Viral Hepatitis in Reproductive Health

Training Course in Sexual and Reproductive Health Research
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Viral Hepatitis Vaccines

GFMER

23 February 2009

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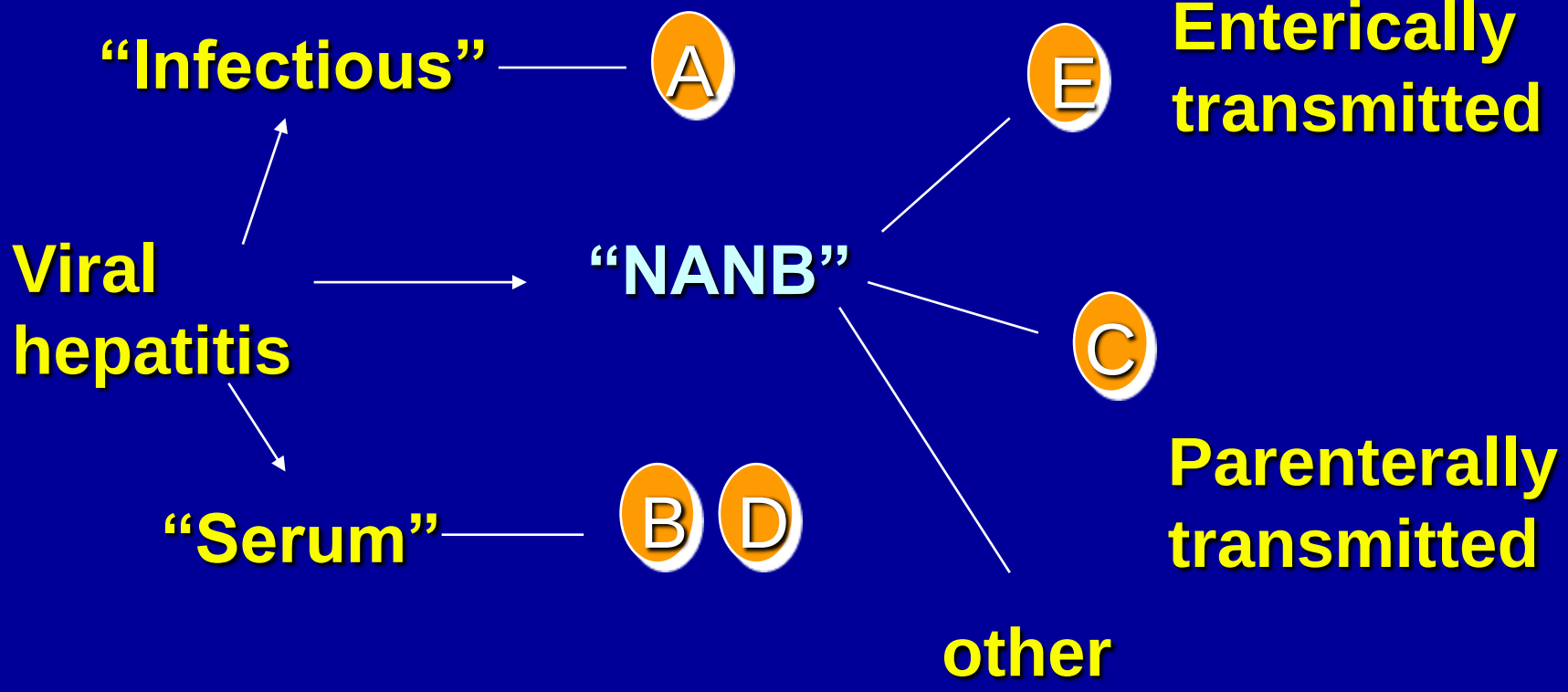
VIRAL HEPATITIS

HISTORICAL PERSPECTIVE



Epidemiology and Prevention of Viral Hepatitis

Worldwide chronic carriers

VHB > 350’000’000

VHC > 200’000’000

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

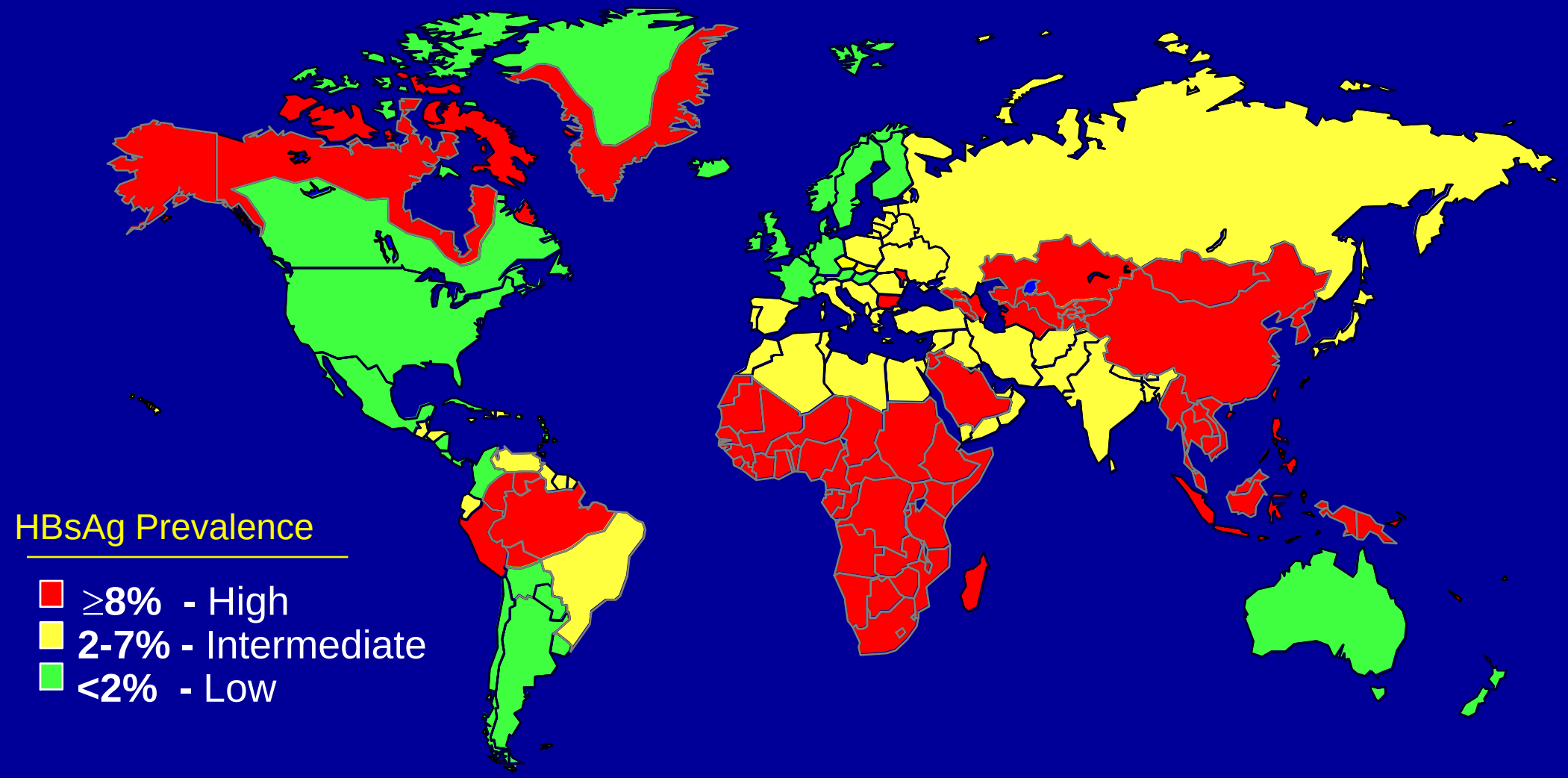
- **A**
  - **fecal-oral spread: hygiene, drug use, men having sex with men, travelers, day care, food**
  - **vaccine-preventable**
- **B**
  - **sexually transmitted – 100x more infectious than HIV**
  - **blood-borne (sex, injection drug use, mother-child, and health care)**
  - **vaccine-preventable**
- **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** **tested in 2006**
- **Hepatitis C** **no vaccine**

