

Légionellose Communautaire chez des patients âgés de 65 ans et plus hospitalisés en France

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Introduction

En Europe (2008), 17% de la population est âgée de 65 ans et plus (*)

La Pneumonie Aiguë Communautaire (PAC) est une cause fréquente de morbidité et de mortalité chez les personnes âgées

(*) Source: http://epp.eurostat.ec.europa.eu/portal/page/portal/statistics/search_database

PAC chez les personnes âgées

Review

Pneumonia in the very old

Pneumonia in the very old

Jean-Paul Janssens and Karl-Heinz Krause

Pneumonia is a major medical problem in the very old. The increased frequency and severity of pneumonia in the elderly is largely explained by the ageing of organ systems (in particular the respiratory tract, immune system, and digestive tract) and the presence of comorbidities due to age-associated diseases. The most striking characteristic of pneumonia in the very old is its clinical presentation: falls and confusion are frequently encountered, while classic symptoms of pneumonia are often absent. Community-acquired pneumonia (CAP) and nursing-home acquired pneumonia (NHAP) have to be distinguished. Although there are no fundamental differences in pathophysiology and microbiology of the two entities, NHAP tends to be much more severe, because milder cases are not referred to the hospital, and residents of nursing homes often suffer from dementia, multiple comorbidities, and decreased functional status. The immune response decays with age, yet pneumococcal and influenza vaccines have their place for the prevention of pneumonia in the very old. Pneumonia in older individuals without terminal disease has to be distinguished from end-of-life pneumonia. In the latter setting, the attributable mortality of pneumonia is low and antibiotics have little effect on the expectancy and should be used only if they provide the best means to alleviate suffering. In this review, we focus on recent publications relative to CAP and NHAP in the very old, and discuss predisposing factors, microorganisms, diagnostic procedures, specific aspects of treatment, prevention, and ethical issues concerning end-of-life pneumonia.



Figure 1. Chest radiograph in an 85-year-old man with bilateral extensive aspiration pneumonia and pleural dysfunction. There are an increased number of pathogenic bacteria (Gram-positive and Gram-negative aerobic bacteria) in the upper-respiratory tract of sick and institutionalized elderly patients, which increased the risk of pneumonia after bronchoscopy.

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Pneumonia is a major threat to older people, with an annual incidence for non-institutionalized patients estimated at between 25 and 48 per 1000 population, up to four times that of patients younger than 65. Older residents of chronic care institutions have an incidence of 33 to 114 cases per 1000 population per year. Few in it state that at any given moment as many as 2% of nursing-home residents may have pneumonia. Mortality rates for older patients in hospital-based studies of community-acquired pneumonia (CAP) are reported to be as high as 30%. For nursing-home acquired pneumonia (NHAP), mortality rates may reach 55%. The diagnosis of pneumonia in this age group is often delayed because of the frequent absence of fever, the paucity or absence of cough, and changes in mental status (delirium), which further contributes to the high morbidity and mortality.¹ Hospitalization for CAP is also an indicator of adverse prognosis at 1 year in older patients. In a case-control study of 154 NHAP patients versus 794 353 hospitalized controls, 1-year mortality was 41% for the CAP patients versus 29% for the control population.²

Physiological changes in the respiratory system associated with ageing

Maximum function of the respiratory system is reached at approximately the age of 20-25 years.³ Thereafter, ageing is associated with a progressive decrease in lung performance; however, unless affected by disease, the respiratory system remains capable of maintaining adequate gas exchange during the entire life span.

Physiological changes associated with ageing have important consequences on the functional reserve of older people, and their ability to cope with the decrease in lung compliance and increase in airway resistance associated with lower-respiratory-tract infection (LRTI).

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ORIGINAL ARTICLE

Community-acquired pneumonia in older patients: Does age influence systemic cytokine levels in community-acquired pneumonia?

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ABSTRACT

Background and objective: Community-acquired pneumonia (CAP) is a major cause of death in the elderly. The age-related increase in comorbid illnesses plays a part but the effect of aging on the immune response may be equally important. We aimed to evaluate patients with CAP for evidence of a muted response to infection in elderly patients admitted to hospital compared with a younger patient group.

Methods: Patients with CAP admitted through the Emergency Department were recruited for this prospective observational study. Clinical data were collected at presentation. Severity of pneumonia was assessed using the British Thoracic Society confusion, urea nitrogen, respiratory rate, blood pressure (CURB) score, the Pneumonia Severity Index (PSI) and the systemic inflammatory response syndrome (SIRS) definition. IL-6 and IL-10 levels were measured within 24 h of admission.

