Vaccine introduction in the Democratic People's Republic of Korea.

F Marks  
B Nyambat  
ZY Xu  
V von Kalckreuth  
Paul E Kilgore, Wayne State University, et al.
Editorial

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ABSTRACT

The feasibility of mass vaccination campaigns for Japanese encephalitis and Haemophilus influenzae type b infections was explored in the Democratic People's Republic of Korea using pilot vaccination studies. The experiences from these initial studies were then used to support larger vaccination campaigns in children at risk of these infections. We discuss the challenges and requirements for the inclusion of additional vaccines into the existing expanded program on immunization in the country.

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Targeted vaccinations have proven to be a most cost-effective public health intervention [1]. However, establishing sustainable immunization programs in resource-limited settings remains a challenge requiring political commitment, trained staff and adequate laboratory facilities. The International Vaccine Institute (IVI) has supported the authorities of the Democratic People's Republic of Korea (DPRK) with preparations for a pilot vaccination campaign against Japanese encephalitis (JE) and Haemophilus influenzae type b (Hib) to determine the feasibility of mass-campaigns and to collect data for future introduction of new-generation vaccines.

The DPRK runs the Expanded Programme on Immunization (EPI) established by WHO in 1974 to ensure basic immunizations throughout the world [2]. Initially, the overall goal was to provide available immunizations against diphtheria, pertussis, tetanus, poliomyelitis, measles and tuberculosis to every child by 1990. The program was extended to include a wider range of vaccines such as those against hepatitis A, hepatitis B (Hep B), Hib, rotavirus, pneumococcus, meningococcus, and human papilloma virus. The EPI was launched in DPRK in 1980 and made available to all target groups by 1990. The national immunization coverage in DPRK remains high; BCG coverage reached 98%, DTP3 93%, OPV3 99%, and MCV3 98% in 2013. Following the worldwide EPI recommendation, the DPRK-EPI was expanded to include vaccination against Hep B, which was added in 2004 and included in the tetravalent diphtheria-tetanus-pertussis-Hepatitis B (DTP-HepB) formulation in 2006. A second dose of measles vaccine was introduced in 2008 at the age of 15 months [3].

JE accounts for a high rate of morbidity and mortality in Asia and Hib remains a cause of death among children in some geographic areas [4–6]. JE and Hib vaccinations have substantially reduced morbidity and mortality in countries that have introduced them into their immunization programs [7–9]. A locally produced JE vaccine was administered to selected risk groups in the south of the DPRK in the 1990s. In 2008, IVI supported the DPRK government with a pilot demonstration project in order to assess the feasibility of mass JE and Hib vaccination campaigns through the DPRK's public health infrastructure. This project was accompanied by efforts to strengthen laboratory capabilities for diagnosing infectious diseases with the goal of establishing appropriate surveillance for these and other pathogens.

A total of 6427 children were targeted in urban settings (3021 with live-attenuated SA 14-14-2 JE vaccine in Sariwon; 3406 with Hib-conjugate vaccine Shan Hib-Liquid® in Nampo). These vaccination target children were selected from Sariwon and Nampo by the Ministry of Public Health of the DPRK (Fig. 1). Operational procedures and training materials were provided and standardized instruments were applied for program evaluation. Posters and flyers were distributed to inform participants about the vaccine and the disease. Several parameters were appraised through the course of vaccination. The cold chain infrastructure was investigated, local staff received training courses and sites were prepared for vaccinations.

Commonly, children under ten years are at highest risk for JE with the highest incidence in the 0–5 years age group. Given the unknown disease burden of JE in the DPRK, children aged one to under six years were eligible to receive JE vaccine. A total of 2987 children received a single dose of JE vaccine after exclusion of 34 children due to receipt of the locally produced JE vaccine or contraindications such as history of hypersensitivity, anaphylactic shock, convulsions and allergic reaction to any previous vaccination, acute moderate to severe illness, presence of high temperature, recent immunosuppresant therapy, persistent crying. The compliance rate was >98%. For Hib vaccination, children were stratified by age to conduct age-appropriate vaccination, three doses or two doses or a single dose were administered to children 6 weeks to 6 months, 7 months to 11 months and 12 months to 36 months of age, respectively. For all three doses of Hib vaccine, compliance rates were 92% or higher. The high participation rate may be explained by the opportunity for children to be protected against two diseases, combined with significant and dedicated efforts put
forward by the DPRK team to mobilize the target population. However, this pilot campaign was relatively small and limited to two cities in close proximity to Pyongyang to facilitate vaccine distribution.

These experiences were taken up and carried forward by DPRK authorities for the implementation of large-scale JE vaccination campaigns with the live, attenuated JE vaccine, SA 14-14-2 (80–95% protective effectiveness). In 2009, 500,000 children between the ages of 12 and 35 months were vaccinated in five provinces and Pyongyang City followed by 1,000,000 eligible children aged 1 year and 4–6 years (2 and 3 year old children received JE vaccination in 2009) in 2010. A third campaign was conducted in 2013 that covered the remaining 3 million eligible children aged between 1–3 years, 9–10 years and 11–16 years in 2013–2014. The five provinces targeted for this JE vaccination campaigns besides Pyongyang included South Hwanghae, North Hwanghae, South Pyongan, North Pyongan, and Kangwon. South Hamkyong and Nampo were added for the 2013–2014 vaccination campaign. Efforts are currently underway to introduce JE vaccines into the routine EPI program, at best to be concomitantly administered with 1st dose of measles vaccine at the age of 9 months.