Geographic Distribution of Chronic HBV Infection



CDC

HBV Modes of Transmission

- Sexual
- Parenteral
- Perinatal

CDC

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

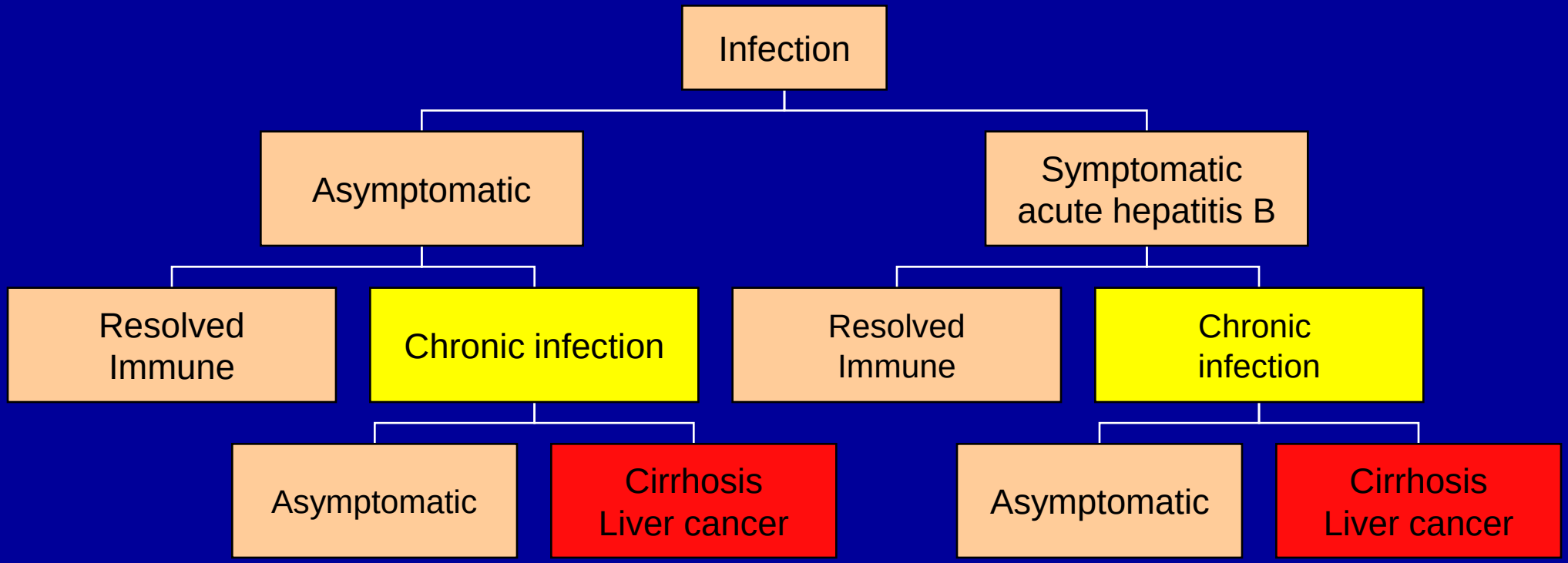
- Chinese/SEA 13%
- drug users 6%
- homosexual males 6%
- HIV infected 8%
- pregnant females 0.4 – 1.5 %

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

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

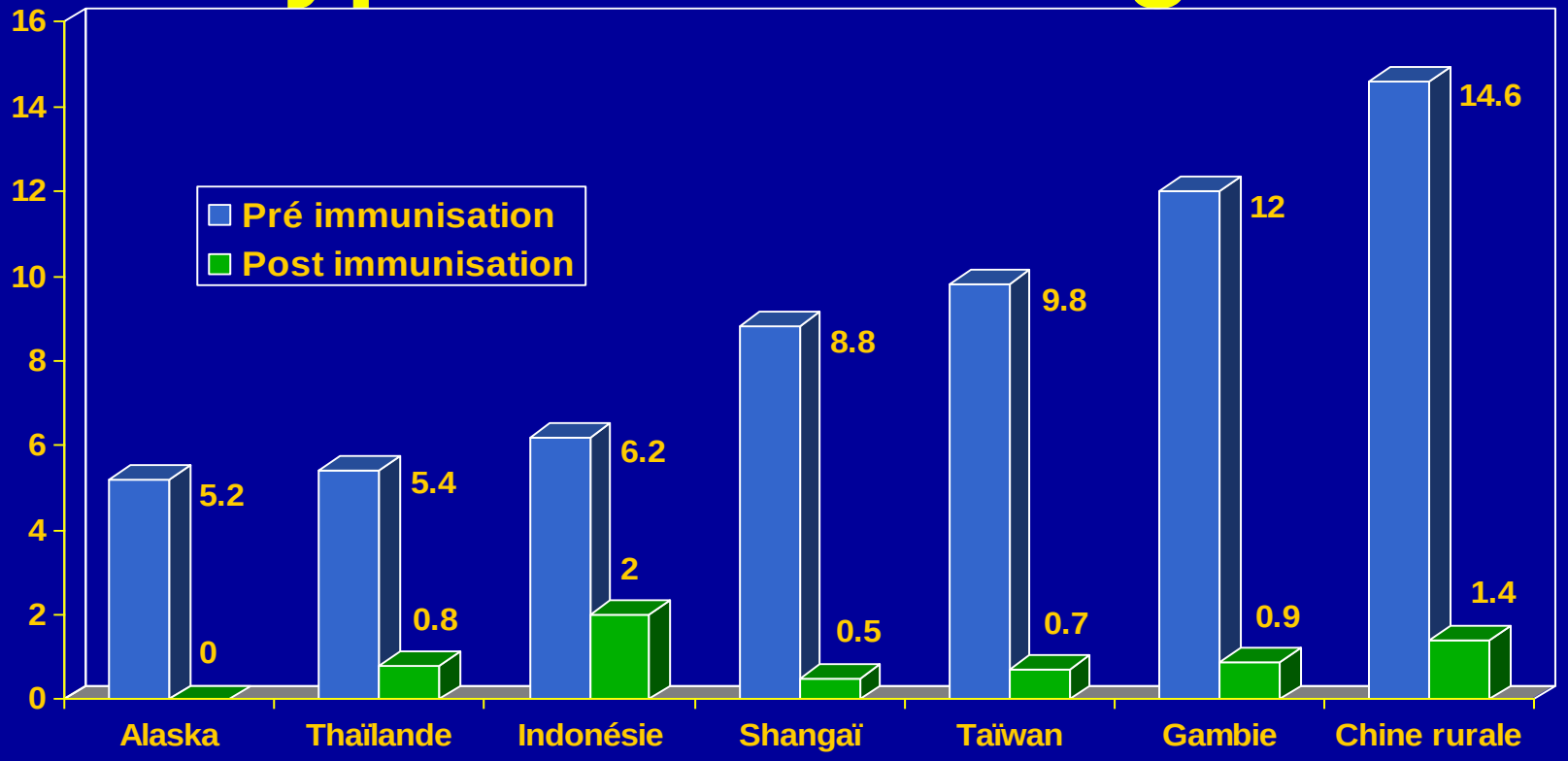
Age of Acquisition of Chronic HBV Infections in High Endemic Countries

