Community-acquired pneumonia through Enterobacteriaceae and *Pseudomonas aeruginosa*: diagnosis, incidence and predictors

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ABSTRACT: The aim of the present study was to determine the relevance of the presence of Enterobacteriaceae (EB) and *Pseudomonas aeruginosa* (PA) in patients with community-acquired pneumonia (CAP) and how the true incidence of these pathogens can be assessed.

Based on prospective data from 5,130 patients with CAP included in the German Competence Network for Community-Acquired Pneumonia (CAPNETZ), the incidence, clinical characteristics, outcome and predictors of patients with CAP due to EB and PA were studied applying strict case definitions.

The incidence of EB was 67 (1.3%) out of 5,130, including 27 patients with bacteraemia. PA was found in 22 (0.4%) out of 5,130 patients. These microorganisms were judged to be indeterminate pathogens in an additional 172 and 27 isolates, respectively. Patients with indeterminate pathogens differed considerably from those with definite isolates in terms of clinical presentation, comorbidity, pneumonia severity and outcome. Independent risk factors for EB included cardiac and cerebrovascular disease, and for PA chronic respiratory disease and enteral tube feeding. The 30-day mortality was significantly higher in patients with definite pathogens.

In the present large population, the incidence of CAP due to EB/ PA was low. The risk of the presence of these pathogens can be assessed using several predictors, which may identify those patients in need of an extended diagnostic work-up and initial antimicrobial treatment.

KEYWORDS: Community-acquired pneumonia, Enterobacteriaceae, *Pseudomonas aeruginosa*

Community-acquired pneumonia (CAP) is characterised by three main criteria. First, it is an acute infectious injury of the lung; secondly, the pneumonia is acquired in the community, *i.e.* not in the hospital; and, thirdly, it occurs in a host without severe immunosuppression, *i.e.* not at significant risk for opportunistic pathogens. The resulting clue is that these three criteria permit a relatively confident prediction of the pathogen patterns to be expected, with *Streptococcus pneumoniae* being the leading pathogen, followed by atypical bacterial and viral pathogens. Thus the diagnosis of CAP and assessment of its severity represent a tough basis for decisions regarding initial treatment settings and empirical initial antimicrobial treatment [1].

Although the concept of CAP usually works well, there remain important uncertainties at its

periphery. These include all pathogens which are only rarely implicated (mainly in at-risk populations), and which are associated with considerable pathogenicity but require a very different antimicrobial coverage, such as Enterobacteriaceae (EB) and *Pseudomonas aeruginosa* (PA). A landmark Spanish study found these pathogens in ~10% of the study population [2], a finding confirmed in a recent Korean study [3]. In contrast, others found these pathogens in ~1–3% [4–7].

Moreover, the concept of CAP has recently been challenged by the definition of the new pneumonia entity healthcare-associated pneumonia (HCAP) [8, 9]. The key perception behind this concept is that elderly and severely disabled patients with constant and/or recent contact with healthcare institutions, such as for dialysis,

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Received:

June 10 2009

Accepted after revision:

Aug 07 2009

First published online:

Aug 13 2009

For editorial comments see page 473.

This article has supplementary material accessible from www.erj.ersjournals.com

European Respiratory Journal

Print ISSN 0903-1936

Online ISSN 1399-3003

nursing homes or hospitals, exhibit a prognostic and aetiological pattern essentially different from CAP. In particular, multiresistant pathogens, including EB and PA, are claimed to occur frequently [10–12].

The incidence, clinical presentation, prognosis and predictors of CAP due to EB/PA were studied. Moreover, patients with definite pneumonia due to EB/PA according to strict definitions were compared with those exhibiting these pathogens but failing to meet these strict criteria in an attempt to improve understanding of what CAP due to EB/PA truly represents.

MATERIALS AND METHODS

Patient population

A detailed description of the Competence Network for Community-Acquired Pneumonia (CAPNETZ) methodology is given elsewhere [13]. The present study was approved by the ethical review board of each of the participating centres, and all patients included provided informed consent.

Data collection

In the present prospective study, all demographic, clinical and diagnostic patient data were recorded using standardised Internet-based data sheets created by 2mt[®] (Ulm, Germany). The study period comprised 61 months, starting on June 1, 2002 and ending on June 30, 2007, thus including four autumn–winter seasons.

