# Viral Hepatitis in Reproductive Health

Training Course in Sexual and Reproductive Health Research
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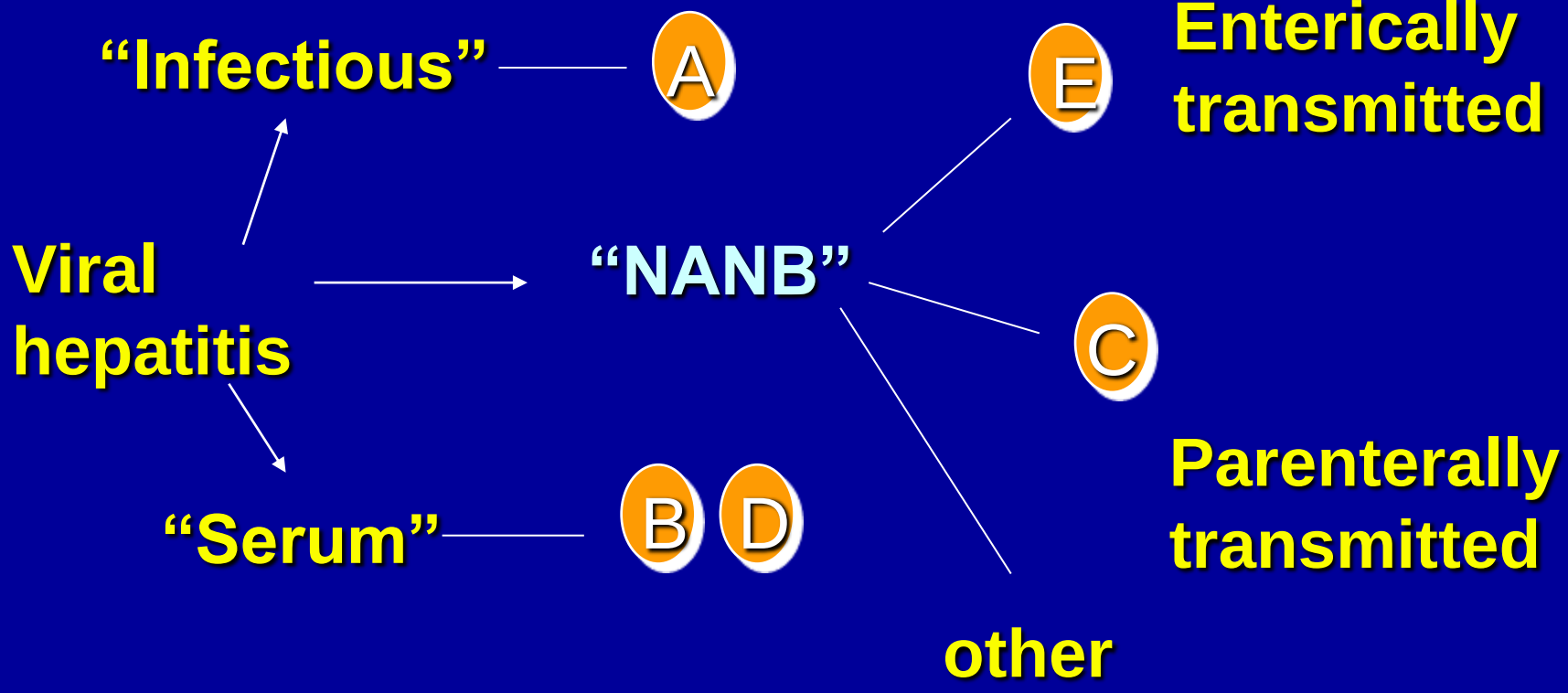
**Reviewed and updated by Dr Willy Urassa, Geneva 15 June 2010**

# VIRAL HEPATITIS

## HISTORICAL PERSPECTIVE



# Epidemiology and Prevention of Viral Hepatitis

Worldwide chronic carriers

VHB > 360000000

VHC > 200000000

# Viral Hepatitis Overview

## Types of Viral Hepatitis

| | A | B | C | D | E |
|---|---|---|---|---|---|
| Source of virus | feces | blood/ blood-derived body fluids | blood/ blood-derived body fluids | blood/ blood-derived body fluids | feces |
| Route of transmission | fecal-oral | percutaneous permucosal | percutaneous permucosal | percutaneous permucosal | fecal-oral |
| Chronic infection | no | yes | yes | yes | no |
| Prevention | pre-exposure immunization | pre/post-exposure immunization | blood donor screening; risk behavior modification | pre/post-exposure immunization; risk behavior modification | ensure safe drinking water |

CDC

# A, B, Cs of Viral Hepatitis

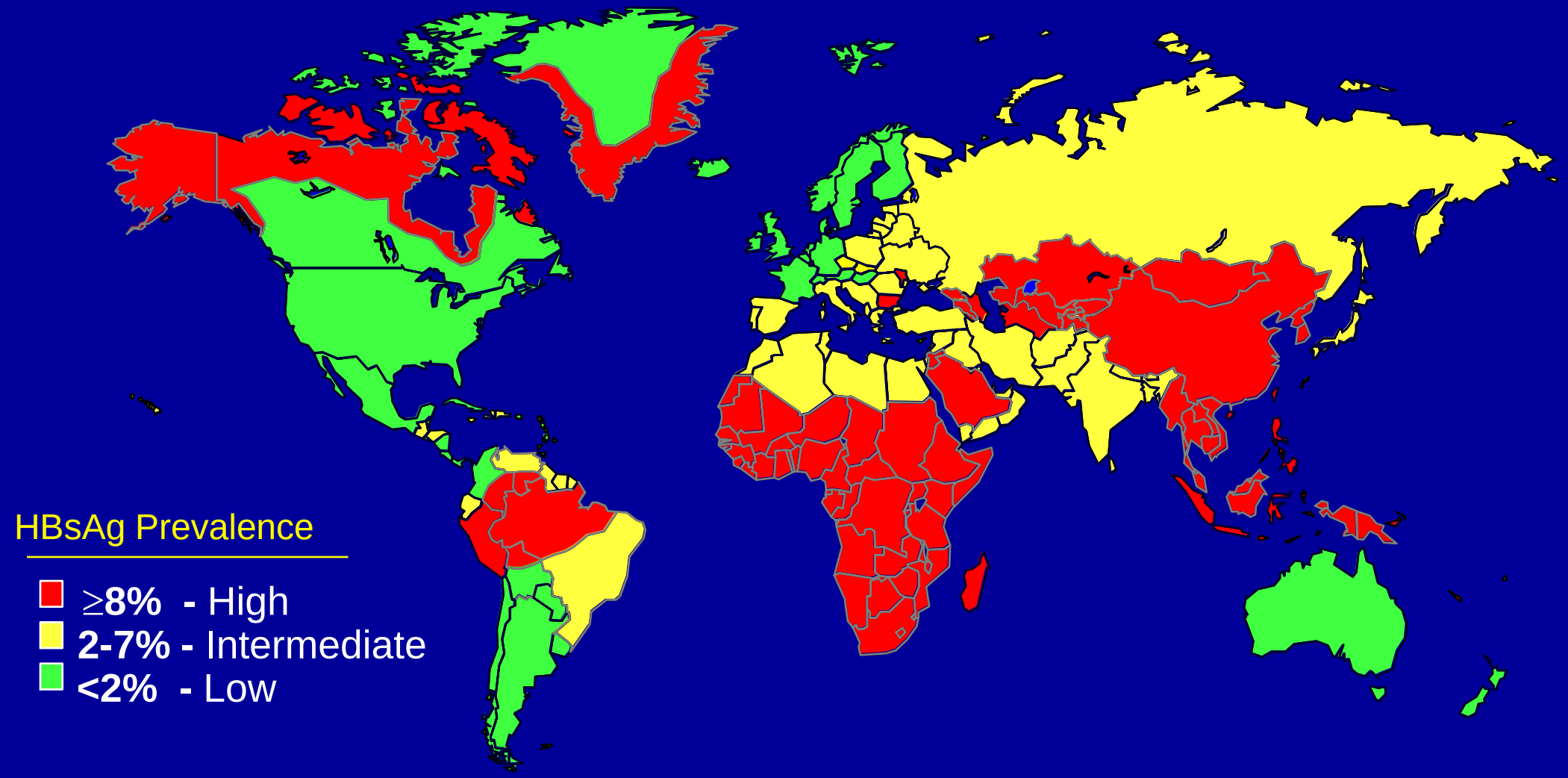
- **Hepatitis A**
  - **fecal-oral spread: hygiene, drug use, men having sex with men, travelers, day care, food**
  - **vaccine-preventable**
- **Hepatitis B**
  - **sexually transmitted – 100x more infectious than HIV**
  - **blood-borne (sex, injection drug use, mother-child, and health care)**
  - **vaccine-preventable**
- **Hepatitis C**
  - **blood borne (injection drug use primarily)**
  - 4-5 times more common than HIV
  - **NOT vaccine-preventable!**