Results: Eighty patients were included in the study, of whom 38 (48%) were female. The median age was 74 years (range 18-95). Patients greater than 65 years of age had a lower incidence of chest pain and a higher incidence of altered mental status on presentation. CURB score and PSI were higher in the older patients. SIRS showed similar frequencies in both groups. IL-6 and IL-10 levels were similar in young (< 65 years), older (> 65 years) and very elderly (> 80 years) patients. This finding was not altered by severity of pneumonia.

Conclusions: Age does not diminish the severity of illness scores in patients with CAP. There was no blunting of the systemic cytokine response with advanced age in this study.

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SUMMARY AT A GLANCE

Evidence for a muted response to infection was evaluated in elderly patients with community-acquired pneumonia (CAP) compared with a younger patient group. Age did not diminish the severity of illness in patients with CAP. There was no blunting of the systemic cytokine response with advanced age.

Key words: elderly, immunology, IL-6, IL-10, pneumonia.

INTRODUCTION

Community-acquired pneumonia (CAP) ranks among the five major causes of death worldwide, despite the availability of potent antibiotic therapy. Increasing age is consistently identified as a risk factor for death due to CAP, a disease classically called the old man's friend.^{1,2} This is not simply because of an increased frequency of comorbid illnesses in older patients because multivariate analysis shows age to be an independent risk factor for mortality.^{3,4} The effect of aging on the body's inflammatory response to infection remains unclear. Reduced *in vitro* and *in vivo* production of inflammatory cytokines in elderly people has been described,⁵ while other studies suggest that the elderly have a more prolonged pro-inflammatory response.⁶

It has previously been demonstrated that IL-6 and IL-10 levels are elevated in patients with CAP accompanied by systemic inflammatory response syndrome (SIRS) when compared with CAP patients without SIRS.⁷ In that previous study of 28 patients, those greater than 70 years of age had a similar cytokine response to patients less than 60 years of age. Limitations of the study included a small sample size and the use of non-specific measures of pneumonia

Community-Acquired Legionella Pneumonia in Elderly Patients: Characteristics and Outcome

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OBJECTIVES: To compare the risk factors, clinical and laboratory features, and outcome of community-acquired pneumonia (CAP) caused by *Legionella pneumophila* in elderly (aged ≥65) and younger patients.

DESIGN: Prospective enrollment of subjects with retrospective data analysis.

SETTING: A 630-bed tertiary center in Badalona (Barcelona), Spain.

PARTICIPANTS: A total of 158 patients diagnosed with CAP caused by *L. pneumophila* from 1994 to 2004: 104 younger than 65 and 54 aged 65 and older.

MEASUREMENTS: Epidemiological, clinical, laboratory, and radiological data and the outcome of the two groups were compared using univariate and multivariate analysis.

RESULTS: Underlying diseases, such as chronic pulmonary diseases, diabetes mellitus, neuromuscular diseases, and heart failure; risk of aspiration; and therapy with corticosteroids were significantly more frequent in patients aged 65 and older. Patients younger than 65 were more likely to be male and have toxic habits (cigarette smoking, alcoholism) and human immunodeficiency virus infection than older patients. Fever, nonrespiratory symptoms (diarrhea and headache), and some laboratory abnormalities (hyponatremia serum sodium concentration < 130 mmol/L and high aspartate aminotransferase and creatinine kinase levels) were significantly less frequent in patients aged 65 and older than in younger patients. No significant differences were observed between the two groups in the frequency of higher-severity risk classes and intensive care unit admission or in outcome (complications and mortality).

CONCLUSION: Elderly patients with CAP caused by *L. pneumophila* had a higher frequency of underlying comorbidities and presented less frequently with fever and

classical nonrespiratory symptoms and laboratory abnormalities of Legionnaires' disease than younger patients, although greater severity of illness at onset and higher mortality were not significantly different between the two age groups. *J Am Geriatr Soc* 55:114-119, 2007.

Key words: community-acquired pneumonia; Legionella; elderly.

In recent decades, there has been a progressive aging of the population in developed countries, such as in Europe, with 16.5% of the citizens being aged 65 and older in 2004.¹ Community-acquired pneumonia (CAP) is a frequent cause of morbidity and mortality in older people, in whom the incidence is three to five times as high as in the remaining adult population.²⁻⁴ Elderly people have a higher risk of legionnaires' disease (LD), and several studies have demonstrated that age is a risk factor for *Legionella pneumophila*.^{5,6} Thus, in four hospital-based series including severe pneumonias, *Legionella* spp. caused 4% to 12% of the CAP occurring in older patients.⁷⁻¹¹ Moreover, nearly half of the people with LD reported to public authorities are aged 60 and older, and the rates of legionellosis are two times as high in this age group.¹² However, the incidence of this disease may be underestimated in older people, because it is not easy to obtain sputum samples, and urinary antigen detection is not systematically performed in all centers.

