

Viral Hepatitis Vaccines

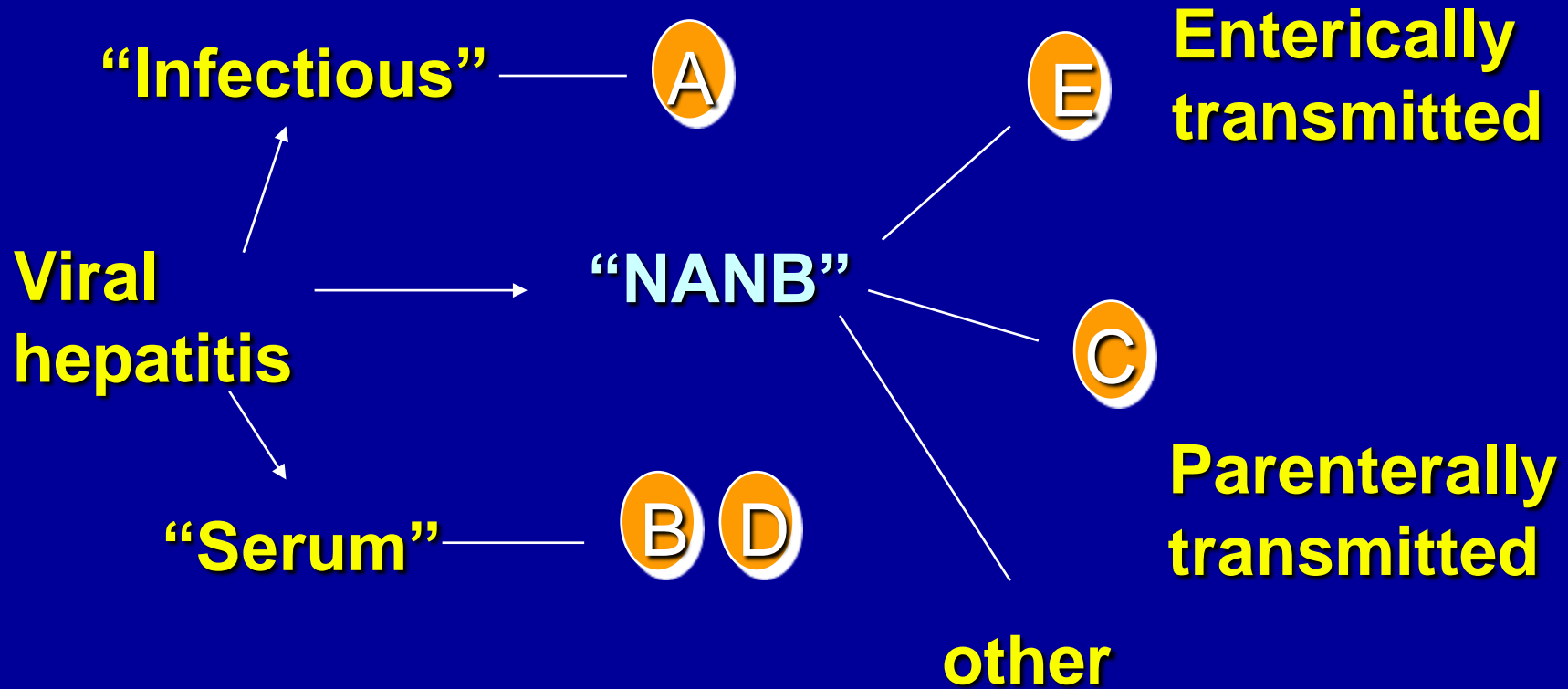
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Training Course in Reproductive Health Research
WHO Geneva 2008

26 February 2008

VIRAL HEPATITIS

HISTORICAL PERSPECTIVE



Viral hepatitis vaccines

- **Hepatitis A** **yes** **2 doses**
- **Hepatitis B** **yes** **3 doses**
- **Hepatitis E** **tested** **in 2006**
- **Hepatitis C** **no vaccine**

