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EDITORIAL

IS THERE A NEED FOR A PUBLIC VACCINE PRODUCTION CAPACITY AT EUROPEAN LEVEL?

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In this issue of *Eurosurveillance*, Rouaud et al report a protracted outbreak of meningococcal B invasive diseases (BMD) in the northern French department of Seine-Maritime, linked to the local expansion of a clonal strain of B:14:P1.7,16 phenotype, belonging to the ST32/ET5 clonal complex.

This strain had already been responsible for an increased incidence in that department in 1997, and the incidence rose again in 2003, and has since remained high.

The paper summarises the main features of this outbreak. First restricted to the city of Dieppe and the surrounding area in 2003 and 2004, cases due to this specific strain were notified from other areas of the department in the first six months of 2005. The proportion of cases presenting with septicaemia was higher than usually observed for invasive meningococcal B diseases in France. However, the initially high case-fatality rate (25% in 2003) has decreased over time. This may in part reflect the impact of local efforts to raise awareness of both the general public and health professionals about the early signs of the disease, in order to optimise the management of cases, including systematic pre-admission parenteral injection of a third-generation cephalosporin for all cases where purpura fulminans is suspected.

Since the paper was first drafted, the situation has evolved, both as regards the epidemiological situation and the implementation of control measures. The hyper-endemicity situation is persisting. The incidence of BMD in the department as of early July for the last 12 months is 2.4 /100 000, compared with 0.7/100 000 for the rest of France. The strain has continued to spread and has been identified in several neighbouring departments, causing moderate increases in incidence.

The hyper-endemicity of meningococcal B invasive diseases in Northern France re-emphasises the need for generic vaccines against meningococcal diseases of serogroup B, and the limitations of the market forces that govern the private vaccine production when faced with such a situation

Mass chemoprophylaxis, which was considered in 2004, has been discarded, after taking into account the geographical spread of the cases due to this specific strain and its long-standing presence in the department. There is no generic serogroup B vaccine available. The only B vaccines to have been used are tailor-made outer membrane vesicle (OMV), protein-based vaccines developed against specific strains. Several of these vaccines have been used in the context of local outbreaks in Cuba, Chile, Brazil, Norway and currently in New Zealand, with efficacy estimates against homologous strains of at least 70% in children over five years [1-5]. Fortunately, the OMV vaccine developed in Norway in 1983 by the National institute of public health (Folkehelseinstituttets, FHI), MenBvac, was directed towards a B:15:P1.7,16 strain, which was responsible for most of the high excess incidence observed nationwide since 1974. As the

response induced by those vaccines is mainly directed towards the Por A protein, defining the sero-subtype, (here P1.7,16), it was anticipated that the Norwegian vaccine could be effective against the Seine-Maritime strain, which shares a common sero-subtype (PorA antigen) with the Norwegian strain. An experiment measuring the response in 19 Norwegian adolescents immunised with the MenBvac vaccine did indeed show a similar bactericidal activity against both the Norwegian and the Seine-Maritime strains. A total of 25 clinical trials have been performed with this MenBvac, including a phase III study carried out with 173 000 students. An immunogenicity study nested in this trial yielded an estimate of protection rate of 87% after 10 months [6]. The safety profile of the vaccine appears satisfactory. With this information on mind, the French Advisory Board on Immunisation, based on the advice of the Meningococcal Emergency Taskforce, which is made up of all the local and national stakeholders involved in the management of meningococcal outbreaks, in December 2005 recommended the vaccination of all children and teenagers under 20 years old living in the department, starting with the Dieppe area. In its statement, the Board urged the French Ministry of Health to take all necessary steps to make a sufficient amount of MenBvac vaccine available as soon as possible. Preliminary discussions held with the drug company that held the rights for MenBvac had been unsuccessful. In the specific context of the use of the vaccine in Seine-Maritime, a direct agreement with the FHI was reached. FHI sold us its available stock and increased its production in order to meet our needs of more than one million doses of the vaccine. The implementation of the vaccination campaign was phased to fit in with the anticipated release of new vaccine lots.

Vaccination started in early June 2006 with the 9000 available doses. It has been targeted at the group of children (considered to be most at risk), based on epidemiological data, that is, children aged between 1 to 5 years living in Dieppe and the surrounding area. Preliminary data suggest that coverage has been close to 80% for the first dose.

This outbreak re-emphasises the need for generic vaccines against meningococcal diseases of serogroup B, which represent 64% of invasive meningococcal diseases in Europe [7]. It shows us once again how little we can fight local outbreaks of BMD, because mass antibioprophylaxis is restricted to very limited situations where outbreaks are restricted in place and time. There was, understandably, considerable distress caused in the general population and among healthcare workers by three consecutive winters of BMD cases in the Seine-Maritime department. Cases were occurring at a rate of more than one per week at the peak of the epidemic, with a significant risk of permanent sequelae or death.

This experience also re-emphasises the importance of close cooperation between epidemiologists and biologists. The contribution of our national reference centre has been crucial in the vaccination decision process, through its ongoing phenotyping and genotyping of the strains and the exchange of the B:14:P1.7,16 strains with the institution involved in the development of OMP vaccines.

Thirdly, this experience has shown the limitations of the market forces that govern the private vaccine production when faced with such a situation. This raises the issue of maintaining a public vaccine production capacity, at European level if not at national level, to deal with public health emergencies. This capacity could be managed at the European level, as it might not be feasible or even necessary to have such a capacity at national level. However, the mechanisms to make such an enterprise work would have to be identified. The Institut de Veille Sanitaire, the French Ministry of Health and its agencies, the local authorities, the families and the health professionals of Seine-Maritime are all greatly indebted to the FHI for its active support in helping us to control this outbreak, but such international collaborations do need more formal mechanisms.

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