The changing epidemiology of hepatitis A in Arizona following intensive immunization programs (1988-2007)

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Objectives

• Describe hepatitis A vaccination recommendations and implementation in U.S. and Arizona since 1995

• Characterize Arizona hepatitis A cases over a 20 year-period (1988-2007)

• Discuss changes in hepatitis A epidemiology now, compared to pre-vaccine era
Background: Hepatitis A

- RNA virus causing acute onset of symptoms
  - Fever, malaise, nausea, jaundice
  - Clinically identical to other acute viral hepatitis
  - No chronic phase
- Fecal-oral route of transmission, primarily
- Incubation period 15-50 days
- Humans are only reservoir
- Occurs globally, with varying levels of endemicity
Hepatitis A Epidemiology, U.S., pre-vaccine

• Cyclic outbreaks every 10 years in endemic regions
• Rates of infection highest among:
  – Children (particularly 5-14 year olds)
  – American Indians/Alaskan Natives and Hispanics
  – Western U.S. states
    • 11 states accounted for 50% of the national cases (1987-1997) but only 22% of the population
• Additional groups at increased risk for hepatitis A:
  – Travelers, men who have sex with men (MSM), injecting drug users
• Most common sources of infection:
  – Household or sexual contact with another hepatitis A case
  – Attending or working at a child care center
Average reported cases of hepatitis A per 100,000 population*, 1987–1997

States with average reported incidence of >20 cases / 100K population — 1987–1997

<table>
<thead>
<tr>
<th>State</th>
<th>Rate (per 100,000)</th>
<th>Cumulative average number of cases per year†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arizona</td>
<td>48</td>
<td>1,852</td>
</tr>
<tr>
<td>Alaska</td>
<td>45</td>
<td>2,137</td>
</tr>
<tr>
<td>Oregon</td>
<td>40</td>
<td>3,297</td>
</tr>
<tr>
<td>New Mexico</td>
<td>40</td>
<td>3,916</td>
</tr>
<tr>
<td>Utah</td>
<td>33</td>
<td>4,519</td>
</tr>
<tr>
<td>Washington</td>
<td>30</td>
<td>6,007</td>
</tr>
<tr>
<td>Oklahoma</td>
<td>24</td>
<td>6,786</td>
</tr>
<tr>
<td>South Dakota</td>
<td>24</td>
<td>6,953</td>
</tr>
<tr>
<td>Idaho</td>
<td>21</td>
<td>7,172</td>
</tr>
<tr>
<td>Nevada</td>
<td>21</td>
<td>7,449</td>
</tr>
<tr>
<td>California</td>
<td>20</td>
<td>13,706</td>
</tr>
</tbody>
</table>

Source: CDC (MMWR 1999;48(No. RR-12) and http://www.cdc.gov/hepatitis/HAV/Historical-USMap.htm)
## Arizona

- Borders Mexico, CA, NV, UT, NM

<table>
<thead>
<tr>
<th>Population Category</th>
<th>1990</th>
<th>2000</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total AZ population</td>
<td>3,665,228</td>
<td>5,130,632</td>
<td>6,392,017</td>
</tr>
<tr>
<td>Native American population</td>
<td>5.9% (222,500)</td>
<td>5.0% (256,000)</td>
<td>4.6% (296,500)</td>
</tr>
<tr>
<td>Hispanic population</td>
<td>18% (695K)</td>
<td>25% (1.3M)</td>
<td>30% (1.9M)</td>
</tr>
<tr>
<td>&lt;18 years of age</td>
<td>27%</td>
<td>28%</td>
<td>26%</td>
</tr>
</tbody>
</table>
1996: CDC recommends vaccine at age 2 years in high prevalence communities

1996: Vaccine available for free to children ages 2-12 years at IHS healthcare facilities

1995: Hepatitis A vaccine becomes available

1998: OUTBREAK; county ordinance requiring vaccination for daycare admittance for children 2-5 years in Maricopa County

1999: CDC recommends vaccine at age 2 years in 11 states with highest prevalence

1999: Vaccine recommended statewide at age 2 years; state rule requiring vaccination for daycare admittance in Maricopa County

2006: CDC recommends vaccine starting at age 1 year for all children (all states)

2006: Vaccine recommended statewide starting at age 1 year
Hepatitis A vaccination coverage, AZ

- Source: Arizona State Immunization Information System (AZ Vaccination Registry)
Methods: Case data source