Microbiological processing and examination

The methods applied have been described previously [14, 15]. In short, sputum and/or other respiratory secretions were immediately processed in the participating local microbiological laboratories according to the German Quality Standards in Clinical Microbiology and Infectious Diseases. The results of virus testing are not included in the present report.

Sample processing

All respiratory specimens and blood cultures, if available, were immediately processed in the local microbiological laboratories of the participating clinical centres. Gram-staining and culture were performed for all respiratory samples. Validated sputum, blood culture, pleural fluid, undiluted and serially diluted tracheobronchial aspirate, protected specimen brush and bronchoalveolar lavage fluid (BALF) samples were plated on sheep blood agar, Centers for Disease Control and Prevention (CDC) anaerobe 5% sheep blood agar and chocolate, as well as Sabouraud, agar. Undiluted protected specimen brush and BALF samples were also cultured on charcoal–yeast extract agar. All Gram-negative pathogens were identified to species level according to standard methods. Standardised susceptibility testing was performed in the local microbiological laboratories. Urine was tested for the presence of *S. pneumoniae* and *Legionella* spp. antigens.

Definitions

Isolates of EB/PA were considered definite causative pathogens when they were: 1) isolated from blood cultures or pleural fluid cultures; or 2) in the presence of a good-quality sputum revealing >25 polymorphonuclear cells and <10 epithelial cells per power field (total magnification 100×) and predominant growth in culture of sputum of $\geq 1 \times 10^6$ colony-forming units (CFU)·mL⁻¹ or BALF of $\geq 1 \times 10^4$ CFU·mL⁻¹. If one of these

criteria was not met, the presence of EB or PA was judged to be indeterminate.

Statistical analysis

Comparisons between groups were performed by means of the Chi-squared test for categorical variables, or Fisher's exact test in the case of small expected frequencies, and ANOVA for continuous variables including multiple comparisons. Multivariate analysis of predictive factors for 30-day mortality and CAP due to definite EB/PA was performed using binary logistic regression analysis. All analyses were performed using SPSS software (SPSS 10.0; SPSS, Inc., Chicago, IL, USA). All tests of significance were two-tailed, and α was set at 0.05.

RESULTS

General characteristics of study population

Overall, 5,130 patients with CAP from 12 clinical centres throughout Germany were included in the analysis during 2002–2007. The 2,842 male and 2,288 female patients had a mean age of 60 ± 18 yrs. Of the patients, 65% ($n=3,334$) were hospitalised when first contacted for participation in CAPNETZ, and 307 (6%) were nursing home residents. Comorbid conditions were present in 3,299 (64%) patients, and 31% were smokers. Severity scores, as assessed using the confusion, respiratory frequency and blood pressure in those aged ≥ 65 yrs (CRB-65) index, were available for 90% of the patients (0: 37%; 1: 38%; 2: 13%; 3: 2%; and 4: 0.3%). Of the patients, 126 (2.5%) required mechanical ventilation and 326 (6.4%) died within 30 days after diagnosis. The clinical characteristics of patients without respiratory samples and no definite EB/PA were significantly different and reflected greater age, greater comorbidity, more frequent nursing home residency, greater pneumonia severity on presentation and increased mortality in the patient group with EB/PA as definite pathogens. The demographic and clinical data of patients with and without EB/PA are given in tables 1 and 2, respectively.

General microbial patterns

S. pneumoniae was identified as the predominant respiratory pathogen in the study population, followed by *Mycoplasma pneumoniae*. In <5% of the patients *Legionella* spp., *Haemophilus influenzae* and *Staphylococcus aureus* were identified. Even less frequent were *Moraxella catarrhalis* and *Chlamydophila pneumoniae*.

Diagnosis and epidemiology of EB and PA

Respiratory samples were available from 2,102 (41%) of the patients. In 40 patients, EB were considered the definite causative pathogen according to the predefined criteria. The most frequent (48%) enterobacterial pathogen isolated was *Escherichia coli*. In contrast, EB were classified as indeterminate in an additional 172 patients. Overall 172 (81%) out of 212 isolates yielding EB were indeterminate rather than definite pathogens.