CDC

# 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

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# HBV Modes of Transmission

- Sexual
- Parenteral
- Perinatal

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# Concentration of HBV in Various Body Fluids

| High | Moderate | Low/Not Detectable |
|---|---|---|
| blood | semen | urine |
| serum | vaginal fluid | feces |
| wound exudates | saliva | sweat |
| | | tears |
| | | breast milk |

CDC

# Prevalence of HBV

HBV serologic markers in USA

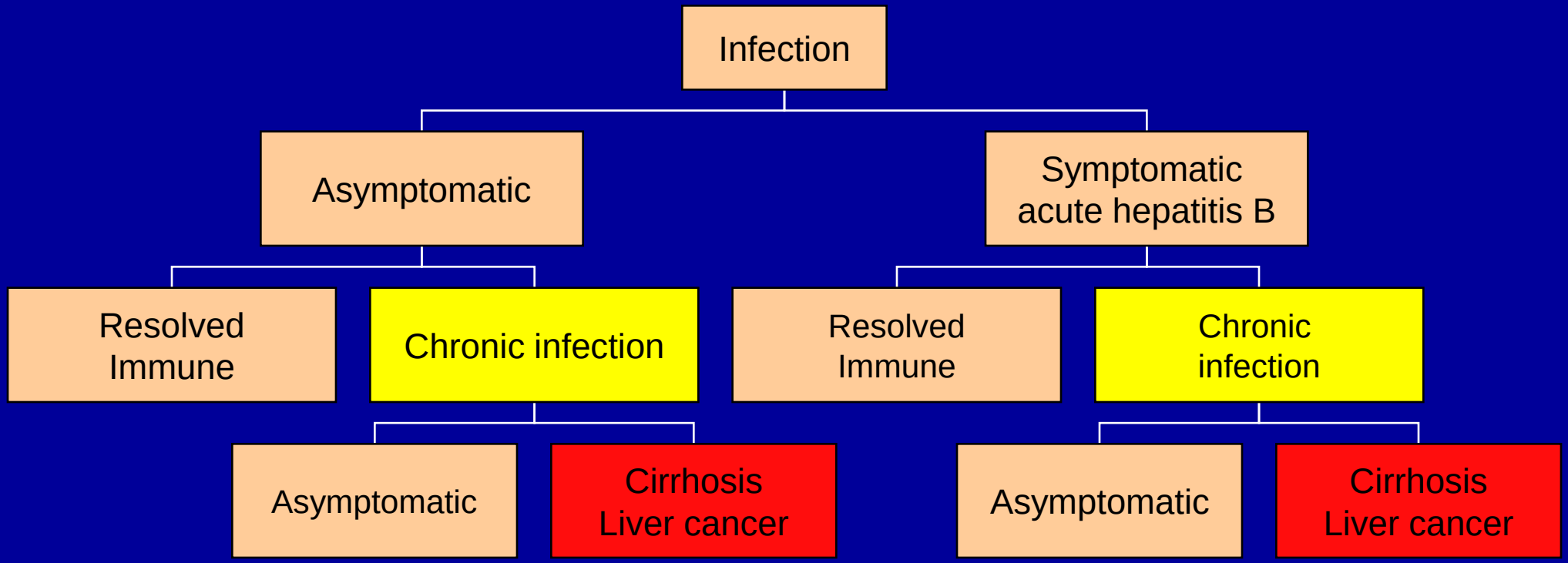
- Chinese/SEA 13%
- Drug users 6%
- Homosexual males 6%
- HIV infected 8%
- Pregnant females 0.4-1.5%

