Hepatitis B vaccination of newborns in rural China: evaluation of an out-of-cold-chain delivery strategy

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Hepatitis B in China

- Hepatitis B (HB) is one of the four major infectious diseases in China
- 120 million people are chronically infected with hepatitis B virus (HBV)—10% of the population
- An estimated 280,000 deaths annually
  >33% of global deaths attributed to HB

Sources:
HBV surface antigen rate among children

- Urban 1992: 7.12%
- Rural 1992: 11.40%
- Urban 2002: 2.10%
- Rural 2002: 8.25%

Rural: 28%
Urban: 71%

Source: Serosurvey adopting the samples from 2002 national nutrition survey (unpublished)
Increase in on-time administration of HB vaccine birth dose

Proportion of children receiving the HB vaccine birth dose on 1st or 2nd day of life

Objective

To evaluate strategies for improving on-time delivery (within 24 hours) of the HB vaccine birth dose in remote areas of China, especially among children born at home.
Study design

- Townships situated at least 20 km from the county capital in three counties in Hunan Province were randomly divided into three groups:
  - Group 1: Ampoule inside the cold chain
  - Group 2: Ampoule outside the cold chain
  - Group 3: HB vaccine in Uniject™* (HB-Uniject) outside the cold chain

- All ampoules of HB vaccine and HB-Uniject packages were marked with vaccine vial monitors (VVMs)

*Uniject is a registered trademark of BD.
Hospital vaccination in the cold chain; home vaccination out of the cold chain

**Group 1:**
- HB vaccine delivered in township hospitals. Vaccine stored in the cold chain

**Group 2 and Group 3:**
- Village-based doctors and midwives trained as vaccine providers. Vaccine stored and delivered out of the cold chain
Preparations

- Held trainings with vaccine providers at township and village levels
- Conducted social mobilization to emphasize the importance of hepatitis B immunization and on-time delivery of the birth dose
- Monitored vaccine storage temperatures with data loggers
Evaluation methods

Baseline and final coverage survey
– Review of children’s immunization cards
– Review of village/township immunization records

Immunologic response survey
– Radioimmunoassay for HBsAg, anti-HBs
Results: Significant improvements in on-time vaccination

- **Raising awareness helps**
- **Out-of-cold-chain storage helps more**
- **Uniject helps even more**

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>Final</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampoule Inside Cold Chain</td>
<td>8.0</td>
<td>57.9</td>
</tr>
<tr>
<td>Ampoule Outside Cold Chain</td>
<td>11.3</td>
<td>67.8</td>
</tr>
<tr>
<td>HB-Uniject Outside Cold Chain</td>
<td>6.8</td>
<td>77.3</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>67.6</td>
</tr>
</tbody>
</table>
Results: Significant improvements in on-time vaccination

- **Hospital births**—improved by raising awareness
- **Home births**—improved by out-of-cold-chain strategy

### Born in the hospital

- **Group 1 (Ampoule Inside Cold Chain):** 77.9%
- **Group 2 (Ampoule Outside Cold Chain):** 80.3%
- **Group 3 (HB-Uniject Outside Cold Chain):** 87.6%

### Born at home

- **Group 1 (Ampoule Inside Cold Chain):** 11.0%
- **Group 2 (Ampoule Outside Cold Chain):** 18.4%
- **Group 3 (HB-Uniject Outside Cold Chain):** 10.7%

- **Group 1 (Ampoule Inside Cold Chain):** 2.4%
- **Group 2 (Ampoule Outside Cold Chain):** 25.2%
- **Group 3 (HB-Uniject Outside Cold Chain):** 51.8%

- **Group 1 (Ampoule Inside Cold Chain):** 0.6%
- **Group 2 (Ampoule Outside Cold Chain):** 2.5%
- **Group 3 (HB-Uniject Outside Cold Chain):** 66.7%
Results: Home-born infants better served when vaccinated at home

Percent of infants who received the first dose of vaccine within 24 hours of birth

