17)	88/265 (33)	>0.2			
Respiratory rate >20·min^{-1}	7/12 (58)	82/226 (36)	0.15	2.5	{0.77,	8.1}
Respiratory rate >30·min^{-1}	6/12 (50)	26/226 (12)	0.001	7.7	{2.31,	25.6}
Shock or mental confusion	2/12 (17)	11/265 (4)	0.12	4.6	{1.18,	17.9}
White blood cells count <9×10^9·l^{-1}	4/12 (33)	56/260 (22)	>0.2			
Serum albumin g·l^{-1}**	26±7	33±5	0.001			
Bacteraemia	3/12 (25)	31/220 (14)	>0.2			
Bilateral shadowing on chest X-ray	6/12 (50)	74/263 (28)	0.13	2.6	{0.82,	8.3}
In hospital						
Complications related to pneumonia§§	4/12 (33)	51/265 (19)	>0.2			
All other complications§§	5/12 (42)	32/265 (12)	0.01	5.2	{1.56,	17.3}
Colonization of respiratory tract	9/10 (90)	84/235 (36)	0.001	16.2	{2.02,	130.3}
Nosocomial infection	4/12 (33)	14/265 (5)	0.01	8.97	{2.41,	33.4}

*: number of patients with positive function/number recorded; **: mean values; †: splenectomied, or treatment with steroids or chemotherapeutics; ††: absence of chills and chest pain, respectively; §: mean duration of illness (days) prior to hospitalization; §§: see table 3; CAP: community-acquired pneumonia.

were analysed with Student's t-test or by linear regression. For patients with complete data, independent variables associated with outcome in the univariate analysis at, or close to, the five percent level of significance, were used in a stepwise logistic regression, using the BMDP software package [30]. The procedure followed that of a multiple regression, where variables are entered into the model one at a time according to which variables produce the best statistical fit, irrespective of their perceived importance. A logarithmic transformation of length of hospital stay was performed before applying multiple linear regression using the BMPD software package.

Results

The mean age of the 277 patients was 62 yrs (range 18–102 yrs), and 57% were female. Two hundred and two patients (73%) had a pre-existing condition (the most important are shown in table 1), and 160 patients (58%) had been hospitalized at least once during the last five years, in 36 cases because of CAP. The median duration of illness prior to admission was three days, with a range of <1–21 days. Ninety patients (32%) had received antibiotics before admission to hospital, mostly penicillin (56%), doxycycline (12%), erythromycin (7%) and amoxycillin or ampicillin (6%).

In 130 patients (47%) the pneumonia had started with an abrupt attack of fever, accompanied by chills in 114. Respiratory symptoms were present in 243 (88%) and 68 (25%) had symptoms from the gastrointestinal tract (vomiting/diarrhoea).

On admission 32 patients (13%, recorded in 226 cases) had a respiratory rate >30 breaths·min^{-1} and 13 (5%) were mentally confused or in shock.

Most patients had elevated white blood cell count, sedimentation rate and C-reactive protein (CRP) levels on admission (table 2). Only two percent of the patients had normal CRP levels (<10 mg·l^{-1}), and ten percent had severe hypoalbuminaemia.

Antimicrobial treatment

Following our departmental routines, penicillin (usually benzylpenicillin 3 g *t.i.d. i.v.*) was the most commonly used drug for initial treatment (165 patients, 60%).

Table 2. – White blood cell count (WBC), sedimentation rate (SR), C-reactive protein (CRP), and serum albumin on admission

Laboratory parameter	Range	n (%)
WBC	$<4\times10^9\cdot l^{-1}$	4 (1)
n=272	10–20	152 (56)
	>20	44 (16)
SR	<20 mm	40 (16)
n=255	≥50	155 (61)
CRP	<10 mg$\cdot l^{-1}$	5 (2)
n=268	≥80	220 (82)
Albumin	≤25 g$\cdot l^{-1}$	25 (10)
n=255	>35	99 (39)

A cephalosporin (usually cefuroxime 750–1,500 mg *t.i.d. i.v.*) was used in 44 patients, erythromycin or doxycyline in 30, ampicillin in 18, ≥2 drugs in 12 and eight patients were given no antibiotics. The initial antibiotic treatment was changed because of failure to respond in 37 (13%) patients. The average duration of treatment, including ambulatory treatment after discharge from hospital, was 12 (±7) days (238 patients recorded).

