Viral Hepatitis in Reproductive Health

Training Course in Sexual and Reproductive Health Research
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VIRAL HEPATITIS

HISTORICAL PERSPECTIVE

"Infectious"

Viral hepatitis

"Serum"

"NANB"

Enterically transmitted

Parenterally transmitted

other

other
Epidemiology and Prevention of Viral Hepatitis

Worldwide chronic carriers

VHB > 3600000000

VHC > 2000000000
# Viral Hepatitis Overview

## Types of Viral Hepatitis

<table>
<thead>
<tr>
<th>Source of virus</th>
<th>Route of transmission</th>
<th>Chronic infection</th>
<th>Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source of virus</td>
<td>Route of transmission</td>
<td>Chronic infection</td>
<td>Prevention</td>
</tr>
<tr>
<td>A</td>
<td>feces</td>
<td>no</td>
<td>pre-exposure immunization</td>
</tr>
<tr>
<td>B</td>
<td>fecal-oral</td>
<td>yes</td>
<td>pre/post-exposure immunization</td>
</tr>
<tr>
<td>C</td>
<td>percutaneous permucosal</td>
<td>yes</td>
<td>blood donor screening; risk behavior modification</td>
</tr>
<tr>
<td>D</td>
<td>percutaneous permucosal</td>
<td>yes</td>
<td>pre/post-exposure immunization; risk behavior modification</td>
</tr>
<tr>
<td>E</td>
<td>fecal-oral</td>
<td>no</td>
<td>ensure safe drinking water</td>
</tr>
</tbody>
</table>

*CDC*
A, B, Cs of Viral Hepatitis

- **Hepatitis A**
  - fecal-oral spread: hygiene, drug use, men having sex with men, travelers, day care, food
  - **vaccine-preventable**

- **Hepatitis B**
  - sexually transmitted – *100x* more infectious than HIV
  - blood-borne (sex, injection drug use, mother-child, and health care)
  - **vaccine-preventable**

- **Hepatitis C**
  - blood borne (injection drug use primarily)
  - 4-5 times more common than HIV
  - **NOT vaccine-preventable!**
Viral hepatitis vaccines

- Hepatitis A: yes, 2 doses
- Hepatitis B: yes, 3 doses
- Hepatitis E: 2 candidates in the pipeline
- Hepatitis C: no vaccine
Geographic Distribution of Chronic HBV Infection

HBsAg Prevalence

- ≥8% - High
- 2-7% - Intermediate
- <2% - Low

CDC
HBV Modes of Transmission

- Sexual
- Parenteral
- Perinatal
## Concentration of HBV in Various Body Fluids

<table>
<thead>
<tr>
<th>High</th>
<th>Moderate</th>
<th>Low/Not Detectable</th>
</tr>
</thead>
<tbody>
<tr>
<td>blood</td>
<td>semen</td>
<td>urine</td>
</tr>
<tr>
<td>serum</td>
<td>vaginal fluid</td>
<td>feces</td>
</tr>
<tr>
<td>wound exudates</td>
<td>saliva</td>
<td>sweat</td>
</tr>
</tbody>
</table>

(CDC)
Prevalence of HBV

HBV serologic markers in USA

• Chinese/SEA 13%
• Drug users 6%
• Homosexual males 6%
• HIV infected 8%
• Pregnant females 0.4-1.5%
Global Patterns of Chronic HBV Infection

• High (>8%): 45% of global population
  – lifetime risk of infection >60%
  – early childhood infections common

• Intermediate (2%-7%): 43% of global population
  – lifetime risk of infection 20%-60%
  – infections occur in all age groups

• Low (<2%): 12% of global population
  – lifetime risk of infection <20%
  – most infections occur in adult risk groups
Outcome of HBV Infection

- Asymptomatic
  - Resolved Immune
    - Asymptomatic
  - Chronic infection
    - Cirrhosis
    - Liver cancer

- Symptomatic acute hepatitis B
  - Resolved Immune
  - Chronic infection
  - Asymptomatic
  - Cirrhosis
  - Liver cancer
Complications of viral hepatitis

Cirrhosis
slow progression over 30 – 40 years
in HBeAg + 3% per year

HCC (hepatocellular carcinoma)
a major cause of death in Asia and Sub Saharan Africa
risk of 2 % per year
increased risk in VHB if high viremia
Objectives of Hepatitis B Immunization Programs

• prevent VHB chronic infections
• prevent liver cirrhosis
• reduce reservoir for 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>
## 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>
Efficacy against hepatitis B even in hyperendemic regions

Prevalence of HBsAg before and after introduction of vaccination in high risk populations