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%

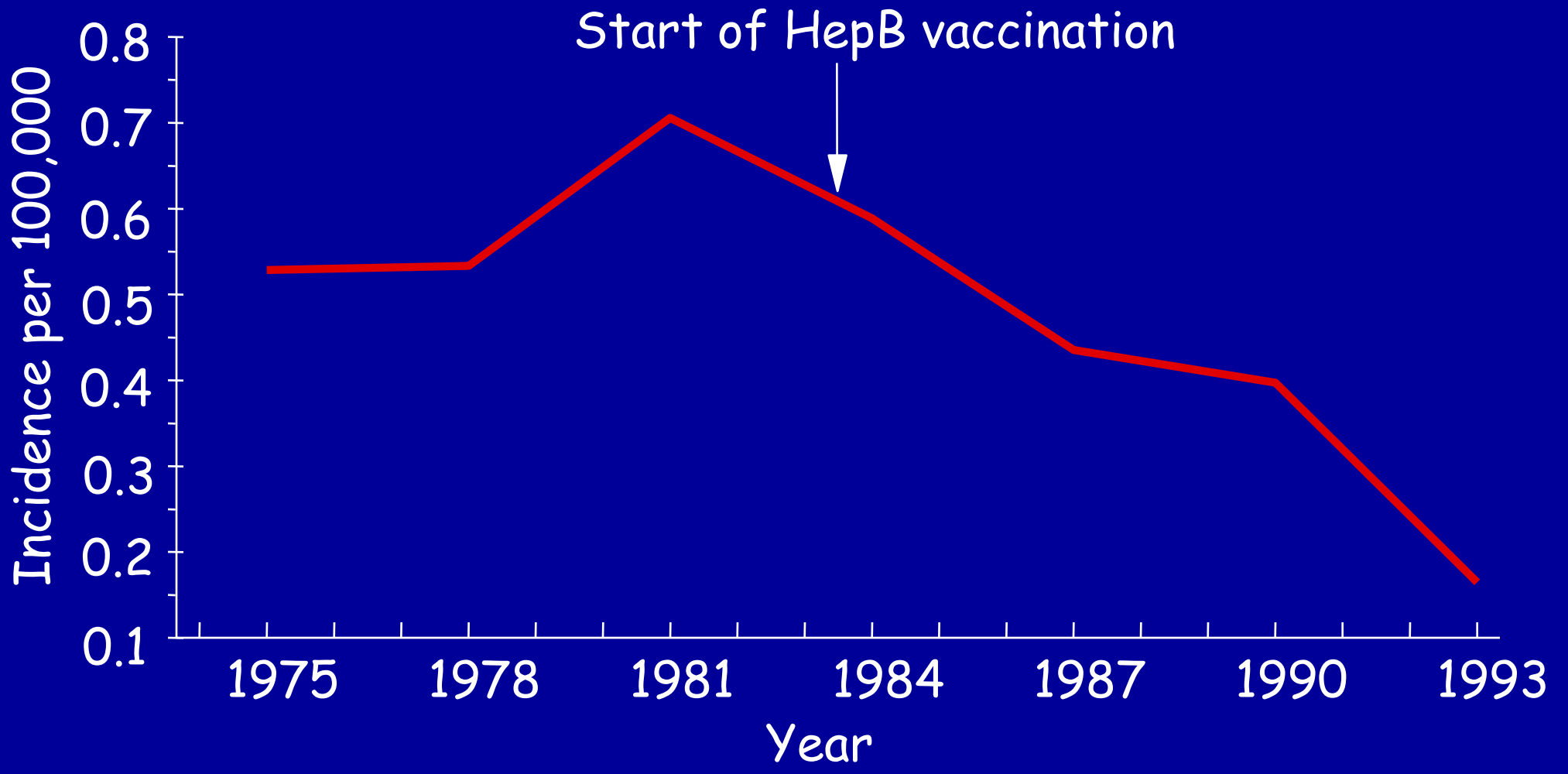
Efficacy against hepatitis B even in hyperendemic regions



