Introducing Hepatitis B Vaccine into National Immunization Programmes

Steven Wiersma
Training in Reproductive Health Research
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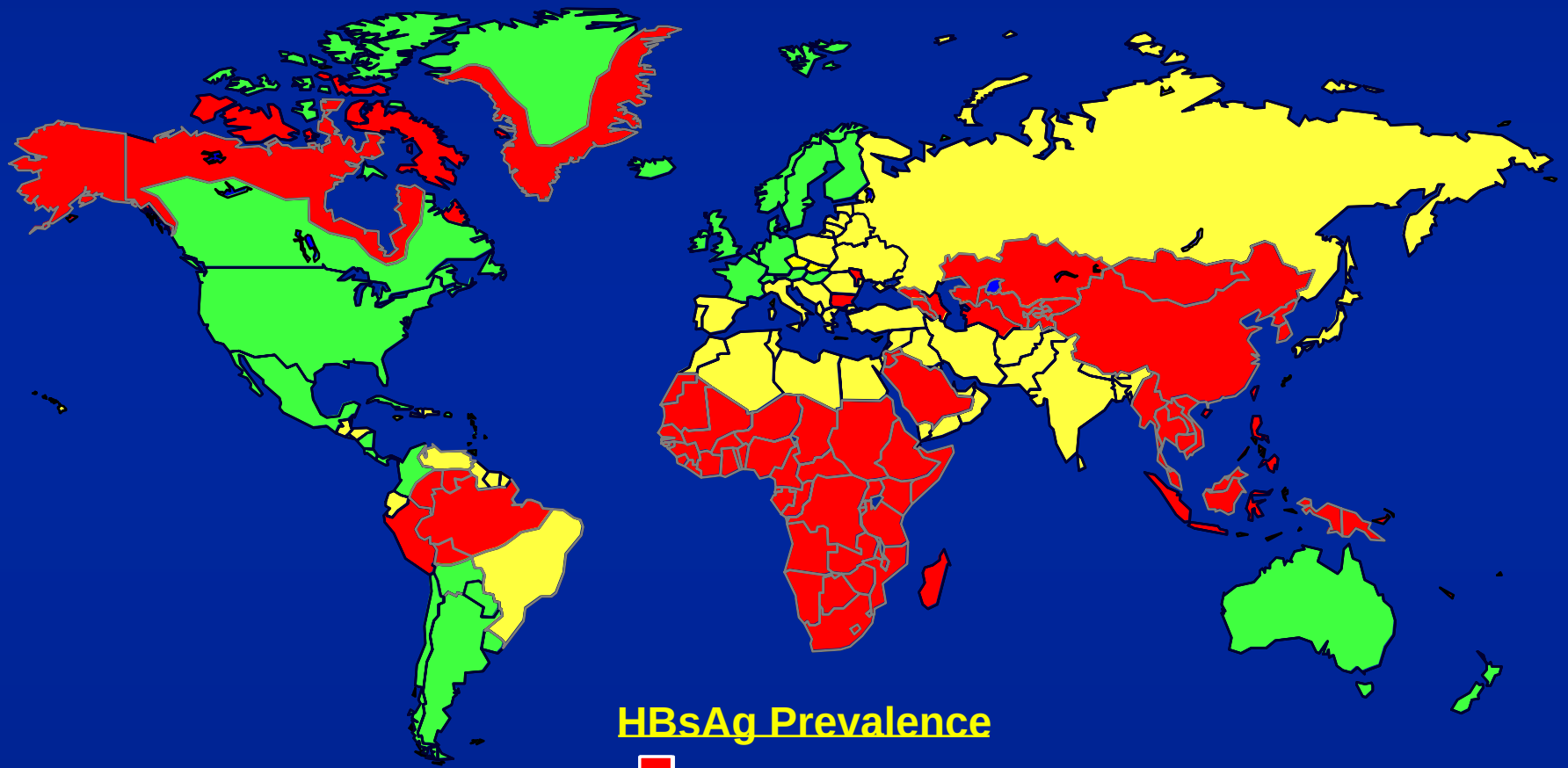
New Vaccine Introduction