Clinical course and complications

In most patients temperature was back to normal (stable level below 37.5°C) within 72 h after admission to hospital (median 2 days, mean 3.1 days). Five patients required treatment in the intensive care unit. A total of 102 complications occurred in 82 of 277 (30%) patients, and of these nearly half could be considered related to hospitalization (table 3).

Table 3. – Complications occurring during hospital treatment in 277 patients with CAP

Related* to the acute infection		Related to hospitalization	
Pleural exudate	12	Nosocomial infection	19
Abscess/empyema	8	Drug reaction	15
Meningitis	2	Pulmonary embolism†	4
Otitis media/sinusitis	3	Other††	7
Myocarditis/ aseptic arthritis	7		
Cardiovascular**	13		
Asthma	5		
Other	7		
Total	57	Total	45

*: new condition caused by the acute infection, or deterioration of an old condition; **: congestive heart failure, atrial fibrillation, severe angina pectoris or myocardial infarction, stroke; †: three verified and one suspected; ††: *e.g.* pressure sores, fractures; CAP: community-acquired pneumonia.

Causes of pneumonia

An aetiological diagnosis was established in 189 patients (68%) (table 4). A single aetiological agent was found in 143 patients, and two or more agents in 46 (table 5). Thirty four patients (12%) had bacteraemia with *S. pneumoniae* (n=26), *Haemophilus influenzae* (n=3), *Enterobacteriacae* (n=3), *Staphylococcus aureus* (n=1) and *Enterococcus* (n=1). Three of these patients died, two with pneumococcal and one with enterococcal bacteraemia.

In the total material *S. pneumoniae* predominated, being diagnosed in 128 patients (46%), 38 of whom showed evidence of mixed infections (tables 4 and 5). *M. pneumoniae* was the second most common pathogen, accounting for the diagnosis in 27 patients (10%). One third of these had mixed infections, most often with *S. pneumoniae*. Of the ten patients with evidence of a *Legionella* infection, one had a positive sputum culture (and a fourfold titre rise against *L. pneumophila* serogroup 4/8). Only one patient had antibodies to *L. pneumophila* serogroup 1, and seven of the remaining eight, with serological diagnoses, showed evidence of mixed infections (table 5). *H. influenzae* was diagnosed in ten patients. Other bacterial pathogens were found in one percent or less of the cases.

Infection with respiratory viruses was detected in 43 patients (16%), but in only 17 of the cases as the only aetiological agent.

S. pneumoniae predominated in all age groups. Infection with Gram-negative enteric bacteria was seen only in the elderly (≥65 yrs), and *Legionella* infections occurred, with one exception, in patients ≥45 yrs old, whilst *M. pneumoniae* was much more common in young patients, being diagnosed in only 2% of patients ≥65 yrs old, but in 18% of those 45–64 yrs old and in 33% of those ≤45 yrs old.

The 88 patients in whom no aetiological diagnosis was obtained were older than the 189 patients with an established diagnosis (65±20 *vs* 60±21 yrs, $p<0.05$). Antibiotic treatment prior to admission had been given equally often in both groups. However, purulent sputum samples before start of antibiotic therapy were obtained from 30% of those with a diagnosed aetiology, but from only 19% of patients with unknown aetiology ($p<0.05$). Also, more blood cultures (89% *vs* 80%, $p<0.09$) and paired sera (86% *vs* 61%, $p<0.001$) had been obtained from patients with established aetiological diagnosis.

