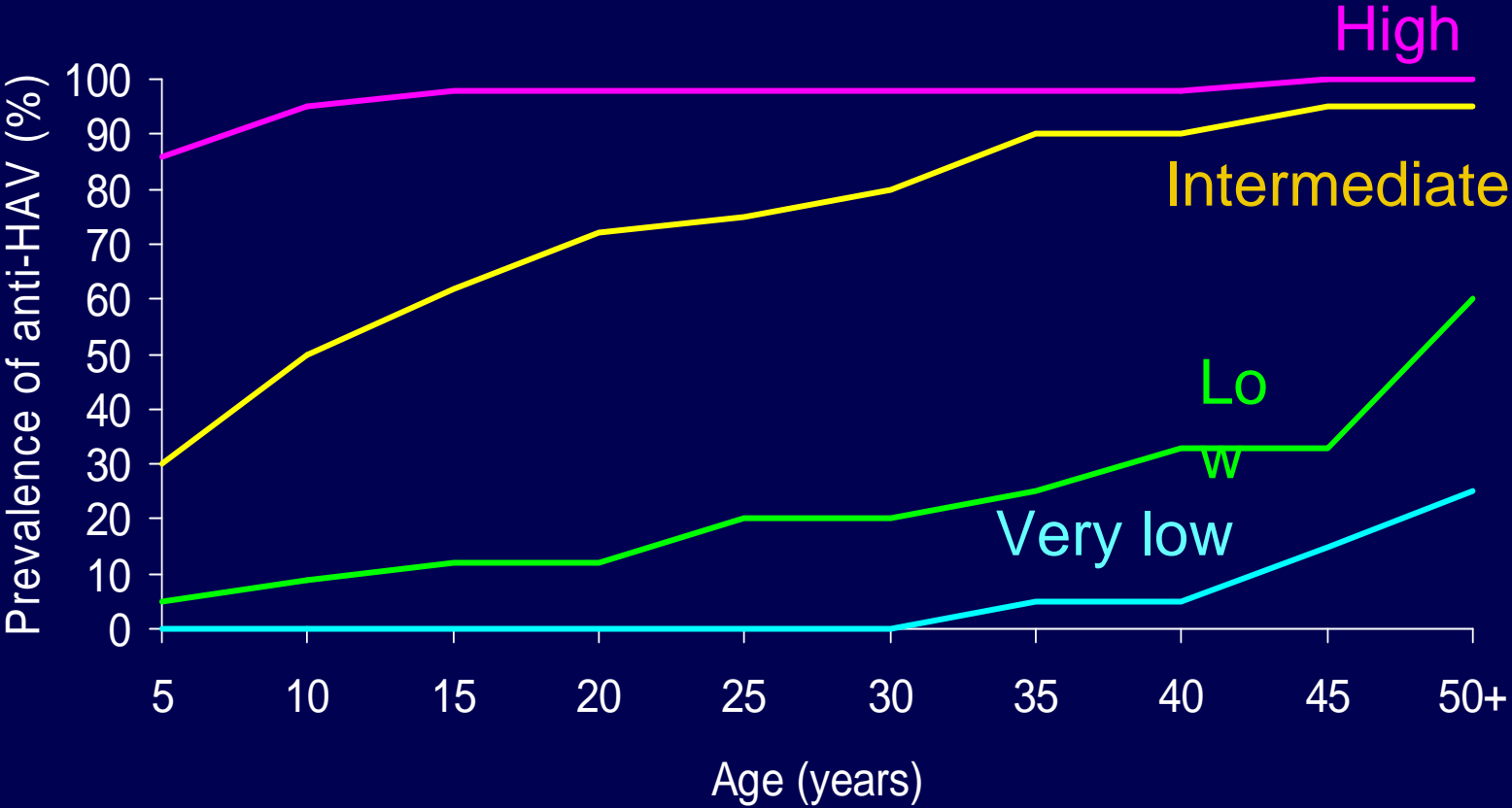

Evolution of Global Hepatitis A Epidemiology

Craig Shapiro, M.D.
World Health Organization
Geneva, Switzerland

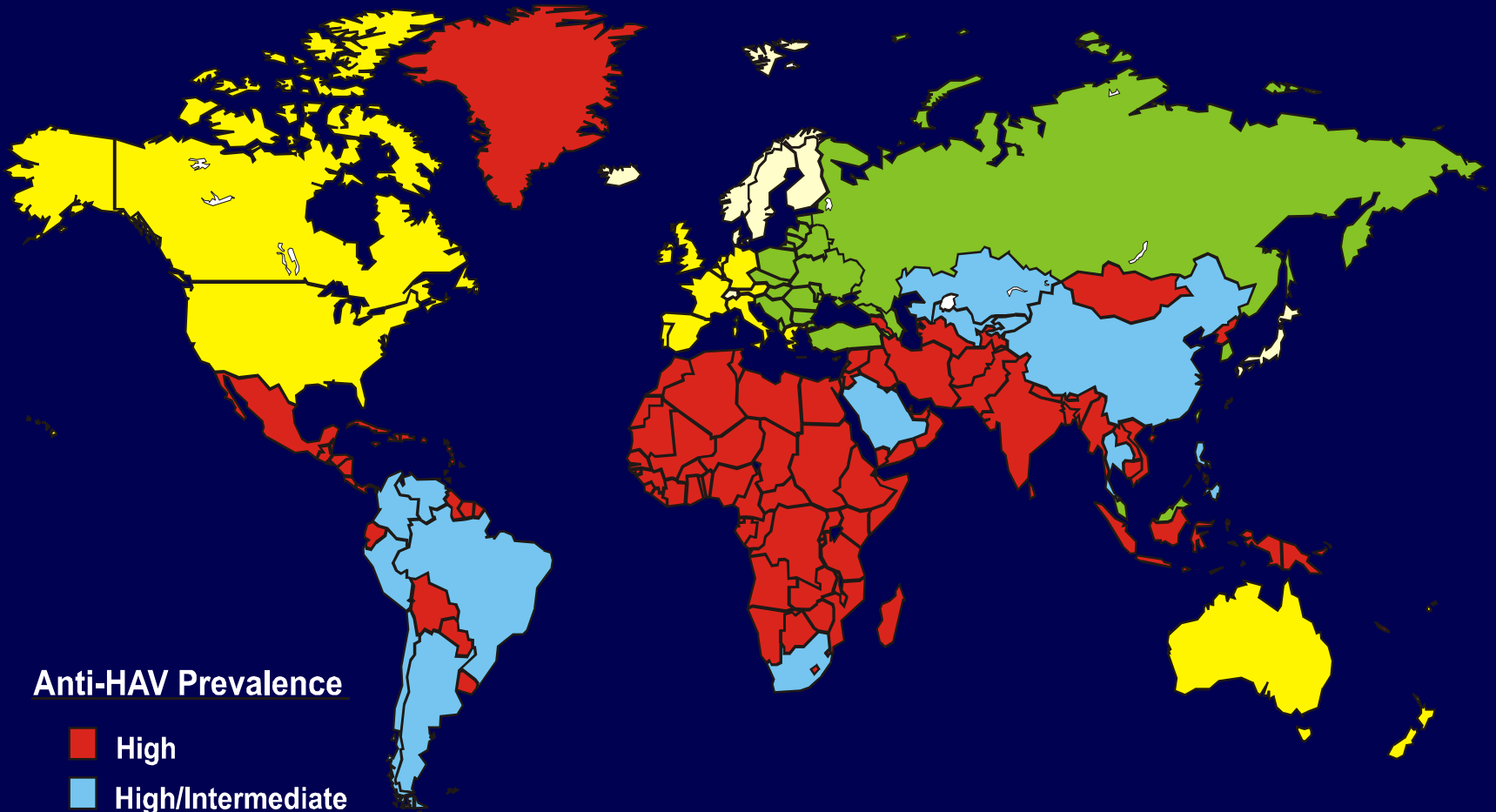
Sources of Hepatitis A Epidemiologic Information

- Surveillance data
 - Acute disease (cases, hospitalizations, transplants, etc.)
 - Reflects recent exposures
- Seroprevalence data
 - Exposures over lifetime
 - Demonstrates underlying pattern of immunity in population
 - Modeling can be used to determine rates of infection

