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SPECIAL ARTICLE

Pneumonia Awareness Year, 2004: Scientific Impact Through Publications in ARCHIVOS DE BRONCONEUMOLOGÍA

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Pneumonia is a common and potentially serious infectious disease. Morbidity and mortality rates continue to be high in spite of major advances and steady progress in diagnosis and treatment. The economic impact of the disease is also great. It is therefore necessary to enlist the public, primary care and emergency physicians, and public policy administrators to join forces to treat and prevent pneumonia for the common good. The annual incidence of pneumonia in the population over the age of 14 years is 1.6 to 2.6 episodes/1000 inhabitants. The mortality rate is 14.1 per 100 000 inhabitants, and the associated costs are €115 million annually. The RESPIRA Foundation and the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) declared 2004 to be pneumonia awareness year with the aim of coordinating efforts to raise awareness, distribute information, and foster debate.

Key words: *Community-acquired pneumonia.* Streptococcus pneumoniae. *Antibiotic resistance. Pneumonia awareness year.*

2004: Año de la Neumonía. Consecuencias e impacto científico en ARCHIVOS DE BRONCONEUMOLOGÍA

La neumonía es una enfermedad infecciosa frecuente y potencialmente grave, con una elevada morbimortalidad a pesar de los continuos y relevantes avances diagnóstico-terapéuticos y con gran impacto económico, por lo que es necesario incidir en la población, los médicos de atención primaria, los médicos de urgencias y las administraciones públicas con el fin de intentar unir esfuerzos para tratarla y prevenirla de manera conveniente. Con una incidencia en > 14 años de 1,6-2,6 episodios/1.000 habitantes, se asocia con una tasa de mortalidad de 14,1 por 100.000 habitantes y un coste anual de alrededor de 115 millones de euros. La Fundación RESPIRA y la Sociedad Española de Neumología y Cirugía Torácica (SEPAR) declararon el año 2004 como «Año de la Neumonía», con la finalidad de elaborar una estrategia conjunta de actividades dirigidas a facilitar el conocimiento, la difusión y el debate en torno a esta enfermedad.

Palabras clave: *Neumonía adquirida en la comunidad.* Streptococcus pneumoniae. *Resistencias antibióticas. Año de la neumonía.*

Pneumologists have long called for greater attention to pneumonia, a common and potentially serious disease with high rates of morbidity and mortality in spite of important, steady progress in diagnosis and treatment. Both hospital and outpatient medical costs are considerable in Spain. It is therefore necessary to mobilize the public, primary care and emergency physicians, and public health administrators to join forces to treat and prevent pneumonia for the common good. The real incidence of community-acquired pneumonia (CAP) is quite difficult to assess because most available epidemiological data come from studies limited to patients who have been diagnosed and treated in hospitals. Very few provide information on cases at the primary care level. The annual incidence rate in European countries is believed to be between 5 to 11 cases/1000 inhabitants,[1] but there are differences from country to country. Precise data is only available for Finland, where the annual incidence is 10.8 cases/1000 adults,[2] and the United Kingdom, where the rate is 4.7 cases/1000 adults.[1] Two Spanish population-based studies of individuals over 14 years of age estimated the incidence to be between 1.6 and 2.6 episodes/1000 inhabitants.[3,4] Younger and older groups suffered higher annual rates of 25 to 35 cases/1000 inhabitants for the age bracket of adults over the age of 65 years or children under 5 years.[1]

World Health Organization (WHO) figures show that of the 50.5 million deaths in 1990, 4.3 million were attributed to pneumonia, 2.2 million to tuberculosis, 2 million to chronic obstructive pulmonary disease (COPD), and 0.95 million to lung cancer.[1] Of the 68.3 million deaths predicted for 2020, 11.9 million are

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expected to be the result of respiratory diseases.[5] CAP is the main cause of death from infectious diseases and ranks in sixth place overall, accounting for 16 deaths/100 000 inhabitants every year.[1] The WHO has estimated the rate of CAP-related mortality in 35 European countries and found great differences indicating uneven data registration.[1] In Spain, respiratory diseases generate the greatest morbidity and mortality, after cardiovascular diseases and cancer,[6] and among the diseases ranking as the main causes of death only Alzheimer's disease and pneumonia were associated with statistically significant increases of 4% in adjusted mortality rates for the 1995 to 1998 period.[7,8] In Spain, 4254 men and 3998 women died of pneumonia in 1999, giving a mortality rate of 14.1 deaths per 100 000 inhabitants; according to figures published in December 2004 by the national statistics institute, the mortality rate was 19.5 per 100 000 inhabitants in 2002, putting pneumonias in ninth place among causes of death in the country, with rates varying between autonomous communities from 11 per 100 000 inhabitants in Catalonia to 34 per 100 000 inhabitants in Aragon.[1] CAP-related mortality is determined by several factors: the manner of clinical presentation, etiology, and patient characteristics. Mortality rates range from 1% when hospitalization is not needed to 5% to 15% in hospitalized patients. Rates rise still higher to around 25% for patients needing intensive care unit (ICU) admission and to 50% if mechanical ventilation is indicated.[9]