# 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

CDC

# Outcome of HBV Infection




CDC

# 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

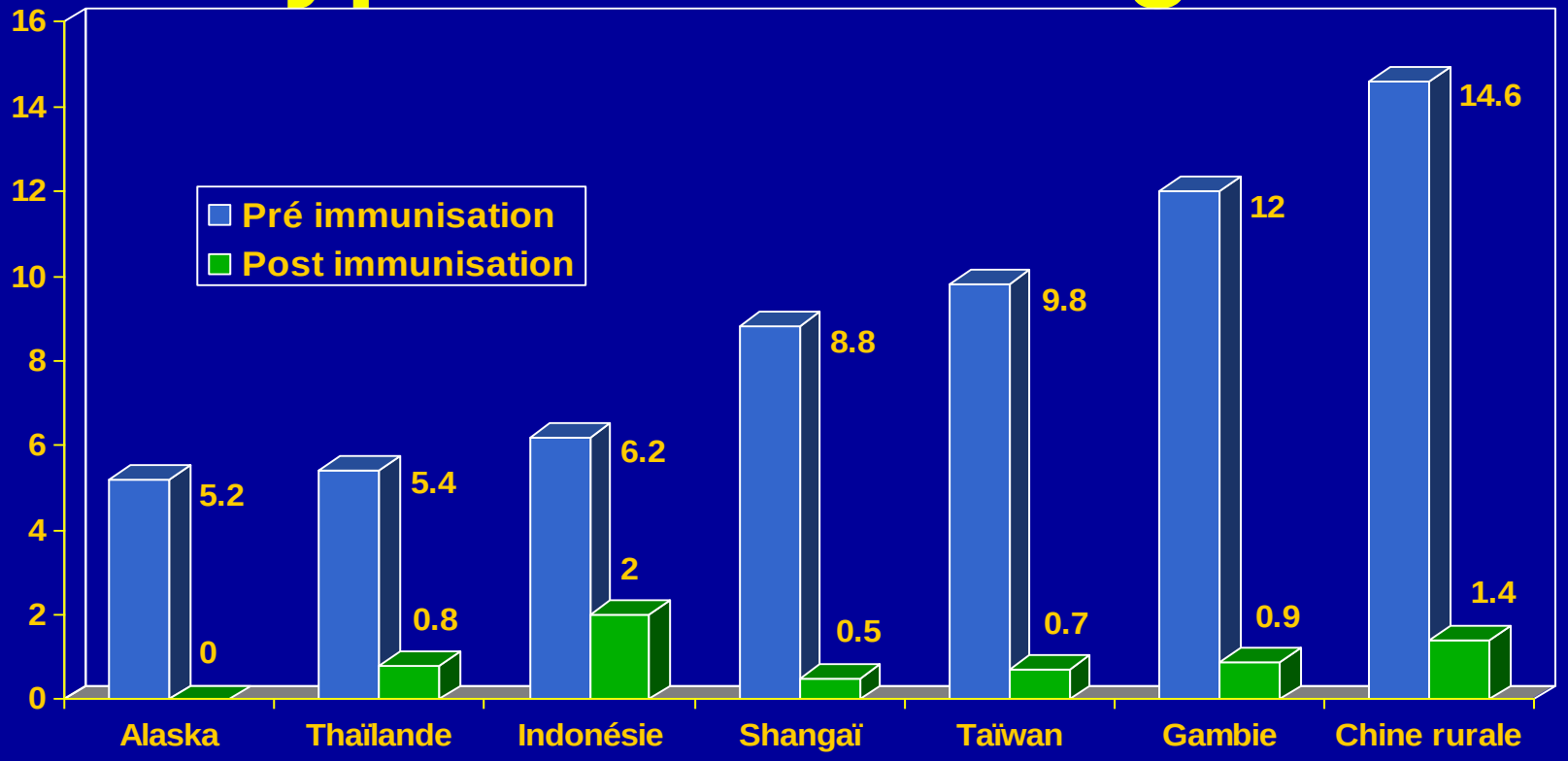
# Age of Acquisition of Chronic HBV Infections in High Endemic Countries

| Age of Acquisition | % of Chronic Infections |
|---|---|
| Perinatal | 10-30 |
| Young children | 65-85 |
| Adolescents/Adults | <5 |

# Effect of Routine Infant Immunization on the Prevalence of Chronic HBV Infection

| Study | Year | No. Tested | Age (yrs) | Vaccine Coverage | Chronic HBV infection: Before Program | Chronic HBV infection: After Program |
|---|---|---|---|---|---|---|
| Alaska | 1995 | 268 | 1-10 | 96% | 16% | 0% |
| Taiwan | 1994 | 424 | 7-10 | 73% | 10% | 1.1% |
| Samoa | 1996 | 435 | 7-8 | 87% | 7% | 0.5% |
| Lombok | 1994 | 2519 | 4 | > 90% | 6.2% | 1.9% |
| Saipan | 1994 | 200 | 3-4 | 94% | 9% | 0.5% |
| Ponape | 1994 | 364 | 3-4 | 82% | NA | 1.0% |
| Micronesia | 1992 | 544 | 2 | 40% | 12% | 3.0% |

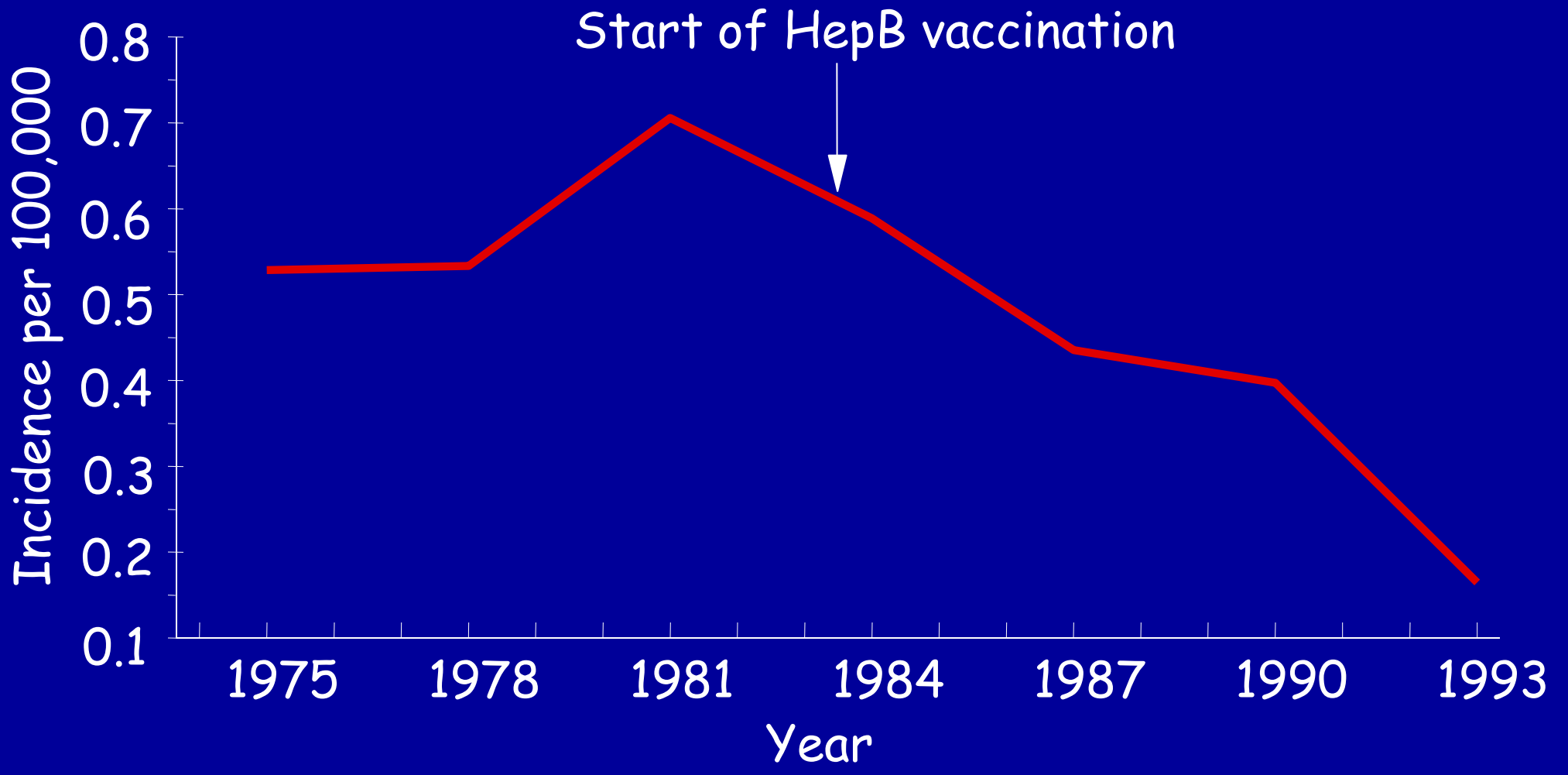
# Efficacy against hepatitis B even in hyperendemic regions