Global Patterns of Anti-HAV Prevalence, by Age and Endemicity



Global Patterns of Hepatitis A Endemicity



Anti-HAV Prevalence

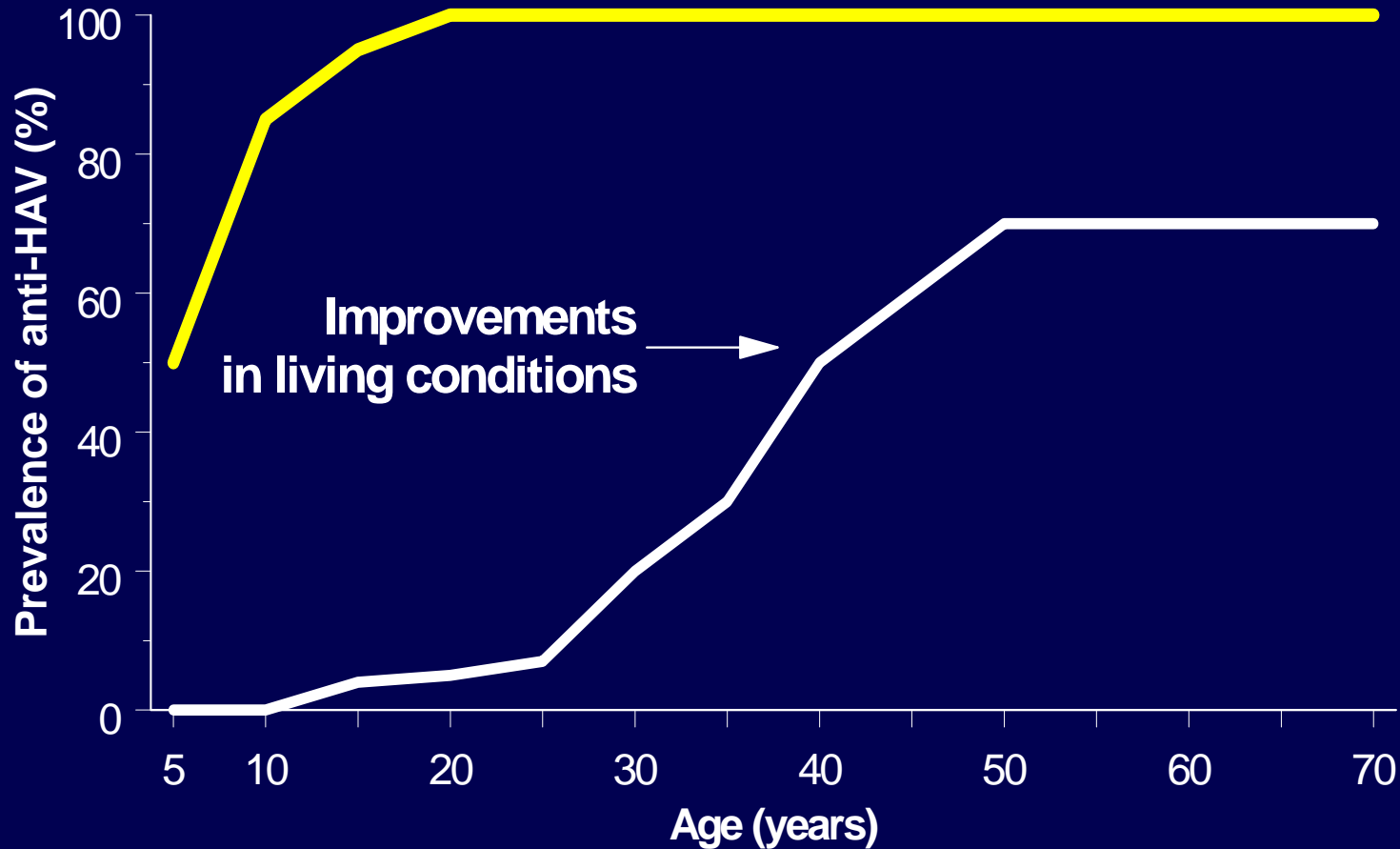
- High
- High/Intermediate
- Intermediate
- Low
- Very Low

Global Patterns of Hepatitis A

Endemicity	Usual Age of Patients (years)	Reported Disease Incidence (per 10 ⁵ /year)	Transmission Patterns
High	5-14	5-150	person to person; outbreaks uncommon
Intermediate	4-24	15-150	person to person; food and waterborne; periodic epidemics;
Low	5-39	5-15	person to person; foodborne; outbreaks
Very Low	> 20	< 5	risk groups