The economic impact of pneumonia is great because of the health care resources consumed, with related costs generated both directly (drugs, medical visits, and hospital admissions) and indirectly (days lost from work and school). In the United States of America, with 4 million episodes and 1.1 million hospital admissions every year, an annual expenditure of US $34 400 milions[1] means the cost of CAP is $7000 for cases treated in hospital and $200 for outpatients.[10] A large part of the direct cost of treatment, therefore, is generated by hospitalization.[1,7] In Spain, Monge and colleagues[11] observed a mean annual rate of hospitalization of 160 cases per 100 000 inhabitants per year, a figure that increased 3-fold in the age bracket over 65 years (5.23 cases/1000 inhabitants per year), although those authors also saw great differences from one Spanish autonomous community to another. Thus, annual rates ranged from 2.4 cases/1000 in Catalonia to 0.8 cases/1000 inhabitants in the Canary Islands. The more than 51 000 patients admitted every year generate the spending of around €115 million annually.[11] Even if we exclude 20% of admissions for being inappropriate, the cost of hospitalization for CAP would still range from €35 to €80 million annually.[7] Another recent study calculated the direct costs generated by patients admitted with CAP to be €1553 (85% for hospitalization), whereas the average cost of outpatient treatment was €196.[12]

The situation of pneumonia in ARCHIVOS DE BRONCONEUMOLOGÍA contrasts with that of other respiratory diseases, such as COPD, about which numerous drug studies have appeared.[6,13,14] Few articles about pneumonia and drug therapies were found when searching the journal, and those that were published pertained to very specific situations or circumstances. Thus, a study by González-Moraleja et al[15] analyzing the cost of inappropriate admissions for pneumonia was undertaken because of the very different costs generated by hospital or outpatient care at a moment in time when rational use of available services and cost cutting is the rule. Another study, by Fernández Álvarez and colleagues,[16] showed that the duration of intravenous antibiotic therapy for CAP had an effect on the mean length of hospital stay and cost of treatment but did not add apparent benefits in selected groups of patients.

Recent years have seen the development of a campaign to disseminate health information, an important and interesting project of the Spanish Lung (RESPIRA) Foundation. The focus is on respiratory diseases that present important health care problems because of their incidence or their cost to the community. The focus of attention was COPD in 2002[17-19] and asthma in 2003.[20,21] Such year-long attention to a single issue has the main purpose of raising awareness of a problem among the general public and public health authorities as well as among physicians themselves. In that context, the RESPIRA Foundation and SEPAR were asked by the Spanish Ministry of Health and Consumer Affairs to declare 2004 to be pneumonia awareness year. The board of directors of SEPAR created a pneumonia awareness committee in 2003 to plan activities to spread information and encourage discussion of the disease.

The principal aims of the pneumonia awareness year were *a)* to raise the general public's awareness of CAP and distribute information about how it is treated and prevented; *b)* to alert health care professionals at different levels (specialists and primary care physicians) to the clinical and therapeutic problems this disease creates and emphasize the role of the pneumologist in treatment and research; *c)* to call the attention of public spokespersons, politicians, and social commentators to the epidemiologic importance of pneumonia; and *d)* to raise the awareness of public health care policy administrators and institutions regarding the importance of pneumonia in our community so that appropriate actions can be taken, especially preventive ones. Particularly targeted for the last goal was the development of comparable criteria for pneumococcus and influenza virus vaccination in the different Spanish autonomous communities with a view to assuring that resources and opportunities are geographically balanced.

The pneumonia awareness campaign was launched in Barcelona, where a press conference brought together journalists from news agencies, the specialist press, radio and television, and digital news media. The announcement received considerable media attention. Later in the year information about planned activities was sent to all members of SEPAR through the association's publications, and national and local press conferences were held in Barcelona, Madrid, Valencia,

Bilbao, and Seville to publicize the events widely. The message conveyed was that SEPAR had named 2004 to be pneumonia awareness year for the following reasons: "Pneumonia is a common and potentially serious disease consisting of lung infection or severe inflammation. Many microorganisms–viruses, bacteria, fungi–can cause pneumonia but the cause remains unknown in 40% to 50% of the cases. In spite of progress in investigating this disease, the overall mortality rate holds steady at around 5%. The real incidence of pneumonia in Spain ranges from 5 to 10 cases for every 1000 inhabitants, and that figure rises to 50 cases per 1000 inhabitants in the population over 65 years of age. Pneumonia is also one of the principal causes of infant death: 4 million children die of pneumonia every year in developing countries. Smoking and alcoholism are risk factors that predispose an individual to pneumonia. It is important to see a doctor at the first appearance of symptoms (cough, fever, chills, chest pain, and shortness of breath). Annual vaccination against the influenza virus and pneumococcus is the main preventive measure. Antibiotics are essential in the therapeutic arsenal for fighting pneumonia, but they should never be used carelessly or without a medical prescription as improper use can lead to the development of resistant strains."

