Eur Respir J 2005; 26: 982–983
DOI: 10.1183/09031936.05.00119705

EDITORIAL

Pneumococcal vaccination

A. de Roux and H. Lode

It has been some time now since AUSTRIAN *et al.* [1] performed a vaccination trial evaluating the effectiveness of a 15-valent pneumococcal polysaccharide vaccine (PPV) in South African gold miners. The receipt of this vaccine was associated with a reduction in the risk of pneumococcal bacteraemia and a >50% risk reduction of any radiographically confirmed cases of pneumonia [1]. However, since the 23-valent PPV has been licensed it has been the subject of numerous debates, studies and controversies. Moreover, the aggregate financial and administrative cost of providing pneumococcal vaccination to all patients at risk is substantial. Nevertheless, pneumococcal vaccination is almost uniformly recommended in Europe for adults who are at high risk from pneumococcal infections because of age, several comorbidities or immunosuppression.

Although many large clinical trials have shown the vaccine to be effective, the results of other studies raise questions regarding the immunogenicity of the vaccine in certain at risk populations [2, 3]. Recent large trials and meta-analyses show a protection from invasive pneumococcal disease; however, a protection from pneumococcal pneumonia and any other pneumonia could not be shown. In contrast, in a recent Cochrane Database systematic review [4] the PPV was not effective in preventing either pneumonia or death in adults with or without chronic illness or in the elderly. Only case-control studies showed a significant efficacy in preventing invasive pneumococcal disease (odds ratio 0.47; 95% confidence interval (CI) 0.37–0.59).

JACKSON *et al.* [5] specifically addressed the efficacy of PPV in preventing invasive pneumococcal disease. By means of a large retrospective cohort study, including data from 47,365 subjects aged ⩾65 yrs, it was convincingly shown that the receipt of the pneumococcal vaccine was associated with a significant reduction in the risk of pneumococcal bacteraemia (hazard ratio (HR) 0.56; 95% CI 0.33–0.93). Again, vaccination did not alter the risk for developing community acquired pneumonia (CAP) of any severity or cause. These data are consistent with other meta-analyses of prospective randomised trials, which concluded that there is no evidence that the vaccine is associated with a reduction in the risk of pneumonia from any cause among older adults [6–8]. So far there is sound evidence that the 23-valent PPV protects from invasive pneumococcal infection in adults of all ages.

Helios Kliniken Emil von Behring, Berlin, Germany.

CORRESPONDENCE: A. de Roux, Helios Kliniken Emil von Behring, Berlin, Germany. Fax: 49 3080022623. E-mail: aderoux@berlin-behring.helios-kliniken.de

In the current issue of the *European Respiratory Journal*, VILA-CORCOLES *et al.* [9] report the results of an interim analysis of a prospective cohort study in individuals aged >65 yrs using the 23-valent PPV. Primary endpoints were the prevention of all-cause CAP and death [9]. Pneumococcal vaccination was associated with a reduction of death from pneumonia (HR 0.28; 95% CI 0.09–0.80) and death from any cause (HR 0.67; 95% CI 0.54–0.83). However, there was only a small, nonsignificant trend towards a reduction in the risk of hospitalisation from pneumonia and the incidence of pneumonia. The authors suggest that the vaccine may not be effective in reducing the incidence of pneumonia, but may reduce the severity of a pneumococcal infection. This interpretation fits with a recent study of a reduction of in-hospital mortality for pneumonia after pneumococcal vaccination [10]. However, the incidence of pneumococcal pneumonia (12 cases) and invasive pneumococcal disease (nine cases) in the present study was low. Therefore, a significant effect of the vaccine on invasive disease may have been missed due to a type-II error. Despite this, the study adds evidence that pneumococcal vaccination is also an important healthcare intervention in the elderly.

The currently available 23-valent PPV induces exclusively humoral immune response. Therefore, impaired B-cell response after vaccination, the lack of possible boosters, rapid antibody washout and decreased avidity of induced antibodies are potential confounders limiting the effectiveness of the polysaccharide vaccine [11–13]. Accordingly, there is evidence that those at highest risk of infection and complications, such as the immunocompromised and aged, benefit least from the vaccine. By covalently linking polysaccharides to carrier proteins, conjugated vaccines have been developed. In contrast to polysaccharide antigens, immune response to protein antigens is T-cell dependent, thereby inducing an enhanced immune response and immunological memory. The currently licensed pneumococcal conjugate vaccine is limited to seven serotypes.