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

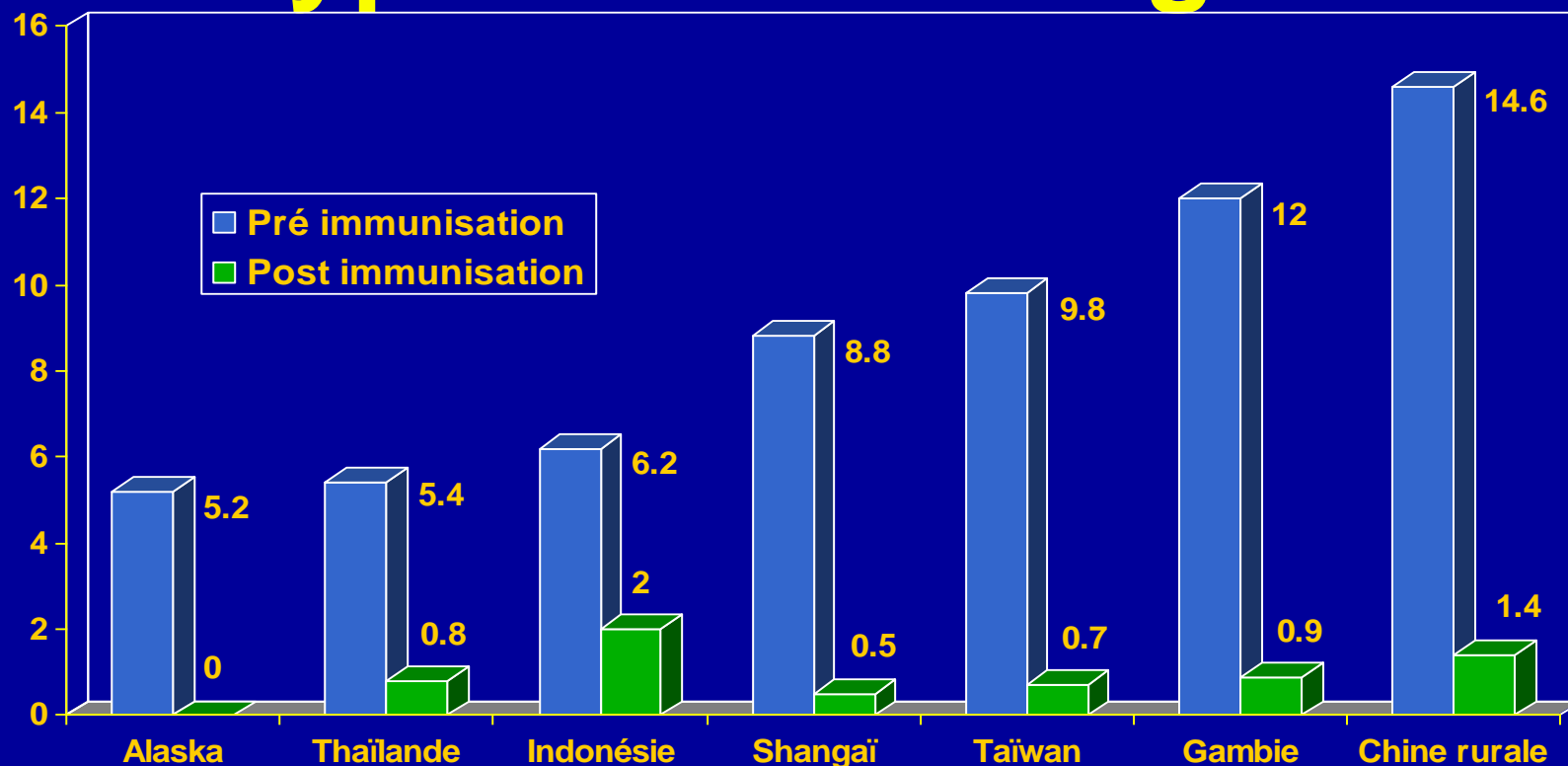
Adolescents/Adults

<5

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

Study	Year	No. Tested	Age (yrs)	Vaccine Coverage	<u>Chronic HBV infection</u>	
					Before Program	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%

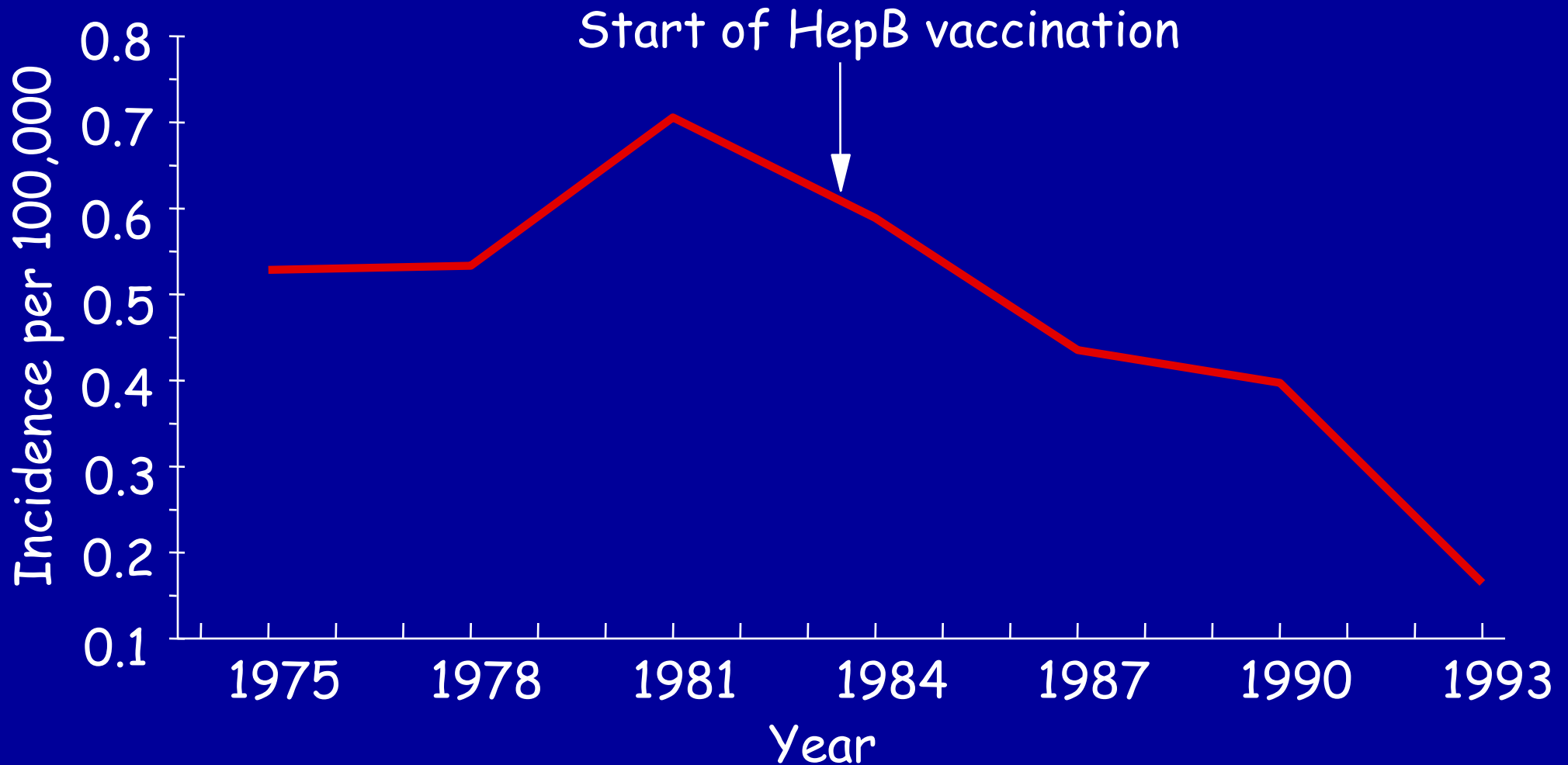
Efficacy against hepatitis B even in hyperendemic regions