**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



# Hepatitis B Vaccination Targets

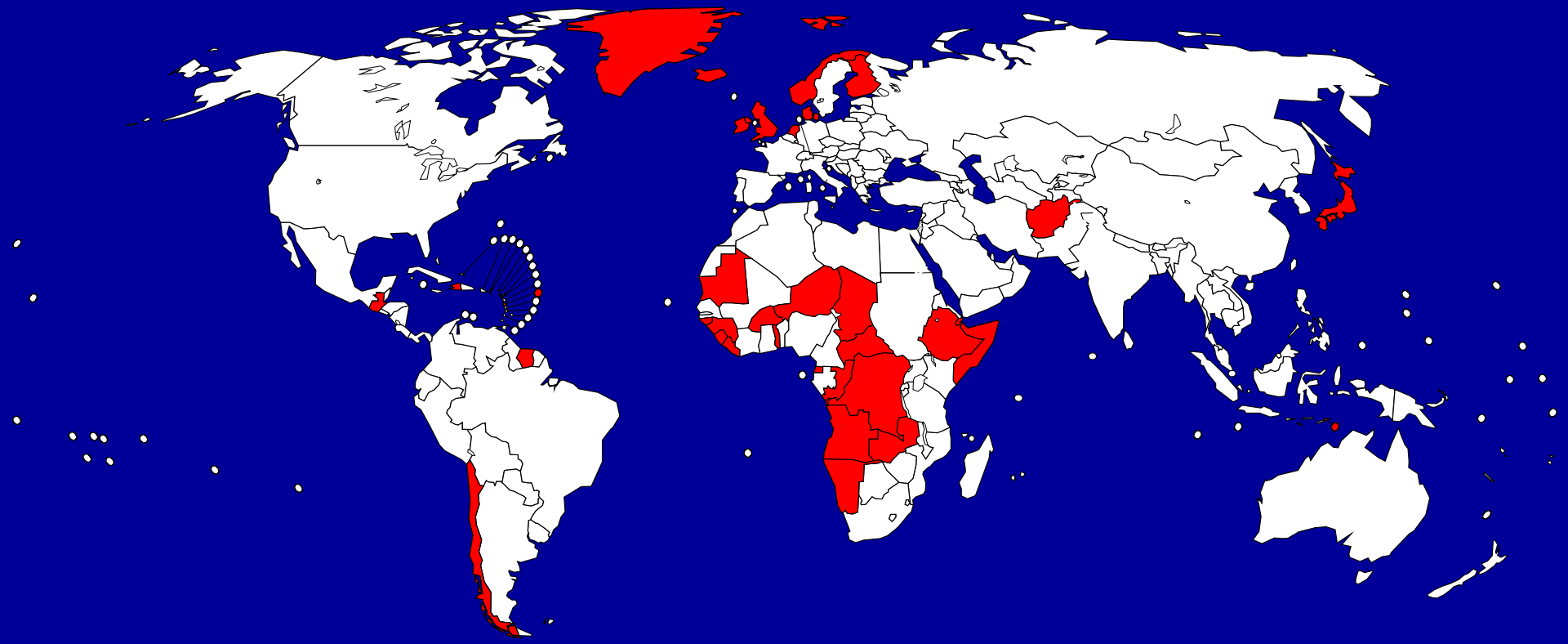
## 45th World Health Assembly, 1992

- 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



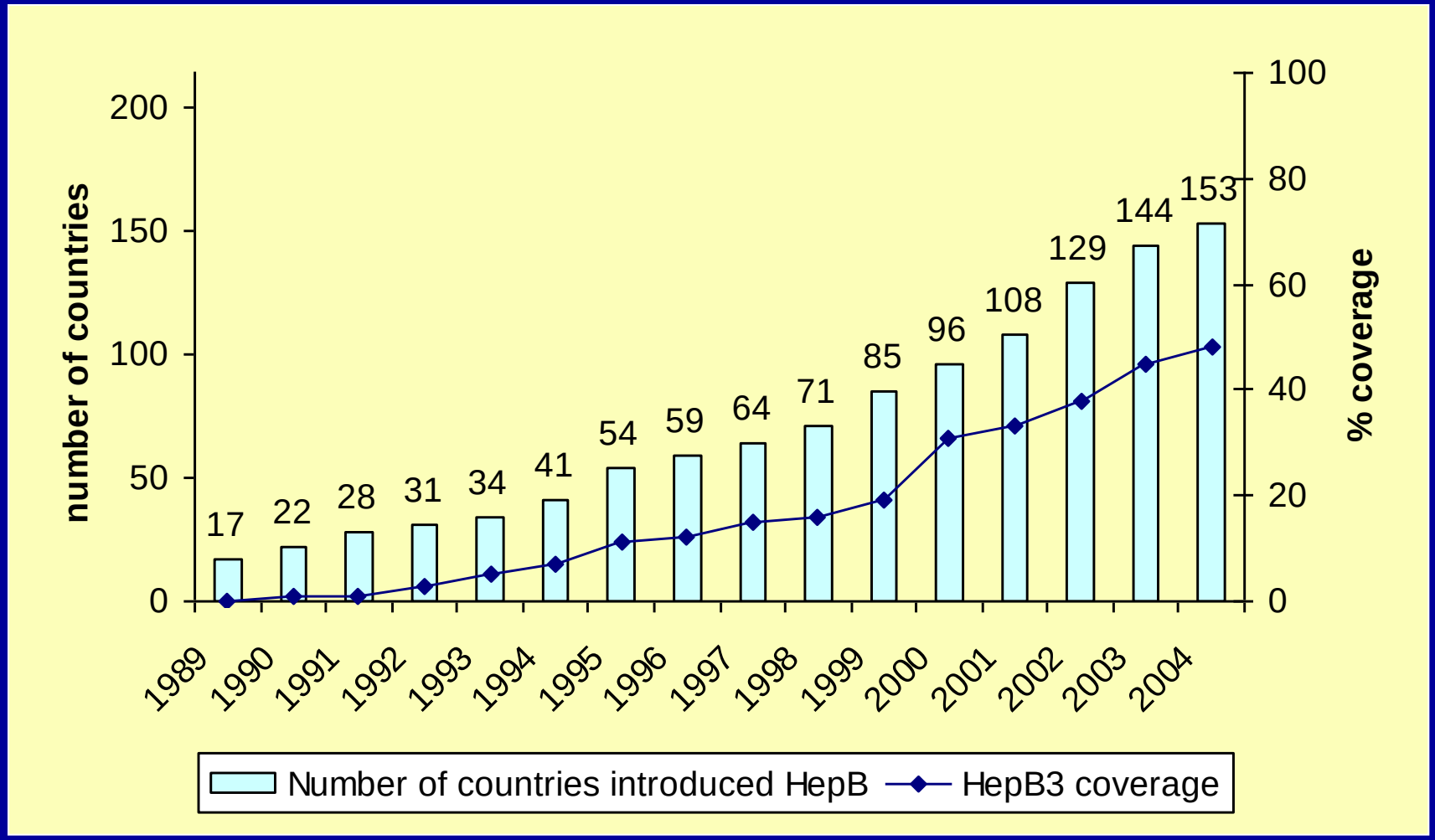
No HepB in schedule *(34 countries or 18%)*

