Hepatitis A Outbreaks

Noele Nelson, MD, PhD, MPH
CDC Lead, ACIP Hepatitis Vaccines Work Group

Advisory Committee on Immunization Practices

October 25, 2017
Hepatitis A Virus Outbreaks – United States, 2016–2017

- CDC has assisted in five hepatitis A virus (HAV) outbreaks since July 1, 2016
  - 2 Foodborne Transmission
  - 3 Person-to-Person Transmission

- Three Epi-Aids

- >1,600 outbreak associated cases reported since July 1, 2016

- Multiple ongoing outbreaks
California

- California is currently experiencing the largest person-to-person hepatitis A outbreak in the United States since the hepatitis A vaccine became available in 1996

Epidemiology

- Transmission - person-to-person and through contact with fecally contaminated environments
- Population - mostly homeless and/or persons who use injection or non-injection drugs
- HAV Genotype - IB

Table. Outbreak Associated Hepatitis A infections by California Jurisdiction

<table>
<thead>
<tr>
<th>Jurisdiction</th>
<th>Cases</th>
<th>Hospitalizations</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>San Diego</td>
<td>507</td>
<td>351</td>
<td>19</td>
</tr>
<tr>
<td>Santa Cruz</td>
<td>73</td>
<td>33</td>
<td>0</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>9</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>11</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>600</td>
<td>395</td>
<td>19</td>
</tr>
</tbody>
</table>

https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/Immunization/Hepatitis-A-Outbreak.aspx
San Diego County

- Since early 2017, the Public Health Services Division, in the County of San Diego Health and Human Services Agency, has been investigating a local Hepatitis A outbreak
- September 1, San Diego County declared a local public health emergency
- **As of October 19, 2017**
  - 516 cases
  - 357 (69.2%) hospitalized
  - 19 (3.7%) died

http://www.sandiegocounty.gov/content/sdc/hhsa/programs/phs/community_epidemiology/dc/Hepatitis_A/outbreak.html
Outbreak-associated hepatitis A cases by week of onset – San Diego

As of 9/11/2017

Of the 325 cases with test results available for review, 64 (20%) have chronic hepatitis C infection, and 17 (5%) have chronic hepatitis B infection.

http://www.sandiegocounty.gov/content/sdc/hhsa/programs/phs/community_epidemiology/dc/Hepatitis_A/outbreak.html
San Diego County Map:
Hepatitis A Outbreak Cases by Zip Code(s)

As of 10/19/2017
## Utah

<table>
<thead>
<tr>
<th>Outbreak-Associated Cases</th>
<th>45</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset Date Range</td>
<td>5/8/2017 - 10/13/2017</td>
</tr>
<tr>
<td>Age Range</td>
<td>23 - 69 years, median age 40 years</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>27 60.0%</td>
</tr>
<tr>
<td>Deaths</td>
<td>0 0.0%</td>
</tr>
<tr>
<td>Risk Factors</td>
<td></td>
</tr>
<tr>
<td>Homelessness and Drug Use</td>
<td>22 48.8%</td>
</tr>
<tr>
<td>Drug Use</td>
<td>9 17.1%</td>
</tr>
<tr>
<td>Homelessness</td>
<td>3 7.3%</td>
</tr>
<tr>
<td>Epi-Linked</td>
<td>5 9.8%</td>
</tr>
<tr>
<td>Travel</td>
<td>2 4.9%</td>
</tr>
<tr>
<td>Unknown</td>
<td>4 9.8%</td>
</tr>
<tr>
<td>Incarcerated</td>
<td>9 20%</td>
</tr>
</tbody>
</table>

### Co-infection

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B (HBV)</td>
<td>7</td>
<td>15.6%</td>
</tr>
<tr>
<td>Hepatitis C (HCV)</td>
<td>15</td>
<td>33.3%</td>
</tr>
<tr>
<td>HBV &amp; HCV</td>
<td>6</td>
<td>13.3%</td>
</tr>
</tbody>
</table>

