Hepatitis A Virus
Hepatitis A - Clinical Features

- Incubation period: Average 30 days
  Range 15-50 days

- Jaundice by age group:
  <6 yrs, <10%
  6-14 yrs, 40%-50%
  >14 yrs, 70%-80%

- Complications:
  Fulminant hepatitis
  Cholestatic hepatitis
  Relapsing hepatitis

- Chronic sequelae:
  None
### Age-specific Mortality Due to Hepatitis A

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Case-Fatality (per 1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>3.0</td>
</tr>
<tr>
<td>5-14</td>
<td>1.6</td>
</tr>
<tr>
<td>15-29</td>
<td>1.6</td>
</tr>
<tr>
<td>30-49</td>
<td>3.8</td>
</tr>
<tr>
<td>&gt;49</td>
<td>17.5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>4.1</strong></td>
</tr>
</tbody>
</table>

Source: Viral Hepatitis Surveillance Program, 1983-1989
Hepatitis A Virus Infection
Typical Serologic Course

- Symptoms
- Fecal HAV
- ALT
- IgM anti-HAV

Total anti-HAV

Titer

Months after Exposure

0 1 2 3 4 5 6 7 8 9 10 11 12
Concentration of Hepatitis A Virus in Various Body Fluids

- Feces
- Serum
- Saliva
- Urine

Infectious Doses per ml

Source: Viral Hepatitis and Liver Disease 1984;9-22
J Infect Dis 1989;160:887-890
Hepatitis A Virus Transmission

- Close personal contact
  (e.g., household contact, sex contact, child day care centers)
- Contaminated food, water
  (e.g., infected food handlers, raw shellfish)
- Blood exposure (rare)
  (e.g., injecting drug use, transfusion)
Incidence of Hepatitis A, United States, 1952-1993

Year

Rate (per 100,000)

Source: CDC, National Notifiable Diseases Surveillance System
Age-specific Incidence of Hepatitis A
United States, 1983-93

Source: CDC, National Notifiable Diseases Surveillance System
Sources of Hepatitis A Virus Infection by Mutually Exclusive Groups, United States, 1983-93

Percentage of Cases

Year


Personal contact
Day care center
Foreign travel
Drug use
Outbreak

Source: CDC, Viral Hepatitis Surveillance Program
## Global Patterns of Hepatitis A Virus Transmission

<table>
<thead>
<tr>
<th>Endemicity</th>
<th>Disease Rate</th>
<th>Peak Age of Infection</th>
<th>Transmission Patterns</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Low to High</td>
<td>Early childhood</td>
<td>Person to person; outbreaks uncommon</td>
</tr>
<tr>
<td>Moderate</td>
<td>High</td>
<td>Late childhood/ young adults</td>
<td>Person to person; food and waterborne outbreaks</td>
</tr>
<tr>
<td>Low</td>
<td>Low</td>
<td>Young adults</td>
<td>Person to person; food and waterborne outbreaks</td>
</tr>
<tr>
<td>Very low</td>
<td>Very low</td>
<td>Adults</td>
<td>Travelers; outbreaks uncommon</td>
</tr>
</tbody>
</table>
# Hepatitis A Vaccine Efficacy Studies

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Site/Age Group</th>
<th>N</th>
<th>Vaccine Efficacy (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAVRIX® (SKB)</td>
<td>Thailand</td>
<td>38,157</td>
<td>94% (79%-99%)</td>
</tr>
<tr>
<td>2 doses 360 EL.U.</td>
<td>1-16 yrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAQTA™ (Merck)</td>
<td>New York</td>
<td>1,037</td>
<td>100% (85%-100%)</td>
</tr>
<tr>
<td>1 dose 25 units</td>
<td>2-16 yrs</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

