Prevention is better than cure: time to change the focus of community-acquired pneumonia management

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Increased awareness of the role of adult vaccination is needed to reduce pneumococcal pneumonia rates http://ow.ly/M3pqj

Community-acquired pneumonia is the leading cause of hospital admission for infectious disease in Europe, and a major cause of morbidity and mortality. According to the results of Global Burden of Disease study, in the World Health Organization European region, community-acquired pneumonia accounted for 230 000 (2.3%) deaths and 2.2 million (1.5%) disability-adjusted life-years in 2010, and was ranked the fifth most common cause of death in the continent [1]. The incidence of community-acquired pneumonia increases with age and the burden is therefore set to become greater and more costly with the ageing worldwide population.

Despite much progress in medicine, and in critical care particularly, short-term mortality of patients admitted to hospital with community-acquired pneumonia remains high: between 10 and 20% [2]. However, unlike nosocomial infections, development of resistance to antimicrobials in the most important pathogens that cause community-acquired pneumonia does not have a role in maintaining this high mortality. Risk factors such as age, chronic comorbidities and disability have a much greater effect on outcome than does the causative pathogen. Unsurprisingly, new antibiotics with broader antimicrobial activity do not produce better results than older antibiotics in general.

Therapeutic options for the future focus on an improvement of the innate immunity of the host; for example, by a local application of growth factors such as granulocyte/macrophage colony-stimulating factor [3] or on a reduction of virulence factors, perhaps by administering IgM-enriched immunoglobulins [4]. However, even in the best case scenario, it will take years until these drugs are available regularly.

The only as yet available method for reducing the burden of disease in community-acquired pneumonia is the use of vaccines for disease prevention. Influenza can cause pneumonia itself, but more often influenza infection is followed by bacterial infection. The effectiveness of influenza vaccination in reducing morbidity and mortality, mainly in elderly patients and in patients with comorbidities, has been demonstrated in a number of studies; therefore, influenza vaccination is recommended worldwide [5].

In contrast, the effectiveness of pneumococcal vaccination is continually being discussed and remains controversial. The most often used 23-valent polysaccharide vaccine (PPV) showed a protective effect with regard to invasive pneumococcal disease (IPD) in healthy adults, not in patients with chronic diseases. A reduction of pneumonia rate has never been shown in huge trials [6]. In children under 5 years of age, in which IPD was the leading cause of death for a long time, PPV was not effective due to the poor immune response in young children. With the introduction of a 7-valent conjugate vaccine (PCV7; including the

Received: April 23 2015 | Accepted: April 23 2015

Conflict of interest: Disclosures can be found alongside the online version of this manuscript at erj.ersjournals.com

pneumococcal serotypes 4, 6B, 9V, 14,18C, 19F and 23F) in children in 2000 a dramatic reduction in IPD rates and in mortality has been recognised [7]. Surprisingly, in parallel, a significant decrease of pneumococcal disease in adulthood was found, as a result of "herd immunity": usually pneumococci colonise the upper respiratory tract of children without infecting them, but the pathogen is transferred to adults, who are then more likely to become severely ill. Conjugate vaccines induce a mucosal immunity in children and therefore prevent colonisation and pathogen transmission to adults, which explains the decline in pneumcoccal pneumonia rates [8].

Since PCV7 has been regularly used in children, a phenomenon known as pneumococcal serotype shift occurred over a period of a few years. The serotypes covered by PCV7 disappeared, but other serotypes appeared. As a consequence, first 10-valent, later a 13-valent vaccine (PCV13) including the new serotypes 1, 3, 5, 6A, 7F and 19A was developed. The effectiveness of this vaccine in children has been proven in a number of studies [9]. In this issue of the *European Respiratory Journal*, Rodrigo *et al.* [10] provided data demonstrating the herd effect in the UK after the introduction of PCV13 for children in 2010. Between the pre- and the post-PCV13 period, an 88% decrease of pneumonia rate caused by the serotypes covered by PCV7 and an additional 30% decline for the six new serotypes added to the PCV13 were observed. The older the patients were, the more pronounced was the protective effect.

The results of this study raise a number of open questions. Does it make sense to vaccinate adults (the elderly and those with chronic diseases) with PCV13 generally? There are some arguments in favour of adult vaccination with PCV13. Despite the herd immunity, there is still a high burden in patients at risk for community-acquired pneumonia. Based on the data of Rodrigo *et al.* [10] for 2013, this corresponds to more than 25 000 hospital admissions for pneumococcal pneumonia due to serotypes included in PCV13. The large increase in numbers of refugees coming to Europe from countries without a vaccination programme for children will decrease the effect on herd immunity. A recently published randomised controlled trial showed a reduction in pneumococcal pneumonia of 46% and in IPD of 75% for serotypes included in PCV13 *versus* placebo [11]. In the UK, 2400 deaths per year could be avoided by PCV13 vaccination.

Conversely, it is still unclear whether sequential vaccination, *i.e.* PPV 8 weeks after PCV13, contributes to improved prevention through broader serotype coverage. Theoretically, the conjugate vaccine could enhance the immune response after polysaccharide vaccination, but well-designed studies on sequential vaccination are missing and are urgently needed.

In summary, Rodrigo *et al.* [10] demonstrated the major effects of childhood PCV13 vaccination on adult pneumococcal pneumonia rates. While vaccination rates in children are high, they are very low in adults, even in the patient population for whom vaccination is recommended. Programmes to improve physicians' knowledge about vaccination effectiveness are necessary. In addition, to raise the awareness of patients themselves must be a main topic for healthcare policy in the future.

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