- 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

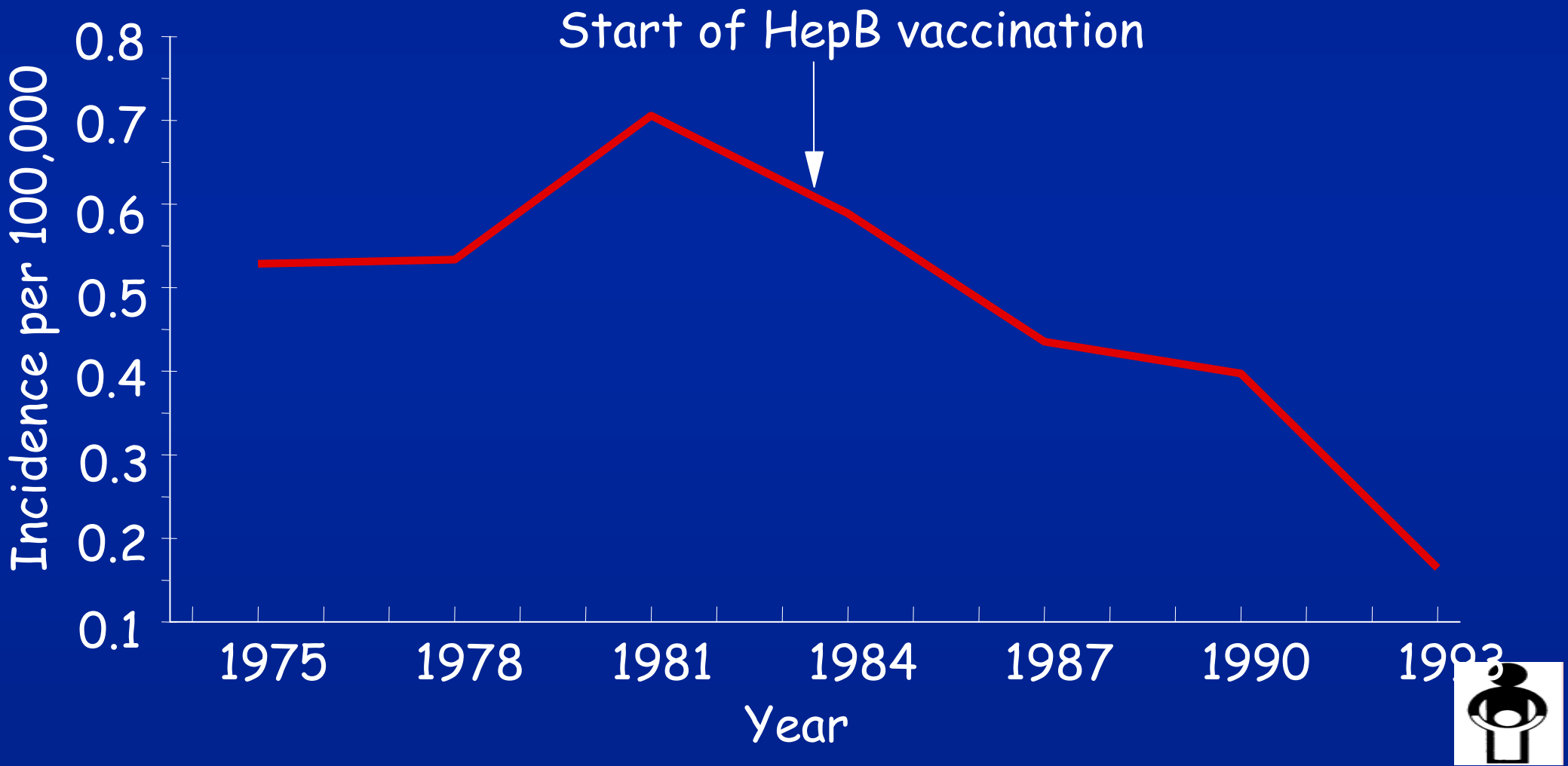
Geographic Distribution of Chronic HBV Infection



