

## **Meningococemia Update: Vaccination and Chemoprophylaxis**

A review article on meningococcal disease by Sachdeva, *et al.* has been published in last issue of Indian Pediatrics(1). The article was written in the wake of an ongoing outbreak of meningococemia and meningococcal meningitis in Delhi; the first case of the outbreak was reported on 29 March 2005. As the temperatures soared to 40°C+ in Delhi during the last weeks of May and early June, the outbreak died its natural death, as predicted earlier. As of 8th June 2005, the cumulative cases were 405 with 48 deaths (CFR = 11.9%)(2). TV channels and newspapers carried out meningococemia as lead news item which not only sensitized the public but also created a panic. Media's interest has subsequently waned.

The scare is gone but the scars remain. It is not easy to forget the physical and mental agony of the affected and their dear ones, the frantic rush for the vaccine resulting in its temporary shortfall, and unjustified mass consumption of ciprofloxacin for chemoprophylaxis. But we have gone back to our routine work till time that another epidemic happens; lessons for future have not been learnt. No national guidelines are available for continued surveillance, management of sporadic cases, reduction of carrier pool, identification of 'at risk' population, and administration of chemoprophylaxis and immunization. Centers for Disease Control, Atlanta remains the leading torch bearer in issuing evidence based guidelines on prevention and control of meningococcal disease(3-5).

As the review article(1) was being published in the last issue; Advisory Committee on Immunization Practices (ACIP) from National Center for Infectious diseases, CDC issued new guidelines for the prevention and control of meningococcal disease on 27th May 2005(6). The recommendations focus on the new tetravalent meningococcal poly-saccharide-protein conjugate vaccine (MCV4) and also updates the recommendations regarding the currently used tetravalent meningococcal polysaccharide vaccine (MPSV4) and on antimicrobial chemoprophylaxis. It would be prudent to discuss and disseminate this information for the benefit of our readers. We also aim to settle some of the queries received in our office regarding mass vaccination and chemoprophylaxis during an outbreak.

### **Pitfalls of Existing Meningococcal Polysaccharide Vaccine (MPSV4)**

MPSV4 is a tetravalent meningococcal polysaccharide vaccine containing A, C, Y, and W-135 purified bacterial capsular polysaccharides. This vaccine has a clinical efficacy of >85% among school-aged children and adults and is useful in controlling out-breaks. Limitations of this vaccine are listed below:

- Bacterial polysaccharides are T-cell-independent antigens and do not elicit a memory response. Thus, subsequent challenge with the same polysaccharide antigen does not result in an anamnestic response(7).
- The serogroup C polysaccharide is poorly immunogenic among children aged <2 years (8).
- The A polysaccharide induces antibody

response in infants, but vaccine efficacy declines rapidly(9).

- Meningococcal polysaccharide vaccines do not confer long-lasting immunity(9,10).
- The vaccine does not reduce the nasopharyngeal carriage of *N. meningitidis*(11).
- Because of the above reason, herd immunity is not generated and transmission continues.

### Graduating to Tetravalent Meningococcal Conjugate Vaccine (MCV4)

Conjugation of polysaccharide to a protein carrier results in shift of the immune response from T-cell-independent to T-cell-dependent. Thus, infants under 2 years can also be protected. A strong anamnestic response is expected at re-exposure. Conjugate Hib vaccine reduces asymptomatic carriage of *H. influenzae* (12), thus protecting unvaccinated persons through a herd immunity effect.

Initial efforts to produce a protein conjugated meningococcal vaccine yielded a monovalent serogroup C conjugate vaccine. CRM 197 (from diphtheria toxin) and tetanus toxoid were the proteins used for conjugation. This was introduced in the United Kingdom in 1999. MCV4 is a tetravalent meningococcal conjugate vaccine (Menactra, manufactured by Sanofi Pasteur, Inc., Swiftwater, Pennsylvania), licensed for use in the United States in January 2005. A single dose of vaccine contains 4 µg each of capsular polysaccharide from serogroups A, C, Y, and W-135 conjugated to 48 µg of diphtheria toxoid. In trials comparing immunogenicity and safety of MCV4 with MPSV4, the two vaccines were found to be equally immunogenic in 11-55 year age groups; the systemic adverse events were also similar. Local adverse reactions were more with MCV4. However, safety and efficacy studies are needed in infants and children. Based on available data, ACIP has recommended

preferential use of MCV4 among persons aged 11-55 years; use of MPSV4 is advocated for children 2-10 years till further data is generated. Both vaccines can be used in control of meningococcal outbreaks. Studies are being conducted to ascertain the duration of protection offered by MCV4. The present data on MCV4 is insufficient on its ability to reduce naso-pharyngeal carriage and produce the herd immunity effect(6).