Source: Hadler; Viral Hepatitis and Liver Disease, 1991

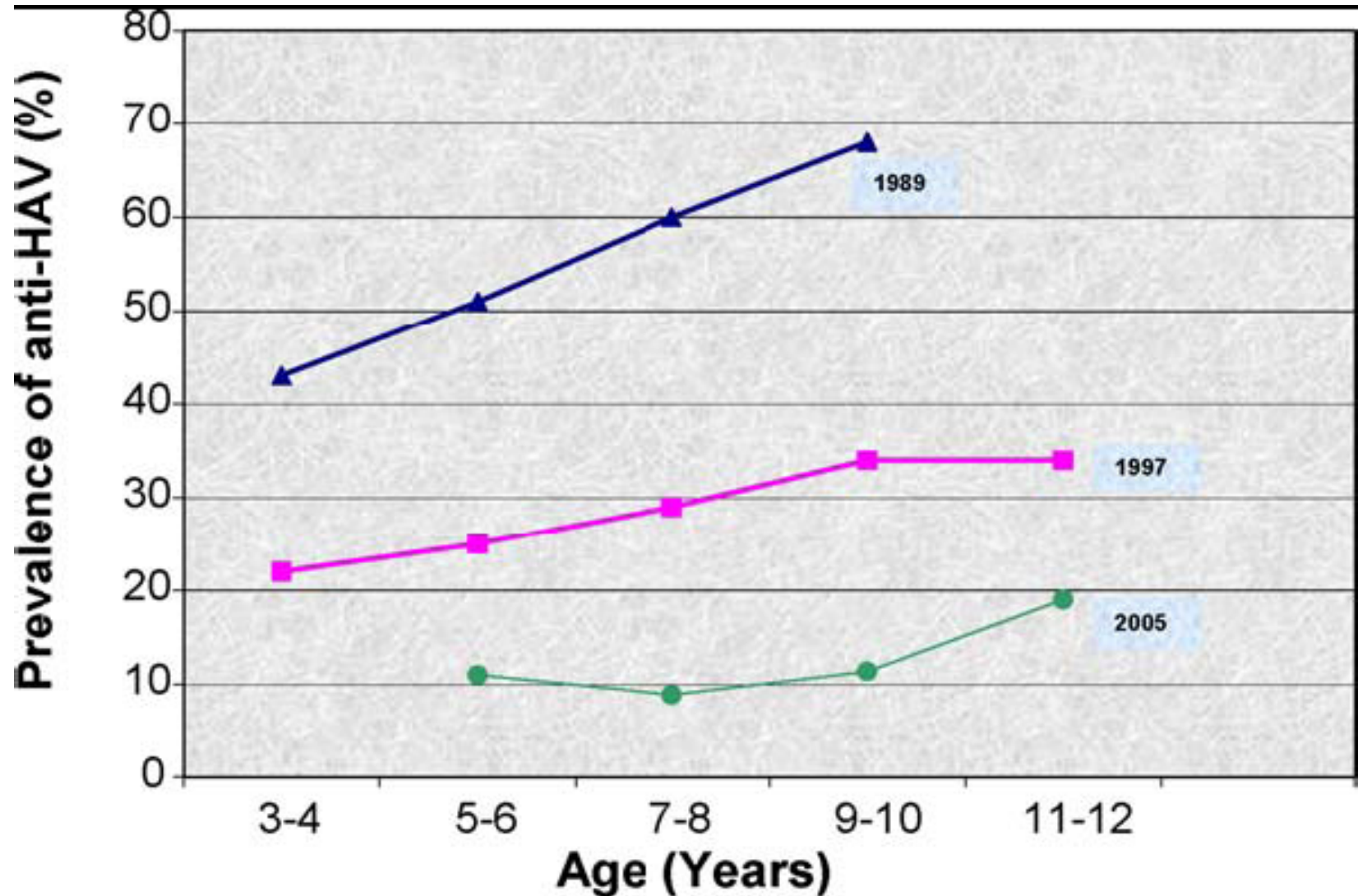
Epidemiologic Shift in Prevalence of Antibodies to Hepatitis A Virus



Hepatitis A: Transition from High to Intermediate Endemicity Features

- Lower prevalence among children
 - Increase in average age of infection
 - Increased morbidity
- Outbreak potential
 - Circulating virus
 - Cohorts of susceptible older children, adolescents, and adults
- Variability in incidence
 - Within regions
 - Within countries and cities
 - urban/rural
 - socioeconomic status

Changes in anti-HAV prevalence in children <12 years of age,
Saudi Arabia, 1989, 1997, 2005



Hepatitis A Outbreaks, Saudi Arabia, 1997 and 2003

Figure 1. An outbreak of hepatitis A by week of onset. Afif town, Riyadh Region, Jan. 1-April 30, 1997

