Editorial

Meningococcal Vaccine: Which, When and for Whom?

Col SP Gorthi*, Brig AK Nagpal+

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Neisseria meningitides, an aerobic gram negative diplococcus is an important cause of devastating acute purulent bacterial meningitis and sepsis that often leads to disabling sequelae like limb loss, renal failure, spastic quadriplegia, cranial nerve palsies, hearing loss and death [1]. It was first isolated in 1887 and is responsible for massive epidemics sweeping through the meningitis belt stretching from Senegal to Ethiopia killing thousands of people. The disease starts as a sporadic case in the presence of favourable environment and host factors, which subsequently progresses into an outbreak and then an epidemic.

N meningitides has 12 identified serogroups based on differences in the capsular polysaccharides and immunological reactivity. The most common serogroups include A, B, C, Y and W-135. Serogroups A, B and C account for approximately 90% of meningococcal diseases. The most common subtype encountered in the Indian subcontinent is serotype-A [2].

Humans are the only natural reservoirs of *N meningitidis* and human nasopharynx is the site from which meningococci are transmitted by aerosol or secretions to others (host-to-host transmission). Meningococcal septicaemia and meningitis have high mortality rates (40% and 10-12% respectively), despite advances in antimicrobial therapy.

Epidemiologically this disease is a prime example of an infection that occurs in closed settings such as military barracks and dormitories, affecting a large number of individuals. New military recruits have consistently been at a higher risk of both sporadic meningococcal disease and outbreaks. This increased risk is probably related to crowded living conditions among persons from various geographic areas who have diverse strains of *N meningitidis*. In Indian Armed Forces the incidence of sporadic meningococcal meningitis cases average 9-10 per year in the last five years. The last major outbreak of 17 cases amongst trained soldiers deployed in counter insurgency operations, reported in this issue of the journal by Kushwaha et al [3], occurred in early 2006. An organization based outbreak of this magnitude is to be addressed with mass chemoprophylaxis or mass vaccination programme to prevent the outbreak from progressing into an epidemic that has the capacity to kill thousands of people.

Since the risk of secondary disease among close contacts is highest during the first few days after the onset of disease in the index patient, chemoprophylaxis (Tablet rifampicin 600 mg every 12 hours for two days or Tablet ciprofloxacin 500 mg single dose or Injection ceftriaxone 250 mg as single IM dose) should be administered as soon as possible. If started more than 14 days after the onset of the disease, chemoprophylaxis is probably of limited or no benefit.

Outbreaks with *N meningitidis* occur once in every 8-12 years in meningitis belt and attack rate is 500-1000 cases per lakh, with a mortality rate of 10%. In households where a case of meningococcal disease has occurred, the risk of invasive disease is increased by a factor of 400-800.

Two types of vaccines are in use for meningococcal meningitis; the polysaccharide vaccines and conjugate vaccine. In India bivalent (A+C) and quadrivalent (A, C, Y, W 135) polysaccharide meningococcal vaccines are marketed by few multinational companies. It is available as a lyophilized vaccine containing 50mcg of polysaccharide per dose. A single dose of 0.5 ml of reconstituted vaccine is administered subcutaneously in the deltoid region for adults. Immunity is conferred for a period of only three to five years. However this vaccine is flawed by the fact that it does not induce herd immunity and does not affect nasopharyngeal carriage

Conjugate vaccines have been developed recently in a few developed countries to overcome these

*Associate Professor, + Professor and Head (Department of Internal Medicine), Armed Forces Medical College, Pune -411040.
E-mail : pgorthi2002@yahoo.com

drawbacks. These vaccines are based on covalent linkage of the polysaccharide to a carrier protein (diphtheria/tetanus toxoid) which connects the polysaccharide to thymus dependent antigen thus enhancing the capsular antibody formation and memory cells. The conjugate vaccine confers herd immunity after 28 days of vaccination and immunity is long lasting. An Indian company is in the process of developing a conjugate vaccine against serogroup A. The vaccine is likely to be available for public use by this year end.

In their recommendation the expert group of the Association of Physicians of India [4] felt that routine vaccination of all adults is not recommended in view of the short lived protection provided by the currently available polysaccharide vaccines. The meningococcal vaccine can be used in selected populations in certain situations such as during an outbreak, during inter epidemic periods to persons living in dormitories and immunocompromised individuals, to travellers, pilgrims, people attending fairs and festivals in large numbers. In these situations a single dose of bivalent vaccine is recommended 10-14 days before the scheduled visit. However for Haj pilgrims, as a national policy, NICD Delhi is administering the quadrivalent polysaccharide vaccine to fulfill the requirements of the Government of Saudi Arabia.

The expert group in India recommends that during outbreaks, a single dose of vaccine (A+C) may be given to health care workers, laboratory workers and close contacts of cases. United Kingdom is the first country to adopt routine immunization with meningococcal conjugate vaccines with phenomenal success in reducing the incidence of the disease. In United States, all military recruits and first year college students residing in dormitories receive the quadrivalent A,C,Y, W-135 meningococcal vaccine and routine vaccination of all children 11-12 years of age has been recommended [5,6].

Since the *N meningitidis* has the capacity to indulge in 'capsular switching' secondary to 'genetic transformation', serogroup specific protection may lead to capsular switching imparting virulence to the strain if bivalent polysaccharide based vaccines are used for mass vaccination programme [7]. However polyvalent conjugate vaccines are generally more immunogenic and efficacious than polysaccharide vaccines. The former provides long lasting host and herd immunity alongwith decreased nasopharyngeal carriage. Future research should provide a polyvalent conjugate vaccine covering all serotypes which is effective in all geographical areas. Till then the use of presently available vaccines is recommended only in specific situations and not as a mass vaccination measure. At present the polysaccharide based vaccines cost approximately one hundred rupees per vial and the conjugated vaccine is likely to cost eight hundred rupees per vial. The cost of routine vaccination will be enormous to prevent nine to ten cases per year.

Military recruits constitute a high risk group for contracting meningococcal meningitis. If we opt for routine vaccination of all recruits, the policy will entail coverage of 80,000 to one lakh recruits every year. This strategy will raise certain issues. Should we resort to polysaccharide vaccines which confer immunity for a limited period of 3-5 years or should one wait for the conjugated vaccines, which provides longer lasting immunity? The dynamics of cost-effectiveness will have to be worked out keeping in mind the incidence of this disease in Indian Armed Forces. The need for revaccination with booster doses for trained soldiers will be another consideration. The existing guidelines on this aspect are silent.

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MJAFI wishes its readers a Happy New Year