Protecting asplenic individuals from fulminant pneumococcal disease

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In this issue of *Eurosurveillance*, Chironna *et al*. report on an unfortunate death of an asplenic individual with fulminant pneumococcal sepsis [1]. Whether or not the death of this particular individual could have been avoided with active preventive interventions remains unanswered. It does, however, raise the alert to revisit the preventive guidelines of asplenic patients in general, and need for reminders both among practicing clinicians as well as asplenic patients.

Asplenia usually results from splenectomy, which is carried out for three main reasons: (i) rupture of the spleen, either because of trauma, during an operation or spontaneous, (ii) as a desired consequence of treatment of certain haematologic disorders, or (iii) because of treatment of neoplasm of the spleen or other organs close to it. Asplenic individuals are at increased risk of fulminant sepsis caused by encapsulated bacteria, especially by *Streptococcus pneumoniae*, but also by *H. influenzae* and *N. meningitidis*. Clinicians should consider recommending that asplenic individuals get vaccinated against the latter two as well. Depending on the underlying cause of asplenia, and the baseline incidence of invasive pneumococcal disease (IPD) in a given country, the risk of IPD in asplenic individuals can be as high as 25 times that of the general population [2]. Approximately half of all episodes of overwhelming post-splenectomy infection (OPSI) occur more than five years after splenectomy [3], and case-fatality rates are 50% or higher, as also demonstrated in the case report by Chironna *et al*. [1].

What is the best means to protect asplenic individuals from fulminant pneumococcal disease? In Europe, the presently available 23-valent polysaccharide pneumococcal vaccine (23PPV) has been recommended at five-year intervals or even more often to asplenic patients [4]. Evidence arising from sufficiently powered randomised controlled trials on the impact of 23PPV in the prevention of OPSI is not available. Concern has been raised about the potential induction of hyporesponse after multiple doses of 23PPV, also after priming with pneumococcal conjugate vaccine [5-6]. The immunological mechanisms behind the hyporesponse to subsequent doses of 23PPV and the clinical relevance of this observation is not fully understood. Immunogenicity studies suggest, however, that certain asplenic individuals might gain protection against IPD even after multiple doses of 23PPV given at five-year intervals [7]. An observational, population-based study carried out in a cohort of asplenic individuals from Denmark is in line with this finding [8], and thus give support to the present clinical practices. On the other hand, there is a subgroup of splenectomised patients with underlying haematologic diseases who clearly do not benefit from 23PPV and who should be identified by measurement of pneumococcal antibodies after vaccination [9] in order to be provided with other means of protection, such as prophylactic or early antimicrobial treatment.

There is a clear need for the development of more broadly acting, protein-based pneumococcal vaccines, given (i) the limitations of 23PPV in the prevention of pneumococcal disease in several medical risk groups as summarised in a recent meta-analysis published by the World Health Organization [10], (ii) the lack of improved immunity provided by conjugated vaccines to risk groups [11] as well as (iii) the suboptimal coverage of the disease causing pneumococcal serotypes of the presently available pneumococcal conjugate vaccines in these groups combined with the observation of replacement of vaccine serotypes by nonvaccine serotypes [12] especially in risk groups. Proof of clinical efficacy of these new vaccines will be needed, not only in healthy individuals, but also in predefined, immunocompromised risk groups who are most in need of pneumococcal vaccination.

While it will take several years before such new vaccines are licensed, clinicians need to guide and protect their asplenic patients according to the best available knowledge. At this moment the combination of 23PPV, measurement of antibody concentrations induced by 23 PPV and early antimicrobial therapy for those whose protective levels remain low, are the best ways to prevent unnecessary deaths among splenectomised individuals.

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