Of the patients, 27 (40% of all EB pneumonia cases) had definite CAP due to EB with bacteraemia through *E. coli* (18 cases) and *Proteus mirabilis* and *Klebsiella* spp. (three cases each), as well as *Enterobacter* spp., *Serratia marcescens* and *Morganella morganii* (one case each) (online supplementary material).

TABLE 1 Demographic and clinical data of patients with and without Enterobacteriaceae (EB)

	No respiratory sample	Respiratory sample with no definite/indeterminate EB/PA isolates	p-value [#]	Definite EB	Indeterminate EB	p-value [†]	p-value [‡]
Subjects n	3009	1833		67 [§]	172		
Age yrs	60 ± 19	58 ± 18	<0.000	73 ± 15	66 ± 14	<0.000	0.002
Male sex	53	58	0.002	61	69	0.553	0.276
Nursing home resident	8	2	<0.000	19	10	<0.000	0.046
Hospitalisation	69	56	<0.000	94	73	<0.000	0.000
CRB-65 score			<0.000			<0.000	0.000
0	36	39		13	24		
1	37	37		28	46		
2	13	11		33	15		
3	3	1		9	2		
4	0.4	0.1		0	1		
Smoking history pack-yrs	28 ± 22	29 ± 23	0.439	46 ± 40	37 ± 31	<0.000	0.179
Dyspnoea	71	74	0.043	90	76	0.005	0.038
Confusion	10	4	<0.000	22	6	<0.000	0.000
Oxygen requirement	44	38	<0.000	85	51	<0.000	0.000
Mechanical ventilation	2.2	2.5	0.598	13.4	3.5	<0.000	0.005
Chronic respiratory disease	34	37	0.074	45	45	0.157	0.853
Renal failure	8	6	0.004	22	11	<0.000	0.029
Congestive heart failure	19	14	<0.000	46	25	<0.000	0.001
Cerebrovascular disease	12	5	<0.000	33	12	<0.000	0.000
Other chronic neurological disorder	8	3	<0.000	15	8	<0.000	0.086
Diabetes mellitus	17	13	<0.000	30	24	<0.000	0.338
Enteral tube feeding	2.0	0.5	<0.000	4.5	6.0	0.008	0.762
CRP mg·L⁻¹	78	74	0.337	153	93	0.026	0.204
Leukocyte count cells·μL⁻¹	11100	11100	0.784	12650	11650	0.006	0.048
Change in antibiotic therapy	27	24	0.009	40	24	0.002	0.016
30-day mortality	220 (7.3)	82 (4.5)	<0.000	14 (20.9)	12 (7.0)	<0.000	0.002

Data are presented as mean ± SD, % or n (%), unless otherwise indicated; C-reactive protein (CRP) concentrations and leukocyte counts are medians. PA: *Pseudomonas aeruginosa*; CRB-65: confusion, respiratory frequency and blood pressure in those aged ≥ 65 yrs. [#]: respiratory sample with no definite/indeterminate EB/PA isolates versus no respiratory sample; [†]: definite EB versus respiratory sample with no definite/indeterminate EB/PA isolates; [‡]: indeterminate EB versus definite EB; [§]: in respiratory samples (n=40) and blood cultures (n=27).

In seven of the bacteraemic patients, respiratory samples were available, two of which yielded an identical bacterial species to the corresponding blood cultures.

Thus the overall incidence of CAP with definite EB was only 67 (1.3%) out of 5,130. It was 63 (1.9%) out of 3,334 in hospitalised patients and four (0.2%) out of 1,796 in ambulatory patients. Taking into account only patients with respiratory samples available, the overall incidence was 67 (3.2%) out of 2,102.

Applying the same criteria, definite PA pneumonia was diagnosed in 22 patients.

PA in the respiratory tract of an additional 27 patients was considered indeterminate (table 2). In nine additional cases, respiratory samples yielded *Pseudomonas* spp. other than PA (not further specified (n=2), *P. fluorescens* (n=5), and *P. putida* and *P. stutzeri* (n=1 each)) and were consequently excluded from the analysis. Overall, 27 (55%) out of 49 isolates yielding PA were indeterminate rather than definite pathogens. Only

one case had PA bacteraemia; respiratory samples from this patient were not available.