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

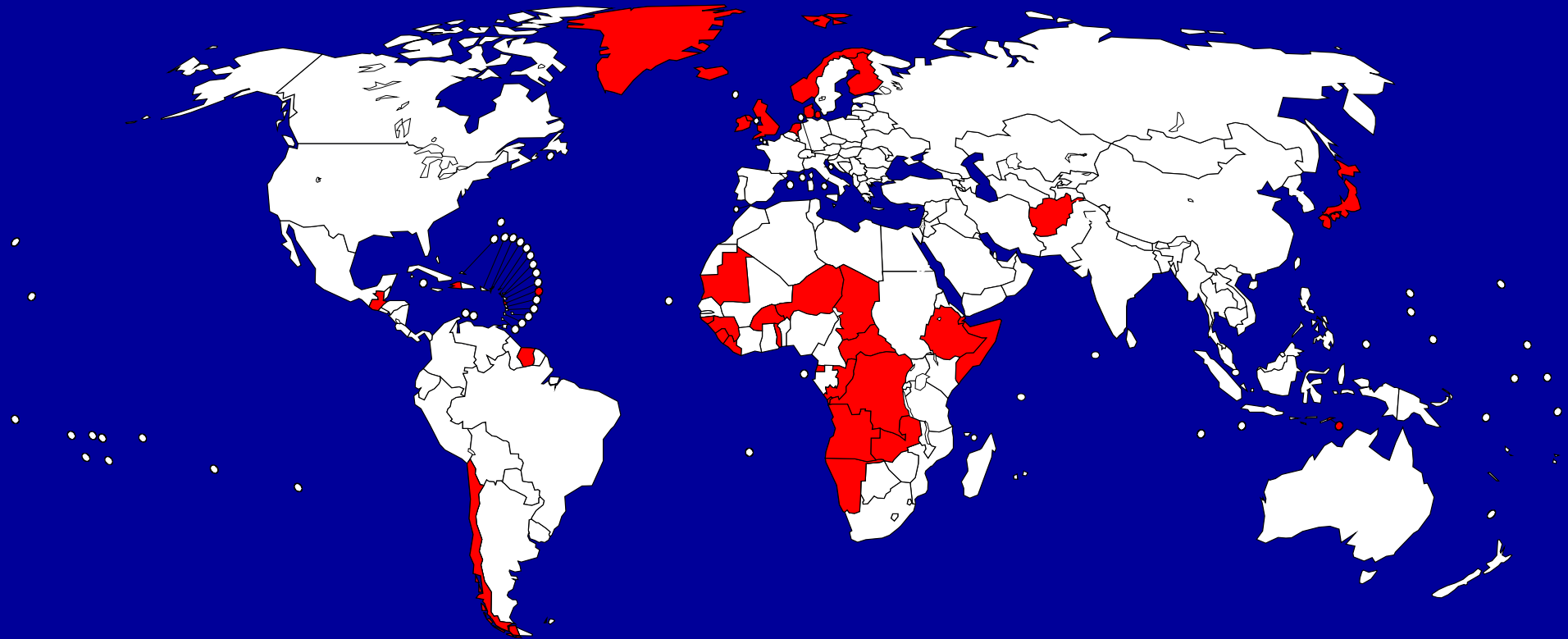
45th World Health Assembly, 1992

- By 1995 HepB vaccine introduced in countries with HBsAg prevalence $\geq 8\%$
- 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

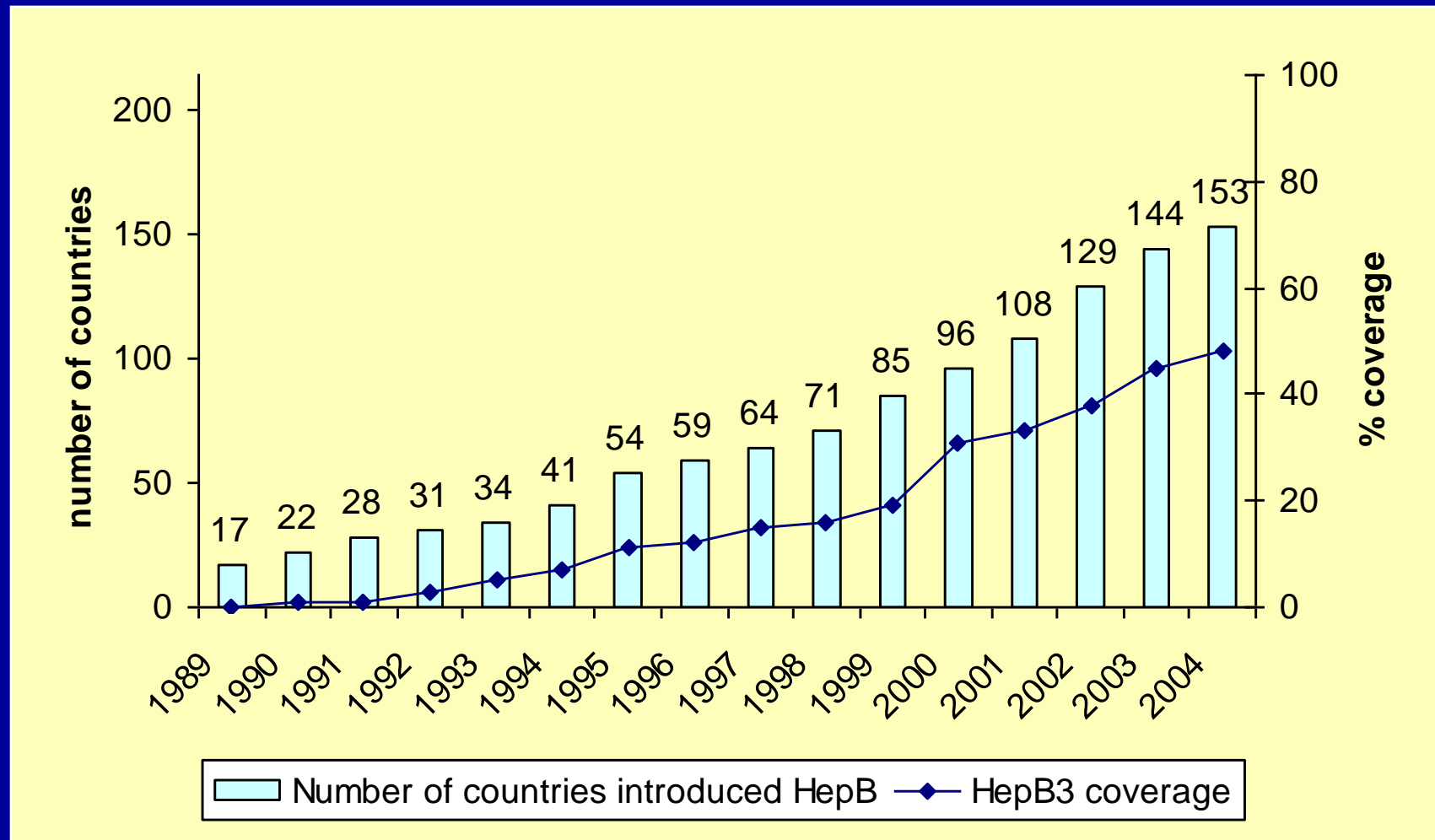
Source: WHO/IVB database, 2005 192 WHO Member States. Data as of September 2005