The content of the 365-day campaign against pneumonia was reflected in a booklet titled *A pleno pulmón*, literally "a full lung" but also a Spanish expression related to calling out news loud and clear. The following activities were listed: *a)* an informative campaign targeting the general population, *b)* scientific studies on pneumonia that were being promoted, *c)* a professional development course to update knowledge on pneumonia, *d)* a telephone survey to ascertain the general public's level of knowledge of the disease, *e)* a campaign to promote vaccination in high-risk groups, and finally, *f)* the preparation of a consensus paper discussing the proper treatment of pneumonia.

A web page was created (www.neumonia2004.com) to make key information available to the public in the form of a comprehensive, easy to understand guide to the disease. Physicians were also offered a complete bibliography of professional literature on the disease. A space for articles in the general press on pneumonia was also provided, as well as a space to convey information to journalists. The site was created to have a way to regularly post updated information on the planned activities throughout the campaign year and to give all participants in this ambitious project their own space.

One of the key activities was to carry out a survey in which computer assisted telephone interviewing technology was used. Various population groups were targeted and the purpose was to ascertain the level of knowledge of pneumonia among Spaniards and their attitudes regarding prevention and treatment. Rates of vaccination against the pneumococcus and the influenza virus were determined by age brackets, sex, urban or rural residence, and geographic area. Items asked about measures the interviewees would take in case of pneumonia. The preliminary results were presented at a press conference in April 2004 and the final paper is still pending publication. Only a single other survey was found among the publications in ARCHIVOS DE BRONCONEUMOLOGÍA since 1998 the aim of the study, published in 1999, was to determine the situation of domiciliary mechanical ventilation in Spain; the target population was health care professionals, however, rather than the general public.[22]

To meet other objectives for the awareness year, a course on pneumonia was developed[23] and accredited by the Spanish commission for continuing professional development for physicians (SEAFORMEC). The course was given through printed reading matter and information was posted online. Online tutoring from specialists was available in all the Spanish autonomous communities. A total of 1153 physicians enrolled in the course, which targeted primary care physicians wishing to update their knowledge of CAP treatment and prevention. Such physicians, who are in direct contact with the community, are the first step in the health care system. To act within the framework of a public health care system, both types of caregivers–pneumologists and primary care physicians–must be coordinated and ready to share responsibility.[24] Such cooperation is essential given the high prevalence of respiratory diseases treated in the primary care setting.

A campaign to promote vaccination against influenza and pneumonia among groups most at risk was initiated in the autumn of 2004.[25]

We must also remember an important aspect of the correct treatment of pneumonia, namely the serious problem of antibiotic resistance. In Spain, the rate of resistance of *Streptococcus pneumoniae*, the main cause of CAP, is among the highest in the world. As this resistance affects treatment options, we must understand our clinical context. One multicenter study carried out by members of the Assembly on Tuberculosis and Respiratory Infections (TIR) of SEPAR had as its objective to study the epidemiology and clinical manifestations of CAP from *S pneumoniae* strains that were resistant to antibiotics.[26] The rates of resistance were 35.7% to penicillin, 27.4% to erythromycin, 2.8% to third-generation cephalosporins, and 0.6% to levofloxacin, although the figures for penicillin resistance appear to have stabilized at this time.

Finally, within the framework of the year dedicated to awareness of pneumonia, the CAP study group of the TIR Assembly brought together a substantial number of pneumologists with the aim of reaching a consensus on the main diagnostic processes and therapeutic regimens for this disease, given the need to create consistent procedures to correct the current differences between Spanish autonomous communities. The efforts of this group were recorded in the SEPAR guidelines for CAP diagnosis and treatment,[25] which brought earlier guidelines up-to-date and into keeping with current scientific evidence, adapted to the Spanish situation with regard to resources, drugs, and patient care capabilities. These recommendations, designed to provide a practical tool for doctors who treat

TABLE 1
Publications Related to Pneumonia in ARCHIVOS DE BRONCONEUMOLOGÍA, by Year: Search on the Web Site of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) (Key Word: Pneumonia)

Year of Publication	No. of Articles
1998	6
1999	9
2000	6
2001	7
2002	4
2003	13
2004	6
2005	11
2006 (January-June)	5
Total	67

TABLE 2
Type of Published Article Related to Pneumonia in ARCHIVOS DE BRONCONEUMOLOGÍA, From January 1998 Through June 2006

Type of Article	No. of Articles
Editorial[7,27-35]	10
Original Article[15,16,36-51]	18
Special Article[52-57]	6
Review Article[58]	1
SEPAR Recommendations[25]	1
Case Report[59-66]	8
Letter to the Editor[67-86]	20
Other Guidelines/Recommendations[87-89]	3
Supplement Article[90-100]	11
Total	78

pneumonia at whatever level of the health care system, are confined in scope to CAP in immunocompetent adults (≥18 years old). Excluded, therefore, are cases found in institutionalized patients, who require special consideration. A key point is the recommendation of vaccination, given that SEPAR and the RESPIRA Foundation favor lowering the age of application, especially for groups at risk.