Accordingly, the overall incidence of CAP due to PA was 22 (0.4%) out of 5,130. PA was absent in ambulatory patients. The incidence was 22 (1.0%) out of 2,102 in the subgroup with respiratory samples available.

Copathogens were isolated from the respiratory materials of six patients with definite EB (three *Legionella* spp., two *S. pneumoniae* and one *H. influenzae*) and eight patients with definite PA pneumonia (three *S. aureus*, two *S. pneumoniae*, one *Streptococcus pyogenes*, one *M. catarrhalis* and one *K. pneumoniae*).

The incidences of EB and PA according to different denominators are summarised in table 3.

Clinical characteristics of CAP due to EB and PA

Comparing the population with respiratory samples (n=1,840) with that classified as having definite EA/PA, patients with EB

TABLE 2 Demographic and clinical data of patients with and without definite *Pseudomonas aeruginosa* (PA)

	Respiratory sample with no definite/indeterminate EB/PA isolates	Definite PA	Indeterminate PA	p-value [#]	p-value [†]
Subjects n	1833	22 ⁺	27		
Age yrs	58 ± 18	64 ± 17	68 ± 11	0.101	0.322
Male sex	58	59	70	0.886	0.406
Nursing home resident	2	23	7	<0.000	0.219
Hospitalisation	56	100	78	<0.000	0.027
CRB-65 score				0.103	0.653
0	39	32	19		
1	37	27	44		
2	11	23	19		
3	1	5	0		
4	0.1	0	4		
Oxygen requirement	38	82	59	<0.000	0.123
Mechanical ventilation	2.5	9	11	0.101	1.000
Chronic respiratory disease	37	68	52	0.002	0.247
Diabetes mellitus	13	27	19	0.039	0.510
Cerebrovascular disease	5	32	7	<0.000	0.060
Other chronic neurological disorder	4	18	11	<0.000	0.685
Enteral tube feeding	0.5	23	11	<0.000	0.440
Leukocyte count cells·μL⁻¹	11100	14100	12100	0.001	0.251
Change in antibiotic therapy	24	64	40	<0.000	0.106
30-day mortality	82 (4.5)	4 (18.2)	1 (3.7)	0.015	0.160

Data are presented as mean ± SD, % or n (%), unless otherwise indicated; leukocyte counts are medians. EB: Enterobacteriaceae; CRB-65: confusion, respiratory frequency and blood pressure in those aged ≥ 65 yrs. [#]: definite PA versus respiratory sample with no definite/indeterminate EB/PA isolates; [†]: indeterminate PA versus definite PA; [‡]: in respiratory samples (n=21) and blood culture (n=1).

or PA were significantly older and had more comorbid conditions. Between a quarter and a fifth were nursing home residents. Severe comorbidity was reflected by more frequent enteral tube feeding. Pneumonia on presentation was more severe. All of the patients with EB bacteraemia and all with PA were hospitalised. Mortality was approximately five times higher (tables 1 and 2).

Comparison of patients with definite EB and PA with those judged to be indeterminate

When comparing the 67 patients with definite EB with the 172 patients with EB judged to be indeterminate, patients with

definite EB were significantly older, were more frequently nursing home residents, had more comorbid conditions, showed greater pneumonia severity on presentation (CRB-65, hospitalisation rate and requirement for mechanical ventilation) and had a higher mortality (table 1). This was similar in terms of nursing home residency, comorbidity and mortality when comparing patients with PA as definite pathogens to the respective group judged to be indeterminate. However, due to small sample sizes, differences were nonsignificant except hospitalisation rate (table 2).

Predictive factors of CAP due to EB/PA

The following factors were predictors of CAP due to EB: age >65 yrs, nursing home residency, enteral tube feeding, congestive heart failure, renal failure, cerebrovascular disease, other chronic neurological disorders, and diabetes. On multivariate analysis, congestive heart failure and cerebrovascular disease were predictive of EB (table 4).

Predictors of PA on univariate analysis included nursing home residency, enteral tube feeding, chronic respiratory disease, cerebrovascular disease, and other chronic neurological disorders. Independent predictors of CAP due to PA included chronic respiratory disease and enteral tube feeding (table 5).

