Hepatitis B seroprevalence in Thailand: 20 years after hepatitis B vaccine integration into the national expanded programme on immunization

Photo by Pitak13
http://pitak13.multiply.com
HBV Prevention Thailand Experience
Hepatitis B immunization program in Thailand

August 1988: Demonstrate methods of incorporating HB vaccine into EPI program

Program sites: 2 provinces
- Chiangmai
- Chonburi
Thailand EPI

- At birth: HB1, BCG
- 2 months: OPV1, DPT1, HB2
- 4 months: OPV2, DPT2
- 6 months: OPV3, DPT3, HB3
- 9-12 months: Measles or MMR
- 18 Months: OPV4, DPT4,
  JE1 & 2
  (2 weeks apart, booster 1 yr after)
- 4-6 years: OPV5, DPT5, Measles
Prevalence of HBsAg in children under 4 years of age in Chonburi and Chiangmai

Chunsuttiwat 1997
Universal HB vaccination in Thailand

- 1988 implemented in 2 provinces
- 1990 included in 10 more provinces
Impact of universal HB immunization

• Reduce acute hepatitis patients
• Reduce the carriers
• Reduce chronic liver diseases
  » Cirrhosis
  » Hepatocellular carcinoma
EPI HB3 vaccine coverage

% coverage

Year

Thai MOPH
Hepatitis B virus markers in children under 18 years in the 1999

Poovorawan Y. Vaccine 2001
Impact of universal HBV vaccination 2004
2004 Specimens collection 6237 samples

Age: 6 mos – 60 yrs

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

Seroprevalence of HBsAg among different age groups in Thailand

Trop Med Int Health 2008
Seroprevalence of anti-HBs among different age groups in Thailand

Trop Med Int Health 2008
Seroprevalence of anti-HBc among different age groups in Thailand

Percent

Age (year)

Trop Med Int Health 2008
Impact of universal HB immunisation as part of Thailand EPI

• Reduced number of acute hepatitis patients

• Reduced number of carriers:
  
  HB carriers in children <15 years
  
  – 5–6 % in 1988
  
  – 0.7% in 1999, 2004

• Reduced incidence of chronic liver disease in the future:
  
  – cirrhosis
  
  – HCC

Vaccine 2001, Trop Med Int Health 2008
Combined DTPw-HB

Public Health benefits

- high compliance & coverage
- fast implementation

Health Economic benefits

- logistical cost-savings
- cost-effectiveness of DTPw
Chiang Rai Field Trial (Thailand)
Combined DTPw-HB DTPw and HB vaccines injected separately

- Project run by Thai CDC (Dr Supamit)
- Study site: Chiang Rai province
- Population: 1.2m - 10% hill tribes
- Study duration: July ‘94 to end Dec ‘97
- Phase I: ~ 4,000 children received DTPw + HB separately
- Phase II: ~ 25,000 children received combined DTPw-HB

Supamit C. Vaccine 2002
Chiang Rai Field Trial (Thailand)

Combined DTPw-HB vs. DTPw and HB vaccines injected separately

- No difference in safety and reactogenicity profile
- Immunogenicity:

<table>
<thead>
<tr>
<th></th>
<th>SP rate</th>
<th>Infection rate*</th>
<th>Carrier rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTPw + HB (separately)</td>
<td>88.4%</td>
<td>6 %</td>
<td>1.15 %</td>
</tr>
<tr>
<td>Combined</td>
<td>94.8%</td>
<td>4 %</td>
<td>0.23 %</td>
</tr>
</tbody>
</table>


* Chunsuttiwat S; Vaccines Today - Protecting the Future, Kuala Lumpur, March 1998
Combine DTPw-HB vaccine into Thailand EPI program
Effect of dose number and interval between the first two doses of hepatitis B vaccine on the carrier rate of infants born to hepatitis B surface antigen positive mothers
(A) Location of Chiangrai, the northern most province of Thailand

(B) 11 district hospitals participating in this study
The number in B stands for 1 - Khun Tan; 2 – Thoeng; 3 - Wiang Kaen; 4 - Phan; 5 - Chiang Saen; 6 - Wiang Pa Pao; 7 - Phaya Mengrai; 8 - Mae Sai; 9 - Mae Chan; 10 - Mae Fa Luang and 11 - Mueang Chiangrai districts.

