Arch Bronconeumol. 2010;**46(6)**:335-342

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Letters to the Editor

Flu Pandemic Consequences in Spain Might Be Minimized With Conjugate Anti-Pneumococcal Vaccine

¿Se podrían minimizar los efectos de la pandemia por gripe A (H1N1) en España con la vacuna antineumocócica conjugada?

To the Editor:

When the influenza pandemic arrives, most of the deaths will be a result of bacterial superinfection, and *Streptococcus pneumoniae* will be the most commonly isolated bacteria. This assertion is neither gratuitous nor original.[1] The big difference between this and previous pandemics is precisely the availability of pneumococcal vaccines, and in particular, the pneumococcal conjugate vaccine. Possibly, routine pneumococcal vaccination is the most effective and efficient measure that we can take to fight the influenza A (H1N1) pandemic, even more while a specific influenza vaccine is not widely available.

If the influenza A virus by itself can cause deaths, when combined with a secondary bacterial infection it becomes really lethal. In nearly all the series published, the *S. pneumoniae* is the most common infectious agent of secondary bacterial pneumonia, present in 25-75% of cases.[1] Severe pneumococcal pneumonia associated with seasonal influenza has also been known. Most of the 40 million deaths during the influenza pandemic in 1918 were due to bacterial pneumonia and, with the methodology available at that time, the pneumococcal bacteria was isolated from the blood in up to half of the victims of pneumonia due to the influenza virus.[1] Furthermore, the time from the start of symptoms until death – an average of around 10 days – is compatible with the time taken until death with bacterial superinfection, and to be specific, bacterial pneumococcal pneumonia[1]. Preliminary data collected since the start of the pandemic in the United States, where routine anti-pneumococcal vaccination has been carried out since 2001, show that most (80%) of the paediatric deaths from Influenza A that have been registered are in children over 5 years, where invasive pneumococcal disease is more frequent. However, in 43% of the cases in which cultures were taken, bacterial superinfection was documented, and *S. pneumoniae* was present in 30% of the isolations.[2] More recently, the CDC referred to bacterial superinfection being identified in a third of autopsy studies, *S. pneumoniae* being the microorganism identified in half of the cases.[3] The most recently published series of influenza A patients show bacterial superinfection in between 20% (Australia) and 33% (USA and Canada) of cases admitted to intensive care.[4,5] These figures are very significant, more so if we take into account that most of the patients admitted to hospital with influenza A received early empirical antibiotherapy in all the series published, which could have led to a significant reduction in the sensitivity of the cultures.

We have a heptavalent pneumococcal conjugate vaccine (and soon there will be 2 more pneumococcal conjugate vaccines with 10 and 13 serotypes), whose effectiveness and safety have been confirmed.[6] Its qualities include the capacity to prevent both invasive and non-invasive pneumococcal pneumonia.[6] Grijalva et al estimated that, on a global scale, the heptavalent vaccine could reduce hospital admissions with pneumonia of any aetiology in children under 2 by 40% (and by 65%, that caused specifically by pneumococcus).[6] More recently, it was published that the pneumococcal vaccine in children, the main reservoirs and transmitters of influenza viruses, was able to reduce pneumonia from airway viruses by 31%. Another study carried out with a pneumococcal conjugate vaccine showed that it was not only able to prevent secondary pneumococcal pneumonia in children but also, that the children who received the pneumococcal vaccine were hospitalized 45% less for influenza virus infections (confirmed by laboratory) than those who received a placebo[1]. Added to this is the fact that routine childhood vaccinations give indirect protection to non-vaccinated subjects (collective or flock immunity)[6] to such an extent that the heptavalent vaccination for children probably provides greater protection to people over 65 years of age than the right vaccination for this age group with the 23-valent *pneumococcal polysaccharide* vaccine.

At present, in our country the interterritorial vaccination schedule only recommends pneumococcal vaccinations with the heptavalent conjugate vaccine for children under 5 in high-risk groups, and with the 23-valent polysaccharide vaccine for the elderly over 65 years of age. Routine vaccinations for children with the heptavalent pneumococcal conjugate vaccine, recommended by the World Health Organisation and in the vaccination schedules of most European countries, is only free in Spain for the children of the Autonomous Community of Madrid, despite both national and international recommendations (by the Vaccination Advisory Committee of the Spanish Paediatric Association). In other words, it is likely that morbimortality from influenza A (H1N1) in the Autonomous Community of Madrid will be lower than the rest of Spain thanks to routine pneumococcal conjugate vaccinations.

Conflict of Interest

Dr. F. Martinón-Torres has received travel grants and/or fees for conferences and/or consultancy work from GSK, Wyeth, Novartis, Sanofi Pasteur MSD y Medimmune.