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



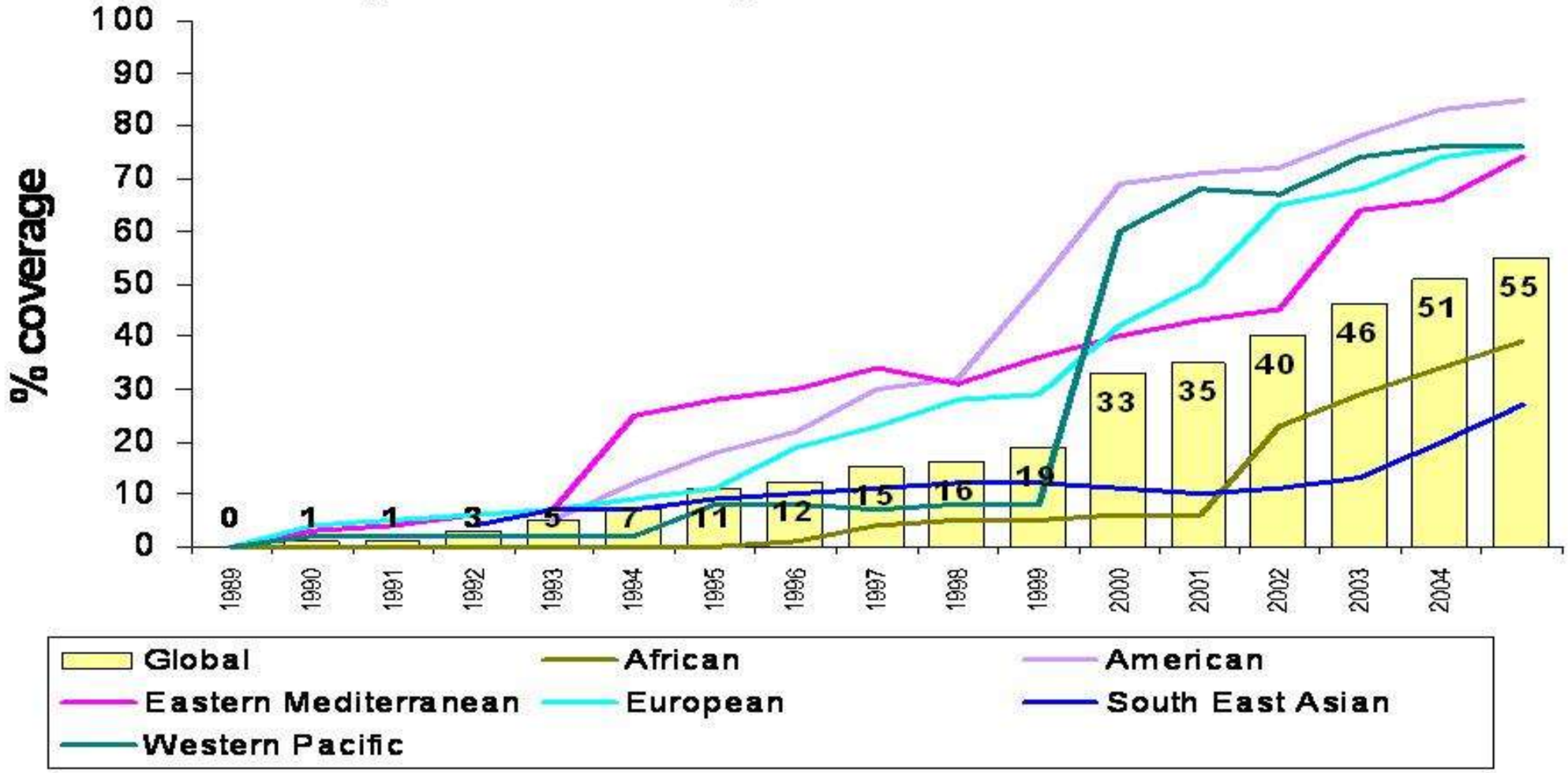

excluding 5 countries where HepB administered for adolescence

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




Source: WHO/UNICEF coverage estimates 1980-2005, August 2006

Date of slide: 4 September 2006

WHO

# 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

| | | | | | HepB Options | | |
|---|---|---|---|---|---|---|---|
| Age | Visit | Other Antigens | | | I | II* | III* |
| Birth | 0 | BCG | OPV0 | | | HepB | HepB |
| 6 weeks | 1 | | OPV1 | DTP1 | HepB/Combination | HepB | Combination |
| 10 weeks | 2 | | OPV2 | DTP2 | HepB/Combination | | Combination |
| 14 weeks | 3 | | OPV3 | DTP3 | HepB/Combination | HepB | Combination |
| 9-12 months | 4 | | | Measles | | | |

*schedule to prevent perinatal HBV infection

# HepB/Hib Vaccine Administration

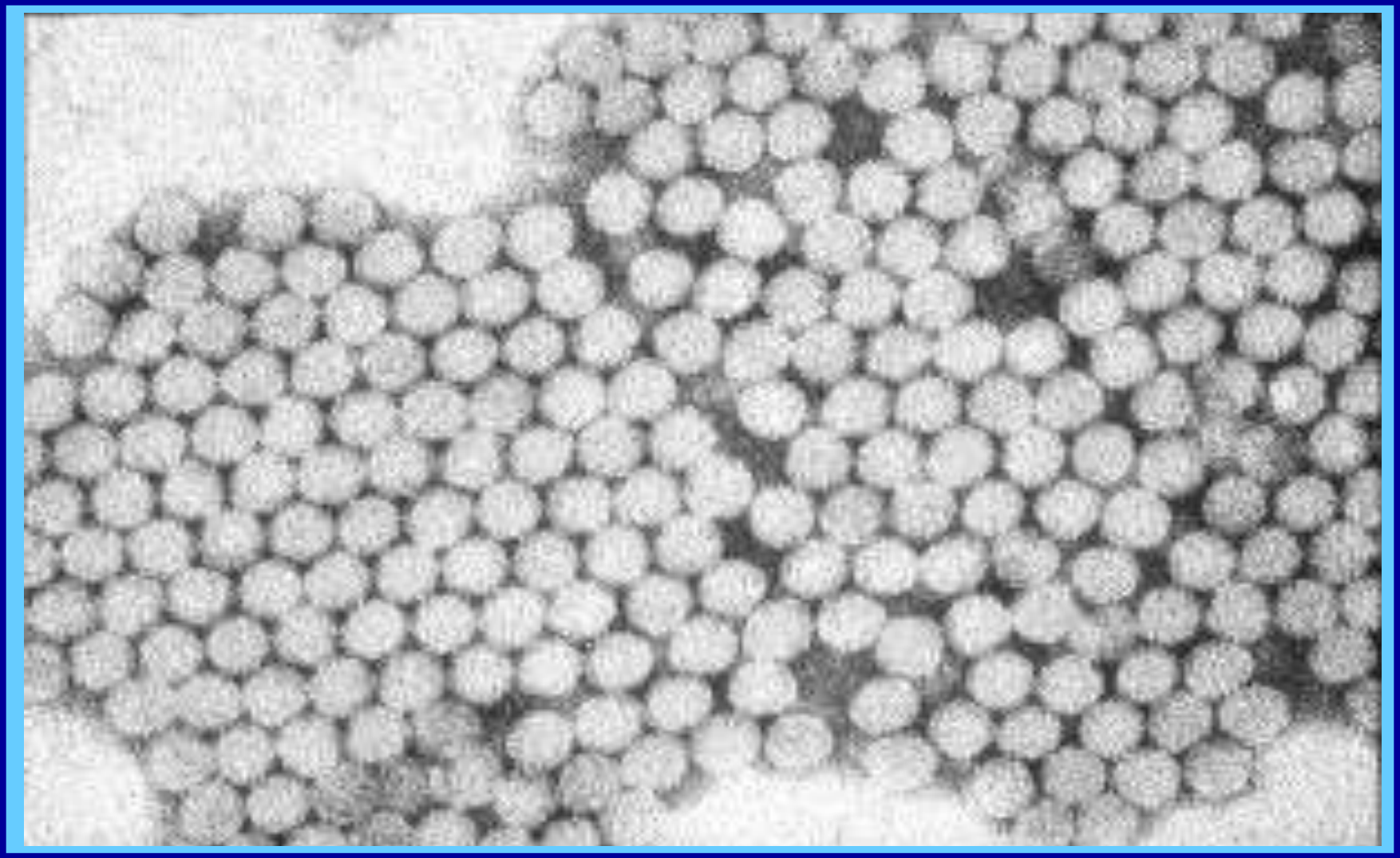
- IM injection:
  - anterolateral thigh (infants)
  - deltoid (older children)
- Can be safely given at the same time as other vaccines:
  - DTP, OPV, Hib/HepB, BCG, measles, yellow fever
- Injection equipment same as for DTP/Hib:
  - 1.0 or 2.0 mL syringe
  - 25 mm, 22 or 23 gauge needle