The consensus paper was presented formally at the national meeting of SEPAR in 2005 in Valencia and published in its full form in ARCHIVOS DE BRONCONEUMOLOGÍA.[25] An abridged version was also published as a tryptic to facilitate quick consultation of main points.

Two years after the designated pneumonia awareness year, we ask what the outcome of the project was, with the aim of summarizing and analyzing the real short-term impact (January 2004 through June 2006) on publications in ARCHIVOS DE BRONCONEUMOLOGÍA. We used the advanced search option on SEPAR's web site, requesting articles with the word *pneumonia* in the title or abstract and specifying the aforementioned date limits. Other related publications were also selected to extend the search, even if *pneumonia* did not appear in the title or abstract; articles in special supplements that were not found in the first search were also located. We excluded articles actually about other entities even if the word *pneumonia* was present (eg, articles concerning bronchiolitis obliterans with organizing pneumonia).

The numbers of articles directly related to pneumonia published from 1998 through June 2006 are shown in Table 1. The distribution of the 67 articles by type of publication is shown in Table 2: 10 editorials,[7,27-35] 18 original articles,[15,16,36-51] 6 special articles,[52-57] 1 review article,[58] 1 paper in the SEPAR recommendations series,[25] 8 case reports,[59-66] 20 letters to the editor,[67-86] and 3 other sets of guidelines.[87-89] The 3 other sets of guidelines included a SEPAR working group's recommendations on the diagnosis of ventilator-associated pneumonia,[87] recommendations issued by a SEPAR working group in cooperation with other societies on the treatment of serious nosocomial pneumonia,[88] and a third giving recommendations from the Latin American Thoracic Association (ALAT) on nosocomial pneumonia.[89] In addition to those 67 articles, 11 more were published in various annual supplements or those related to seminars[90-100] or simply other supplements.[90-99] Some were overviews of hot topics in pneumology.[100] That brought the total to 78. Table 3 shows the types of publication that appeared, by year.

Noteworthy was the number of original articles published, 18 in total, and the activity during 2003, the most productive year with 13 papers, and during 2005, with 11 papers published. The period between 2004 and June 2006 saw 25 articles related to pneumonia, covering nearly all relevant knowledge areas: 3 editorials,[7,34,35] 7 original articles,[45-51] 4 special articles,[54-57] 1 article in the SEPAR recommendations series,[25] 2 case reports,[65-66] 3 letters to the editor,[84-86] 2 other sets of guidelines,[88,89] and 3 articles in special supplements[98-100] (Table 4).

Reviewing the scientific content of articles published since 1998 revealed substantial changes over time in the lines of investigation followed. We were understandably concerned at first with characterizing pneumonias, risk factors, etiologic patterns, diagnostic methods, and treatment–in short, in studying how pneumologists were treating the disease in Spain. The studies were descriptive of the practice setting. One study that helped establish the bases we now work from must be cited. It was a multicenter project carried out by SEPAR's TIR Assembly,[101] a group that has promoted several such studies in recent years and can claim publications in high-impact journals. Referred to as the NACE study,[101] an acronym derived from CAP in Spanish, that TIR project involved 21 Spanish hospitals and 468 patients with the main objective of determining the diagnostic and therapeutic protocols being followed in relation to CAP in this country. The group found that 85% of patients required admission and etiologic diagnoses were reached in few cases (14%). *S pneumoniae* was identified as the most common pathogen. Two thirds of the patients were over 60 years old, consistent with indications that CAP requires admission most often in older age brackets. Comorbidity was present in 75% of the cases, and the presence of chronic diseases such as COPD was a risk factor. It was seen that guidelines for the treatment of CAP were generally being followed

TABLA III
Distribution of Article Type by Year

Year	Editorials	Original Articles	Special Articles	Review Article	Guidelines/ Recommendations	Case Reports	Letters to the Editor	Supplements
1998	–	–	1	1	–	–	4	–
1999	1	3	–	–	–	1	4	–
2000	–	1	–	–	–	1	4	4
2001	1	1	1	–	1	2	1	4
2002	2	2	–	–	–	–	–	–
2003	3	4	–	–	–	2	4	–
2004	–	2	2	–	1	–	1	2
2005	2	3	1	–	2	2	1	1
2006 (January-June)	1	2	1	–	–	–	1	–

and that hospital mortality due to CAP, the percentage of patients needing ICU admission, and the number of complications were in the low range. Good practice by Spanish pneumologists in relation to this disease was confirmed in spite of disparity in diagnostic and treatment criteria.