Mortality

The overall case fatality rate was 4% (12 of 277). Pneumonia was the direct cause of death in five of the fatal cases. In the remaining seven, death occurred on day 7–57 (median 24 days) after admission, and was caused by pulmonary embolism, myocardial infarction, arterial leg gangrene, bleeding ulcer, and cachexia in one patient each, and malignancy in two. Patients who died were older than those who survived (table 1), and

Table 4. – Aetiological agents and mortality in 277 patients hospitalized because of CAP

Aetiological agent	Cases		Fatal cases		
	n *	%	n	%	Percentage of those who died
Streptococcus pneumoniae (negative blood culture)	102	37	1**	1	8
Streptococcus pneumoniae (positive blood culture)	26	9	2	8	17
Mycoplasma pneumoniae	27	10	0		
Chlamydia psittaci	3	1	0		
Chlamydia pneumoniae	0				
Legionella spp.	10	4	0		
Haemophilus influenzae	10	4	0		
Branhamella catarrhalis	3	1	0		
Staphylococcus aureus	2	1	1†	50	8
Alpha-streptococci	4	1	1††	25	8
Enterobacteriacae	4	1	0		
Other bacteria	3	1	2**†	67	
Pneumocystis carinii	1		0		
Influenza A and B	7	3	0		
Respiratory syncytial	8	3	0		
Parainfluenza 1–3	13	5	1††	8	
Adenovirus	15	5	0		
Aetiology unknown	88	32	7	8	58

*: including 46 patients with mixed aetiologies; **: one patient with two causative agents (*S. pneumoniae* + *Enterococcus*); †: one patient with two causative agents (*Streptococcus pyogenes* + *S. aureus*); ††: one patient with two causative agents: (*Alpha-streptococci* + parainfluenza virus); CAP: community-acquired pneumonia.

Table 5. – Occurrence of mixed infections in 277 patients treated in hospital because of CAP

Virus or "atypical" agents	No. cases	No. of cases with mixed infection caused by	
		*S. pneumoniae**	Other bacteria**
Influenza A or B	7	6†	1††
Parainfluenza 1–3	13	3	3§
Adenovirus	15	7	1§
Respiratory syncytial virus	8	4	1§§
M. pneumoniae	27	6	1
Legionella spp.	10	5‡	
Total		31	7

*: seven additional patients with mixed pneumococcal pneumonia (one each with *H. influenzae*, *C. psittaci*, *E. coli*, enterococci and *Pneumocystis carinni*, and two patients with B. catarrhalis); **: one additional patient with mixed *S. aureus* + *S. phyogenes* infection; †: one patient with influenza A + *S. pneumoniae* + *H. influenzae*; ††: one patient with influenza A + *Legionella longbeache 2* + *Klebsiella*; §: one patient with *M. pneumoniae*; §§: respiratory syncytial virus + *Legionella longbeache 1*; ‡: one patient with *S. pneumoniae* + *Klebsiella* + *Legionella micdadei;* CAP: community-acquired pneumonia.

only one of the fatalities was below 60 yrs of age. The patients who died were also less subject to chills ($p<0.06$) and chest pain, had higher respiratory rate and lower serum albumin on admission, and were more subject to colonization and nosocomial infections during hospitalization (table 1).

Of these factors, serum albumin and occurrence of nosocomial infection, and to a lesser extent absence of chills and airway colonization, were associated with higher mortality in the multivariate analysis also (table 6). According to the mathematical model generated in the multivariate analysis the calculated predicted

Table 6. – Multivariate analysis of outcome in 277 patients hospitalized because of CAP

Independent variable	Outcome			
	Death	Length of hospital stay	Delayed recovery[$]	Delayed X-ray resolution[$$]
Age	–	***	–	–
Alcoholism			*	
Any chronic disease		–	–	**
Hospitalized during last 5 yrs		*		
Absence of chills	(*)	–		
Absence of chest pain	–	–		
Patient delay[†]				**
Circulatory shock/ mental confusion[††]		**		
Respiratory rate >30 breaths·min^{-1}[††]	–	*		
Serum albumin[††]	**	***	*	**
Complications related to pneumonia		***		–
Other complications		***	*	–
Colonization of respiratory tract	(*)	*	***	–
Nosocomial infection	*	–	–	

***: p<0.001; **: p<0.01; *: p<0.05; (*): p<0.06–0.1; –: p>0.1. Spaces indicate that the variable was not included in the multivariate test; [$]: the patient had not returned to normal activities at follow-up; [$$]: no, or only partial, resolution of chest X-ray at follow-up; [†]: duration of illness prior to hospitalization; [††]: on admission; CAP: community-acquired pneumonia.