Several studies have shown that CAP in older people usually occurs in individuals with high comorbidity and with fewer symptoms than in younger adults, thereby delaying the diagnosis and worsening the prognosis.^{13,14} However, little is known about the epidemiological characteristics, the presentation, or the evolution of CAP caused by *Legionella* in older people. Knowledge of these data may aid in increasing diagnostic suspicion and improving the healthcare of these patients. Thus, the aim of our study was to compare the risk factors, the clinical presentation and the evolution of CAP caused by *L. pneumophila* in patients aged 65 and older with those of younger patients.

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This study was presented at the 45th Interagency Conference on Antimicrobial Agents and Chemotherapy, Washington, DC, December 2005. Address correspondence to Dr Nieves Sopena, Unidad de Maladies Infeccioses, Hospital Universitari Germans Trias i Pujol, C/Canyet, s/n, CP 08916 Badalona, Barcelona, Spain. E-mail: nsopena.germanistas@gnca.net DOI: 10.1111/j.1532-5415.2006.01021.x

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Incidence des PAC est 3-5 x plus élevée que dans le reste de la population;

Introduction

Les *Legionella spp.* sont responsables de 4% à 12% des PAC chez les personnes âgées.

Plus de la moitié des cas de légionellose déclarés est rapportée chez des personnes de plus de 60 ans;

**** France: 2007 (52,9%, 1428 cas), 2006 (54,4%, 1443 cas) des cas \geq 60 ans.**

Legionella pneumophila séroroupe 1 (Lp1) - principal pathogène, responsable de plus de 80% des cas.

Objectif

L'objectif de cette étude était de comparer les facteurs de risque, les signes cliniques et l'évolution des cas de Légionellose communautaire (LC) dus à *Lp1* en fonction de l'âge au diagnostic (< 65 ans vs \geq 65 ans).

Méthodes et Patients

Données: étude prospective nationale (avril 2006 – juin 2007)

Population: tous les cas de Légionellose communautaire dus à *Lp1* hospitalisés en France ayant un diagnostic clinique, radiologique et microbiologique:

- Isolement de *Legionella* dans un prélèvement clinique,
- Immunofluorescence directe positive,
- Présence d'antigène soluble urinaire,
- ↑ du titre d'anticorps (x4) avec un 2^{ème} titre minimum de 128.

Méthodes et Patients

Questionnaire standardisé:

Données démographiques: âge, sexe

Facteurs favorisants: alcoolisme, tabagisme, corticothérapie, hémopathie/cancer, diabète

Signes cliniques, physiques, radiologiques et biologiques

Sévérité de la légionellose: Score de Fine

Délai de prise en charge thérapeutique:

- délai 1 (délai entre les 1^{ers} symptômes et l'hospitalisation).
- délai 2 (délai entre les 1^{ers} symptômes et la mise en place d'une antibiothérapie adaptée).

Évolution: complications, guérison, décès

Méthodes et Patients

Analyse statistique:

Comparaisons:

- Chi 2 (données catégorielles)
- Mann-Whitney (données continues)
- Valeur de $p < 0,05$ a été considérée comme significative

Analyse de survie:

La survie durant le séjour hospitalier (censurée à 90 jours) a été estimée selon la méthode de Kaplan-Meier et les comparaisons ont été réalisées au moyen du test du Log-rank.



RESULTATS

Avril 2006 à Juin 2007

595 cas de Légionellose

**574 communautaires
(96,5%)**

**21 nosocomiaux
(3,5%)**

17 – 64 ans

**Age < 65 ans
337 (58,7%)**

**Age ≥ 65 ans
237 (41,3%)**

65 – 100 ans

**Age (moyenne ± SD)
60,7 ± 16,8**

Caractéristiques démographiques et facteurs de risque chez les cas de légionellose communautaire.

	Age < 65 ans n=337 (58,7%)	Age ≥ 65 ans n=237 (41,3%)	
	n (%)		p
Sexe			
Hommes	266 (78,9)	158 (66,7)	0,001
Facteurs de risque			
Au moins 1 facteur de risque	290 (86,1)	140 (59,1)	<0,001
Tabagisme	257 (76,3)	52 (21,9)	<0,001
Alcoolisme	90 (26,7)	17 (7,2)	<0,001
Diabète	38 (11,3)	52 (21,9)	0,001
Corticothérapie	21 (6,2)	19 (8,0)	0,411
Hémopathie ou cancer	11 (3,3)	30 (12,7)	<0,001

Signes cliniques avant et/ou à l'admission.