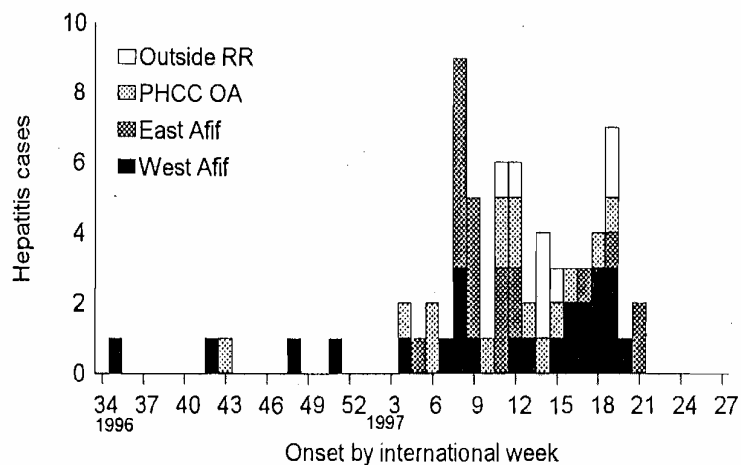
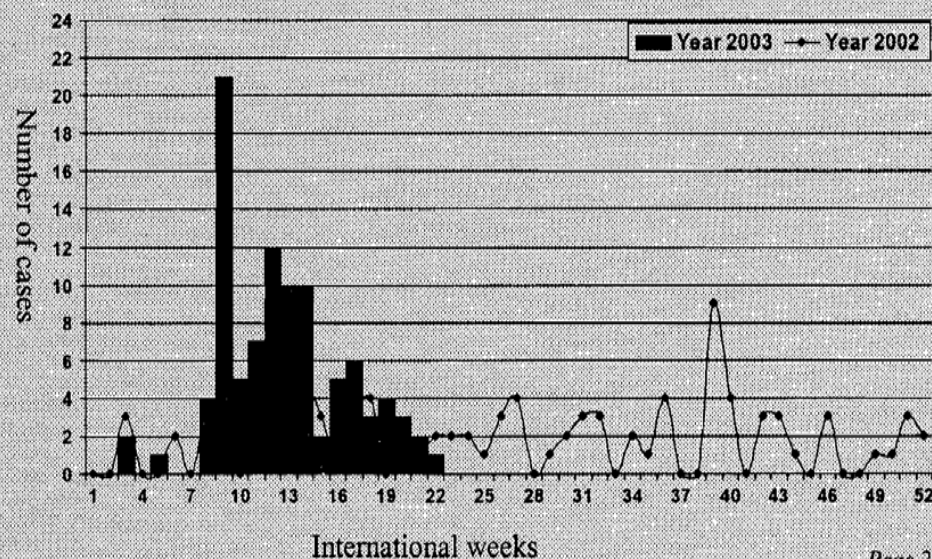


Figure 1: Distribution of Hepatitis A cases by date of onset reported from Bisha Governorate during 2002 and 2003.



Outside RR - Outside Riyadh Region (Madinah, Taif, Qassim Regions)
 PHCC OA - Primary Health Care Center outside Afif

Estimated Force of Infection, by Region

	<u>Total</u>	<u>Afric</u> <u>a</u>	<u>America</u> <u>s</u>	<u>Asia</u>	<u>Europ</u> <u>e</u>	<u>Middle</u> <u>East</u>
<u>Number of Surveys</u>	157	7	31	40	62	17
Decreasing prevalence	66%	0	42%	57%	97%	41%
<u>Estimated mean infection rate per 1000 susceptibles per year</u>						
Surveys before 1990 (n=74)	190	620	680	310	20	230
Surveys after 1989 (n=83)	160	490	250	110	10	210

Implications of Epidemiology for Hepatitis A Vaccine Introduction

- Disease patterns change with improvement in socioeconomic conditions and water/sanitation levels
 - Overall force of infection less
 - Disease among older age groups
 - increased morbidity
 - increased heterogeneity
- General assumption that increased no. of susceptibles among children implies the need for vaccine
- To drive vaccine recommendations, more data is needed
 - Many seroprevalence studies
 - Limited surveillance data (morbidity, mortality) on global, regional, or country level

WHO Vaccine Introduction Guidelines (2006)

