

REGIONAL ADVISORY BOARD POSITION STATEMENT ON OPTIMAL PNEUMOCOCCAL VACCINATION IN ADULTS UPDATE TO 2011 CONSENSUS ON ADULT PNEUMOCOCCAL DISEASE: UPDATE ON OPTIMAL PNEUMOCOCCAL VACCINATION IN ADULTS

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SUMMARY

Background: An important development in the field of adult pneumococcal vaccination since the last Consensus Statement, published by the Expert Panel of Central and Eastern Europe and Israel (the Region) in September 2012, was the licensure of the 13-valent pneumococcal conjugate vaccine (PCV13) for adults aged 50 years and older.

Discussion: The Expert Panel has developed this Position Statement as an update to its previous Consensus to address the following topics which are likely to be on the agenda of national scientific societies during the ongoing updates of vaccination recommendations in the Region: the availability of a pneumococcal conjugate vaccine for adults over 50 years of age, the available clinical evidence on its use in adults, and the future place of conjugate vaccines in adult pneumococcal vaccination. The Expert Panel concluded that there is sufficient epidemiologic immunogenicity and safety evidence to use PCV 13 in adults over 50 years of age.

Results: The use of conjugate vaccine induces immunological memory and can overcome some limitations associated with the plain polysaccharide vaccine (PPV). It was also agreed that, if the use of PPV is considered appropriate, PCV13 should be administered first, regardless of prior pneumococcal vaccination status.

Key words: invasive pneumococcal disease (IPD), community-acquired pneumonia (CAP), Central and Eastern Europe (CEE), Israel, pneumococcal vaccines, vaccination, elderly adults

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BACKGROUND

Despite advances in prevention and medical management, *S. pneumoniae* infections continue to exert a significant burden on the adult population (1). Further, incidence and mortality of pneumococcal disease in adults start to rise at 50 years of age

and reach a second peak among older adults that may exceed the significant disease burden recognized in children less than 5 years of age (2). Incidence of pneumococcal disease is currently underestimated, as bacteriological laboratory confirmation methods are underused and have limitations in their diagnostic yield. The definition of invasive pneumococcal disease (IPD) is ambiguous

and varies in different sources since there is no consensus about whether laboratory methods beyond conventional bacteriological culture should be considered, e.g. PCR, BinaxNOW, etc. Further, limitations of the culture based bacteriology laboratory methods, together with the usually occurring previous antibiotic treatment, make it difficult to detect bacteremia in pneumonia cases and, therefore, to differentiate between bacteremic (invasive) and non-bacteremic (non-invasive) pneumococcal pneumonia. This is an important consideration since pneumococcal disease in adults presents most often as pneumonia.

Significant antibiotic resistance of *S. pneumoniae* in many countries of the Region suggests that there is a need for further optimization of prevention. In the majority of countries within the Region, pneumococcal vaccination in adults has been very limited due to low awareness among primary care professionals and the public, who tend to associate vaccination with children only. Additionally there is often a general, overriding negative connotation associated with vaccination. Data from randomized clinical trials and meta-analyses of studies evaluating the use of the plain polysaccharide vaccine (PPV) in adults have demonstrated a moderate decline of IPD incidence but little or no effect against pneumonia (3, 4). Repeat doses of PPV are generally not recommended for healthy adults by most of the guidelines, reflecting its limitations in providing protection through the long adult age period (3, 4), but may be suggested for specific circumstances in some countries (5). Pneumococcal conjugate vaccines (PCV) have led to significant reductions in disease burden in children, particularly where the vaccine has been incorporated into child vaccination programmes (CVP). Significant reductions in isolation of *S. pneumoniae* resistant to penicillin and macrolides were observed after the introduction of PCV7 vaccination in children (6, 7). A herd effect provided by PCV7, i.e. a reduction in the incidence of IPD caused by vaccine serotypes in unvaccinated age groups, has been observed in countries with national PCV7 CVP (8). However, there are PCV CVP countries which have not observed this, like the Czech Republic (9). The degree of herd effect on IPD and the speed at which it is achieved appears to be dependent in a large part on the vaccination strategy implemented, and coverage rate achieved in the CVP. Vaccine-mediated herd effects may reduce the probability of exposure to the pathogen (colonization) but do not provide personal immunity against disease.

DISCUSSION

Use of Conjugate Pneumococcal Vaccination

The use of conjugate technology in adult pneumococcal vaccination may overcome a number of limitations associated with the characteristics of polysaccharide vaccines (10, 11) including: short duration of effectiveness (12), little or no efficacy on community acquired pneumonia (13), no effect on nasopharyngeal carriage, and depletion of serotype specific memory and B1b-cell subsets (12). Generally, conjugate vaccines provide higher functional antibody levels than polysaccharide vaccines (14) by creating an immune memory and do not blunt immunologic response to secondary vaccination (hyporesponsiveness). Conjugate vaccines can also reduce serotype-specific nasopharyngeal

carriage (15). Conjugate vaccines, such as the ones against *Haemophilus influenzae* Type B (Hib), meningococcal Group C (MenC), and pneumococci, have proven to be effective in children <2 years of age, an age group in which polysaccharide vaccines are known to be non-immunogenic and have no impact. Additionally, in HIV-positive adults, clinical trials with PCV7 have shown significant efficacy in protecting against vaccine serotype-specific IPD (16).