# 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 20years 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

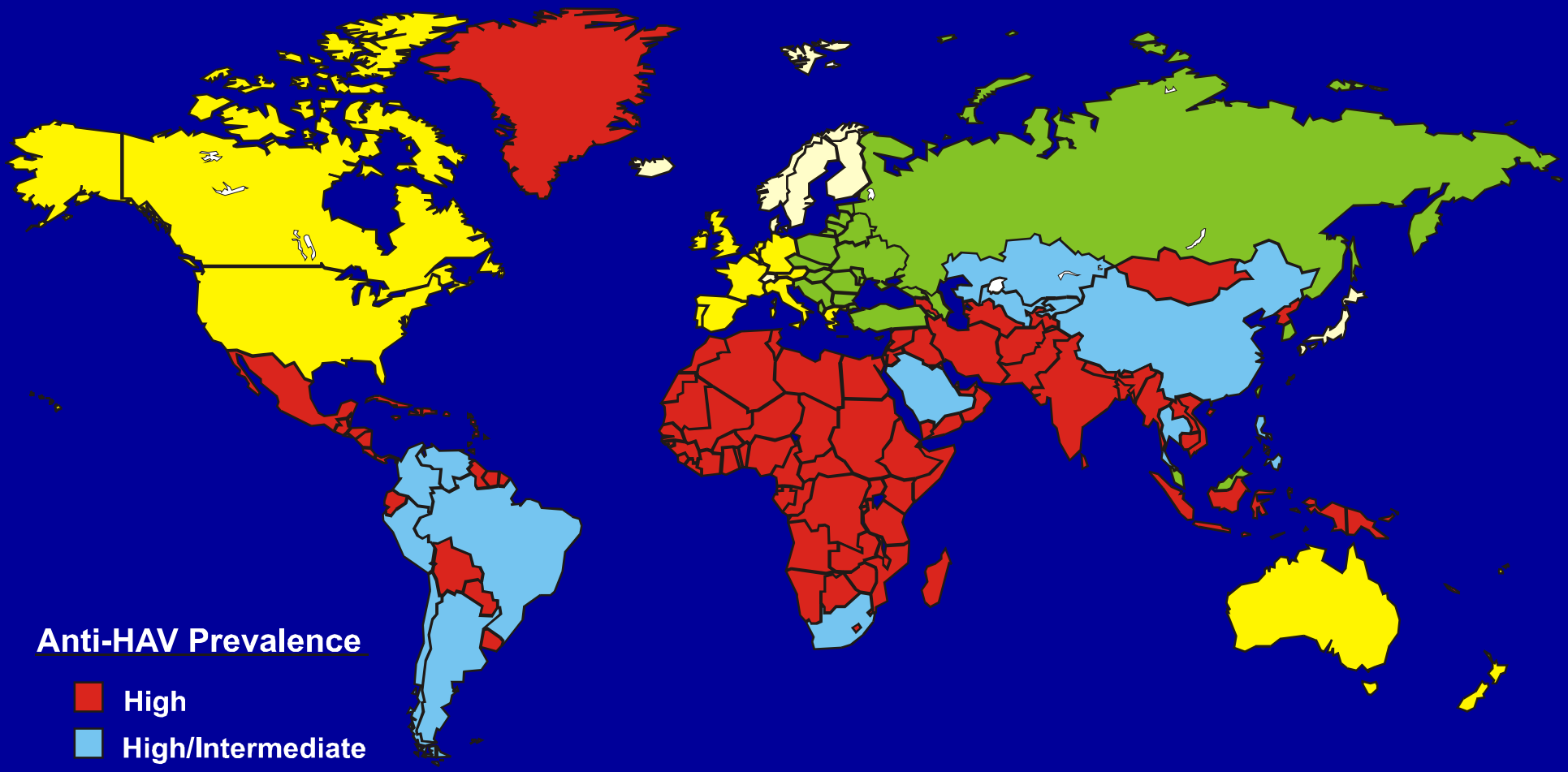
# HEPATITIS A VIRUS



# 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

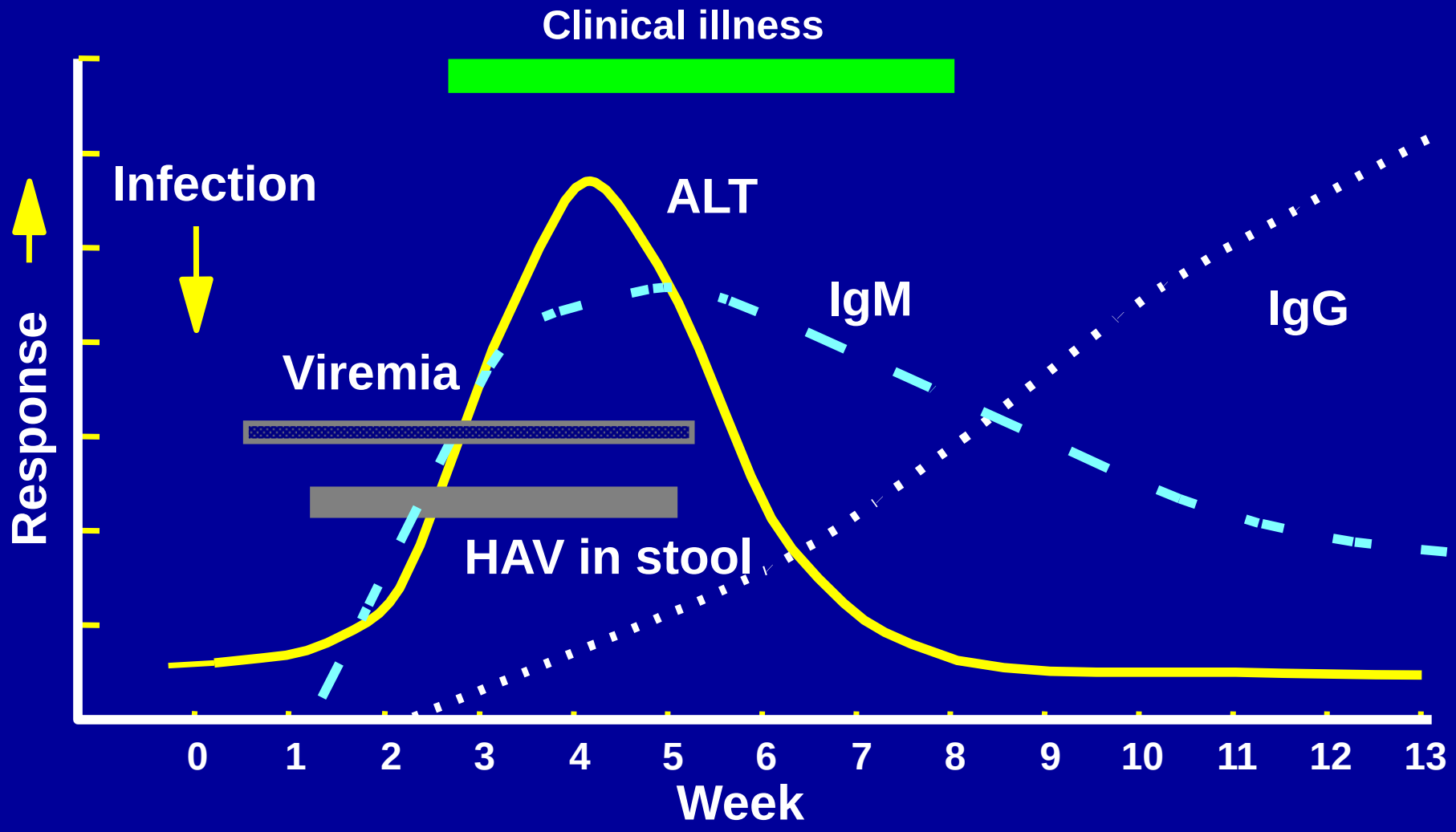
# GEOGRAPHIC DISTRIBUTION OF HEPATITIS A VIRUS INFECTION



# HEPATITIS A - clinical presentation

- Jaundice by age group
  - <6 yrs: <10%
  - 6-14 yrs: 40%-50%
  - >14 yrs: 70%-80%
- Rare complications : fulminant hepatitis, cholestatic hepatitis
- Incubation: average 30 days, 15-50 days
- Chronic sequelae: none