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

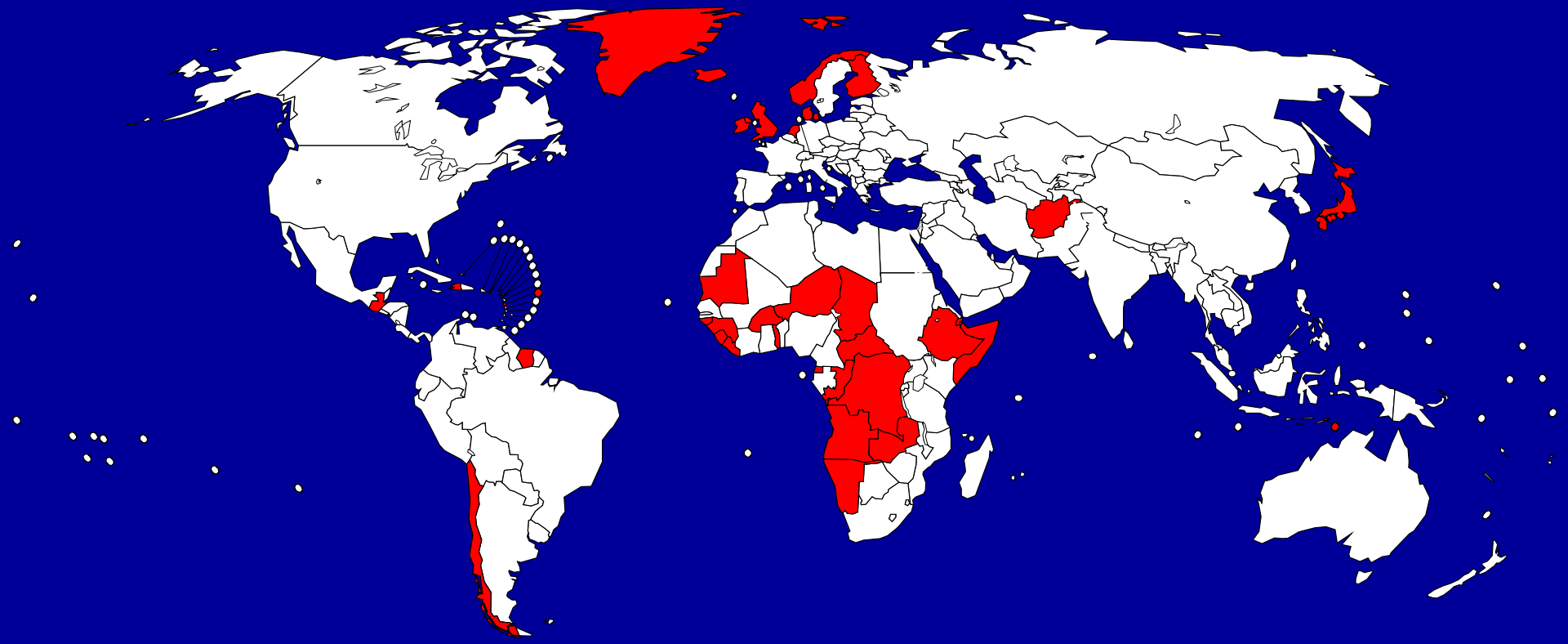
45th World Health Assembly, 1992

- 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



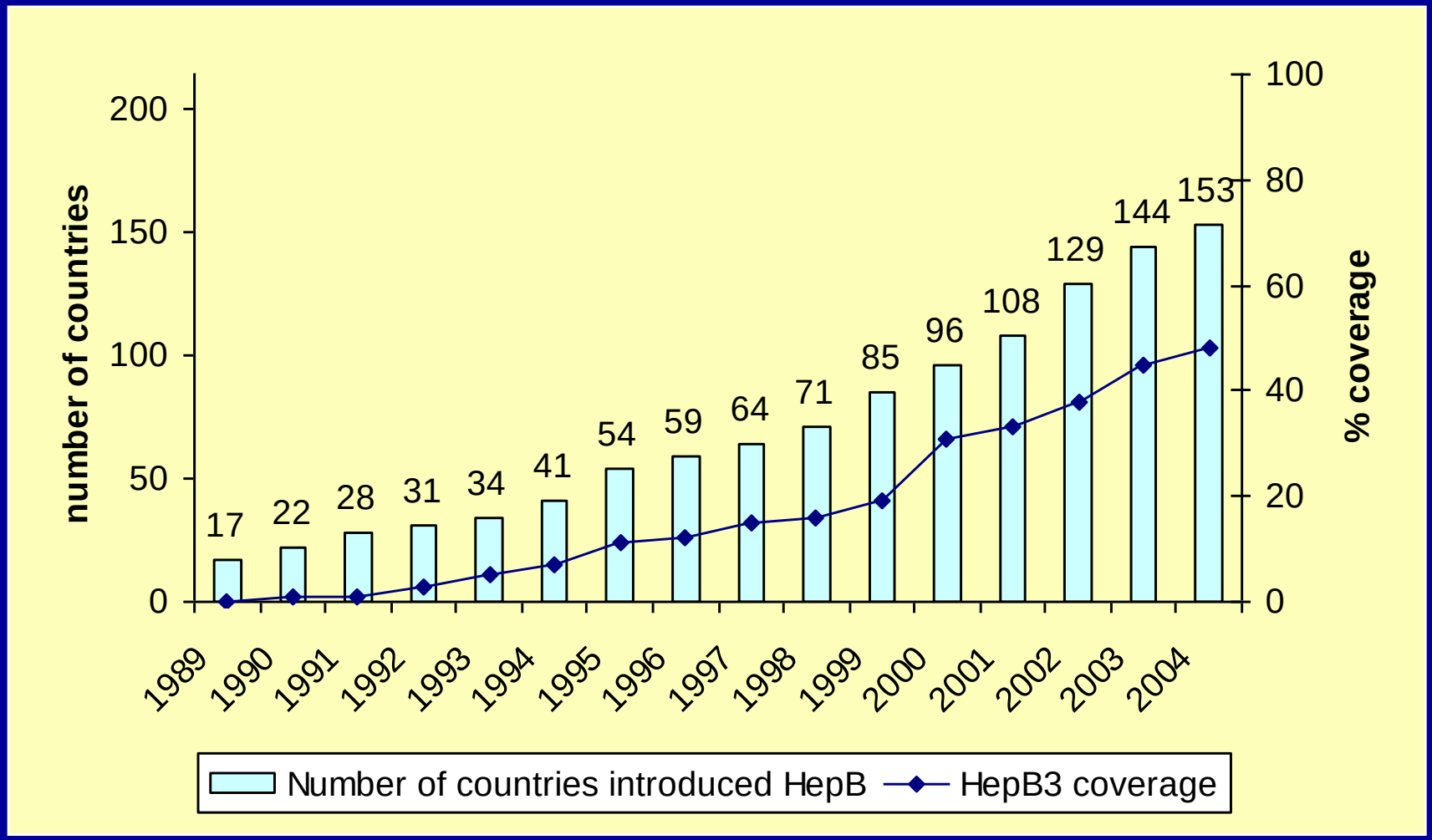
No HepB in schedule *(34 countries or 18%)*