- Home-born and immunized at home: 73.5%
- Home-born and immunized in township hospital: 32.8%
Serology results: No difference between in-the-cold-chain and out-of-cold-chain groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Children observed</th>
<th>Anti-HBs positive</th>
<th>HBsAg positive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Children</td>
<td>%</td>
</tr>
<tr>
<td>Group 1</td>
<td>203</td>
<td>194</td>
<td>95.6</td>
</tr>
<tr>
<td>Group 2</td>
<td>203</td>
<td>195</td>
<td>96.1</td>
</tr>
<tr>
<td>Group 3</td>
<td>200</td>
<td>191</td>
<td>95.5</td>
</tr>
<tr>
<td>Total</td>
<td>606</td>
<td>580</td>
<td>96.0</td>
</tr>
</tbody>
</table>
## Serology results: No difference between in-the-cold-chain and out-of-cold-chain groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Children observed</th>
<th>Children with Anti-HBs +</th>
<th>Anti-HBs&gt;=10 mIU/ml</th>
<th>GMT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Among Anti-HBs positive (%)</td>
<td>Among children observed (%)</td>
</tr>
<tr>
<td>Group 1</td>
<td>203</td>
<td>194</td>
<td>180 (92.8 %)</td>
<td>180 (88.7 %)</td>
</tr>
<tr>
<td>Group 2</td>
<td>203</td>
<td>195</td>
<td>184 (94.4 %)</td>
<td>184 (90.6 %)</td>
</tr>
<tr>
<td>Group 3</td>
<td>200</td>
<td>191</td>
<td>178 (93.2 %)</td>
<td>178 (89.0 %)</td>
</tr>
<tr>
<td><strong>Inside cold chain</strong></td>
<td><strong>203</strong></td>
<td><strong>194</strong></td>
<td><strong>180 (92.8 %)</strong></td>
<td><strong>180 (88.7 %)</strong></td>
</tr>
<tr>
<td><strong>Outside cold chain</strong></td>
<td><strong>403</strong></td>
<td><strong>386</strong></td>
<td><strong>362 (93.8 %)</strong></td>
<td><strong>362 (89.8 %)</strong></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>606</strong></td>
<td><strong>580</strong></td>
<td><strong>542 (93.5 %)</strong></td>
<td><strong>542 (89.4 %)</strong></td>
</tr>
</tbody>
</table>
Storage temperatures: freeze and heat exposure

- In the cold chain: 2/3 township refrigerators below 0 °C
- Out of the cold chain: temperatures 2°C–30°C
  - 0.2% vaccine was discarded due to heat exposure
  - VVMs effective in identifying heat exposure
- No serious adverse events following immunization were reported during the study
Acceptability of Uniject

- Among providers who had used the Uniject device:
  - 98% thought Uniject was easy to carry, transport, and use
  - 95% thought Uniject could administer a full dose of HB vaccine
  - 88% thought Uniject could save immunization time compared with standard syringes

- Almost all immunization providers thought that the village-based out-of-cold-chain strategy could improve the on-time delivery of the HB vaccine birth dose among children born at home
Conclusion 1

- In remote areas in China and other countries where many children are born at home, on-time administration of HB vaccine has been difficult to achieve through routine immunization service.

- Village health workers using an out-of-cold chain immunization strategy can improve the on-time administration of the HB vaccine birth dose among infants born at home.

- Training and monitoring of hospital health workers can improve on-time administration of the HB vaccine birth dose to children born in hospitals.
Conclusion 2

- Simple tools such as VVMs and Uniject can ensure vaccine quality and injection safety when vaccines are administered by village health workers.

- HB vaccine is sufficiently heat stable to withstand routine out-of-cold-chain storage in tropical conditions without loss of immunogenicity.

- Taking vaccine out of the cold chain could potentially decrease the risk of vaccine damage due to inadvertent freezing.
Next steps

- Improve awareness and coordination of the birth dose in hospital settings through increased supervision
- HB vaccine manufacturer will start application of licensure for use of HB-Uniject stored out of the cold chain
- Introduce VVMs on EPI vaccines, in accordance with UNICEF and WHO recommendations
- Adopt national policy of HB vaccine storage out of the cold chain, initially in warm areas among children born at home
Increase in coverage of HB3

Source: National Coverage Survey, 2004
Progress in Hepatitis B Immunization
Western Provinces 1999-2004 *

* Adjusted for corrected data Qinghai (2004), Xinjiang (2003-4)