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

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Number of countries introduced HepB vaccine and global infant HepB3 coverage, 1989-2004



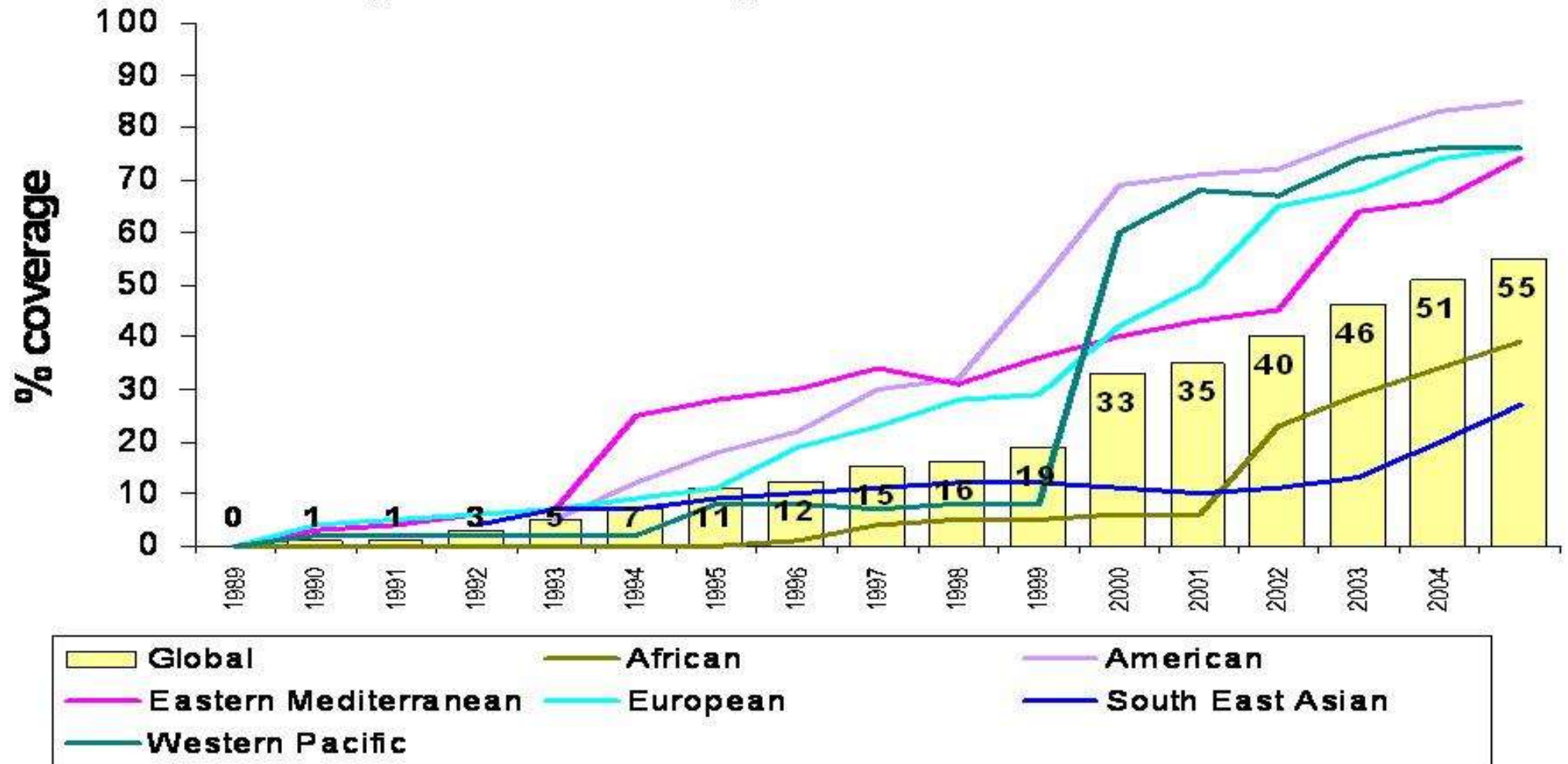
excluding 5 countries where HepB administered for adolescence

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



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

Age	Visit	Other Antigens	HepB Options		
			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