	Age < 65 ans (n=337)	Age ≥ 65 ans (n=237)	p
Signes Physiques			
	Médiane [min-max]		
Température > 38,5°C*	303 (89,9)	192 (81,0)	0,003
PAS (mmHg)	120 [60 - 220]	130 [60 - 210]	<0,001
PAD (mmHg)	70 [35 - 120]	70 [30 - 123]	0,263
FC (bpm)	104 [38 - 180]	97 [50 - 183]	<0,001
FR (cycles/min)	26 [10 - 60]	26 [10 - 84]	0,410
Signes respiratoires			
	n (%)		
Toux	241 (71,5)	150 (63,3)	0,045
Dyspnée	226 (67,1)	183 (77,2)	0,009
Douleur thoracique	81 (24,0)	36 (15,2)	0,011
Expectoration	106 (31,5)	65 (27,4)	0,309
Signes digestifs			
Diarrhées	84 (24,9)	33 (13,9)	0,002
Nausées	84 (24,9)	36 (15,2)	0,005
Douleurs abdominales	58 (17,2)	31 (13,1)	0,198
Signes neurologiques			
Céphalées	121 (35,9)	24 (10,1)	< 0,001
Confusion	94 (27,9)	84 (35,4)	0,067
Signes généraux			
Frissons	244 (72,4)	133 (56,1)	< 0,001
Myalgie	103 (30,6)	73 (30,8)	1,000
Anorexie	84 (24,9)	36 (15,2)	0,005

Caractéristiques biologiques à l'admission.

	Age < 65 ans (n=337)	Age ≥ 65 ans (n=237)		
Biochimie	Médiane [min-max]		p	« Valeurs normales »
Na ⁺ (mmol/L)	132 [117 - 151]	133 [74 - 157]	<0,001	135-145
Na ⁺ <130 mmol/L*	140 (31,8)	48 (20,9)	0,005	
ASAT (UI/L)	64 [61 - 7152]	51 [12 - 7000]	0,021	10-45
ALAT (UI/L)	52 [0,8 - 1468]	42 [6 - 2242]	0,008	
CRP (mg/L)	308 [2,6 - 1108]	315 [9,8 - 1227]	0,652	0-5
CPK (UI/L)	310 [3,9 - 53720]	224 [18 - 40000]	0,261	30-125
Créatinémie (mg/L)	11 [4,9 - 116]	12 [0,9 - 71]	<0,001	7-15
Hématologie				
Lymphocytes (G/L)	0,9 [0,1 - 69]	0,7 [0,02 - 89]	0,001	0,9 - 4,0
Neutrophiles (G/L)	9 [1,2 - 23]	10 [0,4 - 36]	0,007	1,7 - 8,0
Polynucléaires (G/L)	10 [0,1 - 24]	11 [1,8 - 39]	0,014	1,7 - 9,0
Hématose en air ambiant				
PaO ₂ (mmHg)	62 [20 - 166]	58 [28 - 206]	0,056	
PaO ₂ < 60 mmHg*	103 (42,0)	98 (56,0)	0,003	

* Résultats exprimés en n (%).

Délai de prise en charge thérapeutique et durée de séjour.