### Decision for Mass Vaccination

Decision for a mass vaccination campaign has to be taken cautiously because of the associated effort, expense and unwarranted apprehension. The decision to start mass prophylaxis depends on the primary attack rate. For this, it is imperative that the cases are classified as primary, secondary and co-primary(6).

- A primary case of meningococcal disease is one that occurs in the absence of previous known close contact with another patient.
- A secondary case of meningococcal disease is one that occurs among close contacts of a primary patient >24 hours after onset of illness in the primary patient.
- Co-primary cases are two or more cases that occur among a group of close contacts with onset of illness separated by <24 hours.
- Close contacts of a patient who has meningococcal disease include (i) household members; (ii) child-care center contacts; and (iii) persons directly exposed to the patient's oral secretions (*e.g.*, by kissing, mouth-to-mouth resuscitation, endotracheal intubation, or endotracheal tube management).

A community-based outbreak is defined as the occurrence of three or more confirmed or probable cases of meningococcal disease in <3 months among persons residing in the same

area who are not close contacts of each other and who do not share a common affiliation, with a primary disease attack rate of >10 primary cases/100,000 persons. For a primary attack rate to be calculated, all confirmed cases of the same serogroup should be added; secondary cases should be excluded and each set of co-primary cases counted as one case(6).

Attack rate per 100,000 = [(number of primary confirmed or probable cases during a 3-month period) / (number of population at risk)] × 100,000.

In a community outbreak, the population at risk is defined as the smallest geographically contiguous population that includes nearly all patients(6). This could be a neighborhood, village, town, or a city, whose size is obtained from census data. In case the disease is occurring in a certain specified age group only, the population at risk will be age-specific. Almost all parts of Delhi and all age groups were involved (even though the majority of cases were adolescents or young adults); thus the whole population of Delhi should be considered 'at risk'. The primary attack rate is difficult to calculate for the recent Delhi outbreak, since cases were not classified as primary, secondary and co-primary. However, even if we presume all reported cases to be primary, there is clearly no case for mass vaccination as the attack rate in the present outbreak did not exceed the stipulated cut off. The decision to vaccinate, however should also take cognizance of (a) completeness of case reporting and number of possible cases of meningococcal disease for which bacteriologic confirmation or serogroup data are not available; (ii) occurrence of additional cases of meningococcal disease after recognition of a suspected outbreak; and (iii) logistic and financial considerations. Because available vaccines are not effective against *N. meningitidis* serogroup B, vaccination should

not be considered during serogroup B outbreaks.

### Vaccination Group

Those persons designated to be administered vaccine during a vaccination campaign comprise a vaccination group. The vaccination group usually includes either the whole or a subset of the population at risk. Since meningococcal vaccine is not recommended for children <2 years, and the cases were noticed predominantly among persons aged <30 years(1), the vaccination group would have comprised of those aged 2 - 29 years from among the population at risk; provided a mass campaign is justified from calculated attack rate. The decision should also take into account the available finances and human resources.

### Mass Chemoprophylaxis

Mass chemoprophylaxis (to eliminate the carrier pool) is not recommended to control large outbreaks of disease. Emergence of resistant organisms; and logistics and the cost of the drug and administration are the major disadvantages. The approach is also impractical in view of multiple sources and prolonged risk for exposure. Further, it is difficult to ensure simultaneous administration of drug to all targeted persons.

### Adding Azithromycin to the Arsenal

Chemoprophylaxis is meant to prevent occurrence of meningococcal disease in a close contact of a patient with invasive meningococcal disease. A recent study(13) has reported that azithromycin (500 mg single dose in adults) may also be used for eradicating nasopharyngeal carriage of *N. meningitidis*. Further studies are needed to establish efficacy and potential of developing drug resistance to azithromycin, if it is to be used widely for chemoprophylaxis.

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