Older patients admitted with CAP made up a large percentage of the sample and as life expectancy is extended we will need to become accustomed to that pattern. The incidence of CAP is known to be significantly higher in the population aged over 70 years, where we also find higher prevalences of chronic and debilitating diseases that increase risk of pneumonia considerably; that picture also changes the range of etiologic agents responsible for CAP, the clinical manifestations of the disease, and clinical course.[99] Pneumonia in the elderly has special characteristics and can not be managed in the same way as in younger patients. Our review of recent publications in ARCHIVOS DE BRONCONEUMOLOGÍA revealed a concern to deepen our understanding of the disease in this population. Another article from SEPAR's TIR Assembly must be highlighted in this line as it is the first prospective multicenter study of CAP characteristics in patients over 65 years old.[102] Sixteen participating Spanish hospitals treated 503 patients with a mean age of 76 years. Contrary to common belief, CAP was acute in 63% of the cases and *S pneumoniae* was the causal agent in 49% of the cases for which a microbiologic diagnosis was available. Mortality, at 11%, was low compared with the crude mortality rate of 20.8% observed in a retrospective study by Clemente et al[40] in 2002 but was similar to the hospital mortality of 10% and the 30-day mortality of 13% observed by Saldías Peñafiel et al.[42] Risk factors for poor prognosis identified in the TIR study[102] were as follows: patient previously bedridden, altered mental status, absence of chills, plasma creatinine levels over 1.4 mg/dL, a ratio of PaO_2 to inspired oxygen fraction (FiO) less than 200 upon admission, and kidney failure or shock during the pneumonia episode. Other independent risk factors associated with mortality that have been found are serum creatinine level of 1.2 mg/dL (relative risk [RR], 13.9), bedridden patient (RR, 5.7), PaO_2/FiO_2 of 200 (RR, 5), and neoplastic disease (RR, 4.1)[40]; and advanced age (83 years), absence of cough, low blood pressure, and elevated phosphate levels.[42] Clemente et al[40] found that the presence of chest pain was associated with a lower risk of death (RR, 0.11).

TABLE 4
Pneumonia-Related Articles in ARCHIVOS DE BRONCONEUMOLOGÍA Between January 2004 and June 2006, Grouped by Type

Type of Article	No. of Articles
Editorial[7,34,35]	3
Original Article[45-51]	7
Special Article[54-57]	4
Review Article	–
SEPAR Recommendations[25]	1
Case Report[65,66]	2
Letter to the Editor[84-86]	3
Other Guidelines/Recommendations[88,89]	2
Special Supplement Article[98-100]	3
Total	25

In December 2004 Martínez-Moragón et al[45] published an interesting study in which they analyzed differences in CAP in elderly residents of geriatric facilities in comparison with patients living in private homes. CAP in institutionalized geriatric patients is considered different in terms of etiology, presentation, and prognosis. Very few Spanish studies have been done to confirm that profile, however, so Marín and Alsonso[56] made special mention of that study in their 2005 survey of publications in the 2004 volume of ARCHIVOS DE BRONCONEUMOLOGÍA. Martínez-Moragón and coworkers prospectively analyzed CAP in admitted patients over 65 years old over a period of 18 months, with special attention to functional status and comorbidity. Ninety-one patients, 25 from geriatric facilities, were enrolled. The geriatric facility residents were older and had more concomitant diseases (P=.0001) and more functional impairment. Mortality was higher in residents of geriatric facilities (28%) than in those living in private homes (4.5%), although the rate for home-living patients was lower than that reported from earlier studies.[40,42,102] Urea nitrogen level was the best predictor of mortality in this population. Finally, if CAP in the immunocompetent elderly patient requiring admission is a prevalent disease with particular clinical and epidemiologic characteristics,

course, and prognosis[42] in and of itself, it can also be seen from the analysis of source of transfer prior to admission that cases coming from group residential facilities are particularly severe and such provenance is a major risk factor for death even if the etiologic agents do not differ from the usual ones.

With the first issue of 2000, ARCHIVOS DE BRONCONEUMOLOGÍA[103] became the official journal for communicating the scientific activity of the Latin American Thoracic Society (ALAT).[104,105] Since then, SEPAR and ALAT have been in close contact and contributions from ALAT members have been published at a steady rate. Consistent with attention to other diseases, such as COPD, for which the ALAT treatment guidelines were published,[106,107] the journal also published a special article presenting the society's guidelines for CAP treatment in August 2004,[55] thereby providing a useful update of previous recommendations.[53]

Our colleagues across the ocean must also cope with the problem of antibiotic resistances, sharing our concern for *S pneumonia* susceptibility. A search for the appropriate antimicrobial agent motivated an international clinical trial to evaluate the efficacy and safety of treatment with moxifloxacin in comparison with amoxicillin in patients suspected of pneumococcal CAP.[43] That study reflected experience in 5 Latin American countries, listing germs isolated, patterns of antibiotic sensitivity, and clinical and microbiological findings. The high prevalence of *S pneumoniae* with low susceptibility to penicillin was documented and should be taken into account in establishing empirical treatment guidelines for those countries.

