

Introduction of *Haemophilus Influenzae* type b (Hib) as Pentavalent (DPT-HepB-Hib) Vaccine in Two States of India

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H*aemophilus influenzae* type b (Hib) bacterium was estimated to have caused 8.1 million cases of serious Hib diseases, and 371,000 deaths globally in the year 2000 [1]. In India, an annual estimated 2.4 to 3.0 million cases and 72,000 deaths in under-5 children were attributed to Hib diseases [1, 2]. Safe and effective vaccines to prevent Hib diseases have been available for nearly two decades and are being used globally. The National Technical Advisory Group on Immunization (NTAGI) in India recommended the introduction of Hib vaccine in the Universal Immunization Program (UIP) in 2008 [2]. From December 2011, Hib vaccine in combination with diphtheria, pertussis, tetanus and hepatitis B has been introduced in UIP in Kerala and Tamil Nadu states. A comprehensive technical review on Hib diseases and vaccines was published in 2009 in this journal [2]. This paper provides an update on global Hib vaccine use, and reviews the process and steps undertaken in India to introduce Hib-containing pentavalent vaccine in Kerala and Tamil Nadu.

HIB DISEASES

It is estimated that mortality due to Hib disease contributes 4% of all annual under-5 deaths in India [1, 3, 4]. The fastidious nature of the Hib bacterium and poor laboratory infrastructure in developing country settings such as India makes the diagnosis of Hib diseases and calculation of disease burden extremely difficult. Moreover, a combination of limited access to health services and poor health-seeking behavior by rural populations results in many affected children never having the opportunity of being correctly diagnosed or receiving appropriate care [5]. Even for those children who do reach health facilities, the increasing prevalence of antibiotic-resistance makes treatment difficult [6, 7].

HIB VACCINES AND THEIR INTRODUCTION

Hib vaccines are available in liquid and lyophilized formulations and presented in monovalent format or

combined with other antigens such as DPT and/or hepatitis B antigens. Hib vaccines have been shown to be cost-effective in both developed and developing country contexts and are in use for more than two decades. The World Health Organization (WHO) recommends that Hib vaccines be included in routine infant immunization programs of all countries [7]. By June 2011, Hib vaccine, in various formulations, was included in the national immunization program of 170 countries in all regions of the world [8].

Hib vaccination also reduces nasopharyngeal colonization with the bacterium, resulting in further reductions of Hib disease incidence. In addition to the effects directly attributed to the vaccine, there are important indirect effects associated with Hib vaccines. Indirect benefits include herd immunity and reductions in antibiotic resistance by preventing disease and inappropriate use of antibiotics. These benefits have been amply demonstrated by the post-introduction studies where near elimination levels of Hib disease have been reached; near-elimination of the disease occurred in both industrialized and developing countries, even countries with moderate to low immunization coverage rates [9-12].

Decision-making

In April 2008, the NTAGI Sub-committee on Hib vaccine reviewed available literature and information related to disease burden in India, vaccine availability, safety and efficacy, and cost-effectiveness. Based on this information, the Sub-committee recommended that Hib-containing pentavalent vaccine should be introduced in the country [2,3]. In a subsequent NTAGI meeting held in June 2008, the Sub-committee recommendations were discussed. Based on the cumulative weight of supporting evidence, the Sub-committee's recommendation to introduce Hib-containing pentavalent vaccine was endorsed [3]. Importantly, the Indian Academy of

Pediatrics (IAP) had already recommended in 2006 the use of Hib vaccine for all children [13]. The use of Hib vaccines in the private sector is widespread in India for almost a decade. Following the recommendation of NTAGI, the Ministry of Health and Family Welfare (MoHFW), Government of India (GoI), decided to introduce the vaccine initially in two states.

STRATEGY FOR VACCINE INTRODUCTION

Government of India has introduced Hib as liquid pentavalent vaccine (LPV) combined with DPT and HepB in 10-dose presentation. The use of combination formulation has certain clear programmatic advantages. First, the number of injections per completed schedule will be less, consequently requiring fewer syringes and generating less potentially hazardous sharps waste. In addition, cold chain space will be saved as a single vial of LPV replaces DPT and Hep B vials. LPV has been recommended for all infants and will be given in a 3-dose schedule. The first dose is given at 6 weeks of age or older followed by dose 2 after a gap of at least 4 weeks and a gap of at least 4 weeks before dose 3 (**Table I**). The vaccine is offered to all children younger than 1 year of age and the booster dose is not recommended in UIP in India [2, 14].

To facilitate and ease program implementation, Government of India policy states that LPV will be given to a progressive birth cohort whereby all children who present for their first dose of DPT (DPT 1) will be provided their first dose of LPV (LPV 1). Infants who had already initiated their schedule of DTP + HepB will complete the DPT and HepB vaccines schedule. In addition, monovalent Hepatitis B vaccine will continue to be used for birth-dose and DPT vaccines will continue to be used for 16-24 months and 5-6 years of age booster doses [2, 14].

