

Out-of-Cold-Chain Delivery of the Hepatitis B Birth Dose in Four Districts of Vietnam

A study by PATH and the Vietnamese National Expanded Programme on Immunization

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Hepatitis B infection in Vietnam

As in other parts of southeast Asia, hepatitis B (HB) virus is one of the leading causes of liver disease in Vietnam. A 1998 national survey showed a HB infection rate of 18%. Approximately 30% of pregnant women are thought to have chronic HB infection, resulting in high rates of viral transmission to infants at the time of birth.¹ Recent studies in the western pacific region have shown that 3% to 5% of children are infected with HB during birth. To prevent this perinatal transmission of HB from mothers to newborns, World Health Organization (WHO) and the Vietnamese Ministry of Health recommend a birth dose of HB vaccine as soon as possible after birth.

Since 2003, the Vietnamese Expanded Programme on Immunization (EPI) has provided HB vaccination to all Vietnamese children. Following WHO recommendations, the EPI introduced a nationwide birth-dose policy in 2003, requiring all newborns to be vaccinated at the time of birth.

Challenges to on-time coverage

Although Vietnam's current coverage of HB vaccination within 24 hours of birth is 62% (as of 2005 national reporting), coverage rates vary greatly between provinces, with mountainous rural areas below 40%. Challenges to the on-time delivery of the birth dose in these areas include the lack of cold chain refrigerators at commune health centers. In rural areas, a large proportion of children are born at home or in commune health centers, rather than in the cold-chain-equipped district hospitals. Without a regular supply of HB vaccine at health centers, family members are sent to district hospitals to pick up a dose of HB vaccine. No transport or support is provided, so usually the child must wait until the monthly EPI day at the health center to receive the birth dose.

Pilot study of out-of-cold-chain delivery of HB

Following recent experiences in Indonesia and China, where HB vaccine with a vaccine vial monitor (VVM) is used outside the cold chain to improve timeliness of the birth dose, PATH and the Vietnamese EPI began an out-of-cold-chain study in four districts of northern Vietnam in 2005. Utilizing the natural heat stability of HB vaccine and the ability to monitor excessive heat exposure with the VVM, the team designed the study to evaluate the coverage, safety, immunogenicity, and logistics of an out-of-cold-chain delivery strategy for the HB vaccine birth dose in areas where the cold chain does not function. Two groups were compared:

1. In the control group, newborns born at district hospitals were vaccinated with HB vaccine stored in the cold chain. Subsequent doses were stored in the cold chain and delivered during regular monthly EPI days at commune health centers.
2. In the out-of-cold-chain group, infants born at commune health centers and at home were vaccinated with HB vaccine stored at room temperature at commune health facilities. The subsequent doses were stored in the cold chain and delivered during regular monthly EPI days at commune health centers. The single-dose HB vaccine for the birth dose was delivered to the health center twice per month and stored at room temperature in a dark box to protect it from sunlight.

¹ Hipgrave B, Van NT, Huong VM, Long HT, Dat DT, Trung TN, Jolley D, Maynard JE, and Biggs BA. Hepatitis B infection in rural Vietnam and the implications for a national program of infant immunization. *American Journal of Tropical Medicine and Hygiene*. 69(3), 2003, pp. 288-294.

Results

During the 14-month study, over 10,000 children in the 4 study districts received the birth dose, approximately one-third within the cold chain and two-thirds out of the cold chain.

Coverage improvements: Compared to a pre-study baseline, on-time birth-dose coverage doubled with the introduction of the out of cold chain strategy. Baseline data was available only for birth doses delivered within three days of birth. Using the three-day definition, baseline coverage was 45%, while study coverage increased to 90% for all children born within the four districts.

Rural health center coverage equivalent to hospital coverage: Using the out of cold chain approach, health centers were able to achieve the same on-time birth dose coverage as cold chain-equipped hospitals. On-time coverage was 83% for the health center-based out-of-cold-chain group and 82% for the hospital-based in-the-cold-chain group and (no significant difference).

Higher immunogenicity out of cold chain: Serology was conducted on children from both groups. The in-the-cold-chain group showed a protective efficacy level of 86% while the out-of-cold-chain group showed a protective efficacy level of 92% ($p < 0.001$). Although reasons for the higher seroconversion in the out-of-cold-chain group are not clear, a reduction in vaccine freezing is considered a strong possibility.

Next steps

Vietnam is taking steps to expand the out-of-cold-chain approach nationally. An EPI working group is currently adapting WHO/WPRO guidelines for HB birth dose, including out-of-cold-chain procedures, for Vietnamese policy.

Regulatory review will be required to determine whether Vietnamese-produced HB vaccine will be approved for out-of-cold-chain use.

The Vietnamese producer of HB vaccine is establishing the capacity to label its vaccine with VVMs in order to take over the entire supply once GAVI support ends in 2007.

Conclusions

- On-time delivery of the HB birth dose can be increased by using an out-of-cold-chain delivery strategy in regions where a continuous cold chain is impossible to maintain. This approach could be instrumental in achieving the WHO and Vietnamese goal of reducing HB infection in children under 5 to less than 2% by 2012.
- Children vaccinated with a birth dose of HB vaccine using vaccine stored out of the cold chain have an immune response at least as high as those vaccinated using vaccine stored in the cold chain.
- Storing HB vaccine out of the cold chain in commune health centers is practical, compatible with existing logistic systems, and is highly acceptable to health workers.