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%

Liver Cancer Death Rates among 0-9 Year Old Children, 1974-1993, Taiwan



Hepatitis B Vaccination Targets

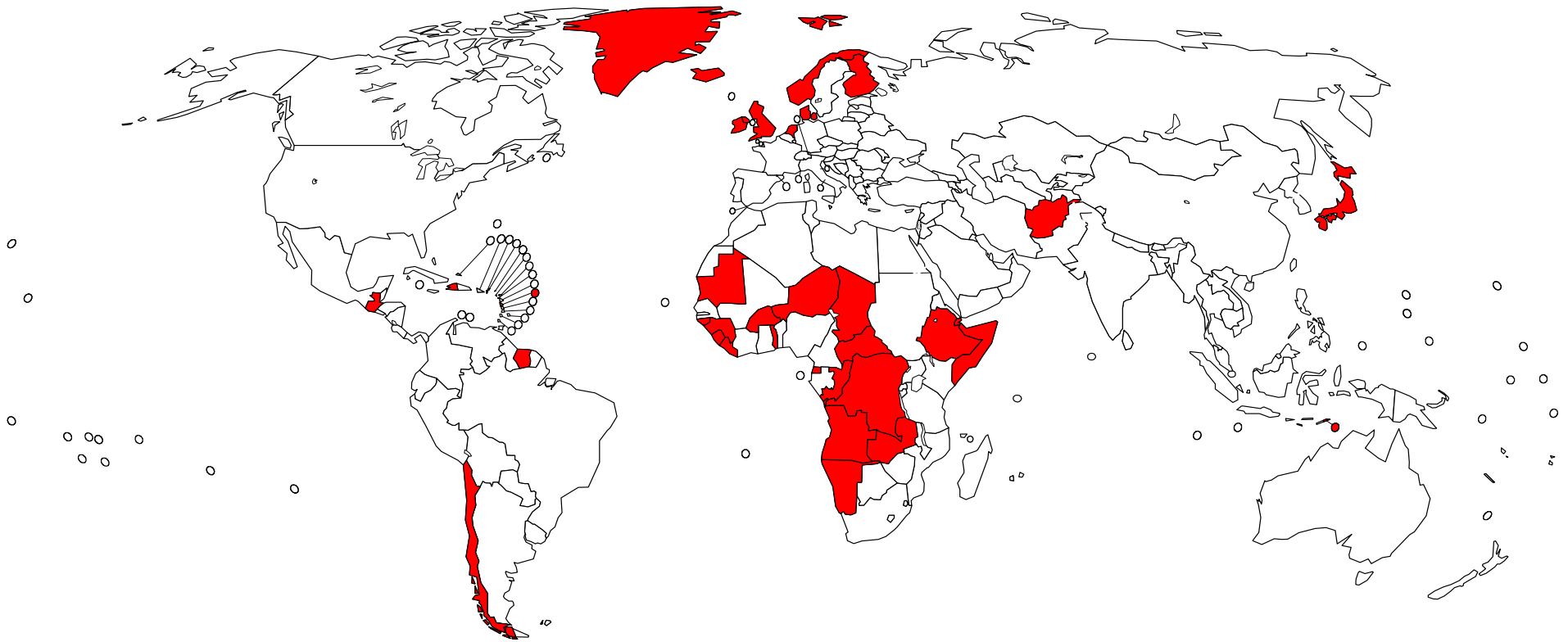
45th World Health Assembly, 1992

- 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%)*

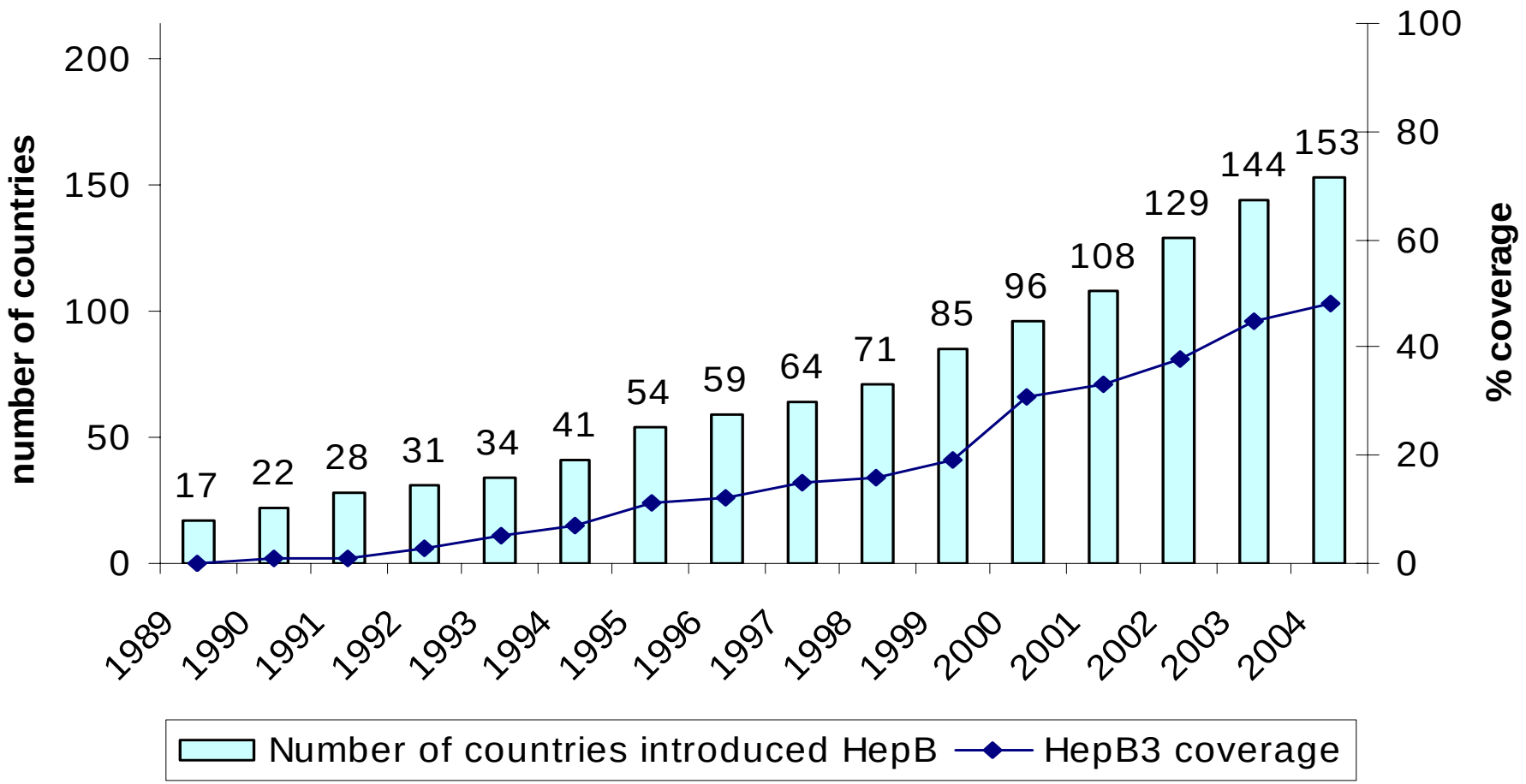
* includes partial and among adolescents

Source: WHO/IVB database, 2005

192 WHO Member States. Data as of September 2005

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

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

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

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

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

Monovalent versus Combination Vaccines: Issues

Issue	Monovalent	Combination
Costs	++ Vaccine ++ Program	+++ Vaccine + Program
Injections	1 additional	No additional
Flexibility	Increased	Less (no monovalent)
Vaccine security	Problem	Problem not likely
Cold chain	Increased	Modest increase
Training	More demand	Less demand
Local DTP production	Not a problem	Could displace

UNICEF Hepatitis B Vaccine Prices, 2001

Vaccine	Type*	Doses	Price, US$
HepB	R	6-20	0.26-0.54
HepB	PD	10	0.35
HepB (incl. syringe)	R	1	0.64-1.31
DTP+HepB (combo-pack)	R	10	0.48
DTP-HepB	R	10	1.10
DTP-HepB+Hib	R	2	3.50

*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 (cm^3/dose) *

Vaccine	1 dose vials	2 dose vials	6 dose vials	10 dose vials
HepB monovalent	9.7	4.8	3.2	3.0
HepB (Unijject)	24.6	---	---	---
HepB + DTP (combo-pack)	---	---	---	8.2
DTP-HepB (combined)	---	---	---	3.0
DTP-HepB+Hib	---	9.7	---	---

*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