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



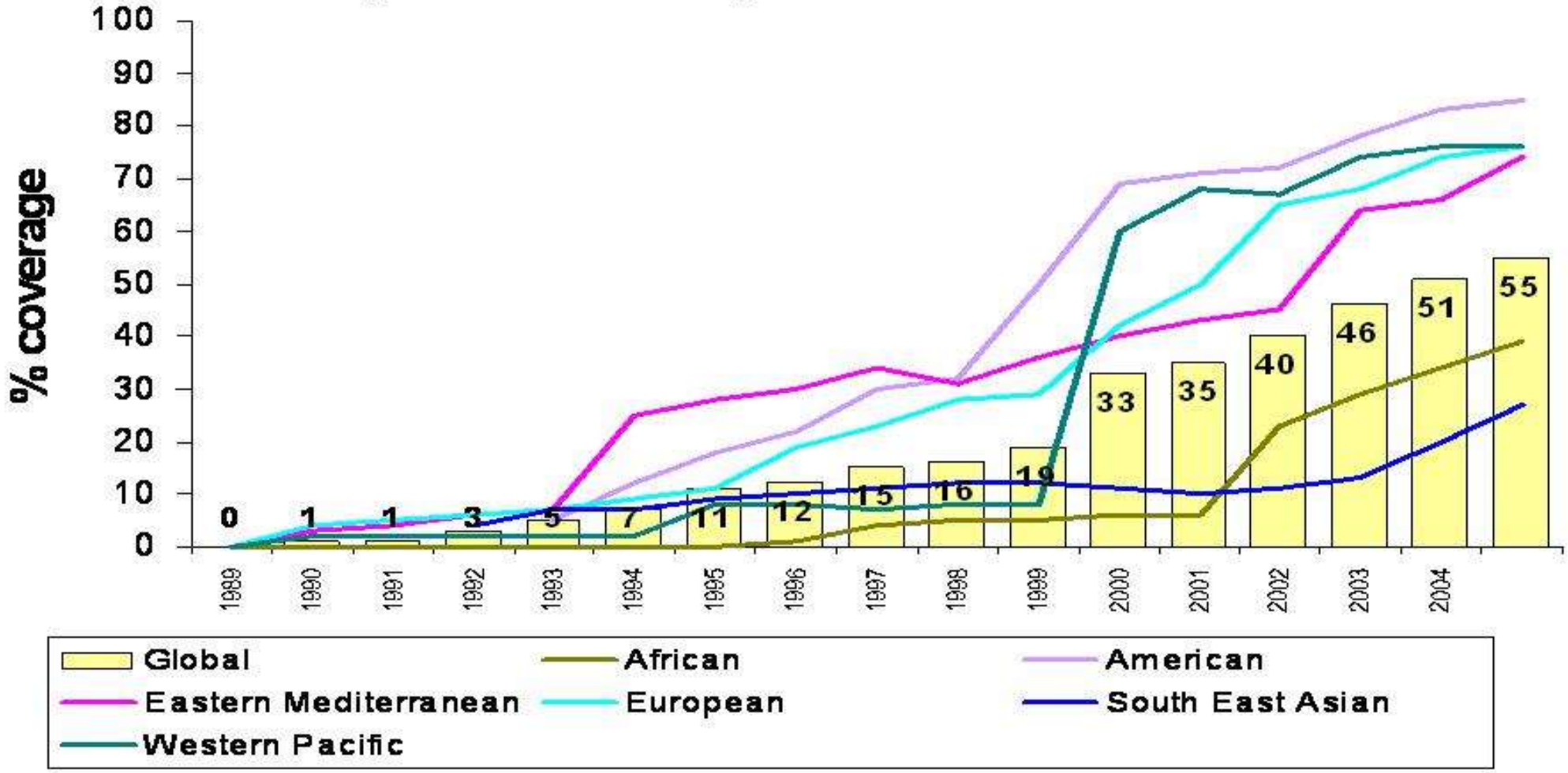
excluding 5 countries where HepB administered for adolescence

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 birth dose 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

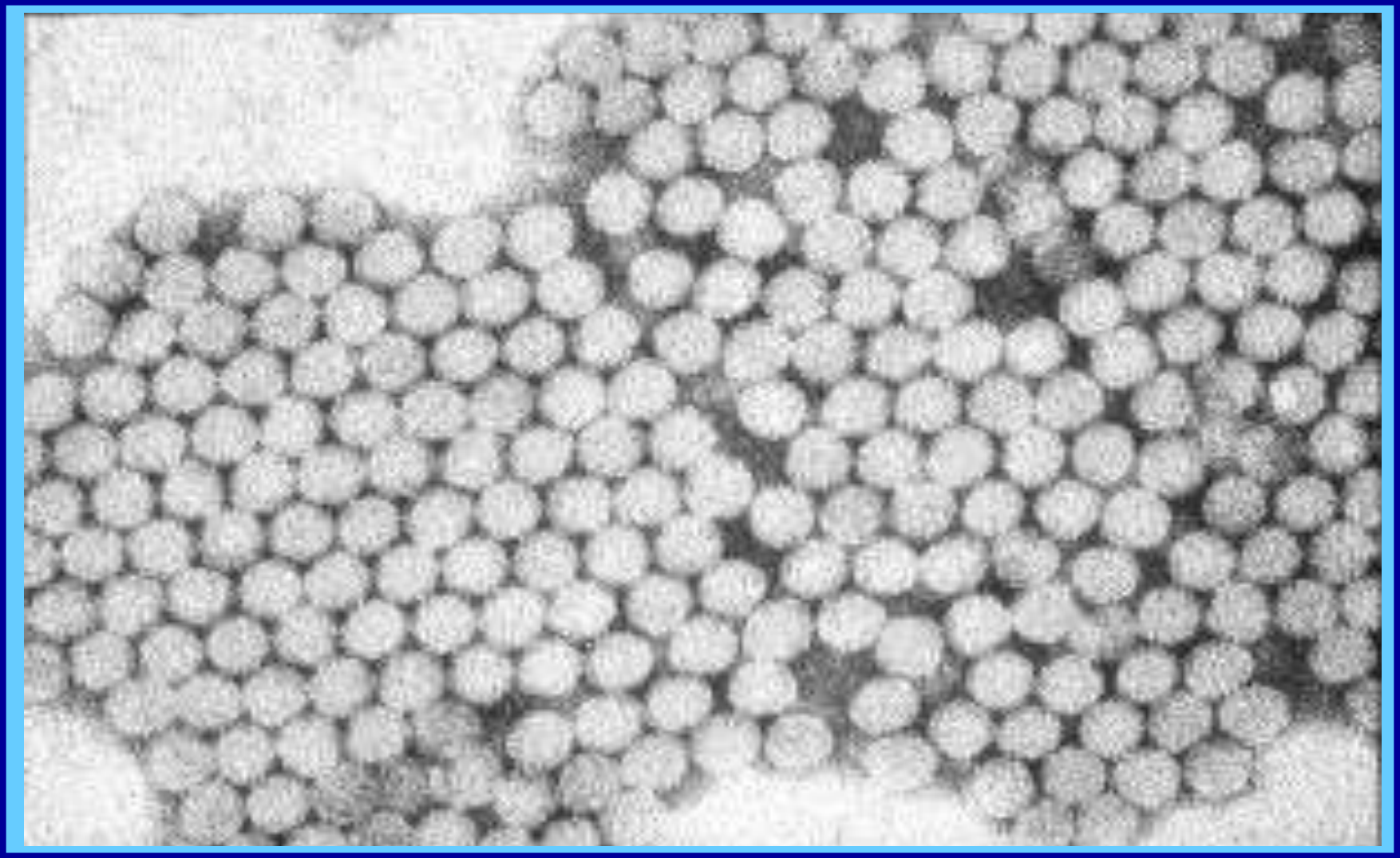
- IM injection:
  - anterolateral thigh (infants)
  - deltoid (older children)
- Can be safely given at the same time as other vaccines:
  - DTP, OPV, Hib/HepB, BCG, measles, yellow fever
- Injection equipment same as for DTP/Hib:
  - 1.0 or 2.0 mL syringe
  - 25 mm, 22 or 23 gauge needle

