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Objectives of Molecular Surveillance

- Determine the genetic characteristics of HAV circulating in the United States
- Determine the genetic relatedness of HAV isolates among cases with a recognized risk factor for infection
- Among persons with an unknown source of infection, use genetic relatedness of HAV isolates to identify possible source or risk factor for infection
- Provide phylogenetic background of HAV for outbreak investigation and molecular tracking of hepatitis A
Methods - Sentinel Counties Study of Acute Viral Hepatitis

- **Population under surveillance**
  
  (n = 4.5 million)

- **Clinical information:**
  - Symptoms or signs of viral hepatitis; ALT/AST and bilirubin; other causes of liver injury

- **Epidemiological interview:**
  
  Demographic data; Missed opportunities for prevention; risk factor history

- **SeroLogic and Molecular testing at CDC**

Conducted by CDC from 1982-2006.

Patients with acute viral hepatitis reported to 6 county health departments through stimulated passive surveillance:

- Pierce (PRC) WA, 1982
- Multnomah (MLT) OR, 1996
- Contra Costa (CCA) CA, 1996-97
- Denver (DEN) CO, 1982
- Jefferson (JFA) AL, 1982
- Pinellas (PNF) FL, 1982
Genetic Relatedness of HAV Isolates in the Sentinel Counties

- A total of 1234 hepatitis A cases shared 407 UNSPs (unique nucleotide sequences pattern)
- Predominant genotype IA (n=1196 or 97%)
- 77% (n=946) of isolates found more than once
  - 119 UNSPs
  - 61% cases (N=756) share 10% (n=40) dominant UNSPs (≥5 cases)
- Only 23% (n=288) of HAV isolates were unique
Persistence of HAV Isolates in the Sentinel Counties (n=1,234)

Year of Sequences First Identified
- 1996
- 1997
- 1998
- 1999
- 2000
- 2001
- 2002
- 2003
- 2004
- 2005
- 2006

Surveillance Year (onset date)
Three major and a few minor IA clusters identified

407 UNSPs, 1996-2006
VP1-P2B Region, 315 bp in Length

5.0% Nucleotide Variation
## Association between Risk Factors and Phylogenetic Clusters

(N=810 Cases with completed epidemiologic data)

<table>
<thead>
<tr>
<th>High Risk Factor</th>
<th>1A Cluster 1</th>
<th>1A Cluster 2</th>
<th>1A Cluster 3</th>
<th>Other IA Clusters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intl-Travel (n=99)</td>
<td>67(67.7)*</td>
<td>11(11.1)</td>
<td>12(12.1)</td>
<td>9(9.1)</td>
</tr>
<tr>
<td>IDU (n=68)</td>
<td>7(10.3)</td>
<td>47(69.1)*</td>
<td>10(14.7)</td>
<td>4(5.9)</td>
</tr>
<tr>
<td>MSM (n=165)</td>
<td>12(7.3)</td>
<td>13(7.9)</td>
<td>137(83.0)*</td>
<td>3(1.8)</td>
</tr>
<tr>
<td><strong>Total (N=810)</strong></td>
<td><strong>261</strong></td>
<td><strong>234</strong></td>
<td><strong>276</strong></td>
<td><strong>39</strong></td>
</tr>
</tbody>
</table>

* Significantly higher proportion (row) than others
Overall, 39.9% cases belong to cluster US-IA1; 25.5% US-IA2, 29.7% US-IA3, and 5.0% others.

Distribution of HAV infected sub-populations varies by county over time:
- US-1A2 strains were particularly dominant in Multnomah before 2002, and US-1A3 strains in Denver before 2001.
- Very few US-IA2 cases in Pinellas and US-IA3 cases in Pierce in the 11 years.
Epidemiological Characteristics of 114 Cases Sharing the Same UNSP  
(Sequence ID = SC9)

- Majority of cases occurred in 1997; the unique isolate circulated for 5 years (1996-2000);
- Predominantly male (92.1%);
- 97% of cases occurred in Denver and Multnomah;
- 76% white, and 24% others;
- 61% of cases reported male homosexual activity (MSM), and 6% of cases reported IDU activity.
Summary

Molecular surveillance and genetic relatedness analysis provide insights into the distribution of distinct HAV variants and predominant specific transmission routes

- A relatively limited number of HAV strains account for the majority of cases before 2002
- Certain strains seem to be associated with certain risk factors
- Identical sequence pattern may suggest epidemiological relatedness
- HAV phylogenetic patterns varies by the county over time
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