



Molecular Surveillance of Hepatitis A Virus in the United States: Sentinel Counties Study of Acute Viral Hepatitis, 1996-2006: an Update

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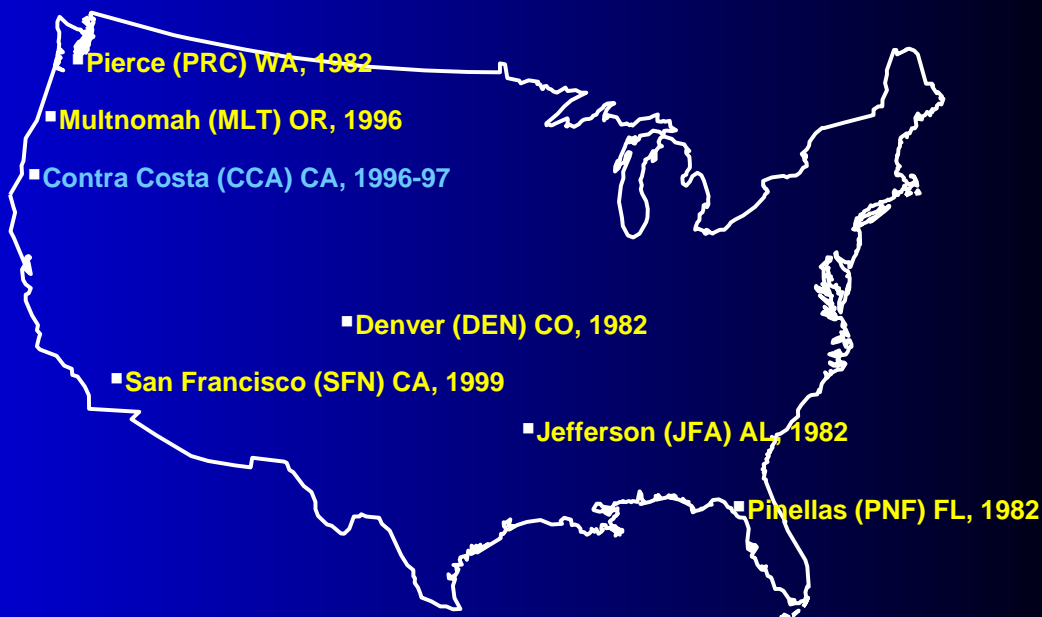
Objectives of Molecular Surveillance

- ❖ 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



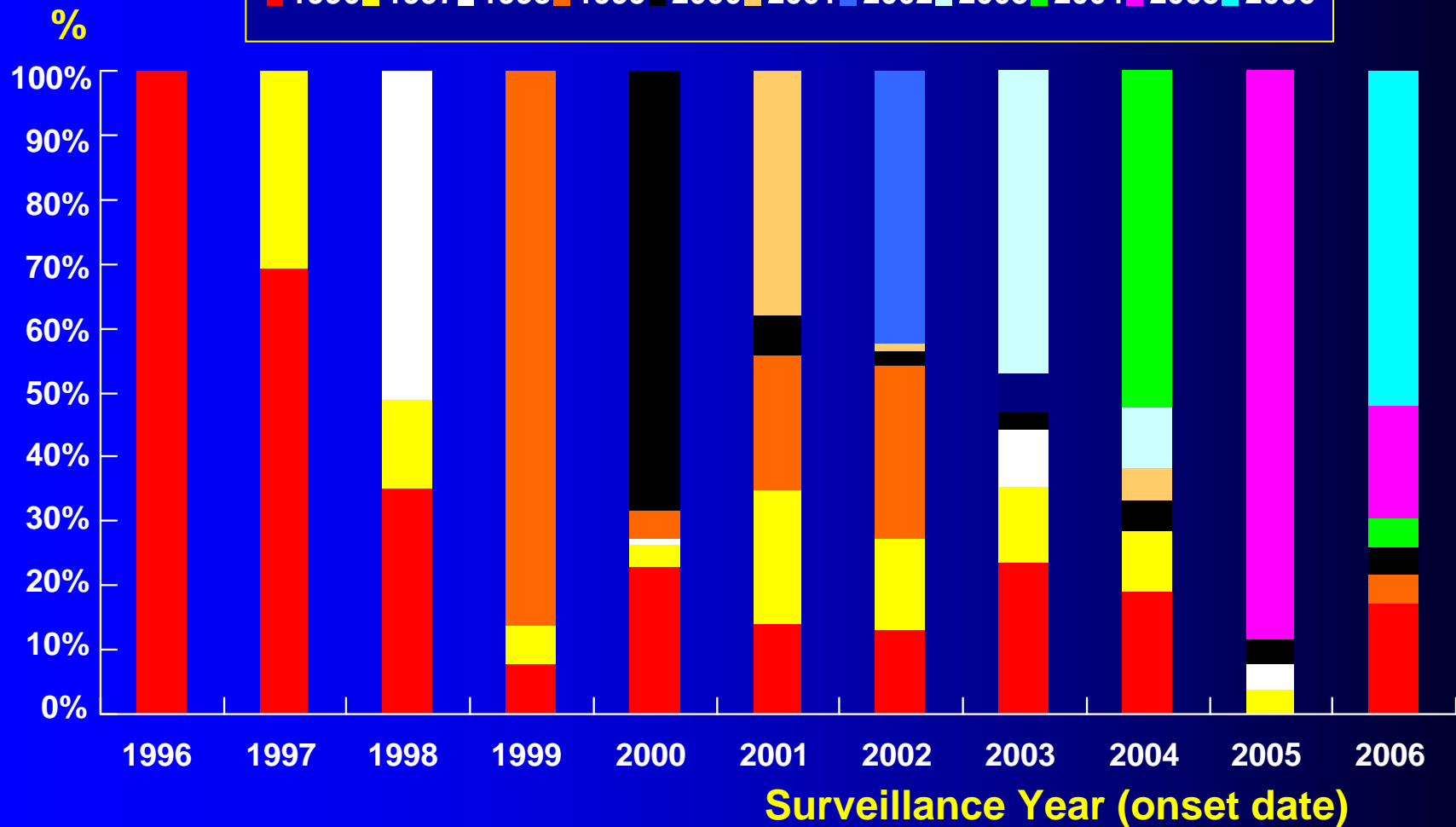
Genetic Relatedness of HAV Isolates in the Sentinel Counties