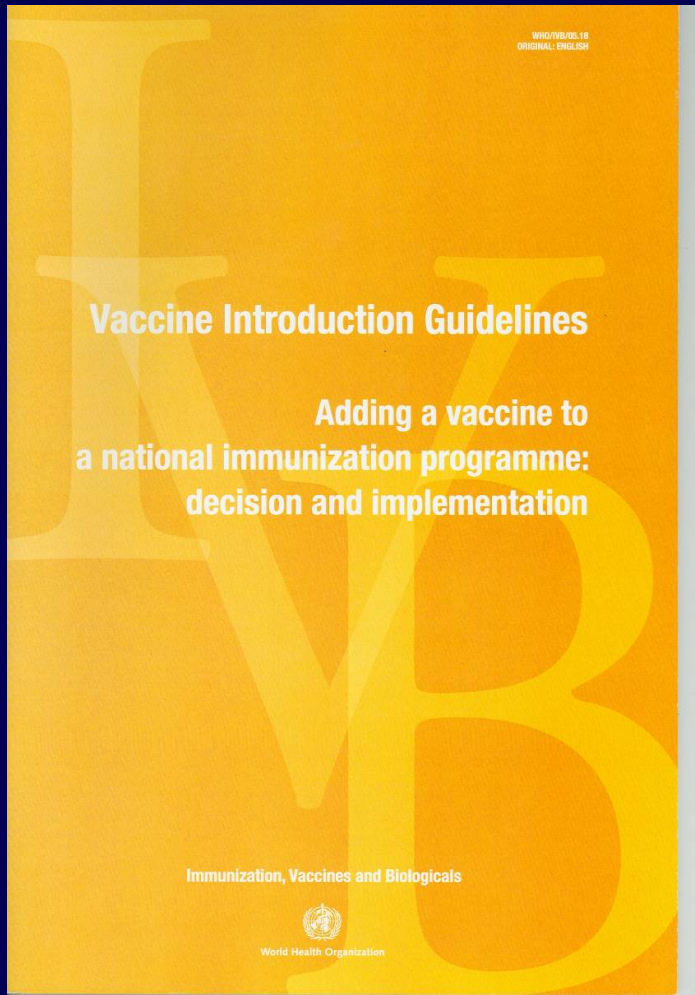
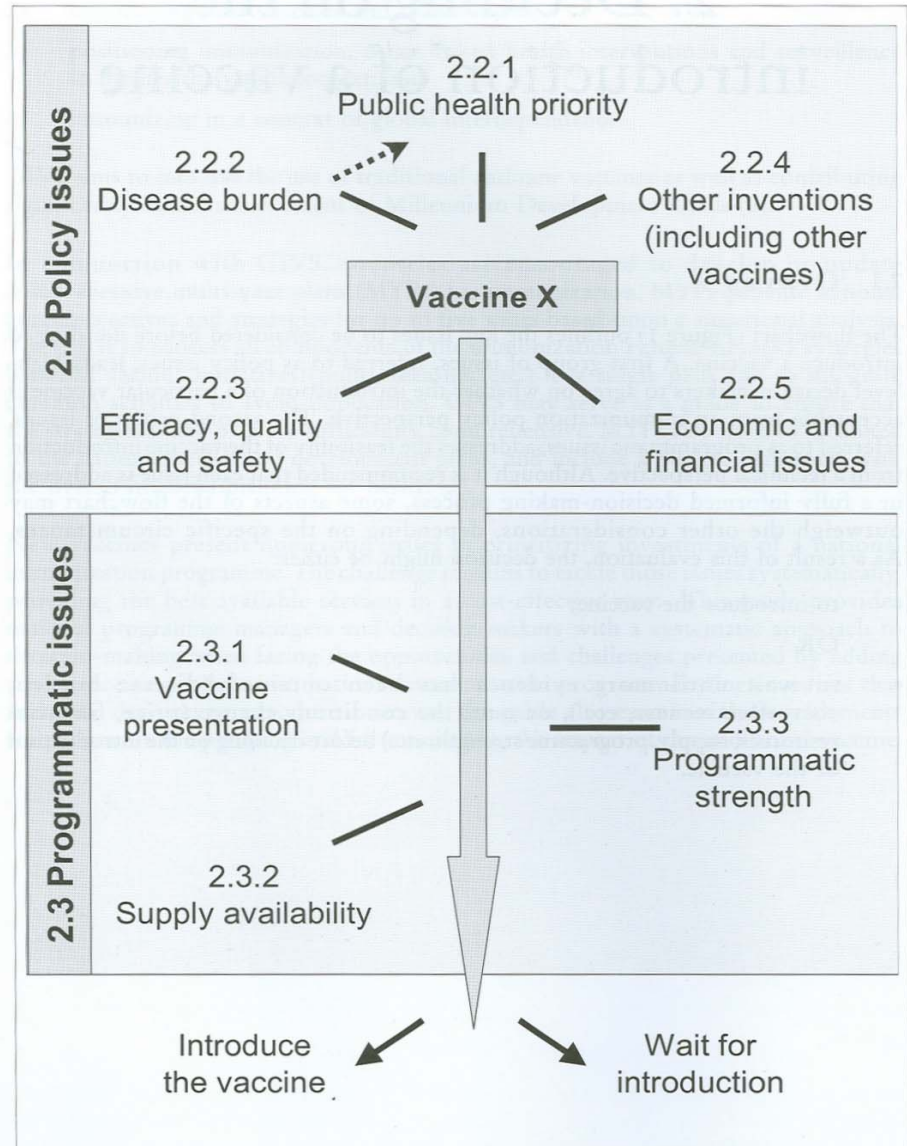