Immunogenicity and Safety of PCV13 in Adults

There is a substantial body of evidence demonstrating immunogenicity and safety of PCV13 in adults who have or have not previously received a dose of pneumococcal polysaccharide vaccine (PPV) (17).

PCV13 provides comparable levels of immunogenicity for all common serotypes (superior immunogenicity for the majority of common serotypes) to those provided by PPV, in both naive and previously PPV-vaccinated adults (17). There is also a demonstration of immunological memory 3–4 years following a primary vaccination with PCV13, whereas PPV was clearly shown not to induce immunological memory (18). Depending on clinical circumstances, PCV13 may also be administered concomitantly with seasonal trivalent inactivated influenza vaccine (17, 19, 20), where this can facilitate vaccination of older adults who might fail to return for a subsequent vaccination (17, 19, 21).

Approvals and Recommendations of PCV13 for Adults

As of March 2012, PCV13 was licensed for use in adults aged 50 years and older by the European Medicines Agency (EMA) and Food & Drug Administration (FDA) in the USA. Based on the available approvals depending on the existing evidence, PCV13 may be used for adults over 50 years of age and can be administered in both naive and PPV-vaccinated adults. If PPV use is considered appropriate, it is recommended that PCV13 should be administered first to enable revaccination with either PCV13 or PPV at a later stage. As mentioned by the latest EMA Committee on Medicinal Products for Human Use (CHMP) assessment report, PCV13 can induce immune memory, which is a favourable and encouraging vaccine characteristic for revaccination. Vaccination decisions would also take into account individuals with conditions which place them at high risk of pneumococcal disease. Vaccination with PCV13 in specific immunocompromised groups should be considered on an individual basis.

After the EMA and FDA approval decisions, the availability of PCV13 for adults has already been addressed in several 2012 updates of national pneumococcal vaccination schedules. A number of European countries including Austria, Greece and five countries of the Region (Bulgaria, Estonia, Hungary, Lithuania, and Poland) have recommended the use of PCV13 for all adults over 50 years of age (22–28). In the Czech Republic, France (29), the Netherlands (30), Spain (31), Switzerland (32), and the USA (5), PCV13 has been recommended for use in adults of certain high-risk groups. The UK (33) and German (34) schedules have remained as they were with PPV use in adults over 65 and 60 years of age, respectively.

Implementation of Vaccination Guidelines

Public awareness campaigns and education of healthcare professionals have to be considered to improve the impact of evidence-based guidelines on real-life healthcare. Guidelines for vaccination are developed by academic societies based on scientific evidence, while their implementation is affected by the level of education, awareness and preconceptions of primary care physicians, public, and policy makers as well as economic factors. Awareness and education programmes for all healthcare and lay audiences should be conducted, not only specifically around adult pneumococcal disease, but also in the broader context of “Healthy Ageing” and the importance of adult vaccination. Currently available data from countries with strong epidemiology networks, which have long shown the significant burden of pneumococcal disease and the causative serotypes across all ages (2, 35) should be communicated to primary care physicians, public and policy makers. Scientific evidence on vaccination against pneumococcal diseases should be communicated in the Region to reinforce the existing general agreement that all at-risk groups should be vaccinated. Practicing physicians will need clear educational and reference materials to make practical choices surrounding vaccination regimens for adult patients.

Future Research

Epidemiologic, microbiologic, clinical, and health economic research is important in the fields of pneumococcal disease in general and specifically in adult pneumococcal vaccination. Development of affordable diagnostic methods with improved sensitivity and specificity for pneumococcal disease would allow for more accurate ascertainment of the true disease burden. International studies with unified robust methodology and centralized data centers are needed to generate comparable data on antibiotic resistance. Health economic models and studies (including those assessing the costs of non-vaccination), can also support decisions on the national funding of age-based pneumococcal vaccination in adults 50 years of age and older. Post-licensure studies in adults will further explore the influence of PCV13 programmes on the distribution and morbidity of *S. pneumoniae* serotypes; they will ultimately demonstrate the impact of PCV13 on adult pneumococcal disease, including IPD and pneumonia, extending the evidence already available on the impact of PCV7 and PCV13 vaccination programmes in children.

CONCLUSIONS

Addressing the preventable burden of disease in older adults is essential in the context of healthy ageing, which is increasingly important in the countries of the Region. Further to the Call to Action published in its recent Consensus paper (1), the Expert Panel agreed, that the international licensure of a conjugate vaccine PCV13 for adults over 50 years of age represent a significant development in the field of adult pneumococcal vaccination. These approvals acknowledge the substantial body of evidence on safety and immunogenicity of PCV13 in adults. The use of the conjugate vaccine can provide additional opportunities for adults, such as the proven immunological memory which may help in lessening the significant burden of adult pneumococcal disease in the Region. The Expert Panel also emphasizes the importance

of evidence-based vaccination recommendations and guidelines and effective educational activities for the relevant health care personnel.

Conflict of Interests

Endre Ludwig: Financial support for participating and working as consultant in advisory boards by Astellas, MSD; Honoraria as speakers in scientific meetings by Bayer.

Roman Chlíbek: Principal investigator in clinical studies supported by GlaxoSmithKline and Novartis; Scientific consultant to Baxter, GlaxoSmithKline, Novartis, Aventis Pasteur and Pfizer; Sponsorship from GlaxoSmithKline and Aventis Pasteur to attend scientific meetings.

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