- ❖ 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

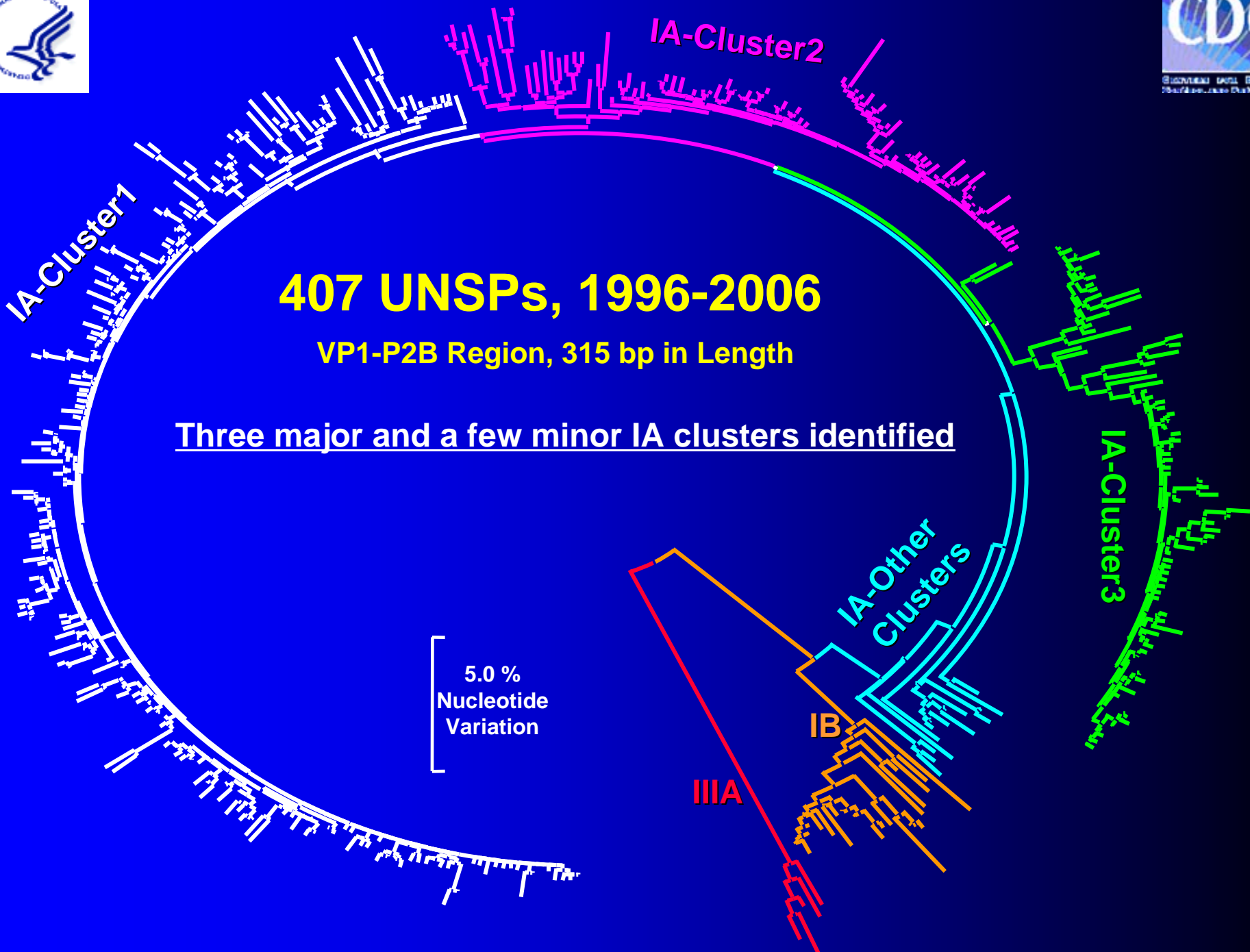




407 UNSPs, 1996-2006

VP1-P2B Region, 315 bp in Length

Three major and a few minor IA clusters identified



Association between Risk Factors and Phylogenetic Clusters

(N=810 Cases with completed epidemiologic data)

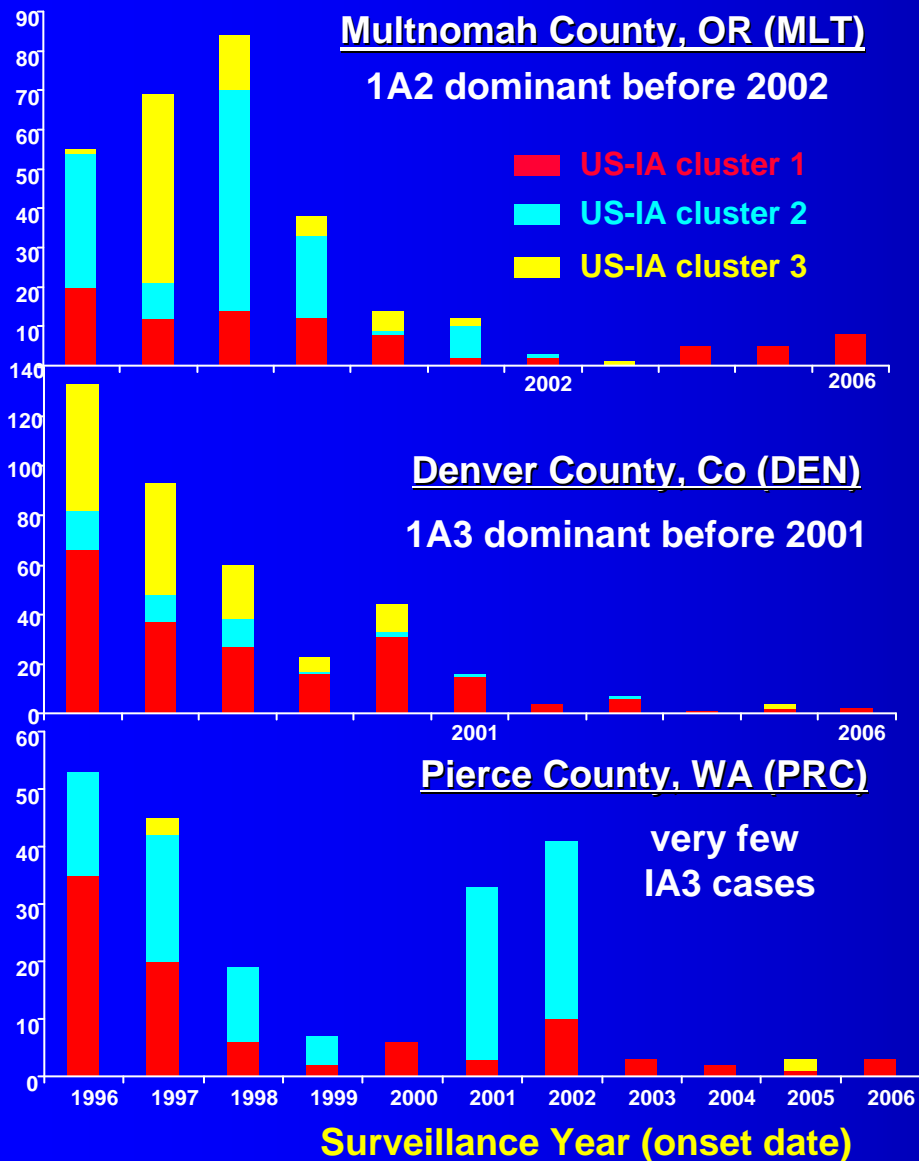
| High Risk Factor | 1A Cluster 1 | 1A Cluster 2 | 1A Cluster 3 | Other IA Clusters |
|--------------------|--------------|--------------|--------------|-------------------|
| Intl-Travel (n=99) | 67(67.7)* | 11(11.1) | 12(12.1) | 9(9.1) |
| IDU (n=68) | 7(10.3) | 47(69.1)* | 10(14.7) | 4(5.9) |
| MSM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