# EVENTS IN HEPATITIS A VIRUS INFECTION

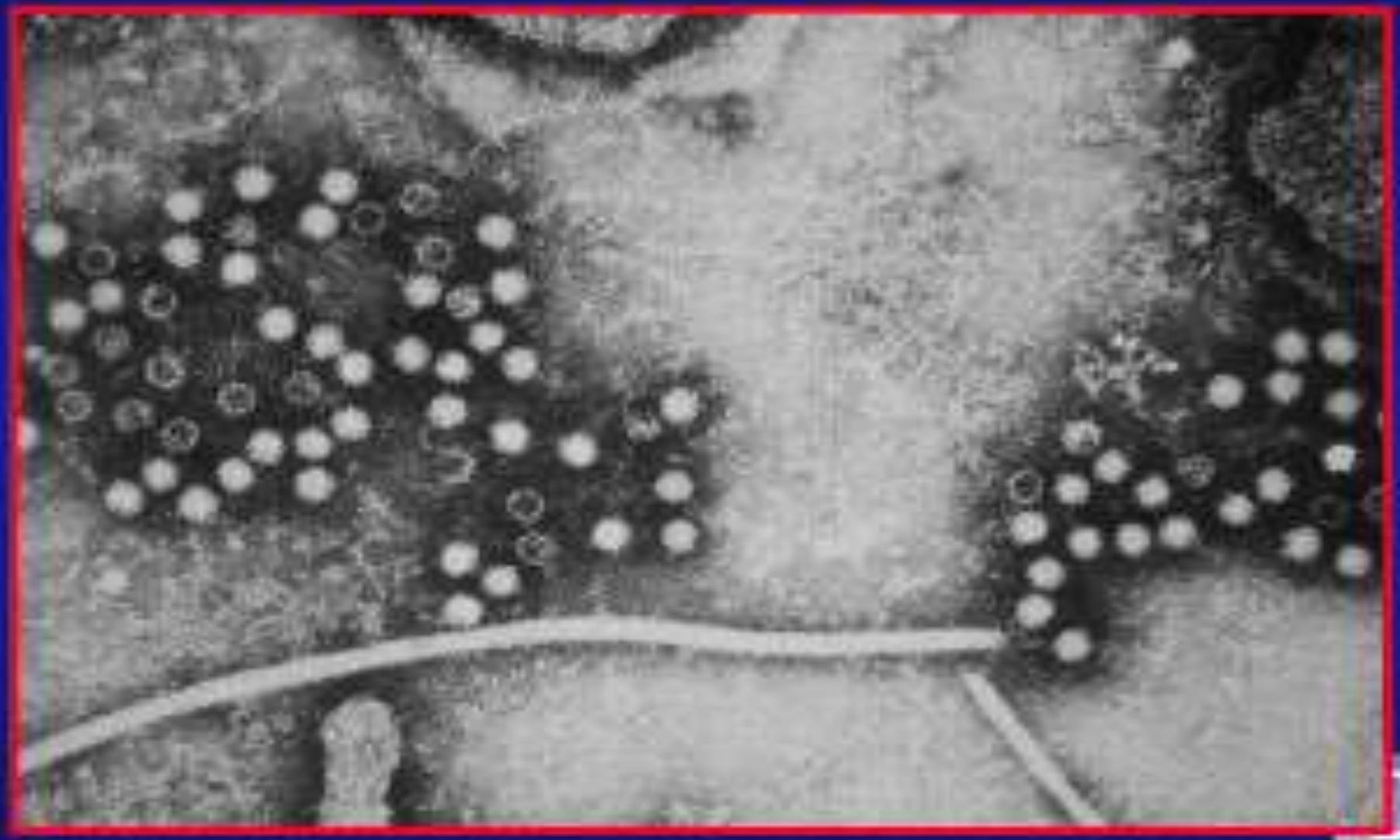


# HEPATITIS A vaccine

- 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

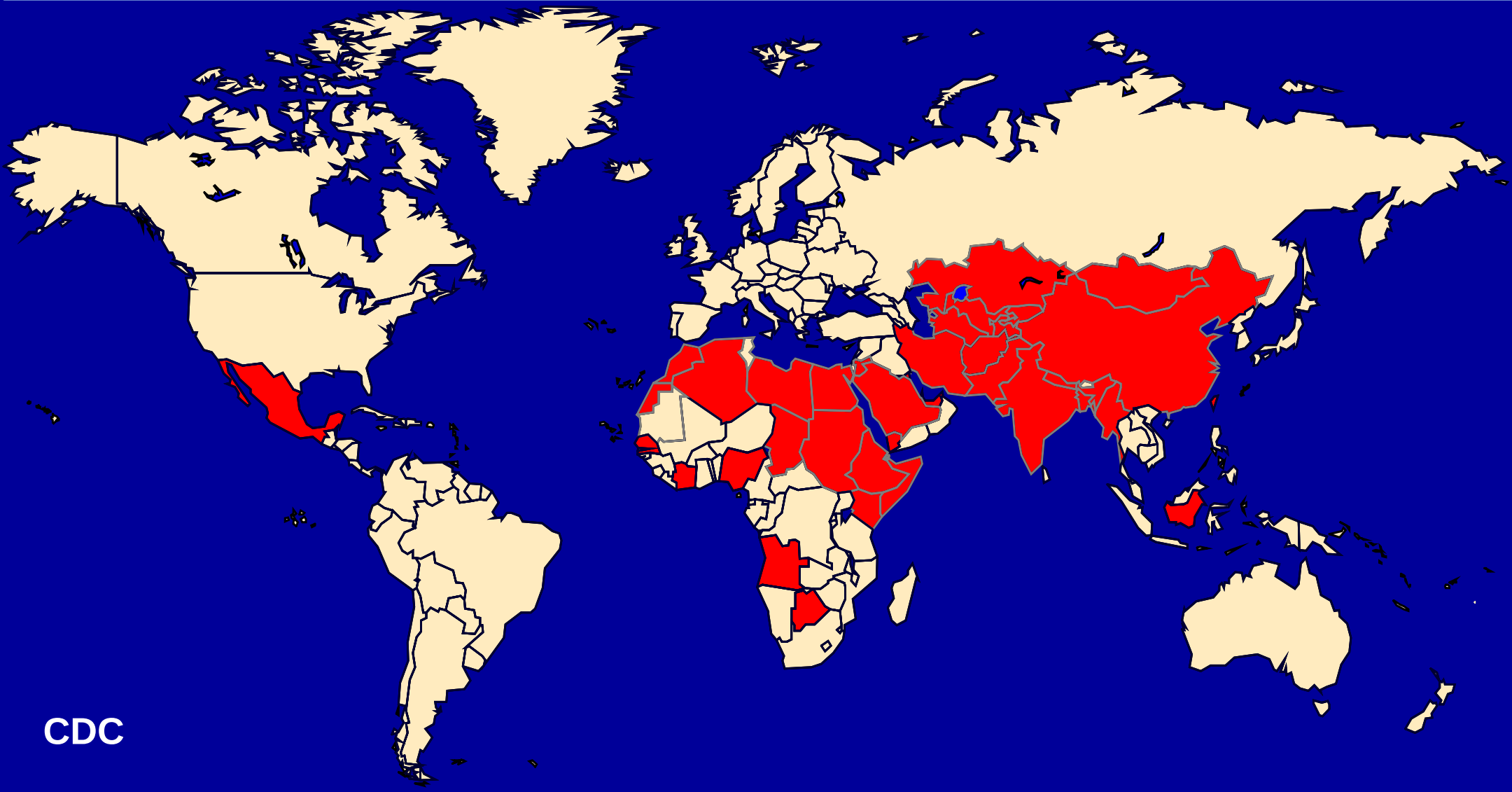
- Highly efficacious
  - 94%-100% of children are protected after one dose

