



Defeating the Scourge of Meningococcal Disease in Africa

A Work in Progress

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Dr F. Marc LaForce reflects on why the Meningitis Vaccine Project is necessary and how MVP's strategy might pave the way for the development of other vaccines for use in developing nations.

The Meningitis Vaccine Project (MVP) is a partnership between the World Health Organization (WHO) and the Program for Appropriate Technology in Health (PATH). Created in 2001 through a \$US 70 million grant from the Bill & Melinda Gates Foundation, its goal is to eliminate epidemic meningitis as a public health problem in Sub-Saharan Africa.

Over the last 100 years sub-Saharan Africa has suffered repeated epidemics of meningitis. These epidemics have been clustered in the so-called "meningitis belt" that stretches from Gambia and Senegal on the Atlantic coast to Ethiopia and Somalia in East Africa. Epidemics have occurred every 8-12 years although the inter-epidemic period appears to have been shrinking during the last two decades. Occurrence of the disease has a high temporal predictability. It takes place in the December to June "dry season" in sub-Saharan Africa and epidemics promptly cease after the first rains.

The human toll from these epidemics has been enormous; the 1996-1997 epidemic resulted in over 188,000 reported cases. However, a simple tally of the numbers of cases does not do justice to the havoc that accompanies meningococcal epidemics. The disease strikes suddenly and unless antibiotics are available and used quickly mortality rates can soar. In addition, long-term sequelae are noted in 10 to 15 per cent of survivors so that death or disability, even with appropriate antibiotic therapy, affects 1 out of 4 individuals. Because the disease occurs in adolescents and young adults as well as infants, the disruption and chaos in the community are considerable. The impact of the disease on individuals and their families is such that an epidemic can quickly turn into a social, human, and economic disaster for the affected countries.

Over the last 20 years control of epidemic meningitis has emphasized surveillance and reactive mass immunizations. Routine immunization programs and other ongoing

public health interventions are suspended as public health officials try to respond to the crisis by preventively immunizing the populations in identified 'at-risk'— districts with meningococcal polysaccharide (PS) vaccine. However, supplies of PS vaccines are limited and uncertain, and notification about an epidemic is frequently delayed so that the intervention only begins in the last phase of the epidemic with a discouragingly low effect.

This reactive approach, which depends on good surveillance, availability of PS vaccine and a properly functioning health infrastructure, is not the most appropriate for Africa. African public health officials have been increasingly frustrated with having to respond to meningococcal epidemics with strategies that are at best, moderately useful and at worst, ineffective.

The Meningitis Vaccine Project (MVP) grew out of a WHO-sponsored effort to improve the public health response to meningitis outbreaks in Africa after the devastating outbreak in 1996 and 1997. This renewed interest led to the creation of WHO-sponsored expert panels that were asked to review vaccine options, particularly the possibility of developing conjugate meningococcal vaccines that offer the promise of a more effective preventive strategy. Indeed, conjugate vaccines are much more immunogenic than polysaccharide vaccines are, they can be confidently used in children under one year of age, and they have been shown to induce herd immunity. The conjugate *Haemophilus influenzae* vaccine has eliminated meningitis due to this organism in every country where the vaccine has been widely used, and the meningococcal C conjugate vaccine has drastically reduced the incidence of meningitis and carriage due to serogroup C *Neisseria meningitidis* in the United Kingdom.

The Meningitis Vaccine Project is working with a Group A meningococcal conjugate vaccine to be widely used in 1- to 29-year-olds to control serogroup A disease, which accounts for most meningococcal epidemics in Africa. The vaccine will also be used as an Expanded Program on Immunization (EPI) antigen in children under one year of age.

Ensuring that this new conjugate vaccine is affordable is one of the core principles of the project. African public health officials have repeatedly emphasized the importance of price as a limiting factor in the sustainable use of vaccines in Africa. This is particularly true in the meningitis belt countries, which are some of the poorest countries in the world. MVP has operationalized these comments and is committed to the development of products well under \$US 1 per dose.

In order to assure a low-priced, high quality vaccine product, MVP is working with a highly respected developing country manufacturer for vaccine production, and it is forming partnerships with other companies for technology development and transfer, and supply of base materials. A contract manufacturer will produce vaccine grade polysaccharide A (Ps A) and a process development company will develop an innovative conjugation methodology whereby Ps A is conjugated to tetanus toxoid (TT). The vaccine manufacturer will accept transfer of the conjugation technology and manufacture a Group A meningococcal conjugate vaccine at a **target** price of less than \$US 0.50 per dose. The vaccine will be licensed and tested in developing countries. Clinical lots of the men A conjugate vaccine will be prepared in 2004 and Phase 1 and 2 trials are scheduled to begin in 2005.

MVP's strategy of developing a low-cost vaccine through facilitating and coordinating numerous public-private partnerships demands a high level of management responsibilities and accountability from the project team. However, the low-cost vaccine resulting from this approach will help ensure accessibility to countries of the meningitis belt in Africa and widespread sustainable uptake of the vaccine. Broad and sustained uptake is critical for achieving public health impact and meeting the goal of the project. In addition, this approach has the potential for providing a new model for vaccine development that could facilitate the introduction of other 'orphan' vaccines whose primary markets are low-income countries in the developing world.