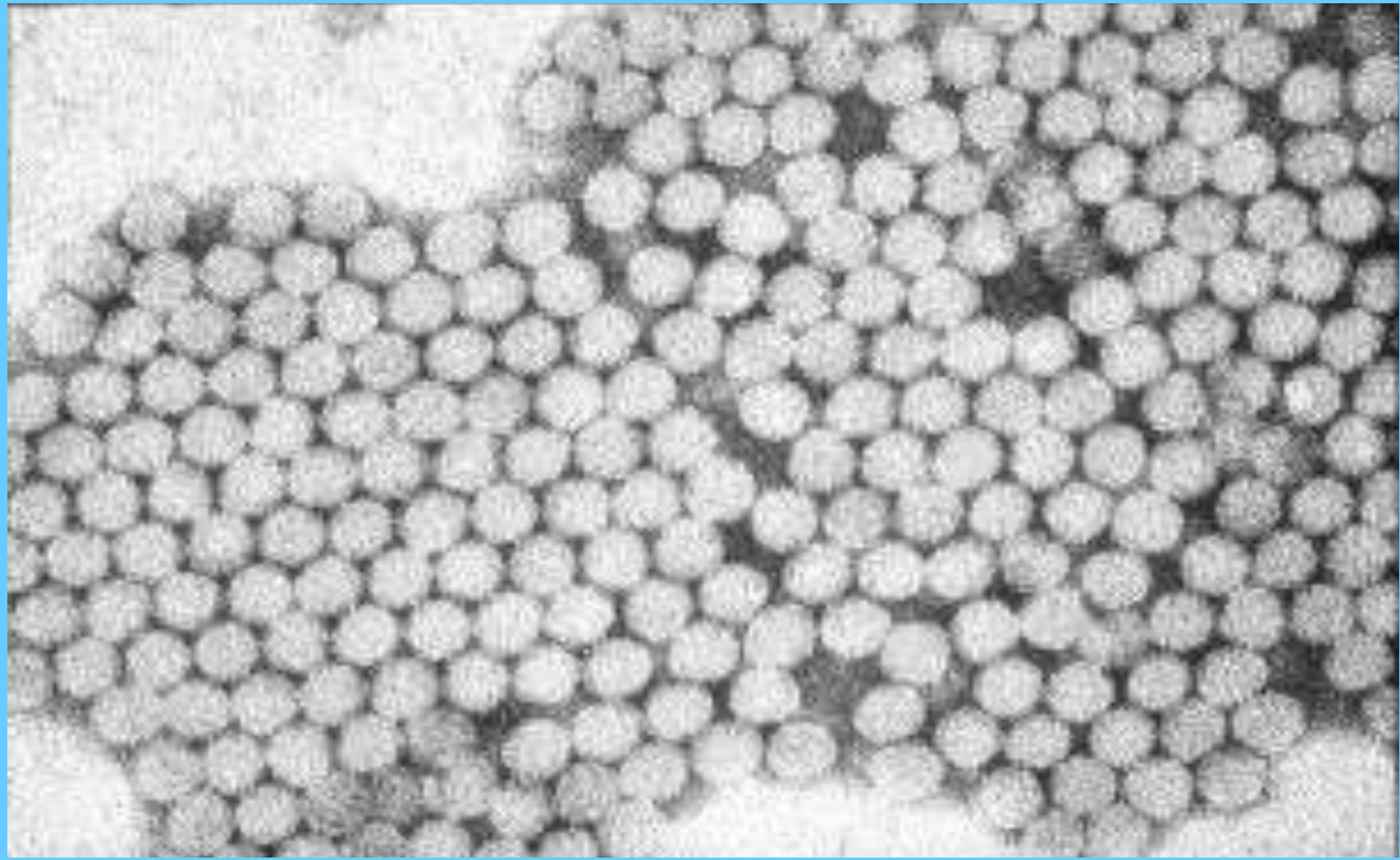
Two Decades of Universal Hepatitis B Vaccination in Taiwan (Gastroenterology 2007;132:1287-1293)