### Recommended HB vaccination schedule for newborns of HBsAg positive and negative mothers, Chiangrai, 2004 - 2006

<table>
<thead>
<tr>
<th>Group</th>
<th>Age</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Birth</td>
<td>1 month</td>
<td>6 weeks</td>
<td>2 months</td>
<td>4 months</td>
</tr>
<tr>
<td>Children born from HBsAg negative mother</td>
<td>HB</td>
<td></td>
<td>DTPw-HB</td>
<td>DTPw - HB</td>
<td>DTPw - HB</td>
</tr>
<tr>
<td>Children born from HBsAg positive mother</td>
<td>HB</td>
<td>HB</td>
<td>DTPw-HB</td>
<td>DTPw - HB</td>
<td>DTPw - HB</td>
</tr>
<tr>
<td>- Group 1 (5 doses HB)</td>
<td>HB</td>
<td>HB</td>
<td>DTPw-HB</td>
<td>DTPw - HB</td>
<td>DTPw - HB</td>
</tr>
<tr>
<td>- Group 2 (4 doses HB)</td>
<td>HB</td>
<td>DTPw- HB</td>
<td>DTPw - HB</td>
<td>DTPw - HB</td>
<td></td>
</tr>
</tbody>
</table>

997 born from HBV carrier mothers (2004 – 2005)

624 met inclusion criteria

523 mothers’ consented to the study

521 available for serum collection

373 children were excluded

101 children were excluded

2 children were excluded (unable to take the blood)

4 children were excluded (missed vaccine schedule)

Group 1
277 children
4 carriers

Group 2
240 children
11 carriers

Eligible, enrolled population and HBV carriers in the study

### HBV carrier rate by HB1-2 interval in the study

<table>
<thead>
<tr>
<th>Interval (Additional 1 dose HB vaccine)</th>
<th>Total children</th>
<th>No of HB carrier</th>
<th>HB carrier rate (%) and 95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>277</td>
<td>4</td>
<td>1.44, 0.46 - 3.91</td>
</tr>
<tr>
<td>Group 2</td>
<td>240</td>
<td>11</td>
<td>4.58, 2.43 - 8.28</td>
</tr>
<tr>
<td>By HB1-2 interval</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Less than 6 weeks</td>
<td>21</td>
<td>1</td>
<td>4.76, 0.25-25.87</td>
</tr>
<tr>
<td>• 6 – 7 weeks</td>
<td>30</td>
<td>1</td>
<td>3.33, 0.17-19.05</td>
</tr>
<tr>
<td>• 8 – 9 weeks</td>
<td>89</td>
<td>2</td>
<td>2.25, 0.39-8.65</td>
</tr>
<tr>
<td>• 10 weeks above</td>
<td>100</td>
<td>7</td>
<td>7.00, 3.1-14.38</td>
</tr>
</tbody>
</table>

- 4 children, received vaccine of different schedule not belong to group 1 or 2, were excluded from this table

# Adjusted OR and 95% confidence interval of children becoming HBV carriers by multiple logistic regression

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Adjusted OR</th>
<th>95% Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBeAg positive mother</td>
<td>34.03</td>
<td>4.19-276.62</td>
</tr>
<tr>
<td>HB1-2 interval of more than 10 weeks</td>
<td>3.74</td>
<td>0.97-14.39</td>
</tr>
</tbody>
</table>

GMT of anti-HBs by number of doses of HB vaccine, relative to time since complete HB vaccination.
Long-term antibody persistence in children primed and boosted with a DTPw-HBV vaccine at 2, 4, 6, 18, months of age

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<table>
<thead>
<tr>
<th>Age</th>
<th>Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>BCG, HB vac</td>
</tr>
<tr>
<td>1 mo (HBsAg+ve mother)</td>
<td>HB vac</td>
</tr>
<tr>
<td>2 mos</td>
<td>OPV, DTPw-HB</td>
</tr>
<tr>
<td>4 mos</td>
<td>OPV, DTPw-HB</td>
</tr>
<tr>
<td>6 mos</td>
<td>OPV, DTPw-HB</td>
</tr>
<tr>
<td>9-12 mos</td>
<td>MMR1</td>
</tr>
<tr>
<td>18 mos</td>
<td>OPV, DTPw (JE vac 0, 1, 6-12)</td>
</tr>
<tr>
<td>4-6 yrs</td>
<td>OPV, DTPw, MMR2</td>
</tr>
</tbody>
</table>
» Evaluating the HBV seroprevalence
» Genetic variability, genotypes, antigenic subtypes and mutations

Picture available from: www.lpnrights.org
Study populations

- 787 Laotians
- 1,103 Myanmarese
- 1,119 Cambodians
HBsAg positive in Migrant workers in Thailand 2008

Sa-nguanmoo et al. 2010
Suwannakarn et al. 2008
We would like to express our gratitude towards the entire staff of the Center of Excellence in Clinical Virology, Faculty of Medicine, Chulalongkorn University and Hospital, for their tireless effort in collecting the multitude of data required. We also would like to thank the Commission on Higher Education, CU Centenary Academic envelopment Project and Chulalongkorn Hospital for supporting our group.