(Vryheid RE. Vaccine 2000)
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 with adequate vaccine delivery
- By 2007 in all countries
Countries where HepB not introduced in national immunization schedule, 2004

No HepB in schedule (34 countries or 18%)

HepB in schedule* (158 countries or 82%)

* includes partial and among adolescents

Source: WHO/IVB database, 2005  192 WHO Member States. Data as of 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
Global Immunization 1989-2005,
3rd dose of Hepatitis B coverage in infants

global coverage at 55% in 2005

% coverage

Date of slide: 4 September 2006
Priority: prevention of perinatal Hepatitis B

Points to consider

1. Relative contribution of perinatal transmission to global Hep B burden
   - % mothers HBsAg + who are HBeAg +
   - Transmission rate: HBeAg + ~85%
     HBeAg - ~10%

2. Possibility to give 1st dose at birth in hospital
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)
# 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 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>
</tr>
<tr>
<td>6 weeks</td>
<td>1</td>
<td>OPV1 DTP1</td>
<td>HepB/Combination</td>
<td>HepB</td>
<td>Combination</td>
</tr>
<tr>
<td>10 weeks</td>
<td>2</td>
<td>OPV2 DTP2</td>
<td>HepB/Combination</td>
<td>Combination</td>
<td></td>
</tr>
<tr>
<td>14 weeks</td>
<td>3</td>
<td>OPV3 DTP3</td>
<td>HepB/Combination</td>
<td>HepB</td>
<td>Combination</td>
</tr>
<tr>
<td>9-12 months</td>
<td>4</td>
<td></td>
<td>Measles</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
Two Decades of Universal Hepatitis B Vaccination in Taiwan (Gastroenterology 2007;132:1287-1293, Pathol Biol. 2010)

- HBV vaccination provides long term protection up to 20 years, a booster is not indicated
- Seroprevalence of HBsAg declined from 9.8% (prevaccination period) to 0.6% in children in Taipei City after 20 years of mass vaccination
- Maternal transmission is the primary reason for immunoprophylaxis failure
- Appropriate HB immunoglobulin strategy for high risk infants (HBeAg + mothers with high DNA)
- Minimize non-compliance
- In Taiwan coverage rate is 97%! 
STOP hepatitis B transmission from one generation to the other
HEPATITIS A VIRUS
Hepatitis A Virus

- RNA picornavirus
  - Unique world serotype
  - Fecal-oral transmission
  - Acute disease and asymptomatic infection
  - No chronic infection
  - Protective antibodies after infection life immunity
GEOGRAPHIC DISTRIBUTION OF HEPATITIS A VIRUS INFECTION

Anti-HAV Prevalence
- Red: High
- Blue: High/Intermediate
- Green: Intermediate
- Yellow: Low
- Black: Very Low
# HEPATITIS A - Clinical Presentation

<table>
<thead>
<tr>
<th>Jaundice by Age Group</th>
<th>&lt;6 yrs</th>
<th>&lt;10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-14 yrs</td>
<td>40%-50%</td>
<td></td>
</tr>
<tr>
<td>&gt;14 yrs</td>
<td>70%-80%</td>
<td></td>
</tr>
</tbody>
</table>

- Rare complications: fulminant hepatitis, cholestatic hepatitis

- Incubation: average 30 days, 15-50 days

- Chronic sequelae: none
EVENTS IN HEPATITIS A VIRUS INFECTION

- Infection
- Viremia
- ALT
- IgM
- IgG
- HAV in stool
- Clinical illness
- Response

Week:
0 1 2 3 4 5 6 7 8 9 10 11 12 13
HEPATITIS A vaccine

• Highly immunogenic
  • 97%-100% of children and adults have protective antibody levels one month after the first dose
  • 100% are protected after the second dose

• Highly efficacious
  • 94%-100% of children are protected after one dose
Hepatitis E Virus
Geographic Distribution of Hepatitis E

Outbreaks or Confirmed Infection in >25% of Sporadic Non-ABC Hepatitis is due to HEV infection
Hepatitis E – clinical presentation

• Incubation: average 40 days
  15-60 days

• Mortality:
  total: 1%-3%
  during pregnancy: 15%-25%

• Chronic disease: none
Typical Serologic Course of Hepatitis E

- **Weeks after exposure**
  - **Titer**
  - **Symptoms**
  - **ALT**
  - **IgG anti-HEV**
  - **IgM anti-HEV**
  - **Virus in stool**

- **Weeks after exposure**: 0-13
Hepatitis E: epidemiology

- Most epidemics are associated with fecal contamination of drinking water (wells)
- Person to person transmission is minimal
- Prevention by control of drinking water
- Two candidate vaccines currently on trial
Prevention of hepatitis A and E transmission by water