Evolution of Global Hepatitis A
Epidemiology

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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

- High
- Intermediate
- Low
- Very low
Global Patterns of Hepatitis A Endemicity

Anti-HAV Prevalence
- High
- High/Intermediate
- Intermediate
- Low
- Very Low
### Global Patterns of Hepatitis A

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

Source: Hadler; Viral Hepatitis and Liver Disease, 1991
Epidemiologic Shift in Prevalence of Antibodies to Hepatitis A Virus

Improvements in living conditions
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

Source: Almuneef et al, Vaccine, 2006
Hepatitis A Outbreaks, Saudi Arabia, 1997 and 2003

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

- Outside RR
- PHCC OA
- East Affif
- West Affif

Hepatitis cases

Onset by international week

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

- Year 2003
- Year 2002

Number of cases

International weeks

Outside RR - Outside Riyadh Region (Madinah, Taif, Qassim Regions)
PHCC OA - Primary Health Care Center outside Affif
# Estimated Force of Infection, by Region

<table>
<thead>
<tr>
<th>Region</th>
<th>Total</th>
<th>Africa</th>
<th>America</th>
<th>Asia</th>
<th>Europe</th>
<th>Middle East</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Surveys</td>
<td>157</td>
<td>7</td>
<td>31</td>
<td>40</td>
<td>62</td>
<td>17</td>
</tr>
<tr>
<td>Decreasing prevalence</td>
<td>66%</td>
<td>0</td>
<td>42%</td>
<td>57%</td>
<td>97%</td>
<td>41%</td>
</tr>
</tbody>
</table>

**Estimated mean infection rate per 1000 susceptibles per year**

<table>
<thead>
<tr>
<th>Surveys</th>
<th>1990 (n=74)</th>
<th>1991 (n=83)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>190</td>
<td>160</td>
</tr>
<tr>
<td>America</td>
<td>620</td>
<td>490</td>
</tr>
<tr>
<td>Asia</td>
<td>680</td>
<td>250</td>
</tr>
<tr>
<td>Europe</td>
<td>310</td>
<td>110</td>
</tr>
<tr>
<td>Middle East</td>
<td>20</td>
<td>10</td>
</tr>
</tbody>
</table>

Source: Jacobsen and Koopman. International J of Epi, 2005
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
The Evolving Vaccine Pipeline (WHO, 2006)

Disease Est. global deaths (2002)

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

Note: The sizes of the globes represent the number of deaths currently estimated to occur (as of 2002). Solid circles indicate deaths that are estimated to occur within the next five years, whereas hollow circles represent deaths that will occur in the next five years. Source: World Health Organization Initiative for Vaccine Research, August 2006
Global Estimates, Hepatitis A

• Projects
  – 1) Institute of Medicine study, 1986 (1979 estimates)
  – 2) International Hepatitis Symposium, Hadler, 1991 (1990 estimates)

• Sources of data
  – 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 case fatality rate (0.3%) and proportion of severe (hospitalized) cases (33%)
## Global Estimates, Hepatitis A, by Region 1979 and 1990

<table>
<thead>
<tr>
<th>Region</th>
<th>Population (millions)</th>
<th>1979</th>
<th>1990</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Estimated Incidence (per 100,000) per year</td>
<td>Estimated Cases (1,000s) per year</td>
</tr>
<tr>
<td>North America</td>
<td>248</td>
<td>10</td>
<td>25</td>
</tr>
<tr>
<td>Central/South America</td>
<td>351</td>
<td>20-40</td>
<td>126</td>
</tr>
<tr>
<td>Europe</td>
<td>748</td>
<td>5-60</td>
<td>261</td>
</tr>
<tr>
<td>Africa/Middle East</td>
<td>575</td>
<td>20-60</td>
<td>173</td>
</tr>
<tr>
<td>Asia</td>
<td>2,339</td>
<td>10-30</td>
<td>551</td>
</tr>
<tr>
<td>Oceania</td>
<td>23</td>
<td>15-30</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>1,141</td>
<td></td>
</tr>
</tbody>
</table>

Sources: Institute of Medicine (1986), Hadler (1991)
Global Estimates (no. cases), Hepatitis A, by Age Group and Severity of Illness, 1984

<table>
<thead>
<tr>
<th>Severity of Illness</th>
<th>&lt; 5 years</th>
<th>5-14 years</th>
<th>15-59 years</th>
<th>60+ years</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical illness</td>
<td>139,843</td>
<td>635,651</td>
<td>2,256,561</td>
<td>149,378</td>
<td>3,181,433</td>
</tr>
<tr>
<td>Severe illness</td>
<td>31,735</td>
<td>158,675</td>
<td>1,221,794</td>
<td>206,277</td>
<td>1,618,481</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>1,144</td>
<td>5,146</td>
<td>8,005</td>
<td>14,295</td>
</tr>
</tbody>
</table>

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

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