As the Hib vaccine in pentavalent formulation (hepatitis B, Hib, diphtheria, pertussis, tetanus) had not been approved by the GAVI Alliance in 2008, the mass campaign was conducted using a monovalent formulation. In the meantime, the tetravalent formulation has been further upgraded in 2012 to a pentavalent formulation.
including Hib (DTP-Hep B-Hib) and was approved for GAVI support in DPRK in September 2011 [10] and subsequently introduced.

Experiences gained in this program raise the importance of identifying prerequisites that should be met prior to introducing new vaccines into the routine program. The decision-making process must be based on evidence of disease prevalence and considerations of the sustainability and long-term outcomes on public health and health economics [11]. All alternative strategies for preventing and controlling the disease must also be explored. Sufficient information on the target vaccine – its safety, efficacy, cost, cost-effectiveness, and supply capacity – must be collected to evaluate its practical application. Finally, the demand for a vaccine must match the capacity of health systems to successfully administer the vaccine and to sustain delivery to targeted populations over a course of time. Public awareness and adequate communication on target vaccines and what diseases will be protected against is also an important aspect of successful administration of vaccination campaigns. Priority weighting and support provided by organizations such as GAVI and UNICEF determine the eligibility of a setting for vaccine introduction.

Information on DPRK’s disease burden largely relies on data supplied by international organizations, NGOs, and DPRK national agencies. The public health agency of the DPRK, the Ministry of Public Health (MOPH), is composed of various departments including the Department for Treatment and Prevention, Department for Public Health Planning, Department for State Hygiene Control, and the Academy of Medical Science (AMS). AMS is the medical research arm comprised of 26 research institutes and branch institutes. Under the structure of the DPRK MOPH, hospitals are located at the county, provincial and central levels and the clinics at the Dong and Ri levels, smallest administrative units in DPRK. The health bureaus, hygienic and anti-epidemic stations (AES) and medical warehouses are also governed from a central level to provincial and county levels. Currently, hospitals and clinics at all levels submit disease surveillance and outbreak reports to their respective AES and public health bureaus, from where reports are channeled up to the MOPH in Pyongyang.

For some vaccines, policy on introduction is determined by external parameters (e.g. disease burden recognized in neighboring countries or the global occurrence of a pathogen), whereas for others, vaccine introduction is contingent on the identification of high-risk areas or populations in the target region. A killed bivalent whole-cell oral cholera vaccine (Shanchol®) is now WHO-prequalified and available and other new vaccines are in late-stage clinical trials (e.g. typhoid conjugate vaccines) and anticipate licensure and possible WHO prequalification in the near future. For these regionally deployable vaccines, relevant disease burden estimates need to be made in order to identify apt target risk groups. To date, primary data on vaccine preventable diseases in the DPRK are largely based on clinical diagnosis; more laboratory support for diagnoses, treatment and prevention measures is necessary for guiding public health policies and the implementation of immunization programs.

Several agencies are engaged in generating such data. The WHO has supported the DPRK MOPH with establishing an integrated disease surveillance system for 13 diseases. Within this framework, syndromic diarrheal disease surveillance is implemented in 2 provinces (South Pyongan province and Pyongan), and there is an aim to extend to an additional 6 provinces. Except for poliomyelitis and measles, for which reference laboratories exist in the DPRK, the other diseases are currently diagnosed based only on clinical presentation without laboratory confirmation. Tuberculosis is diagnosed in a TB hospital in the west of Pyongyang [12]. For adequate diagnostics, especially targeting JE and Hib, standard laboratory investigation via cerebrospinal fluid or blood sample test is ideal.

IVI has, in collaboration with AMS and MOPH, equipped a laboratory on the premises of the Institute of Microbiology (IMB), one of the 26 institutes under AMS, to enable diagnosis of selected diarrheal, enteric, and neurological diseases (JE, infections with Vibrio cholerae, Campylobacter jejuni, rotavirus, Shigella spp., Salmonella spp., Hib). Furthermore, training programs have been conducted both in-country and abroad to augment epidemiology and laboratory skills of DPRK scientists. Five hospitals, located in two provinces (North Hwanghae Province: Pediatric Hospital, Hwangju County People’s Hospital in Sariwon City; South Pyongan Province: Pediatric Hospital, Anju City People’s Hospital, Pyongsong County People’s Hospital) have been selected to start systematic diarrheal and meningeval disease surveillance; once established, surveillance activities could be extended to include diagnoses of invasive bacterial bloodstream infections and beyond such as viral infections.

The international community in the DPRK represented by governmental and non-governmental organizations such as UNICEF, WHO, IVI and others support and collaborate with both MOPH and AMS in public health research and data analysis. A long-term roadmap aiming at a systematic partnership among the participating agencies and stakeholders is essential [13]. All these efforts should under the leadership of the MOPH, lead to a refinement of the disease surveillance system in order to better define the vaccine-preventable diseases. Incremental development will eventually help prioritize public health needs of children and high-risk populations and provide a sound basis for the evaluation of the effectiveness of existing and newly introduced vaccines.

Conflict of interest statement

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