

## Vaccine and Vaccination: Impact and Challenges

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Vaccine and vaccination have a significant impact on global health, saving untold number of lives each year and preventing considerable physical suffering and malnutrition due to repeated illness. In addition, a vaccine may benefit local economies by providing an effective safeguard against the risk of disease. It is obvious that the first decade of the 21st century has been the most productive in the history of vaccine development. Most low-cost traditional vaccines are now produced by vaccine manufacturers in developing countries. Public-private partnerships are accelerating the availability of new vaccines. Systems have been put in place to ensure the safety, effectiveness, and quality of all vaccines. From 2000 to 2007, intensified vaccination campaigns resulted in a 74% reduction in measles deaths globally. Polio has been eradicated in three of WHO's six regions and is today endemic in only four countries – down from 125 countries in 1988. Integrating immunization with the delivery of other health interventions can boost immunization coverage and accelerate the achievement of reducing deaths among children under five years old according to Millennium Development Goals (MDG 4). Vaccination prevents more than 2.5 million child deaths a year. Additionally, available vaccines could prevent an additional two million deaths a year among children under five years old. The introduction of new vaccines against pneumococcal and diarrheal diseases (rotavirus, ETEC) could have a rapid impact within three to five years on reducing the high toll of sickness, disability, and deaths among children under five years old. While new life-saving vaccines have been developed, and others will soon be available, new vaccines are still urgently needed to reduce illness and deaths from high-burden diseases such as malaria, tuberculosis, AIDS and Enterotoxigenic *Escherichia coli* (ETEC) especially in developing countries.

One of major causes of infant mortality in developing countries is diarrheal diseases. Many enteropathogens have been identified; however strains of ETEC have been recognized as the leading bacterial cause of diarrhea in children as well as the most common cause of travellers' diarrhea. Insufficient data exist, but conservative estimates suggest that ETEC are incriminated in approximately 210 million cases and 380,000-500,000 deaths each year, mostly in children under five years old from developing countries. Unfortunately, there is no currently effective vaccine that confers a broad protection against the wide array of ETEC strains, and development of such vaccines is a high priority for international health agencies as endorsed by the World Health Organization. The main hallmarks of this type of bacteria are expression of one or more enterotoxins and presence of Colonization Factors (CFs) used for attachment to host intestinal cells. These virulence factors (enterotoxin/CFs combinations) account for the high prevalence of ETEC diarrhea in endemic areas. While targeting CFs antigen in ETEC vaccine development may help protect against some but not all ETEC strains, these CFs may undergo an antigenic mutations causing failure of the currently used CF-based ETEC vaccines. On the other hand, targeting enterotoxins, heat-labile [LT] and heat-stable [ST], is rationalized by their conservative antigenic structure in all ETEC strains. This strategy was successful to protect against LT because of its immunogenicity which is similar to cholera toxin. However, this approach has been challenged to protect against ST that is present in approximately 75% of all clinical ETEC isolates, and the immediate

mediator of diarrhea in both neonatal animals and children, because of its poor immunogenicity (ST M.W. less than 2 kDa). Additionally, the correlation between ST toxicity and antigenicity hampers the ability to produce a safe ST based- ETEC vaccine. Research is ongoing to construct a non-toxicogenic version of STa immunogen and formulate an effective and safe ST-toxoid based ETEC vaccine. An effective ETEC vaccine could have a significant impact on global health, saving the lives of hundreds of thousands of children under five each year.

Several challenges to the productivity of immunization programmes have been identified such as new emerging diseases and weak health systems. Strong and effective leadership, and national ownership of immunization programmes, are key components of a successful national immunization programme. There is a need to foster increased public demand for vaccines. Disease surveillance and monitoring programmes need to be strengthened at all levels. False or unsubstantiated rumours about vaccine safety can undermine immunization programmes and cost lives. By the 2020s: child deaths from infectious diseases are expected to be at an all-time low; polio should be eradicated, and measles eliminated in all countries. Today's new vaccines against pneumococcal disease, rotavirus, meningococcal disease, and HPV are expected to have inspired new health and development goals. Hopes remain high that new vaccines will be available to combat malaria, tuberculosis, AIDS, ETEC and other diseases.

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Received June 30, 2012; Accepted June 30, 2012; Published July 03, 2012

Citation: Aref NEMM (2012) Vaccine and Vaccination: Impact and Challenges. J Vaccines Vaccin 3:e106. doi:10.4172/2157-7560.1000e106

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