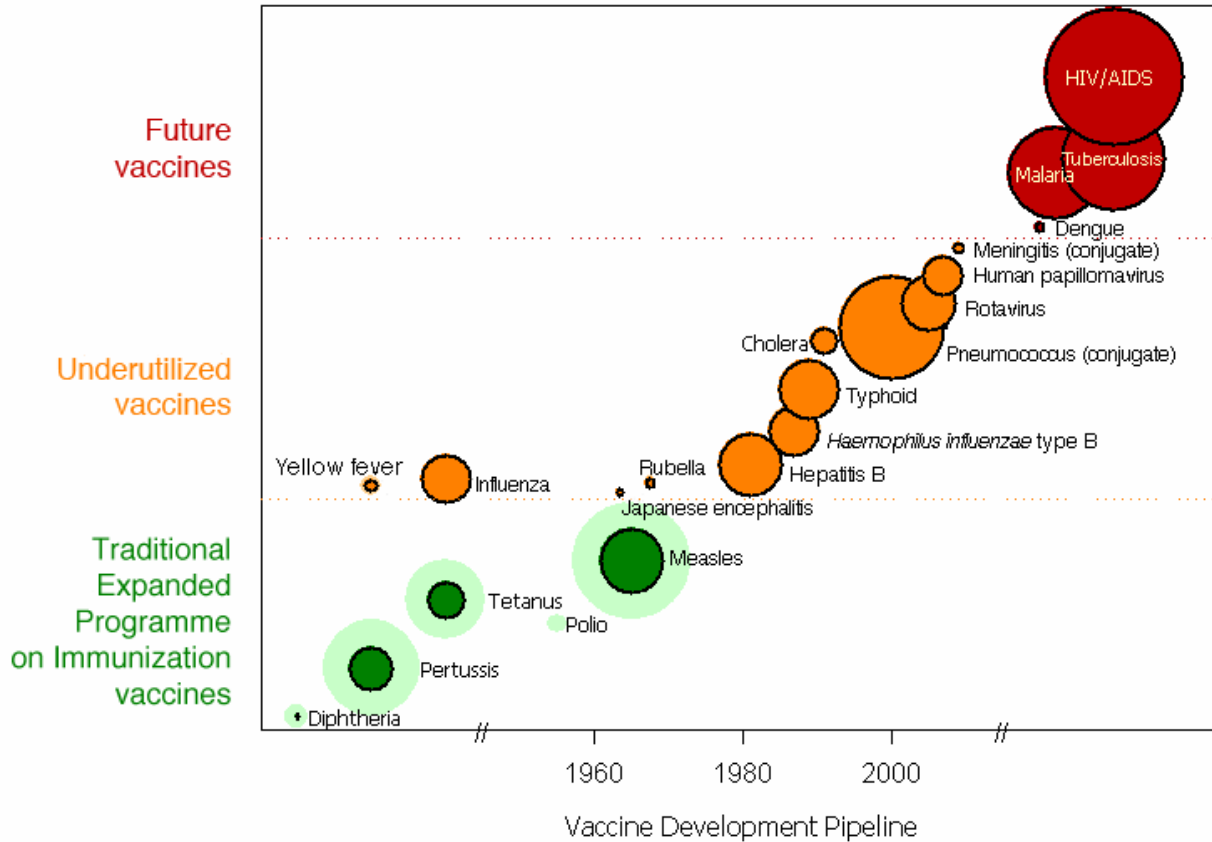