Table 7. – Importance for death of serum albumin level on admission and occurrence of nosocomial infection, in patients hospital treated because of CAP

Occurrence of nosocomial infection	Serum albumin g·l^{-1}		
	40	30	20
No	0.004*	0.04	0.28
Yes	0.02	0.15	0.53

*: the probability of death was calculated using the mathematical model generated in the multivariate analysis of risk factors associated with a fatal outcome:
Predicted probability =

$$\frac{e^{2.4537-0.19166\times\text{serum albumin}+1.6001\times\text{nosocomial inf}}}{1+e^{2.4537-0.19166\times\text{serum albumin}+1.6001\times\text{nosocom. inf}}}$$

(For nosocomial infection, presence of the variable=1 and absence=0). CAP: community-acquired pneumonia.

probability of death was low in a patient with normal serum albumin levels, even where a nosocomial infection occurred during hospitalization (table 7). However, where there was both low serum albumin and nosocomial infection, the calculated risk of death was about 50%.

Course of the survivors

The length of hospital stay for the survivors was on average 7 days. In a univariate analysis, a number of factors were associated with a longer hospital stay (data not shown). Of these, the multivariate analysis showed that high age, hospitalization during the last five years, and high respiratory rate, shock or mental confusion, or low serum albumin on admission, and colonization of the respiratory tract and complications during hospital care correlated significantly with a longer hospitalization (table 6).

At follow-up, about eight weeks after admission to hospital, 234 patients (88% of the survivors) were clinically examined and, of these, 81% had returned to their normal daily activities. Chest X-ray in 219 patients showed complete, or nearly complete, resolution of infiltrates in 84%. According to the multivariate analysis a low serum albumin was significantly associated with both a delayed recovery and a delayed resolution of infiltrates (table 6). Delayed recovery was also associated with alcoholism, airway colonization and complications related to hospital care, while delayed resolution was associated with pre-existing chronic disease and a longer period between onset of illness and admission to hospital. Other factors associated with these two outcome variables in the univariate analysis only (data not shown), included

high age (for both variables), and colonization and complications to the acute infection (for delayed resolution).

Discussion

The present study of 277 patients hospitalized because of CAP, is the first multivariate analysis of prognostic factors for mortality, and outcome of the survivors, including all adult age groups and only community-acquired infections.

The mean age of our patients (62 yrs) was in the same range as in recent studies [16–18], whereas in most earlier studies patients have been younger [9–13]. This may reflect the growing percentage of elderly people in the population [31]. The importance of including the elderly, in contrast to the British multi-centre study material [2], was demonstrated by the fact that one third of our patients were ≥75 yrs of age. Despite high age, only half of our patients had pre-existing illnesses, which contrasts with most [2, 10–12 , 17, 18], but not all [9, 13], previous studies. Also, in contrast to studies from the USA [9–12] and France [17], but more in accordance with those from the UK [2, 13, 14] and Canada [18], the percentage of known alcoholics was low (7%) in the present study.