- 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



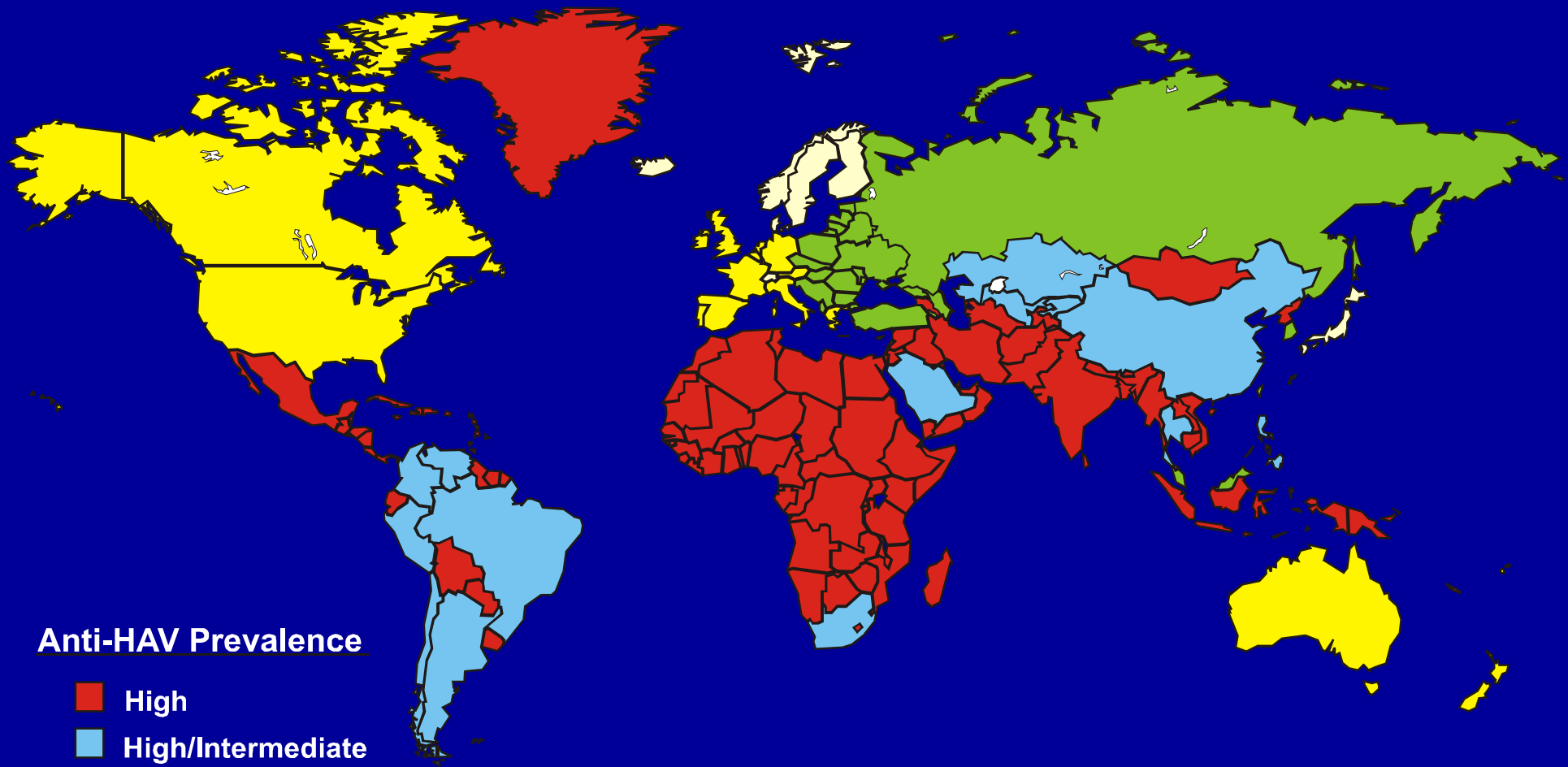
HEPATITIS A VIRUS



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



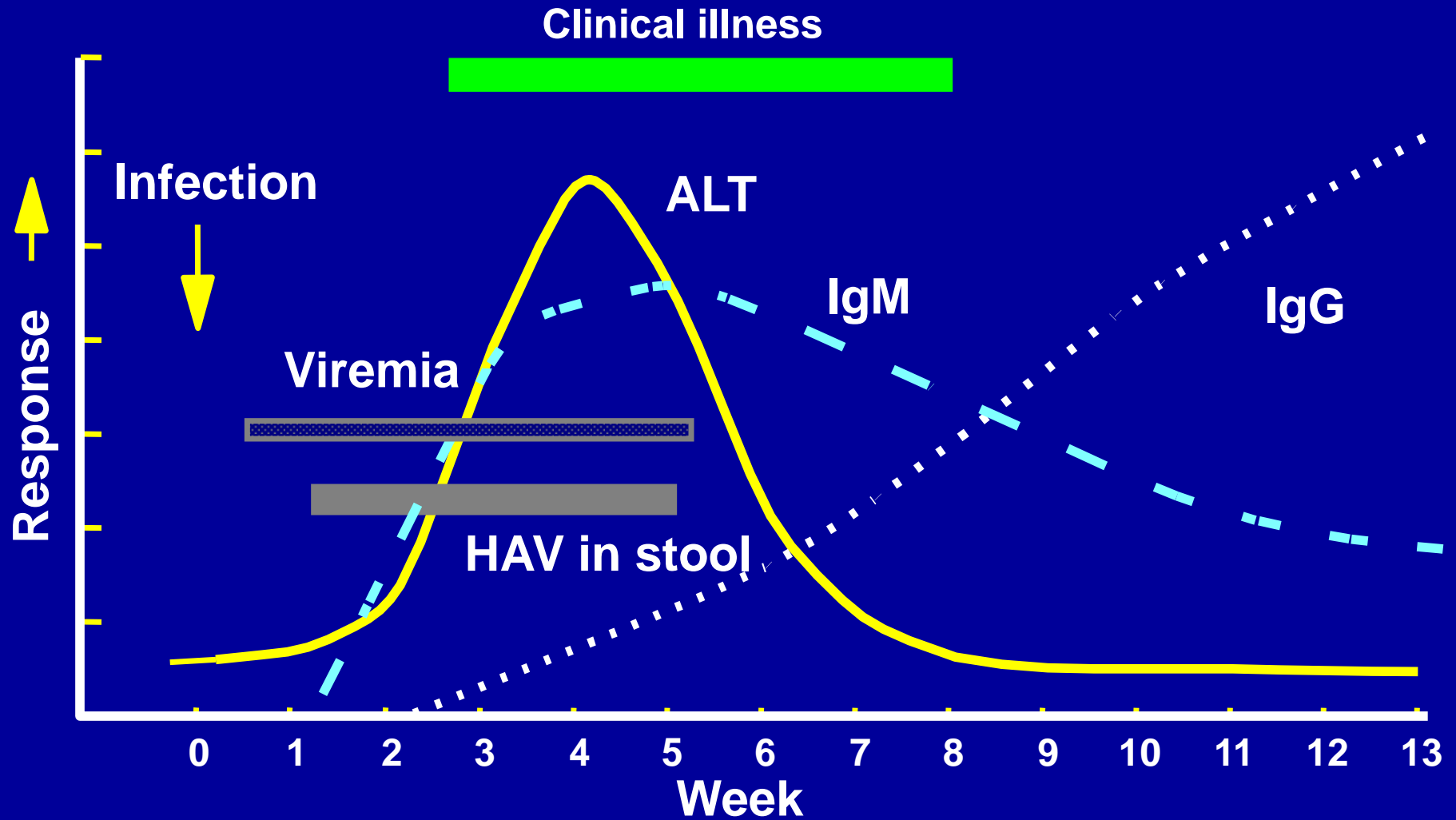
Anti-HAV Prevalence

- High
- High/Intermediate
- Intermediate
- Low
- Very Low

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

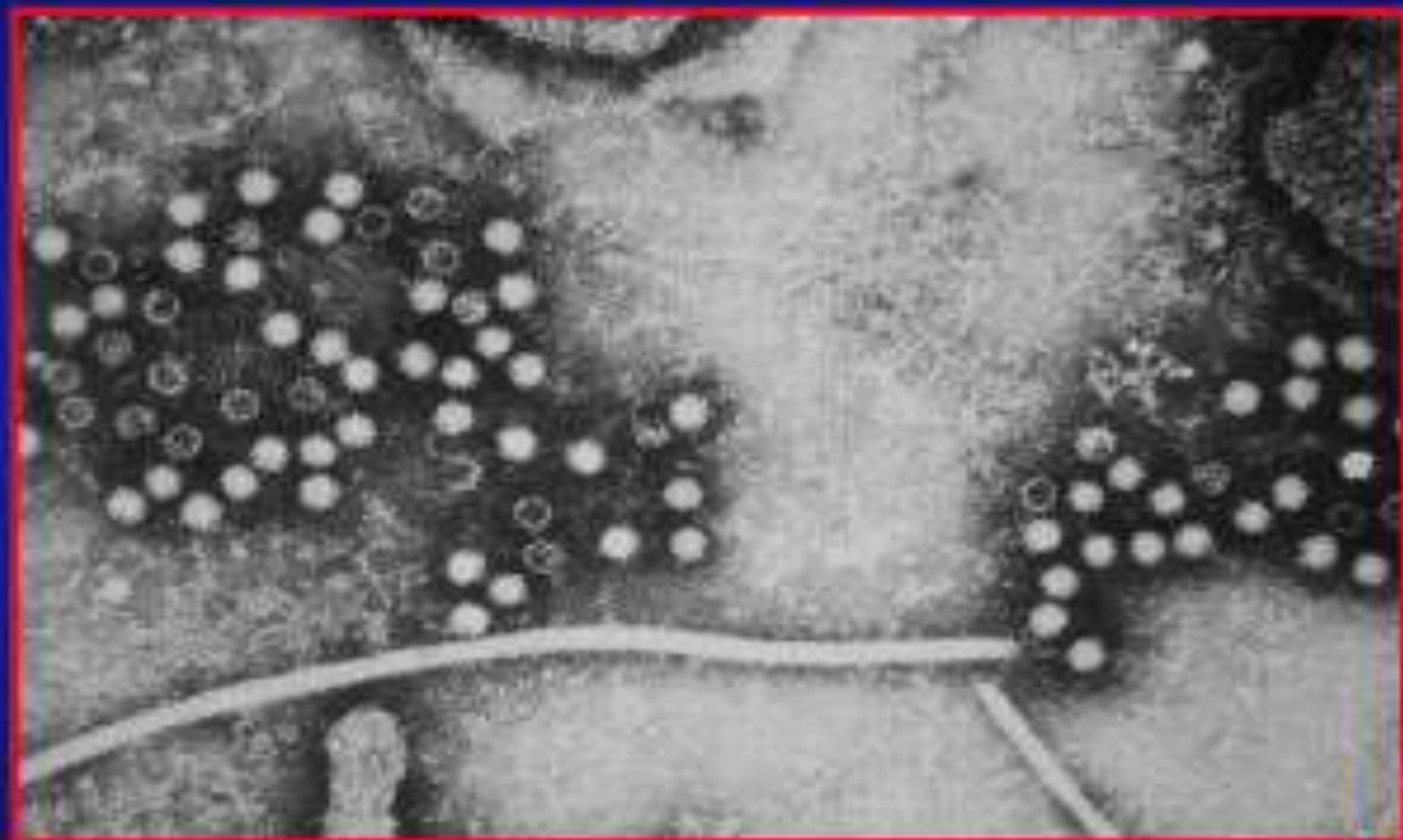
EVENTS IN HEPATITIS A VIRUS INFECTION