Two Decades of Universal Hepatitis B Vaccination in Taiwan (Gastroenterology 2007;132:1287-1293)

- HBV vaccination provides long term protection up to 20 years, a booster is not indicated
- Maternal transmission is the primary reason for vaccine 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

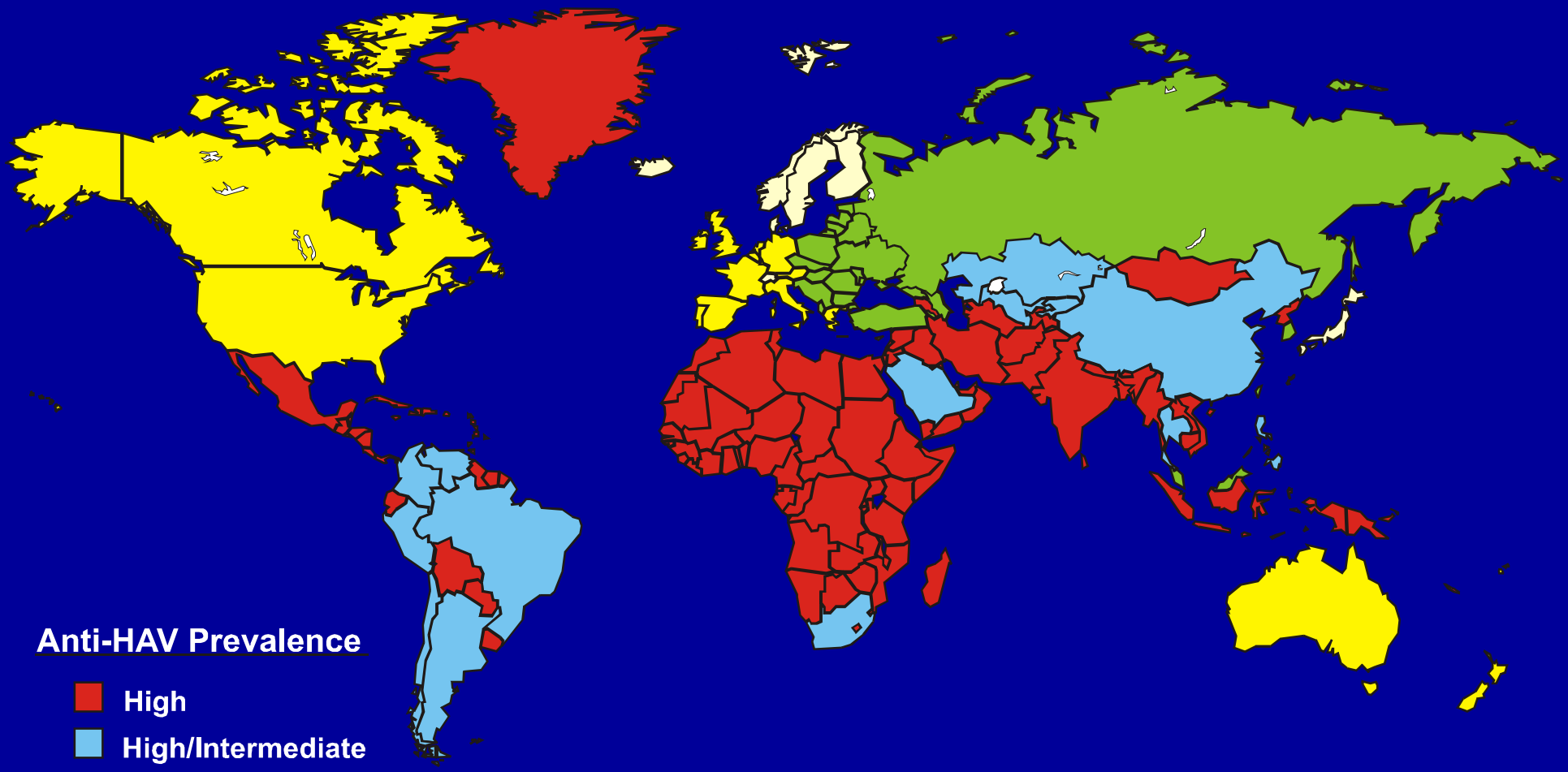


Hepatitis A Virus

- RNA picornavirus
  - Unique world serotype
  - Fecal-oral transmission
  - Acute disease and asymptomatic infection
  - No chronic infection
  - Protective antibodies after infection