Figure 1: Key issues



The Evolving Vaccine Pipeline (WHO, 2006)

The Evolving vaccine pipeline



Note the halos represent deaths currently being averted, and solid circles represent deaths estimated to occur (as of 2002).
 Source: World Health Organization Initiative for Vaccine Research, August 2006

Disease global
 (2002) Est. deaths

- JE 10,000
- Dengue 20,000
- Yellow fever 30,000
- Mening 30,000
- Cholera 100,000
- HPV 250,000
- Influenza 400,000
- Hib 100,000

Global Estimates, Hepatitis A

- Projects
 - 1) Institute of Medicine study, 1986 (1979 estimates)
 - 2) International Hepatitis Symposium, Hadler, 1991 (1990 estimates)
- Sources of data
 - Reported age-specific incidence of “infectious hepatitis” from WHO annual statistics (1975-1981)
 - Data from serologic testing of acute hepatitis (regions available: U.S., western Europe, South America)
 - Assumptions:
 - Children: 80% acute hepatitis is A
 - Adults: 30% of acute hepatitis is A
- Methods
 - Derived estimated number of total cases, severe cases, and deaths by region and age groups
 - For regions where only subregional data available, applied highest rate to entire region
 - Assumed U.S. age distribution of reported cases, where age-specific data not available
 - Assumed U.S. age distribution of severe cases and deaths
 - Assumed U.S. overall case fatality rate (0.3%) and proportion of severe (hospitalized) cases (33%)

Global Estimates, Hepatitis A, by Region 1979 and 1990

Region	1979			1990		
	Population (millions)	Estimated Incidence (per 100,000) per year	Estimated Cases (1,000s) per year	Population (millions)	Estimated Incidence (per 100,000) per year	Estimated Cases (1,000s) per year
North America	248	10	25	275	10	28
Central/South America	351	20-40	126	453	20-40	162
Europe	748	5-60	261	791	5-60	278
Africa/Middle East	575	20-60	173	827	20-60	251
Asia	2,339	10-30	551	2,893	10-30	676
Oceania	23	15-30	5	28	15-30	5
Total			1,141			1,399

Sources: Institute of Medicine (1986), Hadler (1991)

Global Estimates (no. cases), Hepatitis A, by Age Group and Severity of Illness, 1984

	Age group				
Severity of Illness	< 5 years	5-14 years	15-59 years	60+ years	Total
Typical illness (moderate pain/impairment)	139,843	635,651	2,256,561	149,378	3,181,433
Severe illness (e.g. requiring hospitalization)	31,735	158,675	1,221,794	206,277	1,618,481
Death	0	1,144	5,146	8,005	14,295

Source: Institute of Medicine (1986)

Note: Includes 5-fold factor for underreporting

Current data limited

- Old
- Missing country, regional data
- Developed-country data used to estimate proportion of acute hepatitis as hepatitis A; age distribution of cases; distribution of severity of cases (including case fatality rate)

Global Burden of Disease Project

- International collaborative project currently in progress
- Objectives
 - Generate 2005 (and 1990) burden of disease estimates
 - Mortality (no. deaths)
 - Morbidity (no. cases)
 - Disability (DALYs)
- Regional-, age- and sex-specific
- Working group formed and recently met
- For hepatitis A, will involve collection of pre-existing data
 - Surveillance data
 - Seroprevalence data
- Information can be used to help form the basis for more definitive global, regional and country vaccination recommendations

Selected Disease-Related Criteria Considered Important in Decision Making for Vaccine Introduction

Mortality (no. deaths)
Morbidity (no. cases)
Severity of Symptoms/Case Fatality Rate/Long-term sequelae
Epidemic/Pandemic Potential
Disease Incidence in Highest Burden Regions
Inequity
Economic Impact
Alternative Preventive Measures/Treatments

Evaluating Potential for Hepatitis A Vaccine Use

- Global level, relative mortality low
- Multiple seroprevalence studies demonstrating epidemiologic shift
- Need for improved surveillance data, to document:
 - Burden of disease (cases, deaths)
 - Regional, country level
 - Outbreak potential and impact
 - Economic impact of disease