Another Latin American study, carried out in Chile, looked at the role of bronchoalveolar lavage in the diagnosis of pneumonia due to opportunistic germs in immunodepressed children.[46] Complications were assessed and it was found that the approach was safe, provided sufficient diagnostic yield, and allowed an etiologic diagnosis of lung infiltrates to be reached. Still in Chile, Díaz et al[47] undertook a prospective, descriptive study of the clinical presentation, prognostic factors, and treatment of adults admitted to ICUs with severe CAP. Of the 113 patients in the series (mean [SD] age, 73 [15] years), 95% had concomitant diseases and 81% belonged to a high risk category according to the pneumonia severity index (PSI). The etiology was demonstrated for 31% of the cases: *S pneumoniae* (40%), gram-negative bacilli (17%), and *Mycoplasma pneumoniae* (6%). Among the main complications observed were need for mechanical ventilation (45%), septic shock (26%), heart failure (24%), and arrhythmias (15%). The mortality rate at 30 days was 16.8% and factors associated with a higher risk of death were acute kidney failure (odds ratio [OR], 5.1) and blood sugar level over 300 mg/dL (OR, 7.2).

November 2004 saw the publication of recommendations for severe nosocomial pneumonia[88] drafted jointly by several scientific societies such as the Expert Committee on Infectious Diseases of the Spanish Society of Intensive and Critical Care Medicine and Coronary Care Units (GTEI, SEMICYUC), the TIR Assembly of SEPAR, and the Hospital Infection Group of the Spanish Society of Infectious Diseases and Clinical Microbiology (GEIH-SEIMC).

In September 2005, Menéndez et al[34] published an editorial analyzing factors influencing poor outcome and mortality in pneumonia. Starting with the fact that CAP may have a poor outcome even when antibiotic therapy covers an adequately broad spectrum and the pathogen is sensitive, the authors emphasized the development in recent years of prognostic scales for estimating the likelihood of death in CAP in a way that can be applied homogeneously and universally. Such scales have managed to focus attention on signs of unfavorable evolution unrelated to the pathogen itself but rather to the process within the patient. Various papers were published within this line of investigation and yet another project was organized by the TIR Assembly, on CAP treatment failure in Spain (the NEUMOFAIL study).[108-110] A newer approach is to identify risk factors related to response to therapy, as such information is more useful for detecting poor evolution whether the patient's risk classification is high or low for mortality. Nonetheless, it is clear that analyzing response to therapy requires further research on the relationship between the host and the microorganism. One hypothesis that is being investigated holds that an imbalance in the host's response expressed by overproduction of proinflammatory cytokines (tumor necrosis factor [TNF] α and interleukin [IL] 1β) is related to poor outcome. High IL-6 and TNF-α levels have been found in the context of CAP and have been correlated with mortality. Why an exaggerated inflammatory response develops, with negative effects on outcome, is poorly understood, although it is possible that the microorganism itself and the bacterial load might trigger increased production of cytokines and affect antibiotic treatment and the host's susceptibility as well. Given that cytokine production is genetically determined, a line of investigation has developed to look for a relation between genetic polymorphisms and host response to infection along with course of disease.[100] Meanwhile, clinicians need biological markers able to estimate therapeutic response as well as treatments ready to modulate it. Currently, C reactive protein and procalcitonin are the most promising, as elevated concentrations have been found to correlate with treatment failure.

Rodríguez de Castro and coworkers[100] discussed this line of research in a 2005 supplement on related hot topics. It is clear that there is individual variation in susceptibility to infectious diseases and differences in how severely they run their course, and it has always been suspected that genetic factors must play a role in susceptibility in addition to the known environmental factors. Debate is underway and the authors asked how much our genetic make up can account for the different ways of responding to the same infection, independently of other well-known factors such as the prior immunological status (acquired immunity) or variations in virulence of the microorganism. The

human genome project has provided a starting point for analyzing human genetic diversity.[111] Single-nucleotide polymorphisms are the most important and prevalent type of variation in the human genome, accounting for most of the genetic differences between individuals.[100] Among the polymorphisms implicated in antigen recognition are complement system proteins like mannose binding lectin (MBL), a pluripotent molecule of the innate immune system which is able to activate complement once it binds to various sugars on the surface of the microbe. MBL can also act directly as an opsonin. After discussing the varieties of MBL polymorphism, the authors note that while it is true that the allelic variants associated with low protein titers are linked to greater susceptibility to CAP, normal wild-type genotypes confer a greater risk of developing more severe forms of the disease.[100] The next phase in the analysis of genetic associations in infectious diseases will allow us to select candidate genes to study in humans to further our understanding of the molecular events that must take place for a pathogen to invade a host as well as the events required for a host to eliminate the pathogen. That knowledge will undoubtedly revolutionize research and development in the area of vaccines and antimicrobial drugs.

In a June 2005 editorial by Rodríguez de Castro,[7] this question was posed: does a medical specialist provide the patient with better care? Two issues must be considered in responding it seems: on the one hand there is the cost of health care and on the other the course of the patient's illness. A factor that clearly influences the first is the profile of physician giving care and it seems clear that given the same type of patient, a specialist's care costs more, although it is also necessary to assess whether such care improves clinical course. Among respiratory diseases, improved outcome has only been demonstrated for asthma. An objective would be to study the influence of physician profile on the use of resources to treat CAP and on prognosis. We know that CAP patients who are hospitalized generate higher health care costs than do those treated as outpatients; nevertheless, at present there are no consistent criteria for deciding whether to hospitalize a pneumonia patient or not,[30] for deciding duration of hospital stay, or for guiding the use of antibiotics used in different hospitals. Earlier studies, for example, analyzed the influence of duration of intravenous therapy on duration of hospital stay and cost.[16] Although it is possible that differences are related to severity or associated risk factors, it is likely that medical specialty affects variation in care processes followed, the treatment chosen, and therefore in outcome for the patient; it can also be speculated that differences in CAP treatment observed among different specialists could be reduced if structured protocols were followed, according to the editorial.[7] The author noted the scarce differences in treatments prescribed by pneumologists and infectious disease specialists, an observation that underlines the role of medical experience in treating these diseases and, specifically, that the volume of patients treated over the course of a year matters more than the nature of specific academic qualifications.

