Introducing Hepatitis B Vaccine into National Immunization Programmes

Steven Wiersma
Training in Reproductive Health Research
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New Vaccine Introduction

• Assess disease burden
• Assess effectiveness of intervention
• Address programmatic issues
• Assure sustainable vaccine supply
Hepatitis B Virus Infection
Global Disease Burden

- 2,000 million have markers of current or past infection
- 350 million have chronic infection
  - 15%-25% will die from chronic liver disease (liver cancer and cirrhosis)
  - at least 1 million deaths per year
Geographic Distribution of Chronic HBV Infection

HBsAg Prevalence
- ≥8% - High
- 2-7% - Intermediate
- <2% - Low
## Effect of Routine Infant Immunization on the Prevalence of Chronic HBV Infection

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>No. Tested</th>
<th>Age (yrs)</th>
<th>Vaccine Coverage</th>
<th>Before Program</th>
<th>After Program</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alaska</td>
<td>1995</td>
<td>268</td>
<td>1-10</td>
<td>96%</td>
<td>16%</td>
<td>0%</td>
</tr>
<tr>
<td>Taiwan</td>
<td>1994</td>
<td>424</td>
<td>7-10</td>
<td>73%</td>
<td>10%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Samoa</td>
<td>1996</td>
<td>435</td>
<td>7-8</td>
<td>87%</td>
<td>7%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Lombok</td>
<td>1994</td>
<td>2519</td>
<td>4</td>
<td>&gt; 90%</td>
<td>6.2%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Saipan</td>
<td>1994</td>
<td>200</td>
<td>3-4</td>
<td>94%</td>
<td>9%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Ponape</td>
<td>1994</td>
<td>364</td>
<td>3-4</td>
<td>82%</td>
<td>NA</td>
<td>1.0%</td>
</tr>
<tr>
<td>Micronesia</td>
<td>1992</td>
<td>544</td>
<td>2</td>
<td>40%</td>
<td>12%</td>
<td>3.0%</td>
</tr>
</tbody>
</table>
Liver Cancer Death Rates among 0-9 Year Old Children, 1974-1993, Taiwan

Start of HepB vaccination

Incidence per 100,000

Year
Hepatitis B Vaccination Targets

45th World Health Assembly, 1992

• By 1995 HepB vaccine introduced in countries with HBsAg prevalence ≥ 8%
• By 1997 in all countries

GAVI, 2000

• By 2002 HepB introduced in 80% of countries w/adequate vaccine delivery
• By 2007 in all countries
Countries where HepB not introduced in national immunization schedule, 2004

* includes partial and among adolescents

Source: WHO/IVB database, 2005
192 WHO Member States. Data as of September 2005
Date of slide: 15 September 2005
Number of countries introduced HepB vaccine and global infant HepB3 coverage, 1989-2004

excluding 5 countries where HepB administered for adolescence

data provided by Member States through WHO-UNICEF Joint Reporting Form and WHO Regional offices and WHO/UNICEF coverage estimates
Programmatic Issues

- Schedule/Administration
- Formulations
- Cold chain
- Injection equipment/safety
- Vaccine wastage
- Revision of EPI forms and materials
- Training
- IEC needs
- Evaluation of programme impact
Hepatitis B Immunization Programs

Objective

Prevent chronic HBV infections

- prevent chronic liver disease
- reduce the reservoir for transmission of new infections
<table>
<thead>
<tr>
<th>Age of Acquisition</th>
<th>% of Chronic Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perinatal</td>
<td>10-30</td>
</tr>
<tr>
<td>Young children</td>
<td>65-85</td>
</tr>
<tr>
<td>Adolescents/Adults</td>
<td>&lt;5</td>
</tr>
</tbody>
</table>
Priority of Perinatal Hepatitis B Prevention

Issues to Consider

1. Relative contribution of perinatal transmission to overall hepatitis B disease burden
   - % of HBsAg-positive pg women who are HBeAg-positive
   - Rate of transmission: HBeAg-positive ~85%
     HBeAg-negative ~10%

2. Feasibility of delivering the first dose at birth
   - Most feasible in hospitals
Priority of Perinatal Hepatitis B Prevention

High proportion of chronic infections acquired perinatally (e.g., SE Asia)

• A birth dose should be given when feasible (e.g., in birthing hospitals)

• Efforts should be made to administer HepB vaccine to infants who deliver at home

Low proportion of chronic infections acquired perinatally (e.g., Africa)

• A birth dose may be considered after evaluating disease burden, cost-effectiveness, and feasibility
**Options for Adding Hepatitis B Vaccine to Existing EPI Schedules**

<table>
<thead>
<tr>
<th>Age</th>
<th>Visit</th>
<th>Other Antigens</th>
<th>HepB Options</th>
<th>I</th>
<th>II*</th>
<th>III*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>0</td>
<td>BCG OPV0</td>
<td></td>
<td>HepB</td>
<td>HepB</td>
<td>HepB</td>
</tr>
<tr>
<td>6 weeks</td>
<td>1</td>
<td>OPV1 DTP1</td>
<td>HepB/Combination</td>
<td>HepB</td>
<td>Combination</td>
<td>Combination</td>
</tr>
<tr>
<td>10 weeks</td>
<td>2</td>
<td>OPV2 DTP2</td>
<td>HepB/Combination</td>
<td></td>
<td>Combination</td>
<td>Combination</td>
</tr>
<tr>
<td>14 weeks</td>
<td>3</td>
<td>OPV3 DTP3</td>
<td>HepB/Combination</td>
<td>HepB</td>
<td>Combination</td>
<td>Combination</td>
</tr>
<tr>
<td>9-12 months</td>
<td>4</td>
<td></td>
<td>Measles</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*schedule to prevent perinatal HBV infection
HepB/Hib Vaccine Administration