HEPATITIS A vaccine

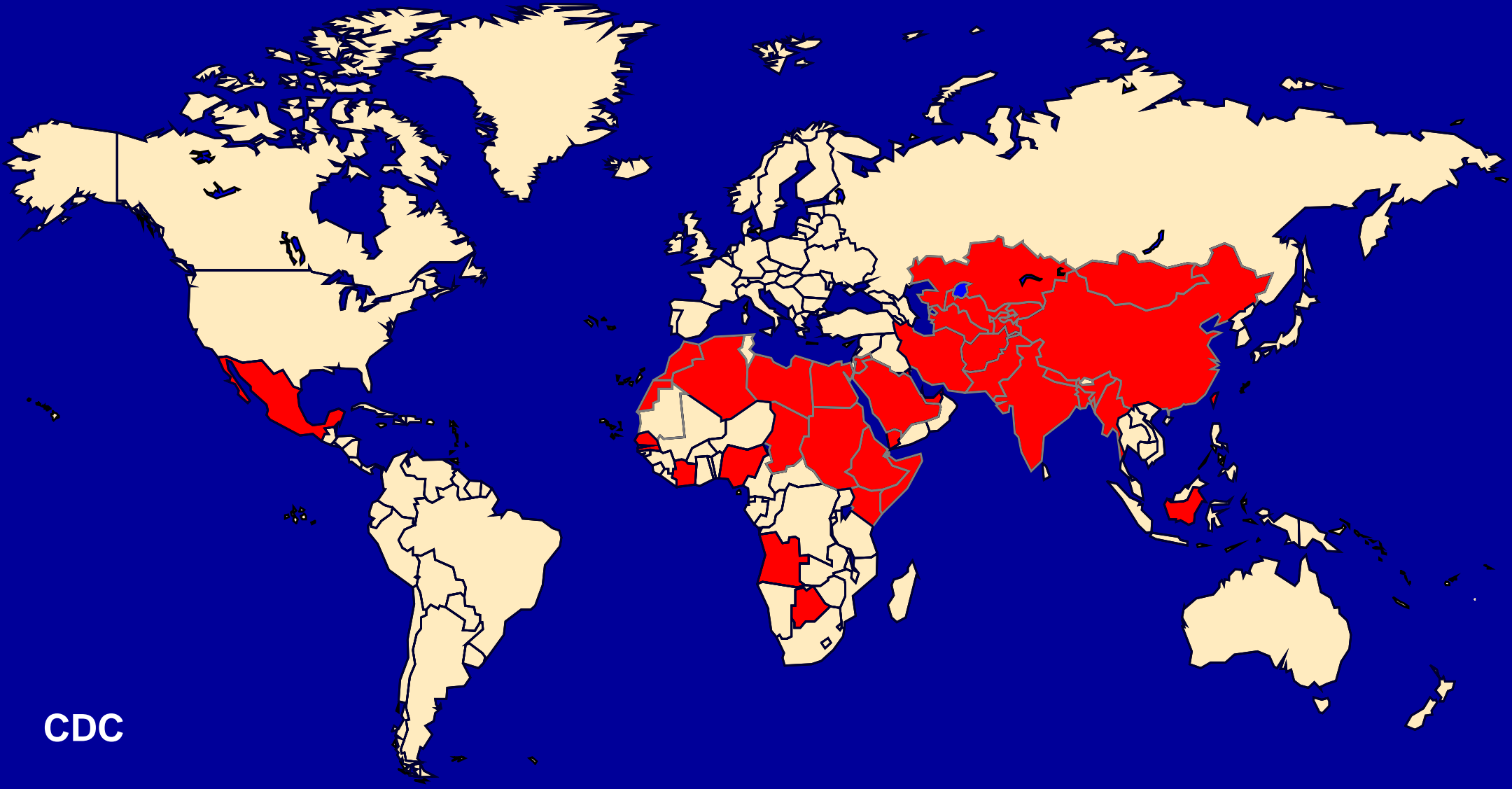
- **Highly immunogenic**
 - **97%-100% of children and adults have protective antibody levels one month after the first dose**
 - **100% are protected after the second dose**
- **Highly efficacious**
 - **94%-100% of children are protected after one dose**

Hepatitis E Virus



Geographic Distribution of Hepatitis E