In the same June 2005 issue of the journal Capelastegui et al[48] also investigated whether variation in CAP treatment was influenced by which hospital department took responsibility and if there was an effect on clinical course. They compared patients treated by departments of pneumology, internal medicine, infectious diseases, and a mixed group of specialties, looking at treatment and outcomes in a random sample of patients drawn from among CAP patients admitted to 4 hospitals. Once severity had been adjusted for, the most severely ill patients treated by pneumologists had hospital and 30-day mortality rates that were lower than those of internists and a duration of intravenous treatment that was significantly shorter. The latter observation seems to partly explain the shorter hospital stays for patients treated by the pneumology department. Other authors, however, have observed that duration of intravenous antibiotic therapy does not appear to add benefits.[16]

The retrospective nature of the study by Capelastegui and colleagues[48] and the lack of homogeneity of the patients admitted by the different departments prevented the authors from reaching definitive conclusions, although the differences in mortality rates observed could be attributed to differences in antimicrobial therapy–pneumologists seem to use more macrolides than internists. The antibiotic therapy was considered appropriate, however, in over 80% of the cases in all departments and in more than 90% of the cases in the internal medicine department. Certain studies suggest that including a macrolide antibiotic in the initially prescribed regimen is associated with lower mortality[112]; other authors, however, have been unable to confirm those findings.[113,114]

Capelastegui and colleagues[50] published another original article in June 2006 in which they assessed the evolution in quality of treatment of patients admitted with CAP over a period of 4 years. Previously it had been demonstrated that applying practice guidelines from March 2000 onward improved results of CAP treatment.[115] In that prospective, observational study, the authors demonstrated statistically significant trends in the following indicators: reduced cost of hospitalization ($P<.001$), shorter hospital stays ($P<.05$), and shorter duration of total antibiotic therapy ($P<.05$), increased coverage of atypical pathogens ($P<.001$), and greater administration of antibiotics within the first 8 hours ($P<.001$). They found no significant differences in hospital mortality, 30-day mortality, or readmissions within 30 days. They also identified 2 areas for improvement: the low percentage of admissions to the intensive care unit (4.4%) and inappropriate admissions of low-risk patients (PSI I-III) (36.8%). Therefore, their main conclusions were that the systematic monitoring of indicators in the guide allowed them to understand and assess their clinical practice, verify favorable evolution of many of the indicators, and identify aspects to improve. For clinicians, the use of guidelines and the systematic monitoring of indicators should become

features of usual clinical practice, as ongoing quality assessment of practice and control of variability will then be possible.

Another area of content reviewed was that of CAP patients who also have COPD. An article by Merino-Sánchez et al[49] published in November 2005 analyzed the incidence, severity (PSI class), and mortality rates associated with pneumonias occurring in a cohort of 596 patients with a diagnosis of COPD over a period of 3 years. They found the overall incidence of pneumonia to be 55.1/1000 person-years. The severity of COPD, based on FEV_1 as a percentage of predicted was mild in 9 patients, moderate in 24, and severe in 42. Seventy-six (86.3%) episodes were CAP and 12 (13.6%) were nosocomial. Fourteen CAP episodes were class V severity, 28 were class IV, 20 class III, and 14 classes I and II. Overall mortality was 12.5%; among nosocomial pneumonias the rate was 41.7% and among CAP cases it was 7.8% (OR, 6.67; 95% confidence interval, 1.65-26.93). Assessing CAP mortality rates by severity, class V mortality was 35.7%, class IV was 3.5%. No deaths occurred in the other severity classes. Thus, COPD patients have a high incidence of pneumonia, and over half the cases of CAP (55.2%) fall into risk classes IV and V in these patients. In another study, Ruiz de Oña et al[41] observed retrospectively that COPD patients with CAP had a mortality rate and duration of hospital stay comparable to those of other CAP patients of higher risk levels (classes IV and V). These authors found significant differences in the percentage of patients with COPD who used home oxygen therapy between those who died (75% used oxygen) and those who did not (37% used oxygen), as well as differences by risk class. Solsona et al[116] reported a mortality rate of 23% for COPD patients requiring ICU admission and mechanical ventilation to treat severe CAP.