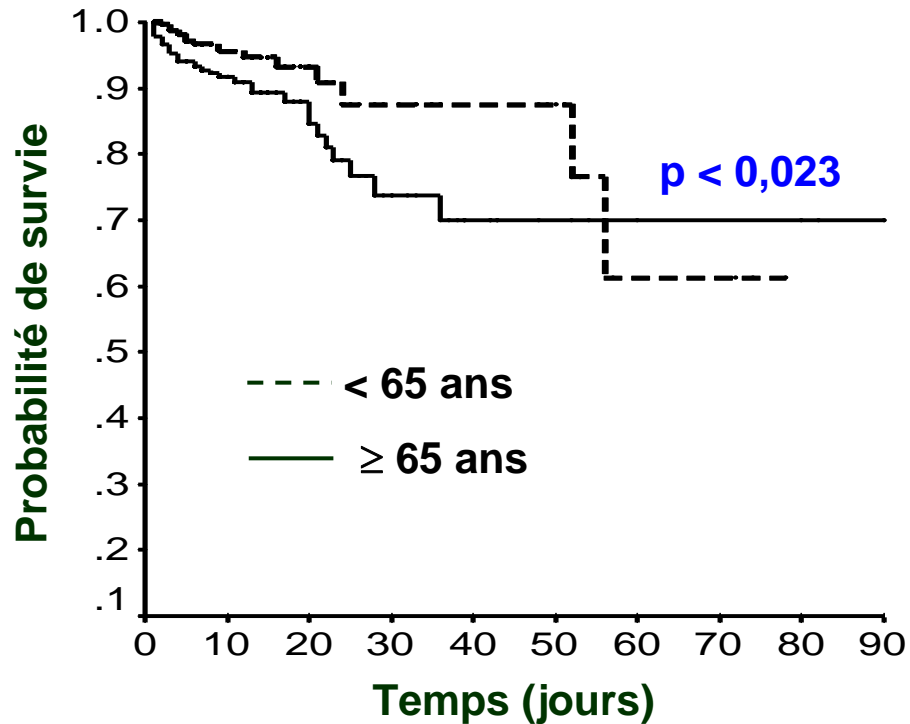
	Age < 65 ans (n=337)	Age ≥ 65 ans (n=237)	
	Médiane (jours) [min-max]		<i>p</i>
Délai 1 (1 ^{ers} signes -DH)	4,0 [0 - 33]	3,0 [0 - 21]	<0,001
Délai 2 (1 ^{ers} signes – ATB adaptée)	5,0 [0 - 33]	4,0 [0 - 23]	0,007
Durée de séjour	8,0 [0 - 78]	12,0 [1 - 92]	<0,001

Complications et évolution des patients.

	Age < 65 ans (n=337)	Age ≥ 65 ans (n=237)	
Variable	n (%)		p
Score de Fine IV, V	92 (27,3)	124 (52,3)	< 0,001
Séjour en Réanimation	102 (30,3)	60 (25,3)	0,221
Complications			
Infection Pulmonaire	25 (7,4)	16 (6,8)	0,870
Insuffisance rénale	28 (8,3)	48 (20,3)	< 0,001
Cytolyse hépatique	62 (18,4)	46 (19,4)	0,828
Décompensation mal. préexistante	14 (4,2)	35 (14,8)	< 0,001
Evolution			
Vivants	315 (93,5)	197 (83,1)	
Décès intra-hospitalier	18 (5,3)	31 (13,1)	< 0,001
Décès imputable à la légionellose (*)	12 (63,2)	17 (56,7)	0,769

(*) Légio seule = 17 et légio + autre cause = 12

Survie chez les patients âgés < 65 ans et ≥ 65 ans hospitalisés pour LC en France (avril/2006 à juin/2007)



	Probabilité de survie (%) à					
	2 j	10 j	20 j	30 j	60 j	90 j
< 65 ans	99,7	95,6	93,3	87,5	61,3	61,3
≥ 65 ans	97,9	91,7	88,0	73,8	69,9	69,9

Discussion

- **Biais de recrutement.**
- **Personnes âgées rapportent moins leurs symptômes.**
- **Age \geq 65 ans : comorbidités.**

Conclusion

Les cas LC \geq 65 ans présentent moins de signes respiratoires (dyspnée exceptée) et digestifs et moins de facteurs de risque que les cas LC $<$ 65 ans.

Cependant la gravité (Fine IV-V) et la mortalité de la maladie sont plus importantes dans ce groupe.

Ces résultats suggèrent que le diagnostic de LC doit être évoqué chez des personnes \geq 65 ans en présence de signes infectieux modérés (test antigène urinaire).



Perspectives

Analyse multivariée (en cours)

Efficacité des traitements: macrolides, fluoroquinolones...

Étude: qualité de vie

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**MERCI POUR
VOTRE
ATTENTION**

Calcul du score de Fine (somme des points)

Facteurs démographiques		Points	Données de l'examen physique		Points
Homme		Age	Atteinte des fonctions supérieures		+20
Femme		Age -10	Fréquence respiratoire ?30/mn		+20
Vie en institution		+10	TA systolique < 90 mm Hg		+20
Comorbidités			Température < 35°C ou ? 40°C		+15
Maladie néoplasique		+30	Fréquence cardiaque ? 125/mn		+10
Maladie hépatique		+20	Données biologiques et radiologique		
Insuffisance cardiaque congestive		+10	pH artériel < 7,35		+35
Maladie cérébrovasculaire		+10	Urée ? 11mmol/l		+20
Maladie rénale		+10	Na < 130 mmol/l		+20
Score			Glycémie ? 14 mmol/l		+10
< 71 points	➤	classe II	Hématocrite ? 30%		+10
71 à 90 points	➤	classe III	PaO2 < 60 mmHg		+10
91 à 130 points	➤	classe IV	Epanchement pleural		+10
> 130 points	➤	classe V			