Last updated 10/24/17

Michigan

- Transmission - direct person-to-person spread
- HAV Genotype 1B
- Greater risk thought to be associated with:
  - Injection and non-injection drug use,
  - Homelessness or transient housing, and

Southeast Michigan Hepatitis A Outbreak Cases and Deaths as of October 18, 2017*
*Table will be updated weekly by 4:00pm each Friday

<table>
<thead>
<tr>
<th>Cases</th>
<th>Hospitalizations</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>431</td>
<td>348 (85.7%)</td>
<td>17 (4.2%)</td>
</tr>
</tbody>
</table>

Please note: Affected jurisdictions include City of Detroit, and Lapeer, Livingston, Macomb, Monroe, Oakland, St. Clair, Sanilac, Washtenaw & Wayne Counties. Table does not include all reported hepatitis A cases in the region; only those that are identified as outbreak-related. More descriptive data on the current outbreak can be found within the Comprehensive Summary. Data are provisional and subject to change.

http://www.michigan.gov/mdhhs/0,5885,7-339-71550_2955_2976_82305_82310-447907--,00.html
Confirmed Hepatitis A Case Onset by Week for Detroit City, Lapeer, Livingston, Macomb, Monroe, Oakland, St. Clair, Sanilac, Washtenaw and Wayne Counties for cases referred Aug 1, 2016 to Oct 18, 2017

http://www.michigan.gov/mdhhs/0,5885,7-339-71550_2955_2976_82305_82310-447907--,00.html
New York City, January – August, 2017

- Increase in reported hepatitis A infections among MSM, 51 cases
- Genotype 1A
  - 24/25 serum specimens matched strains circulating in Europe among European MSM

Shifting Hepatitis A Virus Epidemiology

- Past outbreaks were associated with asymptomatic children
- A large population of adults are not immune to hepatitis A virus
  - Prevalence anti-HAV, NHANES 2009-2010
    - Overall 26.5%
    - 22.2%, age 20-29
    - ~13.5%, age 30-49
    - 20.9%, age 50-59
    - 36.9%, age ≥60
- Older individuals are more likely to experience severe disease and adverse outcomes
- Vaccination uptake among at-risk adults is low
  - 2-dose Coverage for Ages 19-49 years (NHIS)
    - 2015, overall 12.3%
    - 2014, chronic liver disease, 18.2%
An Emerging Genotype?

- Genotype IA commonly circulates in North and South America
- Most recent outbreaks are genotype IB
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

- **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
Hepatitis A Outbreaks Identified in the United States – 1994–2017


CDC FoodTool
Hepatitis A Outbreaks Identified in the United States – 1994–2017

CDC FoodTool
Reported Cases Associated with HAV Outbreaks – United States, 2007–2017

Vaccine Supply, I

- In light of the ongoing outbreaks of Hepatitis A among adults in the US, the demand for adult Hepatitis A vaccine has increased substantially over the past 6 months and vaccine supply to meet this unexpected demand in the US has become constrained.

- Both manufacturers are exploring options to increase domestic supply to address increased demand for the vaccine.

- Both manufacturers are working collaboratively with CDC to monitor and manage public and private vaccine orders to make the best use of adult Hepatitis A vaccine during this period of unexpected increased demand.

- To address constrained supplies, CDC staff are working directly with public health officials to provide guidance about how best to target vaccine distribution.

- These constraints do not apply to the pediatric Hepatitis A vaccine supply in the US.
Vaccine Supply, II

In terms of current product availability

- **Merck:**
  - Supply of available Hepatitis A vaccine will be intermittent through 2017. Following an outage during part of October, orders are anticipated to ship beginning the week of 10/30.

