Meningococcal Disease Prevention in India

WESTERN PERSPECTIVE

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Pediatricians who care for children with meningococcal disease know that it is a disease which is difficult to recognise in its early stages, difficult to manage when the patient is critically ill, and can have devastating consequences amongst survivors [1]. Taken with the propensity for explosive epidemics of disease in some parts of the world, including South Asia, its prevention through vaccination is clearly an important goal for child health.

However, Indian data are sparse on the epidemiology of meningococcal disease [2], and it is difficult to provide informed comment on the potential use of meningococcal vaccines in the region. Most documented cases have been caused by capsular group A [2], and it is not clear why there is a relative lack of disease caused by other capsular groups in the region; this picture has been largely mirrored by experience in Sub-Saharan Africa. Epidemic disease in India has been documented over the last century, and likely relates to the intermittent emergence of highly invasive clones of capsular group A meningococci – as in Africa – so that availability of a Meningococcal A vaccine is an important public health need for the region for outbreak control.

Fortunately, in 2014, there is an unprecedented opportunity for the global reduction of cases of meningococcal disease caused by the major capsular groups of *Neisseria meningitidis* (A, B, C, Y and W) as a result of the development and licensure – in various parts of the world – of more than 10 new generation vaccines containing meningococcal capsular polysaccharides conjugated to a carrier protein (either alone or in combination with other antigens), or containing subcapsular proteins from the organism.

The astonishing experience of the many high income countries – which implemented programs with monovalent capsular group C meningococcal (MenC) vaccines over the last one and half decades – is that MenC disease has now almost disappeared, and the data indicate that high efficacy is likely for quadrivalent (ACYW) meningococcal vaccines (MenACYW) following its use in the United States [3]. Moreover, an Indian glycoconjugate vaccine directed against capsular group A meningococci is interrupting epidemic meningitis following its deployment across the meningitis belt in Sub-Saharan Africa [4]. The main cause of meningococcal disease in most high income countries is serogroup B *N. Meningitidis;* a 4-component protein vaccine was recently recommended for use in the UK to reduce cases of serogroup B meningococcal disease [5], and the impact of this vaccine is eagerly anticipated. While other meningococci only rarely cause disease, outbreaks of serogroup X meningococcal disease in Sub-Saharan Africa are a cause for concern [6], since no vaccine is currently available and development timelines for a new product are long.

The licensure of each of these vaccines in the various regional jurisdictions followed collection of a substantial body of evidence demonstrating immunogenicity and safety, and the likely effectiveness by extrapolation from the immune response data. In this edition of *Indian Pediatrics*, Yadav, *et al*. [7] describe a clinical trial of a quadrivalent meningococcal glycoconjugate vaccine – undertaken in Delhi, Bangalore and Mumbai – which found the vaccine to be both immunogenic and safe in both children (from 2 years of age) and adults. The findings are expected, as the four meningococcal capsular polysaccharides have been chemically conjugated to diphtheria toxin in this vaccine; it has been used for almost a decade in the United States and its impact has been evaluated by the US Center for Disease Prevention and Control indicating up to 85% effectiveness against disease [3]. The publication of clinical trial data on meningococcal vaccines in this region provides important bridging from experience of these vaccines elsewhere.

Key questions, not addressed in the paper by Yadav, *et al*. [7] are the duration of protection following immunization with this meningococcal vaccine and the impact on carriage of the organism in the oropharynx, and

thus the potential for induction of herd immunity. Duration of protection against disease and carriage are important in estimating how many cases can be prevented and thus the potential cost-effectiveness of the vaccine. The impact of such vaccines in high income countries may have resulted more from the excellent direct and herd protection amongst adolescents and young adults than from the short duration responses induced by the vaccination of young children [8]. The reasons for these age-dependent differences in immunity are not completely understood but may relate to developmental differences in the immune system, or be driven by environmental factors. There is also evidence of genetic control of the duration of protection [9] which points to the importance of monitoring duration of protection induced by vaccines in populations with differing genetic backgrounds.

With prevention of meningococcal disease using glycoconjugate vaccines demonstrated elsewhere, bridging data on immunogenicity in India, and leadership in this field from Indian vaccine manufacturers, it is lamentable that there is so little surveillance data available in India to inform policy, to determine the need for programs and to direct the response to outbreaks.

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Preventing Meningococcal Infections in India

INDIAN PERSPECTIVE

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Neisseria meningitidis causes invasive diseases like meningococcemia and meningitis with a case fatality rate of 10-15% and a disability rate of 11-19% among survivors [1]. Although the bacterium largely continue to be sensitive to antibiotics but rapid course of illness and emerging antibiotic resistance warrants that the disease be prevented as far as possible [2,3]. Currently, several vaccines against meningococcus are available, but one has to choose wisely to ensure maximum efficacy. At least