Are immunogenicity and protective efficacy of hepatitis B vaccine related to different administration schedules?
Outcome of HBV Infection by Age at Infection

<table>
<thead>
<tr>
<th>Age at Infection</th>
<th>Chronic Infection (%)</th>
<th>Symptomatic Infection (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>1-6 mos</td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td>7-12 mos</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>1-4 yrs</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>Older Children and Adults</td>
<td>0</td>
<td>80</td>
</tr>
</tbody>
</table>
Infant of HBsAg + /HBeAg + mother

The risk for chronic HBV infection is 70%-90% by age 6 months in the absence of postexposure immunoprophylaxis

Infant of HBsAg + /HBeAg - mother

The risk for chronic infection is <10% in the absence of postexposure immunoprophylaxis

Perinatal HBV transmission is responsible for 35–40% of HBV infections every year worldwide

Hepatitis B vaccination
Thailand Experience

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Faculty of Medicine
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### Hepatitis B Immunization Program in Thailand

<table>
<thead>
<tr>
<th>Year</th>
<th>Description</th>
</tr>
</thead>
</table>
| 1988 | - Demonstrate methods of incorporating HB vaccine into EPI  
- Sites: 2 provinces  
- Chiangmai  
- Chonburi |
<p>| 1992 | Universal HB vaccination |</p>
<table>
<thead>
<tr>
<th>Age</th>
<th>Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>At birth</td>
<td>HB1, BCG</td>
</tr>
<tr>
<td>2 months</td>
<td>OPV1, DPT1, HB2</td>
</tr>
<tr>
<td>4 months</td>
<td>OPV2, DPT2</td>
</tr>
<tr>
<td>6 months</td>
<td>OPV3, DPT3, HB3</td>
</tr>
<tr>
<td>9-12 months</td>
<td>Measles or MMR</td>
</tr>
<tr>
<td>18 months</td>
<td>OPV4, DPT4, JE1 &amp; 2</td>
</tr>
<tr>
<td></td>
<td>(2 weeks apart, booster 1 yr after)</td>
</tr>
<tr>
<td>4-6 years</td>
<td>OPV5, DPT5, MMR</td>
</tr>
</tbody>
</table>
### Efficacy of HB vaccine in infants of HBeAg + mothers (n=263)

<table>
<thead>
<tr>
<th>Group</th>
<th>Vaccine (mo)</th>
<th>HBIG</th>
<th>Protective efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0,1,2,12</td>
<td>-</td>
<td>94.8%</td>
</tr>
<tr>
<td>2</td>
<td>0,1,2,12</td>
<td>+</td>
<td>97.6%</td>
</tr>
<tr>
<td>3</td>
<td>0,1,6</td>
<td>-</td>
<td>92.2%</td>
</tr>
<tr>
<td>4</td>
<td>0,1,6</td>
<td>+</td>
<td>100%</td>
</tr>
</tbody>
</table>

## Immunogenicity of HB vaccine in infants of HBeAg + mothers (n=263)

<table>
<thead>
<tr>
<th>Group</th>
<th>GMT (mIU/ml)</th>
<th>No. with anti-HBs≥10 mIU/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mo 12</td>
<td>mo 24</td>
</tr>
<tr>
<td>1</td>
<td>165</td>
<td>380</td>
</tr>
<tr>
<td>2</td>
<td>161</td>
<td>523</td>
</tr>
<tr>
<td>3</td>
<td>317</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>180</td>
<td>67</td>
</tr>
</tbody>
</table>

Long term follow-up of high risk neonates vaccinated against hepatitis B vaccine in Thailand

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GMT evolution 0, 1, 2, 12 months schedule

A : booster + HBIG  B : booster no HBIG  C: no booster no HBIG
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GMT evolution 0, 1, 6 months schedule

D: booster + HBIG
F: booster no HBIG
E: no booster + HBIG
G: no booster no HBIG

Time (Months)
Impact of Universal Hepatitis B Vaccination in Thailand in 2000
### Population examined for HB markers per province in relation to HB vaccine integration into EPI