An aetiological diagnosis was established in 68% of the patients, a rate similar to [2, 16, 17], or higher than [10, 13, 18, 32] that in most previous studies. We confirmed that *S. pneumoniae* seems to be responsible for about half of the CAP in adults who require hospitalization [2, 9–11, 14, 16–18, 32–34]. The second most common pathogen found in the present study was *M. pneumoniae* (10%). In accordance with earlier findings mycoplasmal pneumonia affected all age groups [35], but was more common in the young [36]. The relative frequency of mycoplasmal pneumonias in earlier studies has varied between 2–3% [14, 31] and 14–18% [2, 13], probably due to differences in the ages of the populations studied, and to cyclical epidemic outbreaks of this agent [35]. Serological evidence of recent *C. pneumoniae* infection was not found in any patient. This is in some contrast to two previous reports [37, 38], both conducted during 2.5 yr periods, in which *C. pneumoniae* infection was diagnosed in 6–12% of the cases. The fact that no cases of *C. pneumoniae* were diagnosed in the present study could be explained by the seemingly epidemic nature of this infection [39, 40]. *H. influenzae* was demonstrated in only ten patients, six of whom were smokers and/or had chronic bronchitis. Evidence has been accumulating that *B. catarrhalis* is a primary respiratory pathogen, particularly in patients with chronic chest disease [41]. Such an underlying disease was uncommon in our patients (19%), which might explain why only three patients were infected with *B. catarrhalis*. In accordance with earlier findings in Sweden [16, 34], except for an epidemic outbreak [24], *Legionella* spp. were an infrequent cause (4%) of CAP in this study. Evidence of mixed infections was found in nearly 25% of patients with an aetiological diagnosis, most commonly, as often described previously, a virus together with *S. pneumoniae*. In 22 of 46 patients with mixed infections, two or more bacteria were found: in six cases *S. pneumoniae* and *M. pneumoniae*, in five *S. pneumoniae* and *Legionella* spp., and in the remaining cases other combinations of aerobic organisms. Similar rates of mixed bacterial infection have been reported in several other studies [2, 16, 17, 32, 34, 42]. Mixed infections with anaerobic bacteria may well be rather common, but cannot be diagnosed from sputum cultures. However, of 12 of our patients who underwent bronchoscopy because of therapy failure a mixed infection was documented in only one [21]. However, the possibility of a mixed infection in a patient who fails to respond to therapy should be considered.

The overall mortality of 4% was at the same level as in some [2, 12, 16], but lower than in most [9–11, 13, 14, 17, 18], previous studies. The diverging case fatality rates in these studies might in part reflect differences in patient materials, since 2% of our patients required ventilatory support, compared to 18% in a study where the mortality was 21% [18].

The aetiological diagnosis was known in only five of the 12 patients who died, three of whom had pneumococcal pneumonia. Three of the seven patients with unknown aetiology died within a week, two of pneumonia and one of pulmonary embolism, and the remaining four patients, 81–90 yrs of age, died of other illnesses after more than two weeks in hospital. Only one of these seven patients had received antibiotics before admission, and before start of treatment blood cultures were obtained from five, and purulent sputum samples from two patients.

The prognostic predictors that appear important according to a multivariate analysis may differ depending on the method used [2]. Also, the low case fatality rate in the present study must be kept in mind when interpreting the results of both the univariate and multivariate test, especially because of the risk for "false negative" results (type II, or beta, errors). For example, although just one of 111 patients below 60 yrs of age died, compared to 11 of 166 of those 60 yrs or older, we found in contrast to both the British multi-centre study [2] and the study by MARRIE *et al.* [18] that age was of importance only in the univariate analysis.

A subtle presentation of pneumonia, without "classical" symptoms such as chills and chest pain has been noted especially in patients of high age or with coexisting diseases [43, 44]. Such an atypical onset was associated with a poorer prognosis of lobar pneumonia as early as the beginning of the century [43], and this has now been confirmed both by the recent British study [2] and the present study. We also confirmed the finding of the British study [2] that tachypnoea on admission was associated with higher mortality. However, the great impact on mortality of low serum albumin levels on admission in the present study, was seen in neither of the two previous

prognostic CAP studies that used multivariate analyses [2, 18]. In the present material of mostly elderly patients, chronic malnutrition may have been a major cause of the lowered serum albumin. We have recently shown that low serum albumin was correlated also with colonization of the respiratory tract and development of secondary infections [27]. The present study demonstrates that both colonization and nosocomial infection were associated with higher mortality. Since malnutrition has multiple adverse influences on host defence mechanisms [44], the patient's nutritional status may play a major role in the prognosis of CAP.