Antimicrobial treatment of CAP due to EB/PA

Based on the available susceptibility testing, first-line antimicrobial therapy in patients with EB in respiratory samples

TABLE 3 Overview of incidences of definite and indeterminate Enterobacteriaceae (EB)/ *Pseudomonas aeruginosa* (PA) according to different denominators

	Subjects n	EB in total population [#] %	EB in population with respiratory samples [†] %
Definite EB[‡]	67	1.3	3.2
Indeterminate EB	172	3.4	8.2
Definite PA[‡]	22	1.0	0.4
Indeterminate PA	27	0.5	1.3

[#]: n=5,130; [†]: n=2,102; [‡]: from respiratory samples.

TABLE 4 Predictors of community-acquired pneumonia due to definite Enterobacteriaceae

	Univariate analysis		Multivariate analysis	
	p-value	OR (95% CI)	p-value	OR (95% CI)
Age >65 yrs	0.000	2.67 (1.59–4.48)	0.278	
Nursing home residency	0.000	4.05 (2.18–7.50)	0.531	
Congestive heart failure	0.000	4.26 (2.62–6.93)	0.007	2.23 (1.25–3.99)
Renal failure	0.000	3.58 (1.99–6.41)	0.080	
Chronic respiratory disease	0.089			
Enteral tube feeding	0.026	3.53 (1.08–11.53)	0.918	
Cerebrovascular disease	0.000	4.87 (2.90–8.19)	0.006	2.45 (1.29–4.66)
Other chronic neurological disorder	0.002	2.77 (1.40–5.47)	0.442	
Diabetes mellitus	0.001	2.41 (1.42–4.10)	0.315	

OR: odds ratio; CI: confidence interval.

and/or blood cultures was adequate in 17 (25%) patients, inadequate in 15 (22%) and indeterminate in 35 (53%) (tables 1 and 2 of online supplementary material).

Likewise, in patients with definite PA pneumonia, initial antimicrobial treatment was inadequate in 14 (64%) out of 22 cases due to innate resistance of the pathogen to the chosen antimicrobial agents. Four (18%) patients received adequate antibiotic therapy according to susceptibility testing, and, in the remaining four (18%) cases, adequacy remained indeterminate (table 3 of online supplementary material).

Outcome of CAP due to EB/PA

The 30-day mortality of CAP due to EB/PA was substantially higher than in patients without respiratory samples available and without these pathogens. The mortality of CAP with EB as definite pathogens in respiratory samples was 20%, EB bacteraemia 22% and PA pneumonia 18% (tables 1 and 2).

Predictors of mortality

Amongst others, the presence of either EB or PA as definite pathogen, but not as indeterminate, was identified as a risk

factor on univariate analysis. However, only EB, and not PA, remained an independent predictor on multivariate analysis (table 6).

DISCUSSION

In earlier studies, including a general population of hospitalised patients with CAP, only few showed a proportion of >3% of CAP due to EB [16, 17], the highest reaching 9% [18]. Likewise, in a recent study addressing this particular issue, the incidence was 3% [2]. The incidence of EB in severe CAP was up to 15%, which is 2–3-fold higher than in the general hospitalised population [19, 20]. However, in a large study of patients aged ≥65 yrs, the incidence was 9.6% [21]. Moreover, in a study addressing the impact of HCAP, the incidence was 11.6% in CAP and even reached 19.7% in HCAP patients [10]. In the present study, the overall incidence was 1.3%. It should be noted that the incidence was minimal in ambulatory patients.

The reasons for this wide range of observed incidences are complex. First, a very strict definition was used, relying on not only quality criteria for sputum samples but also semi-quantitative and quantitative cultures. Indeed, four out of five

TABLE 5 Predictors of community-acquired pneumonia due to definite *Pseudomonas aeruginosa*

	Univariate analysis		Multivariate analysis	
	p-value	OR (95% CI)	p-value	OR (95% CI)
Age >65 yrs	0.374			
Nursing home residency	0.001	4.94 (1.81–13.50)	0.885	
Congestive heart failure	0.461			
Renal failure	0.678			
Chronic respiratory disease	0.010	4.01 (1.63–9.86)	0.001	4.78 (1.89–12.07)
Enteral tube feeding	0.000	21.79 (7.80–60.90)	0.000	13.87 (3.39–56.65)
Cerebrovascular disease	0.000	4.64 (1.88–11.44)	0.107	
Other chronic neurological disorder	0.040	3.49 (1.17–10.39)	0.698	
Diabetes mellitus	0.108			

OR: odds ratio; CI: confidence interval.

