Update on Hepatitis A Disease Burden and Hepatitis A Population Protection

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October 29, 2014
Hepatitis A Vaccine History in the United States
ACIP hepatitis A vaccine recommendations

- **Targeted vaccination, 1996-1999**
  - **1996**
    - Children at age 2 years in communities with high rates of disease
    - Children through teen years in outbreaks
  - **1999**
    - Recommended in 11 states with rates 2x the national average
    - Considered in 6 states with rates above the national average

MMWR 1996;45(RR-15); MMWR 1999;48(RR-12); MMWR 2006;55(RR-7)
ACIP hepatitis A vaccine recommendations-II

Universal childhood vaccination, 2006

- Recommended for use at age 12-23 months in all states
- Continue existing vaccination programs for ages 2-18 years
- Consider catch-up vaccination in outbreaks and areas with increasing disease rates
- Any person wishing to obtain immunity

Note: No routine recommendation for children ages >23 months
ACIP hepatitis A vaccine recommendations-III
Groups at increased risk of HAV or severe HAV disease

- Travelers
- Men who have sex with men
- Users of injection and non-injection drugs
- Persons with clotting-factor disorders
- Persons who work with nonhuman primates
- Persons who anticipate close personal contact with an international adoptee
- Persons with chronic liver disease
- Post-exposure prophylaxis for healthy persons aged 12 months-40 years
Rates of Reported Acute Hepatitis A Cases
United States, 1966-2012

1971: 59,606 cases, Rate = 28.9

1996: Vaccine recommended
31,032 cases, Rate = 11.7

2011: 1,398 cases,
Rate = 0.4

1996-2011: 95.5% decrease in reported cases

National Notifiable Diseases Surveillance System (NNDSS); Armstrong GL. Pediatrics 2007;119:e22-9
Number and rate of reported cases of hepatitis A (2008-2013)

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Reported Cases</th>
<th>Rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>2585</td>
<td>0.9</td>
</tr>
<tr>
<td>2009</td>
<td>1987</td>
<td>0.6</td>
</tr>
<tr>
<td>2010</td>
<td>1670</td>
<td>0.5</td>
</tr>
<tr>
<td>2011</td>
<td>1398</td>
<td>0.4</td>
</tr>
<tr>
<td>2012</td>
<td>1562</td>
<td>0.5</td>
</tr>
<tr>
<td>2013</td>
<td>1781</td>
<td>0.6</td>
</tr>
</tbody>
</table>

### Rate of hepatitis A by US region (2011-2013)

<table>
<thead>
<tr>
<th>US Region</th>
<th>Rate per 100,000 pop</th>
</tr>
</thead>
<tbody>
<tr>
<td>New England</td>
<td>0.5</td>
</tr>
<tr>
<td>Mid. Atlantic</td>
<td>0.6</td>
</tr>
<tr>
<td>E.N. Central</td>
<td>0.5</td>
</tr>
<tr>
<td>W.N. Central</td>
<td>0.6</td>
</tr>
<tr>
<td>S. Atlantic</td>
<td>0.5</td>
</tr>
<tr>
<td>E.S. Central</td>
<td>0.5</td>
</tr>
<tr>
<td>W.S. Central</td>
<td>0.5</td>
</tr>
<tr>
<td>Mountain</td>
<td>0.8</td>
</tr>
<tr>
<td>Pacific</td>
<td>0.7</td>
</tr>
</tbody>
</table>

**Rate per 100,000 pop**

**2011**

**2012**

**2013**

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Rates of reported acute hepatitis A
United States, 2007-2012

Healthy People 2020 Target:
0.3 cases per 100,000 population

National Notifiable Diseases Surveillance System (NNDSS);
Percent of cases by year in age groups (0-9, 10-19, ≥20)

Hepatitis A hospitalization trends, 2002-2011

- National Inpatient Sample (Healthcare Utilization Project or HCUP)
  - Primary discharge diagnosis of hepatitis A

- Mean age of persons hospitalized for hepatitis A has increased significantly over the study time period (mean age 37.6 years in 2002-2003 compared to 45.5 years in 2010-2011)

![Graph showing mean age trends](image)

### Hospitalizations in reported cases of hepatitis A — United States, 2009-2012

<table>
<thead>
<tr>
<th>Year</th>
<th>Hepatitis A cases reported</th>
<th>Availability of valid data† for hospitalization</th>
<th>Cases hospitalized§</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No.</td>
<td>No.</td>
</tr>
<tr>
<td>2009</td>
<td>1,987</td>
<td>1,182</td>
<td>59.5</td>
</tr>
<tr>
<td>2010</td>
<td>1,670</td>
<td>1,020</td>
<td>61.1</td>
</tr>
<tr>
<td>2011</td>
<td>1,398</td>
<td>798</td>
<td>57.1</td>
</tr>
<tr>
<td>2012</td>
<td>1,562</td>
<td>1,022</td>
<td>65.4</td>
</tr>
</tbody>
</table>

†Case reports for which questions regarding hospitalization were answered with “yes” or “no.”  
§Numbers and percentages represent only cases with data regarding hospitalization; numbers likely are underestimates.