PREPARING FOR VACCINE INTRODUCTION

The operational guidelines and frequently asked questions for the introduction of LPV in UIP were

developed and provided to Kerala and Tamil Nadu states for wider dissemination, several months prior to the initiation of LPV use. State immunization program managers were sensitized on the strategies and principles of LPV introduction during a National level UIP review meeting held in May 2011 in New Delhi. In addition, LPV introduction training materials were produced for medical officers and health workers.

Training and sensitization within states then followed a cascade format. State level orientations and training workshops were held and attended by district immunization officers, medical college faculty and other stakeholders. District authorities, program managers, and PHC-block medical officers were sensitized. In turn, block medical officers trained frontline health workers on key aspects related to LPV and its introduction. Representatives of professional associations, such as IAP Indian Medical Association (IMA), and other stakeholders were also sensitized at various levels.

In synergy with trainings, information, education and communication (IEC) material including frequently asked questions, were prepared in local languages and widely disseminated. A media-sensitization workshop on Hib diseases and vaccination was conducted in each state just prior to LPV introduction. The program was launched by the State Ministers of Health and other senior health department officials in Kerala and Tamil Nadu.

CAPITALIZING ON OPPORTUNITY

Lessons from the introduction of Hepatitis B vaccine in 10 states of India in 2007-08 illustrated the immunization system strengthening opportunities that introducing a new vaccine affords. Likewise, the introduction of LPV has been used to strengthen Kerala and Tamil Nadu immunization systems by training/re-training health personnel on proper injection techniques, assessing and correcting existing cold chain problems, improving program monitoring and supervision, and enhancing reporting of adverse events following immunization. In addition, pre-introduction training phase emphasized the

TABLE I IMMUNIZATION SCHEDULE FOLLOWING PENTAVALENT VACCINE INTRODUCTION

Age	Current schedule	After introduction of Pentavalent vaccine
At Birth	BCG, OPV-0, HepB-Birth dose	BCG, OPV-0, HepB-Birth dose
6 weeks	OPV-1, DPT-1, HepB1	OPV-1, Pentavalent-1
10 weeks	OPV-2, DPT-2, HepB2	OPV-2, Pentavalent-2
14 weeks	OPV-3, DPT-3, HepB3	OPV-3, Pentavalent -3
16-24 months	DPT-B1, MCV2, OPV-B1	DPT-B1, MCV2, OPV-B1
5-6 year	DPT-B2	DPT-B2

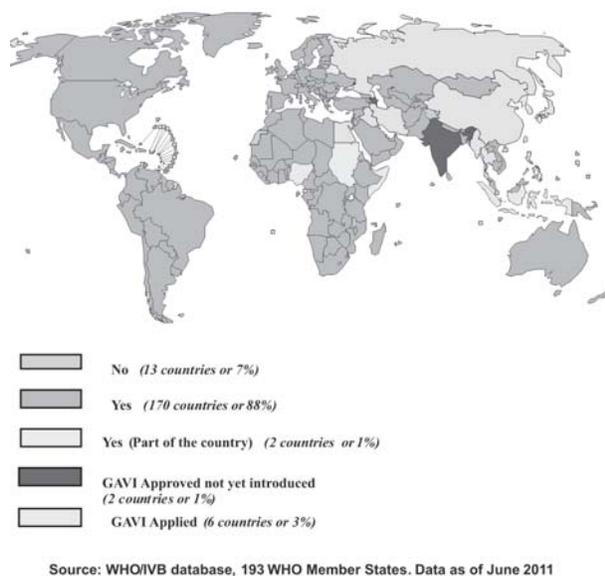


FIG. 1 Countries which have introduced Hib vaccine in the National Immunization Program.

importance of maintaining sufficient stocks of mono-valent Hepatitis B and DPT vaccines to ensure the application of birth-dose and DPT booster (at 16-24 months and 5-6 years of age).

Moreover, the introduction of Hib-containing pentavalent vaccine offers poorer families the opportunity to provide the same life-saving protection to their children as wealthier families who can afford vaccine services in the private sector. Therefore, the introduction of Hib vaccine, free of cost in the government system, helps to ensure equity in health service availability – a stated objective of India's National Health Policy [15].

From a public health perspective, this is not a trivial issue: Hib is one of the leading cause of bacterial meningitis in India and a major cause of childhood pneumonia, the largest killer of Indian children less than 5 years of age. It is estimated that Hib disease prevention through vaccine use has the potential to reduce India's under-5 mortality rate by 4 percentage points. The introduction of LPV in India is a major milestone and a step forward to accelerate child survival in India, and progress towards achieving national health goals and Millennium Development Goal 4.

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