JAMA 1994;271:1363-4
Hepatitis A Vaccination Strategies

Epidemiologic Considerations

- Many cases occur in community-wide outbreaks
  - no risk factor identified for most cases
  - highest attack rates in 5-14 year olds
  - children serve as reservoir of infection
- Persons at increased risk of infection
  - travelers
  - homosexual men
  - injecting drug users
Routine Childhood Hepatitis A Vaccination

• Benefits
  – established delivery system
  – vaccination before risk period
  – potential to interrupt transmission

• Unresolved issues/considerations
  – immunogenicity in infants
  – development of combination vaccines
  – duration of protection
  – cost-effectiveness
ACIP Recommendations - Hepatitis A Vaccine
Preexposure Vaccination

• Persons at increased risk for infection
  – travelers to intermediate and high HAV-endemic countries
  – homosexual and bisexual men
  – drug users
  – persons with chronic liver disease

• Communities with high rates of hepatitis A (e.g., Alaska Natives, American Indians)
  – routine childhood vaccination
## Features of Community-wide Hepatitis A Outbreaks

<table>
<thead>
<tr>
<th>Type of Community</th>
<th>Anti-HAV Prevalence</th>
<th>Usual Age of Case-patients</th>
<th>Annual Incidence/100,000</th>
<th>Outbreak Periodicity</th>
<th>Populations</th>
</tr>
</thead>
<tbody>
<tr>
<td>High rate</td>
<td>&lt;5 yrs old</td>
<td>5-14 yrs</td>
<td>700-1000</td>
<td>5-10 yrs</td>
<td>well defined geographically or ethnically</td>
</tr>
<tr>
<td></td>
<td>30%-40%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;15 yrs old</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>70% -100%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate rate</td>
<td>&lt;5 yrs old</td>
<td>5-29 yrs</td>
<td>50-200</td>
<td>may be periodic</td>
<td>less defined than in high-rate communities</td>
</tr>
<tr>
<td></td>
<td>10%-25%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;15 yrs old</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;50%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
ACIP Recommendations - Hepatitis A Vaccine
Control of Community-wide Outbreaks

High-rate communities

• Routine vaccination of young children
• Accelerated catch-up vaccination of older children
Intermediate-rate communities

- Targeted vaccination can be considered for groups or areas with highest disease rates (e.g., specific age groups, census tracts, drug users)

- Factors to consider:
  - feasibility of vaccinating target groups
  - program cost
  - ability to sustain vaccination of young children
ACIP Recommendations - Hepatitis A Vaccine
Prevaccination Testing

• Considerations:
  – cost of vaccine
  – cost of serologic testing (including visit)
  – prevalence of infection
  – impact on compliance with vaccination

• Likely to be cost-effective for:
  – adults born, or who lived in, high endemic areas
  – adults >40 years of age
  – older adolescents and young adults in certain groups (American Indians, Alaska Natives, Pacific Islanders)
ACIP Recommendations - Hepatitis A Vaccine

Postvaccination Testing

- Not recommended because of the high response rate among vaccinees
- No commercially available test to measure vaccine response
## Recommended Doses and Schedules of Hepatitis A Vaccine

<table>
<thead>
<tr>
<th>Group</th>
<th>Age</th>
<th>No. Doses</th>
<th>Doses EL.U.* (ml)</th>
<th>Schedule (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children and adolescents</td>
<td>2-18 years</td>
<td>3</td>
<td>360 (0.5)</td>
<td>0, 1, 6-12</td>
</tr>
<tr>
<td>Adults</td>
<td>&gt;18 years</td>
<td>2</td>
<td>1,440 (1.0)</td>
<td>0, 6-12</td>
</tr>
</tbody>
</table>

*ELISA units
Hepatitis A Prevention - Immune Globulin

• Preexposure
  – travelers to intermediate and high HAV-endemic regions

• Postexposure (within 14 days)
  Routine
  – household and other intimate contacts
  Selected situations
  – institutions (e.g., day care centers)
  – common source exposure (e.g., food prepared by infected food handler)