- **IM injection:**
  - anterolateral thigh (infants)
  - deltoid (older children)
- Can be safely given at the same time as other vaccines:
  - DTP, OPV, Hib/HepB, BCG, measles, yellow fever
- Injection equipment same as for DTP/Hib:
  - 1.0 or 2.0 mL syringe
  - 25 mm, 22 or 23 gauge needle
Available HepB Products

- Monovalent HepB (1, 2, 6, or 10 dose vials)
  - Recombinant
  - Plasma-derived (discontinued in 2003)
- Monovalent HepB in Uniject
- Hep B and DTP combo-pack (2 and 10 dose vials)
- DTP-Hep B (10 dose vials)
- DTP-Hep B + lyophilized Hib (2 dose vials)
Formulation Choices - Issues to Consider

- Monovalent vs. combination vaccines
- Liquid vs. lyophilized vaccines (Hib)
- Recombinant vs. plasma-derived vaccines (HepB)
- Cost
- Available cold chain storage capacity
- Single vs. multi-dose vials
- Limited supplies of some desirable products
Hepatitis B Vaccine Formulations

- **Monovalent**
  - can be used for any dose in the HepB schedule
  - must be used for vaccination at birth
- **Combination (DTP-HepB, DTP-Hib-HepB, Hib-HepB)**
  - can be used any time all antigens are indicated
  - cannot be used before 6 weeks of age (because of reduced DTP/Hib immunogenicity)
Types of Hepatitis B Vaccine

- **Recombinant**
  - Prepared from HBsAg synthesized by yeast or mammalian cells
- **Plasma-derived**
  - Prepared from HBsAg obtained from plasma of persons with chronic HBV infection
- Both have excellent safety and efficacy
- Until recently, plasma-derived was cheaper
- Plasma-derived discontinued in 2003
<table>
<thead>
<tr>
<th>Issue</th>
<th>Monovalent</th>
<th>Combination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costs</td>
<td>++ Vaccine</td>
<td>+++ Vaccine</td>
</tr>
<tr>
<td></td>
<td>++ Program</td>
<td>+ Program</td>
</tr>
<tr>
<td>Injections</td>
<td>1 additional</td>
<td>No additional</td>
</tr>
<tr>
<td>Flexibility</td>
<td>Increased</td>
<td>Less (no monovalent)</td>
</tr>
<tr>
<td>Vaccine security</td>
<td>Problem</td>
<td>Problem not likely</td>
</tr>
<tr>
<td>Cold chain</td>
<td>Increased</td>
<td>Modest increase</td>
</tr>
<tr>
<td>Training</td>
<td>More demand</td>
<td>Less demand</td>
</tr>
<tr>
<td>Local DTP production</td>
<td>Not a problem</td>
<td>Could displace</td>
</tr>
<tr>
<td>Vaccine</td>
<td>Type*</td>
<td>Doses</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-------</td>
<td>-------</td>
</tr>
<tr>
<td>HepB</td>
<td>R</td>
<td>6-20</td>
</tr>
<tr>
<td>HepB (incl. syringe)</td>
<td>R</td>
<td>1</td>
</tr>
<tr>
<td>DTP+HepB (combo-pack)</td>
<td>R</td>
<td>10</td>
</tr>
<tr>
<td>DTP-HepB</td>
<td>R</td>
<td>10</td>
</tr>
<tr>
<td>DTP-HepB+Hib</td>
<td>R</td>
<td>2</td>
</tr>
</tbody>
</table>

*R = recombinant; PD = plasma-derived
Cold Chain Issues

Introduction of HepB/Hib vaccines will require assessments at all administrative levels:

• to assure adequate cold chain storage capacity
• to assure policies and procedures are in place to prevent freezing vaccine
## HepB Vaccine Storage Volumes (cm³/dose) *

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>1 dose vials</th>
<th>2 dose vials</th>
<th>6 dose vials</th>
<th>10 dose vials</th>
</tr>
</thead>
<tbody>
<tr>
<td>HepB monovalent</td>
<td>9.7</td>
<td>4.8</td>
<td>3.2</td>
<td>3.0</td>
</tr>
<tr>
<td>HepB (Uniject)</td>
<td>24.6</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>HepB + DTP (combo-pack)</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>8.2</td>
</tr>
<tr>
<td>DTP-HepB (combined)</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>3.0</td>
</tr>
<tr>
<td>DTP-HepB+Hib</td>
<td>---</td>
<td>9.7</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>

* vial plus packet containing vial plus other packaging
Single-Dose vs. Multi-Dose Vials

**Single dose vials**
- less wastage
- higher cost/dose
- more storage volume

**Multi dose vials**
- more wastage
- lower cost/dose
- less storage volume