    life immunity

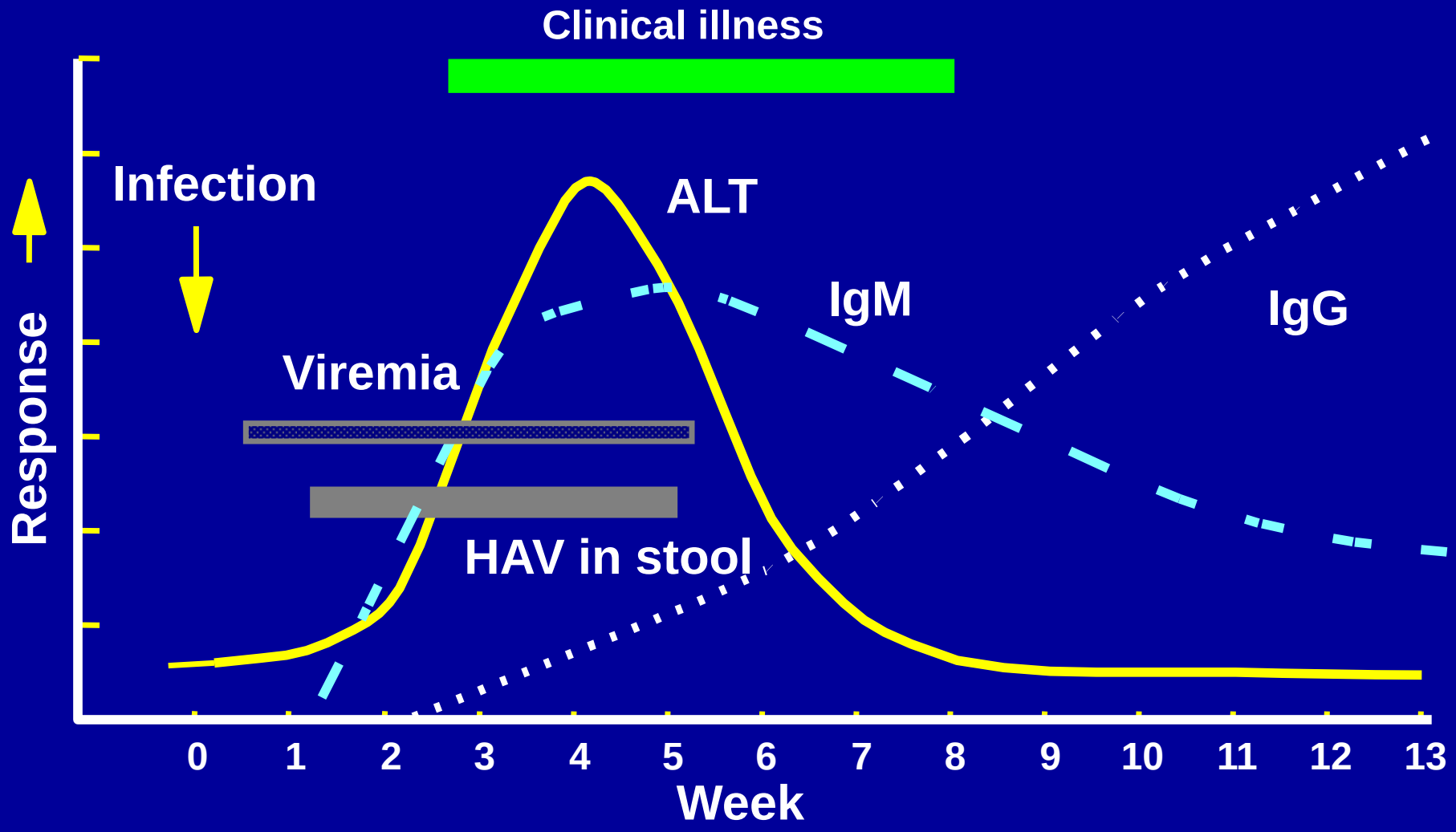
GEOGRAPHIC DISTRIBUTION OF HEPATITIS A VIRUS INFECTION



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 sequellae: none

EVENTS IN HEPATITIS A VIRUS INFECTION

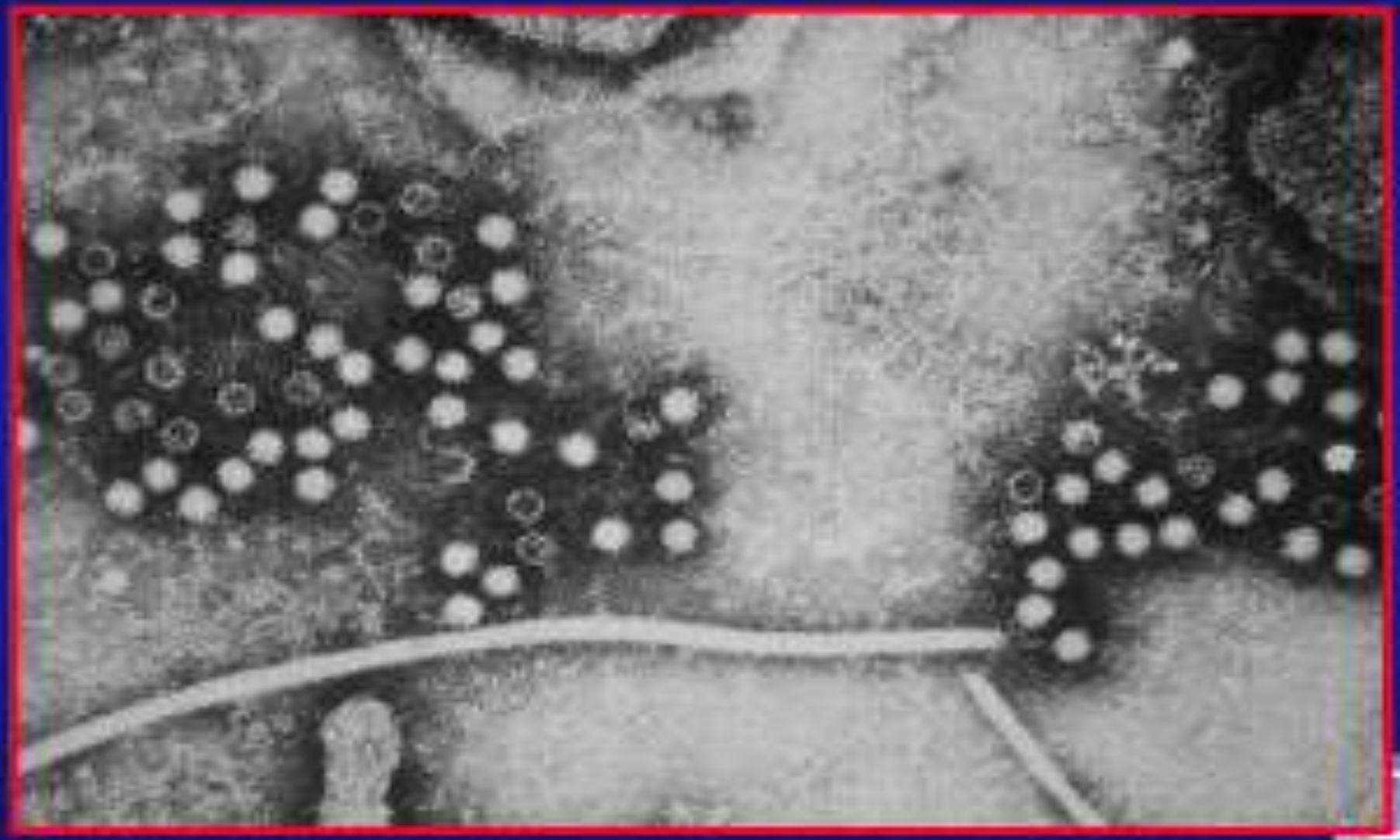


HEPATITIS A vaccine

- 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

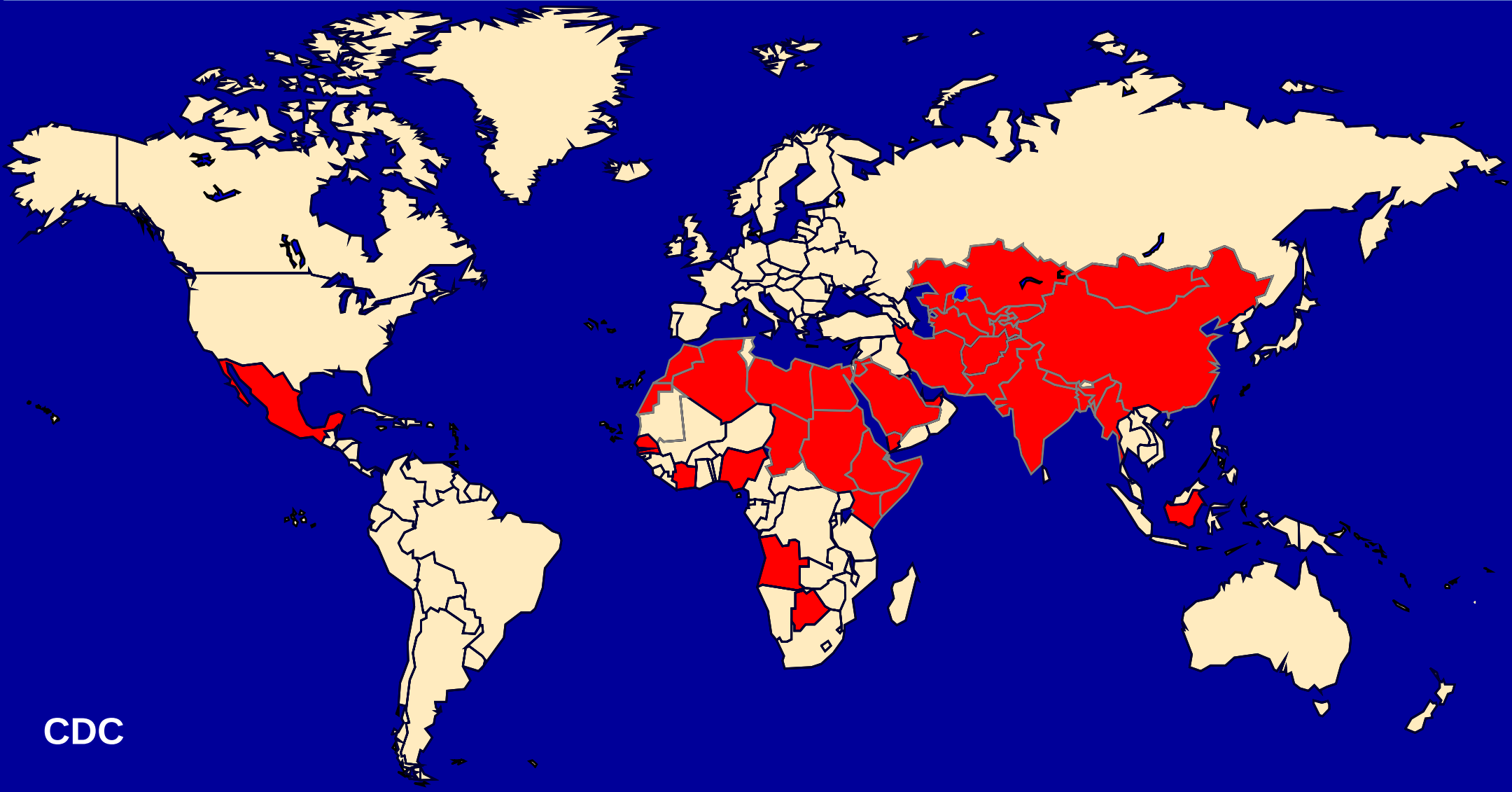
- Highly efficacious