Regarding other factors earlier found to correlate with a high risk of death, we were unable to confirm the importance of confusion, absence of vomiting, number of leucocytes [2], or number of complications during hospital stay [18]. We did not include the recording of blood urea levels, diastolic hypotension, number of lobes involved, or requirement for ventilatory support, factors also found to be of importance [2, 18].

As in the British study [2], about 80% of our survivors were fit for normal activities at follow-up, whilst chest X-ray resolution was seen in 84% of our patients about eight weeks after admission, compared to 55% of theirs after six weeks. Eight weeks, therefore, seems to be a more appropriate time for a control chest X-ray. Low serum albumin on admission was of importance also for the course of the survivors, being associated, partly in accordance with the British study [2], with a longer hospital stay, delayed recovery, and delayed X-ray resolution. A prolonged hospital stay was also, not surprisingly, associated with high age, previous illnesses, severeness of the acute disease and complications during hospital stay. Delayed X-ray resolution was associated with pre-existing illness, but also with a longer patient delay, indicating that early recognition and treatment of pneumonia may limit the extent of pulmonary tissue damage.

In conclusion, although the mortality was low in this material of mostly elderly patients hospitalized because of CAP, some deaths could have been prevented, and it is probably possible to influence the course of the disease in the survivors.

Pneumoccocal vaccination in Sweden is used only occasionally. However, since *S. pneumoniae* is the predominating cause of CAP, vaccination of the elderly should be considered in Sweden as elsewhere [45, 46]. Immunization of all hospitalized patients ≥55 yrs of age, as has recently been suggested as a cost-effective strategy [45], also seems well-founded on the basis of our figures, since nearly 60% of our patients had been hospitalized at least once during the last five years. Intensified observation and treatment is indicated in patients being admitted with atypical presentation of the pneumonia or with high respiratory rate. The patients' nutritional status should be assessed on admission, and in patients with respiratory tract colonization, surveillance should be increased. Finally, there is probably much to be gained by improved prevention of nosocomial infections and thrombo-embolic complications.

Acknowledgements: The authors are grateful to B. Wretlind, and his staff, at the microbiological laboratory at Danderyd Hospital, and to B. Svensson, for their assistance with-this study. They also want to thank E. Berg for assistance with the statistical analysis.

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Etiologie, évolution et facteurs pronostiques dans les pneumonies acquises dans la collectivité et nécessitant l'hospitalisation. Å. Örtqvist, J. Hedlund, L. Grillner, E. Jalonen, I. Kallings, M. Leinonen, M. Kalin.

RÉSUMÉ: Nous avons étudié de mainère prospective, chez 277 patients adultes (âge moyen 62 ans), atteints d'une pneumonie acquise dans la collectivité mais nécessitant l'hospitalisation, l'évolution et les facteurs pronostiques de cette maladie. L'étiologie a été établie dans 68% des cas, *S. pneumoniae* étant l'agent prédominant. La mortalité fut de 4% (12/277), et tous les patients sauf un, qui sont décédés, étaient âgés de plus de 60 ans. Les facteurs associés à une mortalité élévée comportent l'âge avancé, l'absence de frissons et de douleurs thoraciques, les rythmes respiratoires élevés (>30·minute^{-1}) et un taux bas d'albumine sérique à l'admissoin, ainsi que l'apparition d'une colonisation des voies aériennes et d'une infection secondaire au cours de l'hospitilisation. L'analyse multivariée a montré qu'un taux bas d'albumine et l'apparition d'une infection secondaire, mais également l'absence de frissons et de colonisation des voies aériennes, sont en corrélation avec une mortalité élevée. Chez les patients qui ont survécu, la durée médiane du séjour hospitalier fut de 7 jours, et lors du suivi, environ huit semaines après l'admission, l'on a noté un taux de guérison de 81% et une normalisation des clichés thoraciques dans 84% des cas. En conclusion, nous croyons que l'evolution de la pneumonie acquise dans la collectivité peut être influencée par des mesures préventives contre l'infection pneumococcique, et par une surveillance accrue des patients à risque.
Eur Respir J., 1990, 3, 1105–1113.