# Hepatitis E Virus



# Geographic Distribution of Hepatitis E

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

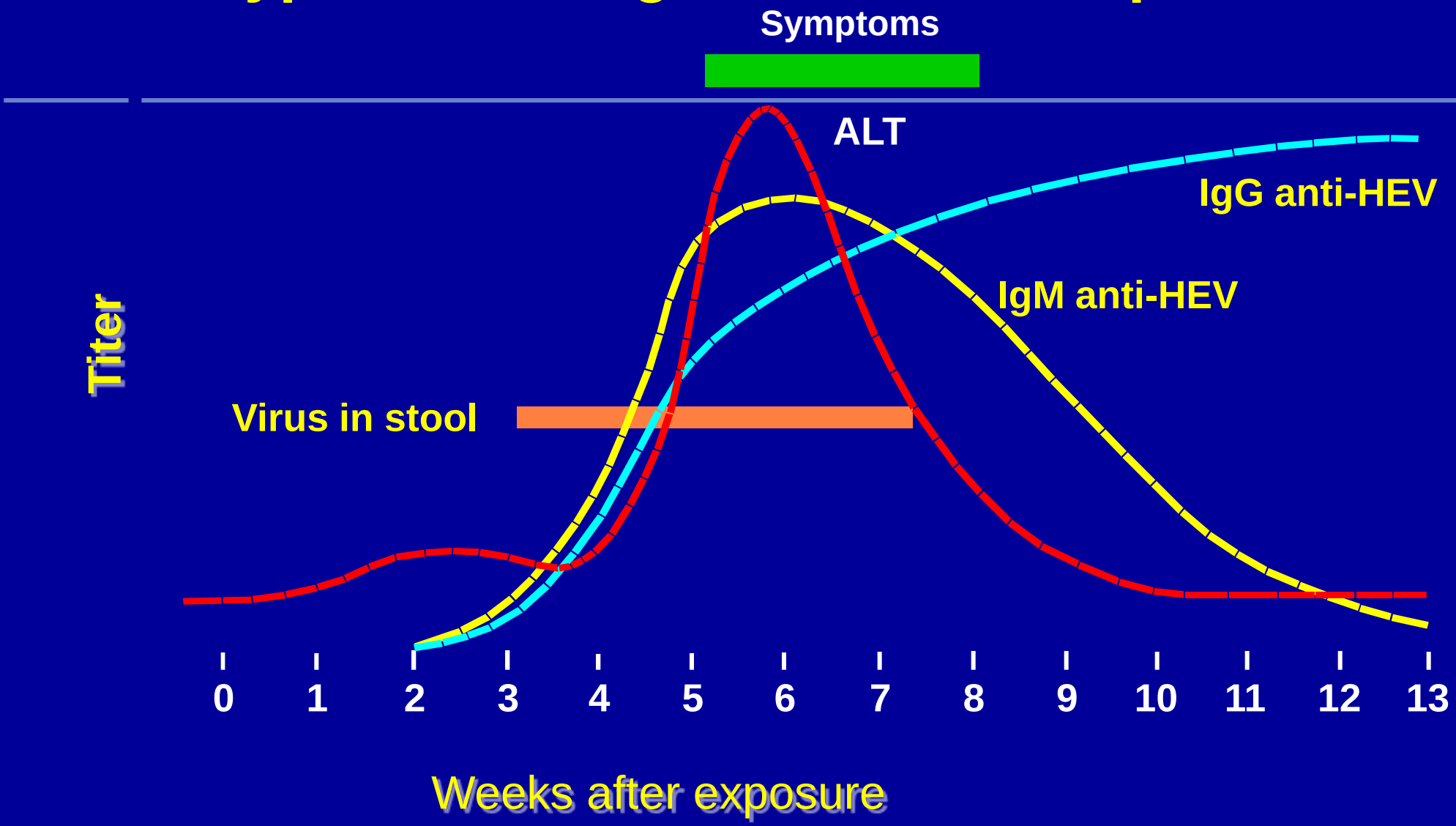


CDC

# 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



# 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