  - 94%-100% of children are protected after one dose

Hepatitis E Virus



Geographic Distribution of Hepatitis E

Outbreaks or Confirmed Infection in >25% of Sporadic Non-ABC Hepatitis

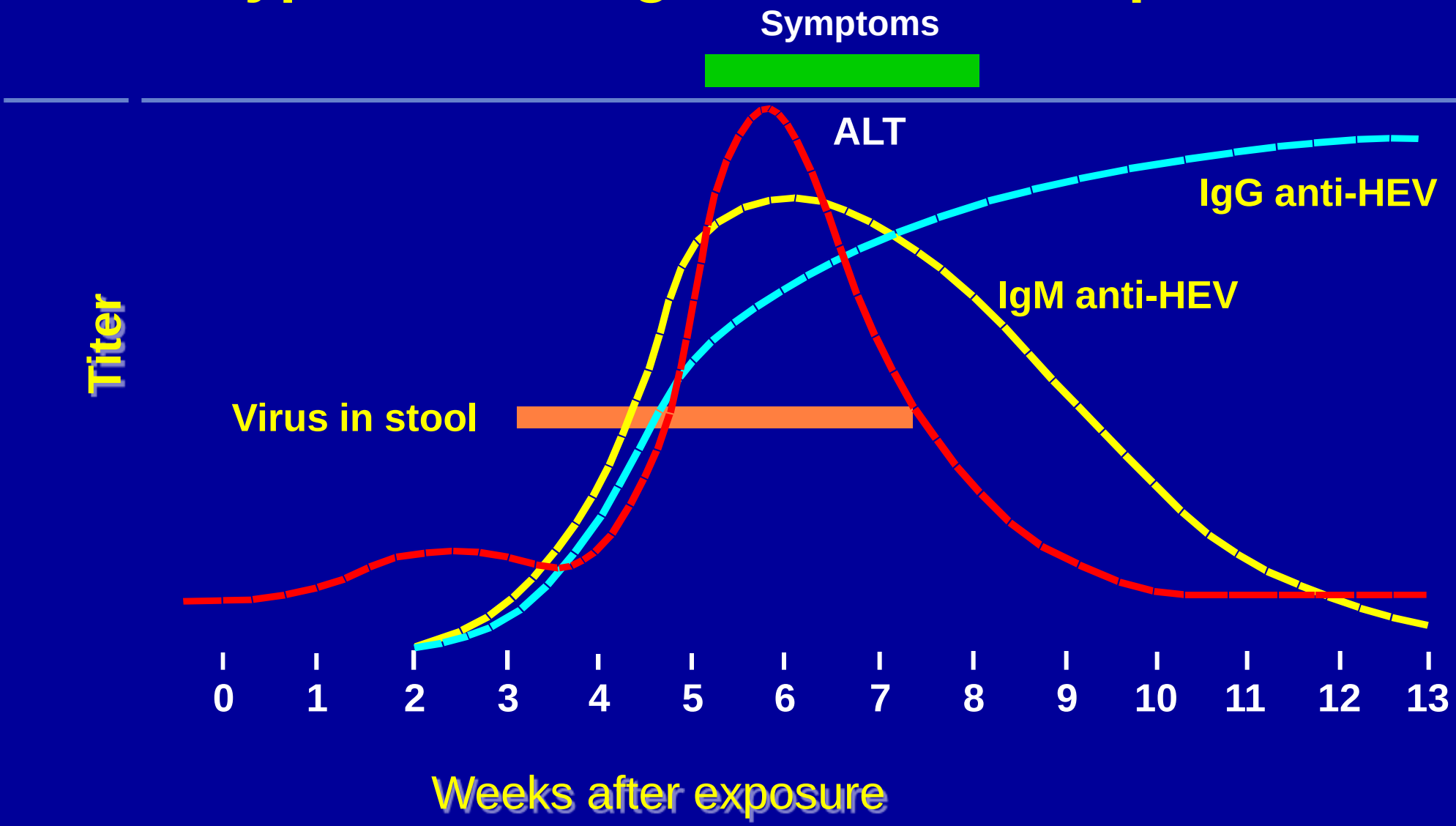


CDC

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 oof drinking water
- A vaccine has been tested in India

Prevention of hepatitis A and E transmission by water