- **GSK’s**
  - Pre-filled syringes are currently out of stock but a limited number of vials are available to order, with ordering controls in place.
  - In addition, GSK is maintaining a limited medical reserve and continues to consult with public health officials to help support urgent public health needs.
  - GSK anticipates limited resupply of pre-filled syringes in early/mid November 2017.
  - Twinrix, GSK’s combination Hep A/Hep B vaccine is currently available for order.
Hepatitis A Among Homeless Populations

- Little is known about hepatitis A immunity among homeless populations in the US

- Homelessness is not considered an independent risk factor for HAV infection

- Older age, duration of homelessness, and injection drug use may indicate HAV immunity

Work Group Considerations

- Should Homeless be included as a hepatitis A risk group for vaccination?
  - Routine?
  - Outbreak setting?
Work Group Considerations – Homeless

- Higher risk for high morbidity and death
  - Often have associated co-morbidities
  - Often have additional risk factors
    • Malnutrition
    • Alcoholism
    • Injection and non-injection drug use
  - Live in poor hygienic settings
    - Increased transmission

- Routine vaccination (e.g., shelters, ED visits) over time
  - Easier implementation than in outbreaks and less vaccine supply constraints

- Catch-up vaccine or universal hepatitis A vaccination discussed
References - I

  - Homeless people attending a clinic were offered hep A vaccine at 0 and 6 to 12 months and hep B vaccine on varying schedules and followed-up for 18 months from the first dose. Once starting the schedule, completion rates were high relative to other studies of vulnerable populations.

  - Reports on data and blood samples collected in 1999 on marginally housed and homeless adults. 52% of 1,138 tested were anti-HAV-positive. IV drug use, being foreign-born, being Hispanic, and increasing age were associated with anti-HAV positivity. Concluded that homelessness may be an independent risk factor for anti-HAV positivity.

- James et al., 2009. Response to hepatitis A epidemic: emergency department collaboration with public health commission
  - Summary of a response to a hep A outbreak in Boston among homeless, PWIDs, and incarcerated. The ED began offering hep A vaccine to everyone >21 years who was homeless, PWID, or incarcerated. The outbreak declined after.
References - II

  - Describes parent study (also discussed in Nyamathi et al. 2012 and Greengold et al. 2009) looking at interventions to increase HAV/HBV vaccination in homeless adults. It found that completion rates were higher for a 2-dose series in 2 months vs. a 3-dose series in 6 months and that the group that got nurse case management was more likely to complete either series.

  - Describes interventions aimed at increasing vaccination rates among homeless/formerly incarcerated men in LA County. Participants were divided into study arms that included combinations of nurse case management, incentives, and tracking.

  - RCT looking at use of peer coaching and nurse case management to increase HAV vaccination among recent parolees.

  - Based on the clinical trial described in Nyamathi et al. 2009. Looked at combined HAV/HBV vaccination in homeless persons. No results presented for HAV alone because the model did not demonstrate HAV vaccination under any strategy to be cost-effective.
Acknowledgments

- **Division of Viral Hepatitis**
  - Jeff Efird
  - Monique Foster
  - Megan Hofmeister
  - Scott Holmberg
  - Cynthia Jorgensen
  - Alaya Koneru
  - Blythe Ryerson
  - Phil Spradling
  - Eyasu Teshale
  - Brigette Ulin
  - Claudia Vellozzi
  - John Ward
  - Winston Abara (former DVH EIS Officer)
  - CDC Division of Emergency Operations

- **Immunization Services Division**
  - Jeanne Santoli
  - Cindy Weinbaum
  - Frank Whitlatch
  - Nathan Crawford

- **Division of Viral Hepatitis Laboratory**
  - Tonya Hayden
  - Yulin Jin
  - Saleem Kamili
  - Yury Khudyakov
  - Amanda Poe
  - Lili Punkova
  - Sumathi Ramachandran
  - Guo-Liang Xia

- **County of San Diego Health and Human Services Agency**

- **California Department of Public Health**

- **Utah Department of Health**

- **Michigan Department of Health and Human Services**

- **New York City Department of Health and Mental Hygiene**
For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.