<table>
<thead>
<tr>
<th>Location</th>
<th>No. of children studied</th>
<th>Male</th>
<th>Female</th>
<th>Start of EPI (date)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chonburi</td>
<td>458</td>
<td>245</td>
<td>213</td>
<td>1 Jan 1989</td>
</tr>
<tr>
<td>Lopburi</td>
<td>488</td>
<td>210</td>
<td>278</td>
<td>1 May 1992</td>
</tr>
<tr>
<td>Udon Thani</td>
<td>400</td>
<td>196</td>
<td>204</td>
<td>1 Oct 1992</td>
</tr>
<tr>
<td>Nakhon Si</td>
<td>411</td>
<td>190</td>
<td>221</td>
<td>1 Oct 1992</td>
</tr>
<tr>
<td>Thammarat</td>
<td>472</td>
<td>196</td>
<td>276</td>
<td>1 Oct 1992</td>
</tr>
<tr>
<td>Lampang</td>
<td>411</td>
<td>190</td>
<td>221</td>
<td>1 Oct 1992</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2229</strong></td>
<td><strong>1037</strong></td>
<td><strong>1192</strong></td>
<td></td>
</tr>
</tbody>
</table>

Hepatitis B virus markers in children under 18 years in 1999

Impact of universal HBV vaccination 2004
2004 survey (6200 samples)

Age: 6 mos - 60 yrs

Provinces:
Geographical area
1 city hospital
2 district hospitals
Seroprevalence of HBsAg among different age groups in Thailand

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Percent

Age (year)

0-2 3-5 6-10 11-15 16-20 21-30 31-40 41-50 51-60

Udon (1725)
ChaingRai (1579)
Nakorn (1492)
Chonburi (1359)
Seroprevalence of anti-HBs among different age groups in Thailand
Seroprevalence of anti-HBc among different age groups in Thailand
Prevalence of HB markers in children < 18 years

- HBsAg: 2.3% in 1999 (n=2229), 1.4% in 2004 (n=2883)
- Anti-HBs: 11.9% in 2004 (n=2883)
- Anti-HBc: 5.5% in 2004 (n=2883)
Vaccine Efficacy

HB vaccine & HBIG administered 12-24 hrs after birth, followed by completion of a 3-dose vaccine series, has been demonstrated to be 85%-95% effective in preventing acute & chronic HBV infection in high-risk infants

Vaccine Efficacy

High-risk babies

- HBIG at birth & 2 mo
- Vaccines at 2, 3 & 5 mo

RESULTS: efficacy = 95.1%

Vaccine Efficacy

In RCTs, HB vaccine (3- or 4-dose schedule) without HBIG beginning \( \leq 12 \) hours after birth has been demonstrated to prevent 70\%-95\% of perinatal HBV infections among high-risk infants

Spacing of vaccine

- No apparent effect on immunogenicity when minimum spacing of doses is not achieved precisely
- Increasing the interval between the first 2 doses has little effect on immunogenicity or final antibody concentration

Combined DTPw-HB vaccines

- Compare combined DTPw-HB vaccines vs separate administration of DTPw & HB vaccines in 124 children of HBsAg-negative mothers
- Higher anti-HBs response in combined vaccine group than in monovalent vaccine group

Combined DTPw-HB vaccines

- One month after the booster dose of DTPw-HB vaccine, at least 97.8% of subjects had seroprotective anti-HBs levels.
- One year later at least 93.9% of these subjects remained seroprotected.

Serological survey in 7-12-mo-old children

Combination vaccine

The immunogenicity of DTaP-HB-IPV/Hib (3 doses) with & without single-antigen HB vaccine at birth is comparable

Conclusion

HB vaccines with or without HBIG have comparable immunogenicity and protective efficacy in prevention of perinatal HBV transmission
Conclusion

**Combined DTP-HB vaccine:**

- Good immunogenicity
- Replace separate vaccines in areas of high HBV endemicity in terms of clinical, economic & strategic benefits
Acknowledgements

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Thank you for your attention