The seven-valent pneumococcal conjugate vaccine has been shown to induce antibody production and immunological memory in very young children with an immature immune system and is currently licensed for children <2 yrs of age [14]. The impact of its use has been dramatic. Apart from an overwhelming reduction of invasive pneumococcal infections in this age group, a decrease of pneumococcal disease in parents and grandparents has been described [15]. A recent study examined the incidence of invasive pneumococcal disease after the introduction of the conjugate vaccine for children in the year 2000. The mean annual incidence between 1994–1999 in the city of Atlanta (GA, USA) fell from 30.2 to

13.1 per 100,000 in 2002 ($p<0.0001$). Striking reductions were observed in children <2 yrs of age (82% decrease) and in those 2–4 yrs of age (71% decrease). Further significant declines were also noted in adults aged 20–39 yrs (54%), 40–64 yrs (25%), and ⩾65 yrs (39%). Macrolide resistance dropped from 9.3 per 100,000 in 1999 to 2.9 per 100,000 by 2002 [16]. Recent data suggest that the seven-valent conjugate vaccine can be safely given to elderly subjects >70 yrs of age. The conjugate vaccine is more effective in inducing immunity to the included serotypes, compared with the 23-valent PPV [17]. Nevertheless, there seems to remain a place for the polysaccharide vaccine as it can be effectively used as a booster after initial vaccination with the conjugate vaccine [17]. A possible drawback is the risk of increasing incidences of nonvaccine serotypes.

In conclusion, there is sufficient evidence to support current pneumococcal vaccine recommendations. This is true particularly in combination with the influenza vaccination as it has been shown that the two vaccines are additive in preventing pneumonia and invasive pneumococcal disease [10]. However, there is a need for new pneumococcal vaccines that provide longer-term protection and better efficacy in high-risk groups.

REFERENCES

1 Austrian R, Douglas RM, Schiffman G, *et al.* Prevention of pneumococcal pneumonia by vaccination. *Trans Assoc Am Physicians* 1976; 89: 184–194.

2 Christenson B, Lundbergh P, Hedlund J, Ortqvist A. Effects of a large-scale intervention with influenza and 23-valent pneumococcal vaccines in adults aged 65 years or older: a prospective study. *Lancet* 2001; 357: 1008–1011.

3 French N, Nakiyingi J, Carpenter LM, *et al.* 23-valent pneumococcal polysaccharide vaccine in HIV-1-infected Ugandan adults: double-blind, randomised and placebo controlled trial. *Lancet* 2000; 355: 2106–2111.

4 Dear K, Holden J, Andrews R, Tatham D. Vaccines for preventing pneumococcal infection in adults. *Cochrane Database Syst Rev* 2003; 3.

5 Jackson LA, Neuzil KM, Yu O, *et al.* Effectiveness of pneumococcal polysaccharide vaccine in older adults. *N Engl J Med* 2003; 348: 1747–1755.

6 Watson L, Wilson BJ, Waugh N. Pneumococcal polysaccharide vaccine: a systematic review of clinical effectiveness in adults. *Vaccine* 2002; 20: 2166–2173.

7 Fine MJ, Smith MA, Carson CA, *et al.* Efficacy of pneumococcal vaccination in adults: a meta-analysis of randomized controlled trials. *Arch Intern Med* 1994; 154: 2666–2677.

8 Cornu C, Yzebe D, Leophonte P, Gaillat J, Boissel JP, Cucherat M. Efficacy of pneumococcal polysaccharide vaccine in immunocompetent adults: a meta-analysis of randomized trials. *Vaccine* 2001; 19: 4780–4790.

9 Vila-Corcoles A, Ochoa Gondar O, Hospital I, Gomez A. Protective effect of pneumococcal vaccine against mortality from pneumonia. EVAN-65 Study. *Eur Respir J* 2005; 1086–1091.

10 Christenson B, Hedlund J, Lundbergh P, Ortqvist A. Additive preventive effect of influenza and pneumococcal vaccines in elderly persons. *Eur Respir J* 2004; 23: 363–368.

11 Rubins JB, Puri AK, Loch J, *et al.* Magnitude, duration, quality, and function of pneumococcal vaccine responses in elderly adults. *J Infect Dis* 1998; 178: 431–440.

12 de Roux A, Schmidt N, Rose M, Zielen S, Pletz M, Lode H. Immunogenity of the pneumococcal polysaccharide vaccine in COPD patients. The effect of systemic steroids. *Respir Med* 2004; 98: 1187–1194.

13 Romero-Steiner S, Musher DM, Cetron MS, *et al.* Reduction in functional antibody activity against *Streptococcus pneumoniae* in vaccinated elderly individuals highly correlates with decreased IgG antibody avidity. *Clin Infect Dis* 1999; 29: 281–288.

14 Eskola J, Anttila M. Pneumococcal conjugate vaccines. *Pediatr Infect Dis J* 1999; 18: 543–551.

15 Whitney CG, Farley MM, Hadler J, *et al.* Active bacterial core surveillance of the emerging infections program network. Invasive pneumococcal disease after the introduction of protein–polysaccharide conjugate vaccine. *N Engl J Med* 2003; 348: 1737–1746.

16 Stephens DS, Zughaier SM, Whitney CG, *et al.* Georgia Emerging Infections Program. Incidence of macrolide resistance in *Streptococcus pneumoniae* after introduction of the pneumococcal conjugate vaccine: population-based assessment. *Lancet* 2005; 365: 855–863.

17 de Roux A, Kuhnke A, Schmoele-Thoma B, *et al.*, Immunogenicity, safety and tolerability of a seven valent pneumococcal conjugate (7vPnC) and pneumococcal polysaccharide (23vPS) vaccine booster dose 12 months after first injection in elderly individuals. 43rd annual meeting of the IDSA: Abstract 980; 2005.