* Significantly higher proportion (row) than others

Dynamics of HAV Infected Sub-populations

(IA Cases N=1,196)

Cases #



❖ 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

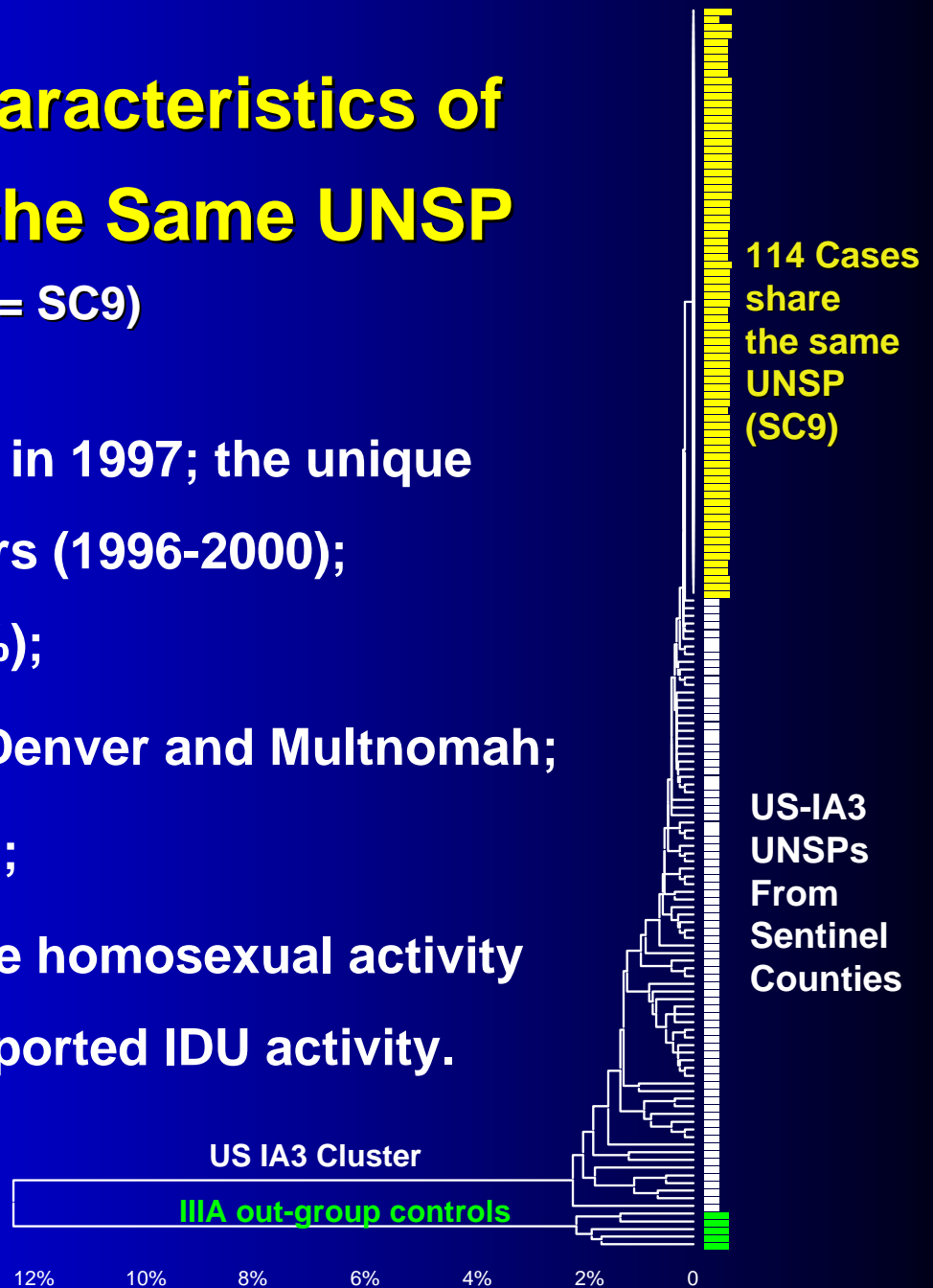
✓ US-1A2 strains were particularly dominant in Multnomah before 2002, and US-1A3 strains in Denver before 2001

✓ 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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