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



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

Symptoms



Titer

Virus in stool



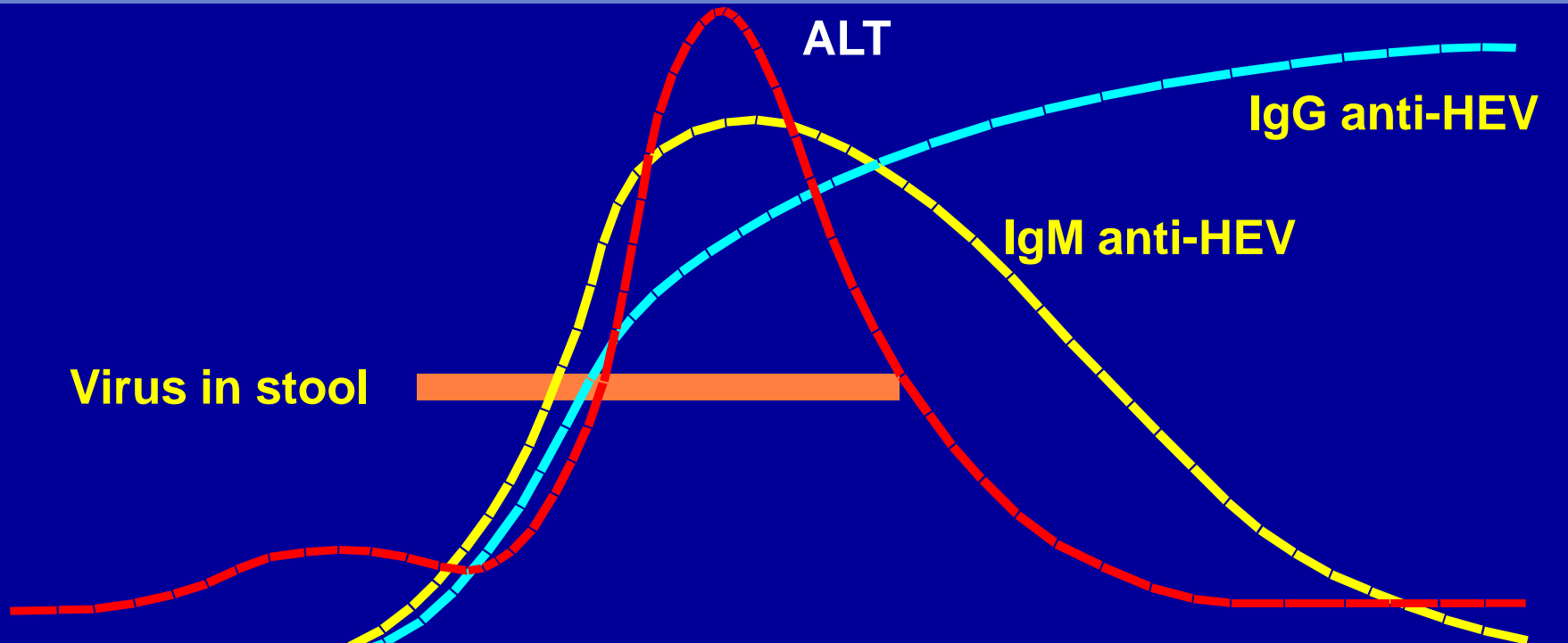
ALT

IgG anti-HEV

IgM anti-HEV

0 1 2 3 4 5 6 7 8 9 10 11 12 13

Weeks after exposure



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**
- **A vaccine has been tested in India**

Prevention
of hepatitis
A and E
transmission
by water