In this review of publications on pneumonia, studies of diagnostic methods must be included. Thus, a March 2006 editorial by Molinos[35] noted that the simple methods such as detection of urinary antigen components of *Legionella* species and *S pneumoniae* have progressed considerably and brought benefits applicable to daily clinical practice. It is clear that the availability of an etiologic diagnosis of CAP contributes to fast, reliable prescription of directed antibiotic therapy and, in the words of the author, would mean prescription of narrower spectrum antimicrobial agents or avoidance of combinations. The basis for urine testing is the fact that microbial antigens concentrate in that fluid more than in others and that there is a lack of antibodies to affect the results. The sensitivity of the *S pneumoniae* urinary antigen test in patients with bacteriemia is 75% to 85%. In patients who are not bacteremic the sensitivity is 50% to 80%. Specificity exceeds 95%. We have sufficient experience to consider that urinary antigen testing is a development that is useful for early, reliable diagnosis of pneumonia due to *Legionella* species and *S pneumoniae*.

Prevention of CAP is another knowledge area to consider. Prevention can take the form of fighting against causative pathogens, the typical action being specific vaccination against the pneumococcus. Alternatively, it can involve attempts to eliminate risk factors that favor the development of the disease, for instance through influenza vaccination or anti-smoking campaigns.[25,52,54,58,99,117] Escribano Montaner et al[54] pointed out the importance of influenza vaccination for pneumonia prevention, given that the influenza virus frequently predisposes the patient to develop serious bacterial pneumonia by altering the ability of the lung to eliminate *S pneumoniae*. The bacterial load therefore increases and along with it the inflammatory response to that pathogen. As noted by Vilá et al,[99] influenza vaccination reduces the need for hospitalization for either influenza or pneumonia and reduces mortality as well. The SEPAR guidelines on CAP[25] give thorough coverage of the use of the pneumococcal vaccine.

In March 2006, Rodenstein[57] reflected on the world-wide panic engendered by the severe acute respiratory syndrome (SARS). In an editorial in June 2003, Blanquer[33] had discussed a situation that began in November 2002 in several cities in the Guandong region of China with the outbreak of an atypical pneumonia whose etiology was unknown at first and which was later attributed to coronavirus. SARS initially infected 8098 persons, of whom 774 died. Health care professionals who were on the front line made up 21% of the patients. Now, the avian flu had caught our attention over the past several months as Rodenstein wrote.

We come to the last of the original articles published in the period under review: a study of the non-invasive diagnosis of pulmonary inflammation that appeared in March 2006.[51] Diverse approaches have been used to achieve that complex goal, and the level of efficacy and safety has varied a great deal. The normal lung balance between oxidants and antioxidants is able to maintain the fluids that line airways and fill extracellular spaces in a highly reduced state. Increasing the concentration of oxidants or decreasing or overusing antioxidants will lead to imbalance. The result is oxidative stress, a phenomenon that forms part of the essential chain of events that results in a state of airway inflammation after bacterial infection. Collection and freezing of exhaled breath condensate (EBC) is a technique for sampling fluids coating the airways for analysis of substances that become dissolved as air passes through. EBC analysis is the subject of a certain amount of debate because of great variability in results and the scarcity of systematic studies on the technique. Romero et al[51] asked whether EBC analysis could reflect the oxidative stress intrinsic to pulmonary inflammation in the context of severe pulmonary infection, as oxidants become more abundant. The authors studied 48 patients in 4 groups: subjects without respiratory disease and patients with multilobar pneumonia of various etiologies, COPD, or severe pneumonia necessitating mechanical ventilation. An EBC sample taken within 72 hours of admission was analyzed for nitrite, nitrate, 8-isoprostane, and myeloperoxidase (MPO). Significant differences were detected between the control group and the patients but not between the different patient

groups. The authors therefore concluded that EBC analysis of 8-isoprostane and MPO could provide an indication of oxidative stress in the airways of patients with lung infections.

Approximately a year and a half has passed since the pneumonia awareness year and the project has left us with important scientific contributions. The objectives were ambitious and, when a project of this scope comes to an end, one is always left with the feeling that more could have been accomplished or something could have been done better. In the end, we are aware that a single year is little time for a discussion of any disease–whether COPD, asthma, pneumonia, sleep disorders, or cancer–but we hope to have contributed to furthering knowledge in some measure and improving the treatment of pneumonia in Spain. We are aware that we must defend our specialty and broaden the horizons of clinical research, which plays an increasingly important role in pneumology.[118] Our commitment to our community obliges us to move into new areas and face new challenges, such as involving ourselves more in caring for the critically ill respiratory patient and promoting the creation of intermediate respiratory care units where pneumologists can themselves manage severe pneumonia.[119] We must remember that other respiratory infections loom. Imported respiratory infections have been rare in Spain, yet recent years have seen more travel to exotic destinations and immigration has increased appreciably. These trends suppose new challenges and dangers. In fact, such contacts should now enter into the differential diagnosis of pneumonia.[120-122]

In the end, the RESPIRA Foundation and SEPAR are scientific associations that work within the framework of the society that created them. These associations, therefore, have as their aims to increase scientific knowledge and promote better health and habits in the community served. In a modern developed society like ours, health campaigns can only be based on making appropriate, accurate, and adequate information available to the public.

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