Hospitalizations of HAV cases has increased since 2009

National Notifiable Diseases Surveillance System (NNDSS); Division of Viral Hepatitis Surveillance Report (2009-2012)
Hepatitis A deaths, 1990-2012

NCHS mortality files for vaccine preventable diseases (1990-2012)
Includes case reports indicating the presence of at least one of the following risks 2–6 weeks prior to onset of acute, symptomatic hepatitis A: 1) having traveled to hepatitis A-endemic regions of Mexico, South/Central America, Africa, Asia/South Pacific, or the Middle East; 2) having sexual/household or other contact with suspected/confirmed hepatitis A patient; 3) being a child/employee in day care center/nursery/preschool or having had contact with such persons; 4) being involved in a foodborne/waterborne outbreak; 5) being a man who has sex with men; and 6) using injection drugs.
Potential source of infection or risk factor for hepatitis A, Emerging Infections Program (EIP) hepatitis surveillance sites, 2005-2007

Hepatitis A Vaccine Coverage

2012
HepA ≥ 1-dose = 81.5%
HepA ≥ 2-dose = 53.0%

Healthy People 2020 target for hepatitis A: 85% 2-dose coverage

Estimated vaccination coverage among Adolescents 13-17 years, NIS Teen, 2006-2012

* ≥1 dose Tdap vaccine on or after age 10 years.
† ≥1 dose MenACWY vaccine.
§ HPV vaccine, either bivalent or quadrivalent, among females.
ACIP recommends either bivalent or quadrivalent vaccine for females.
¶ HPV vaccine quadrivalent, among males. ACIP recommends the quadrivalent vaccine for males; however, some males might have received bivalent vaccine

2012 Preliminary Data
HepA ≥ 1-dose = ~60%
HepA ≥ 2-dose = ~48%

Hepatitis A vaccine ≥2-dose coverage for ages 19-49 years, National Health Interview Survey (NHIS), 2011, overall and two risk groups

- 12.5% of 19-49 year olds traveled outside the U.S. to countries other than Japan, Australia, New Zealand, Canada or the other countries of Europe since 1995.
- 20.1% of 19-49 year olds were no travel outside the U.S. to countries other than Japan, Australia, New Zealand, Canada or the other countries of Europe since 1995.
- 8.4% of 19-49 year olds had chronic liver disease (CLD).

Anti-HAV Seroprevalence
Prevalence of anti-HAV by age group
NHANES, United States

*P ≤ 0.005
Hepatitis A Outbreak
Food Associated Exposure Risk
Food associated outbreaks-2013

- Multi-state outbreak associated with frozen pomegranate arils imported from Turkey
  - 165 cases
    - 7% aged <18 years
    - 93% aged ≥18 years
  - Complications
    - Overall 44% hospitalized
      - 18% aged <18 years
      - 45% aged ≥18 years
    - 2 cases fulminant hepatitis
    - 1 case liver transplant

- Ongoing berry-associated outbreaks in multiple European countries

Trends in the volume of fruit and vegetables imported into the US, 1999-2013

1000 Metric Tons


Fruit
Vegetables

12,383.8
8,974.7

Examples of countries with intermediate and high hepatitis A viral prevalence exporting fruits and vegetables to United States

- **Fruit**
  - Mexico
  - Chile
  - Costa Rica
  - Guatemala
  - Ecuador
  - Argentina
  - Brazil

- **Vegetables**
  - Mexico
  - Peru
  - Guatemala
  - India

Estimated prevalence of hepatitis A virus, 2005

Summary
Summary

- Increasing proportion of adults in United States are susceptible to hepatitis A
  - Reduced exposure to HAV early in life
  - Significant decreases in anti-HAV seroprevalence in older adults (≥ 40 years)
  - Low 2-dose vaccination coverage exists in adults, including high risk adults (e.g., travelers -20%, chronic liver disease -17%)
  - Morbidity and mortality increases with age

- Suboptimal hepatitis A vaccination 1 and 2-dose coverage among young children
Increasing HAV cases and rates in United States

- Increase in HAV cases in 2012 and 2013; first since 1995-1996
- HAV infection rates increased from 2011-2012 for ages 20-29 years, and ages ≥40 years

Hospitalization

- Mean age of persons hospitalized for hepatitis A has increased significantly from 2002-2003 to 2010-2011
- Hospitalization rates for reported hepatitis A cases have increased from 2005 to 2011
HAV remains endemic in many areas of the world

- Risk for travelers to intermediate, high endemic countries
- Risk for consumption of imported HAV contaminated food from global sources
  - Herd immunity does not protect against foodborne exposure

- No routine or catch-up hepatitis A vaccine recommendation for adolescents or adults
Hepatitis A vaccination - Considerations

- ACIP Hepatitis Work Group
  - Strategies to address increasing number/rate of acute hepatitis A and continue progress to HP2020 goal
    - Catch-up vaccination for children/teens age 2 -18 years
      - Continuing exposure to hepatitis A virus
      - Future protection of the adult population
      - Maximize herd immunity from childhood vaccination by expanding the age range of routine/catch-up vaccination
    - Other strategies (e.g., vaccination for other ages)
    - Additional information is needed
Hepatitis A vaccination - Additional information

- Model hepatitis A disease and cost-effectiveness with higher hepatitis A vaccination coverage among children and adolescents, and/or subsets of adults
  - Planning underway

- GRADE for hepatitis A one and two dose vaccine efficacy (immunogenicity), safety, long term protection
  - Systematic review in progress

- Study of hepatitis A vaccine immune response 2 weeks after first dose to consider vaccine for post-exposure prophylaxis among adults ages >40 years
  - Planning underway
Acknowledgements

- **NCHHSTP/ Division of Viral Hepatitis**
  - Mona Doshani
  - Alaya Koneru
  - Kashif Iqbal
  - John Ward

- **NCIRD/ Immunization Services Division**

- **ACIP Hepatitis Work Group**

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    - Melissa Collier
    - Mark Gershman
    - Aaron Harris
    - Scott Holmberg
    - Shahed Iqbal
    - Ruth Jiles
    - Erin Kennedy
    - Monina Klevens
    - Trudy Murphy
    - Sarah Schillie
    - Philip Spradling
    - Donna Weaver
    - Matthew Wise