TABLE 6 Predictors of 30-day mortality on univariate and multivariate analysis

	Univariate analysis		Multivariate analysis	
	p-value	OR (95% CI)	p-value	OR (95% CI)
Age >65 yrs	0.000	5.38 (4.03–7.20)	0.001	2.15 (1.35–3.42)
Male sex	0.000	1.50 (1.18–1.90)	0.232	
Nursing home residency	0.000	8.73 (6.56–11.61)	0.232	
Congestive heart failure	0.000	4.39 (3.46–5.57)	0.005	1.87 (1.21–2.89)
Malignancy	0.000	2.43 (1.79–3.30)	0.000	2.45 (1.52–3.94)
Heavy smoker [#]	0.000	2.31 (1.45–3.69)	0.110	
Dyspnoea	0.000	3.06 (2.12–4.42)	0.211	
Hospitalisation	0.000	31.70 (14.10–71.23)	0.001	5.63 (2.03–15.63)
Mechanical ventilation	0.000	13.03 (8.82–19.24)	0.000	4.36 (2.13–8.91)
EB as definite pathogen	0.000	4.02 (2.11–7.56)	0.469	
EB classified indeterminate	0.749			
PA as definite pathogen	0.047	3.3 (1.11–9.81)	0.999	
PA classified indeterminate	1.0			

OR: odds ratio; CI: confidence interval; EB: Enterobacteriaceae; PA: *Pseudomonas aeruginosa*. [#]: >20 pack-yrs.

EB isolates were judged to represent an indeterminate status. Although it cannot be ruled out that the present case definition may have missed a few additional patients with CAP due to EB, the finding of striking differences as regards pneumonia severity on presentation and clinical outcome in the groups with definite EB compared to the group judged to be indeterminate are in support of the case definition. Secondly, the incidence of EB seems to be highly dependent upon the population studied. It was found that CAP due to EB was associated with greater age, a broad range of comorbid conditions and more severe pneumonia on admission. Thus, since the proportion of patients with severe pneumonia was limited, a higher rate might be expected in studies including a higher proportion of patients with severe CAP.

Although the incidence of CAP due to EB was low, mortality was very high, reaching 20% in definite cases diagnosed from a respiratory sample and 22% in bacteraemic cases. This rate was three to five times higher than that in the general study population. It should be noted that this finding does not necessarily imply excess mortality from these pathogens, and may simply indicate an elderly and more severely disabled population. Indeed, every fifth patient with CAP due to definite EB resided in a nursing home, and comorbidity was extensive. The mortality rate exceeded the rate of mechanical ventilation (21 *versus* 13%), indicating that treatment restrictions due to prognostic considerations were applied. Although the yield of blood cultures in CAP is generally low, and their routine use has, therefore, been questioned [22, 23], it was found that a large proportion of CAP due to EB presents with bacteraemia. Therefore, we argue that blood cultures should be obtained, especially in patients at risk of EB.

The patients typically at risk of CAP due to EB can be characterised quite confidently. They are elderly, highly comorbid and highly acutely disabled patients. Surprisingly, chronic respiratory disease could not be confirmed as a risk factor [2, 20]. However, comorbid conditions, such as cardiac

and cerebral disease, could be identified as independent predictors. Unfortunately, no data were available regarding antimicrobial pretreatment and hospitalisation in the preceding 3–6 months, nor were there any data regarding aspiration at our disposal, factors which have been implicated in CAP due to EB in a previous study [2].