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The Need for New Techniques in the Diagnosis and Staging of Lung Cancer

Necesidades de las nuevas técnicas en el diagnóstico y estadificación del carcinoma de pulmón

To the Editor:

The right mediastinal staging of lung cancer (LC) is essential to assess the prognosis of non-microcytic lung cancer (NMLC) and design a therapeutic strategy. The low sensitivity and specificity of non-invasive radiological techniques mean that, for correct staging and, in many cases, an accurate diagnosis of the pathology, it is necessary to resort to cytohistological techniques.[1-2] To do this, at the present time, there are various more or less invasive techniques, such as conventional transbronchial needle aspiration (TBNA) or those guided by endoscopic ultrasound (EUS-TBNA) and, more recently, endobronchial ultrasound (EBUS-guided TBNA). There are also different surgical mediastinal exploration techniques (SME) such as mediastinoscopy, mediastinostomy and video-assisted thoracoscopy.[1,2] Several studies have shown that the combination of relatively recent techniques, such as positron emission tomography/computerized tomography (PET-CT) and real-time endoscopic ultrasound-guided needle aspiration improve the diagnostic and mediastinal staging process and make it possible to avoid more aggressive and costly diagnostic tests, such as the different SME techniques[1]. For this reason, different scientific societies and experts on the matter have published algorithms which already include these initial assessment techniques with patients with suspected LC.[1,3] However, hardly any studies have been performed which analyse in depth the relationship between the real cost and effectiveness of the general application of these diagnostic algorithms. A recent study based on a theoretical cohort of patients with NMLC concluded that the most cost-effective strategy in the cytological confirmation of possible mediastinal lymph node lesions was to perform standard TBNA in steps, EBUS-guided TBNA if the standard TBNA did not provide with a diagnosis and, lastly, mediastinoscopy in cases where EBUS-guided TBNA results were negative or inconclusive.[4] But we must take into account that these new techniques are more complex to perform, requiring specific infrastructure and more specialized healthcare professionals.[4-6] This has raised the question about the need or not to centralize these techniques in certain hospitals which handle a minimum volume of patients in order to improve cost-effectiveness.[4-6] Up until now, no studies have been published which have estimated how many patients of a real cohort of suspected LC cases would need these techniques for their disease to be correctly diagnosed and staged. The arrival at the beginning of the year of EBUS-guided TBNA and PET-CT to our centre has meant us changing our handling algorithm for these patients (fig. 1), which is very similar to the one proposed by Disdier et al[6] in an excellent review, recently published in *Archivos* de Bronconeumologia. Until now, PET was performed in another centre in Galicia and, if the suspected N2 or N3 disease was not confirmed by standard TBNA, the SME technique appropriate to each case was then carried out. In order to estimate the required number of patients for these new techniques, we performed a retrospective study of a cohort of 380 patients strongly suspected of having LC who were treated in one of the hospitals forming the University Hospital of Vigo Complex over the last 4 years. The average age of the patients was 65 years, 78% of whom were males. The most frequent clinical presentation was general syndrome or cough (? 40% each) and the most common radiological alterations were the presence of a nodule or lung mass (71%). Following the algorithm shown, after performing the CT scan and fibrobronchoscopy (FB) with standard TBNA, or other cytohistological techniques when necessary, we diagnosed 60 patients (15.7%) with other types of pathologies (mainly inflammatory or infectious); 56 (14.7%) had microcytic LC, and we diagnosed and staged 51 cases of NMLC in stage IIIB (13.6%) and 117 (30.7%) in stage IV. That is, using the classic techniques which are accessible to most pulmonologists and centres, it is possible to correctly diagnose and stage 75% of patients. In 31 cases (8.1%) it was necessary to follow the central branch of the algorithm and in 65 (17.1%) the right branch. By applying the diagnostic yield described for the PET-CT and the EBUS real time TBNA,[1-3] it would only have been necessary to perform EBUS-guided TBNA and/or EUS-TBNA in 30 or 40 (8-10 a year) patients in order for them to have been dealt with correctly. Based on the algorithm shown, in our centre, PET would be necessary to study appropriately 25% of the patients with a strong suspicion of LC and endoscopic ultrasound techniques, only for 8-11% of these cases. The results of this study could answer the doubts raised by Disdier et al[6] regarding whether it is necessary to use ultrasound bronchoscopy with all patients subsidiary of diagnosis and mediastinal staging as most cannot be operated due to the presence of comorbidities (an aspect not considered in our analysis), distant metastases, microcytic lung cancer or gross adenopathies. This number of patients is