Many findings regarding CAP due to EB can also be applied to CAP due to PA. Again, the reported incidence varied considerably in previous studies. Of 10 recent studies including >250 patients, six did not find any cases due to PA [6, 7, 16, 17, 24, 25], and the incidence in the remaining four was only 1–5% [4, 21, 26, 27]. Likewise, in severe CAP, the incidence was higher, reaching 12% [19]. In a previous Spanish study, PA was the third most common pathogen, with an incidence of 7% [2]. Interestingly, this finding could not be reproduced in the most recent study from this group, where the incidence of PA reached only 2 and 3% in non-intensive care unit (ICU) and ICU patients, respectively [28]. Consistent with previous findings, PA was absent in ambulatory patients [29]. In hospitalised patients also, only very few cases due to PA were found. Similarly to EB, most (55%) isolates of PA were considered to be indeterminate, an assumption once again confirmed by dramatic differences in mortality. Whereas CAP due to definite PA exhibited a mortality of 18%, mortality was 6% in the general population, and only 4% in the population judged to be indeterminate with regard to PA.

Only very few cases of CAP due to PA have been described in previously healthy patients [30]. Accordingly, only one patient without pre-existing comorbid conditions was found in the present population. In hospitalised patients, it appears that the clinical characteristics of patients with CAP due to PA are similar to those of EB. However, the clinical predictors were not identical; CAP due to PA was associated with chronic respiratory disease and enteral tube feeding, the latter being the most powerful predictor. As in CAP due to EB, the mortality rate exceeded the rate of mechanical ventilation (18

versus 9%). Again, this does not necessarily imply excess mortality due to PA.

The present findings do not support the concept of HCAP to be generally applicable in Germany and countries with a comparable epidemiological situation. First, the incidence of unusual pathogens, such as methicillin-resistant *S. aureus*, EB or PA, was very low in the present study, although 6% of the population consisted of nursing home residents. This might be due to significant differences in the characteristics of nursing home residents and infection control procedures when comparing German and US nursing homes [31]. Secondly, resistance rates in EB were low in the present study, with only one *E. coli* isolate identified as an extended-spectrum β -lactamase-positive microorganism. Likewise, none of the patients in the present study with PA had a multidrug-resistant isolate.

The present study has some limitations. First, respiratory samples and blood cultures were not available for all of the patients studied. Indeed, the group without respiratory samples was older, more comorbid, and showed greater pneumonia severity and higher mortality. Thus some cases with EB/PA may have been missed in this group. However, the mortality was still substantially lower than that in the definite EB/PA group (7.3 versus 20.9% for EB and 18.2% for PA), and was similar to the indeterminate groups (7% for EB; 3.7% for PA). Secondly, the number of patients with severe CAP was limited. Since pneumonia severity is a risk factor for CAP due to EB/PA, the incidence of both may have been underestimated in severe cases. However, it appears improbable that patients presenting with severe CAP exhibit risk factors substantially different to those described in the present study. Therefore, the data are still of help in identifying those patients at risk. Finally, standardised susceptibility testing was not available for the majority of patients with EB, limiting the analysis regarding appropriate treatment.

In conclusion, strict diagnostic criteria have to be applied in order to avoid overestimation of EA and PA. We argue that the present data provide sufficient support for the view that these pathogens show a low incidence and are mainly observed in patients at defined risk. A risk-adapted approach of initial antimicrobial treatment and consistent microbial investigation in patients at increased risk and not assigned to treatment restrictions remains mandatory. At least in Germany and countries with a comparable epidemiological situation, such an approach probably permits better guidance of patient management than the concept of HCAP.

SUPPORT STATEMENT

The Competence Network for Community-Acquired Pneumonia is supported by the German Ministry of Education and Research (Berlin, Germany).

STATEMENT OF INTEREST

None declared.

ACKNOWLEDGEMENTS

The German Competence Network for Community-Acquired Pneumonia (CAPNETZ) is a multidisciplinary approach to the better understanding and treatment of patients with community-acquired pneumonia. The network has only been made possible by the

contribution of many investigators. We are especially indebted to the work of the investigators in the local clinical centres who established and maintained contact with all practitioners, physicians and respiratory specialists cooperating within the network.

In addition, we would like to acknowledge the work of the central computing unit and the central service unit, with A. Sawazki (Institute for Medical Microbiology and Hygiene, Ulm University Hospital, Ulm, Germany) providing excellent technical support.

It is also our responsibility and pleasure to express our appreciation to all of the clinical physicians and physicians in private practice who saw and identified patients with community-acquired pneumonia for their work dedicated to CAPNETZ.

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