• Passive surveillance by ADHS & local health departments (National Notifiable Diseases Surveillance System)
• Reportable in AZ by health care providers and laboratories for many years (AAC R9-6-202 and 204)
• CSTE case definition:
  – Acute illness with discrete onset of symptoms, and jaundice or elevated serum aminotransferase levels.
  – AND positive hepatitis A IgM results
  – Or clinical criteria and epi-linked to lab-confirmed case
• Public health investigations ask about risk factors or possible sources of infection in 2-6 weeks prior to onset
  – CDC forms through 2004; ADHS forms 2005 and later
  – Risk factors questions identical
Methods: Analysis

• Calculations of annual incidence rates by various demographic factors
  – ADHS population denominators (derived from U.S. Census)

• Comparisons of demographic and risk-factor data in selected pre-vaccine years (1994-1995) and vaccine years (2006-2007)
  – 95% confidence intervals around estimated proportions


1988: 58/100K
1989: 79/100K
US: 12/100K
US: 1.0/100K
2000: 9.1/100K
2007 (AZ): 2.3/100K

Vaccine licensed (1995)
1st vaccine recs (1996)
County daycare ordinance (1998)
Vaccinate age 2y, 11 states (1999)

Vaccinate age 1 yr, all states (2006)

N = 22,760 (AZ)  
Source (US data): MMWR Vol. 58, SS-3
Hepatitis A incidence by age (1988-2007, AZ)

Incidence per 100,000

- < 5 years
- 5-14 years
- 15-19 years
- 20-39 years
- 40-64 years
- 65+
- Total

Age distribution of hepatitis A cases

### Age Groups (years)

<table>
<thead>
<tr>
<th>Age Groups (years)</th>
<th>1994-1995 (n = 3575)</th>
<th>2006-2007 (n = 328)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>56 (2%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>1 – 4</td>
<td>440 (12%)</td>
<td>5 (2%)</td>
</tr>
<tr>
<td>5 – 9</td>
<td>927 (26%)</td>
<td>15 (5%)</td>
</tr>
<tr>
<td>10 – 14</td>
<td>472 (13%)</td>
<td>43 (13%)</td>
</tr>
<tr>
<td>15 – 19</td>
<td>315 (9%)</td>
<td>39 (12%)</td>
</tr>
<tr>
<td>20 – 39</td>
<td>1038 (29%)</td>
<td>126 (38%)</td>
</tr>
<tr>
<td>40 – 64</td>
<td>272 (8%)</td>
<td>80 (24%)</td>
</tr>
<tr>
<td>65 or older</td>
<td>48 (1%)</td>
<td>17 (5%)</td>
</tr>
</tbody>
</table>

Children age <15 years:
- 53% of 1994-1995 cases
- 20% of 2006-2007 cases
Hepatitis A incidence by race/ethnicity (1988-2007, AZ)
Distribution of hepatitis A cases by race/ethnicity

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>1994-1995 (n = 3,575)</th>
<th>2006-2007 (n = 328)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. Cases (%)</td>
<td>No. Cases (%)</td>
<td></td>
</tr>
<tr>
<td>White, non-Hispanic</td>
<td>1141 (32%)</td>
<td>117 (36%)</td>
</tr>
<tr>
<td>Hispanic, all races</td>
<td>613 (17%)</td>
<td>137 (42%)</td>
</tr>
<tr>
<td>Native American</td>
<td>1438 (40%)</td>
<td>6 (2%)</td>
</tr>
<tr>
<td>Black, non-Hispanic</td>
<td>48 (1%)</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Asian</td>
<td>9 (0.3%)</td>
<td>4 (1%)</td>
</tr>
<tr>
<td>Missing/Unknown</td>
<td>326 (9%)</td>
<td>63 (19%)</td>
</tr>
</tbody>
</table>

Arizona population, U.S. Census 2000:
- White, non-Hispanic: 64%
- Hispanic: 25%
- Black: 3%
- Native American: 5%
- Asian: 2%
Geographic distribution of cases

- Average annual age-adjusted incidence calculated for the state and Community Health Analysis Areas (CHAAs).
- Maps are displayed by number of standard deviations of each CHAA from the mean age-adjusted incidence of that time period.

In each map:
- Highest rates = red; lowest = green
- Rate associated with each color varies in each map.

Average annual incidence = 43 cases / 100,000 population
Geographic distribution of cases

1998-2002

Average annual incidence = 14 cases / 100,000 population

2003-2007

Average annual incidence = 3 cases / 100,000 population
# Geographic distribution of cases

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. Cases (%); Average Annual Incidence / 100000</td>
<td>No. Cases (%); Average Annual Incidence / 100000</td>
<td></td>
</tr>
<tr>
<td>Central</td>
<td>1413 (40%); 26</td>
<td>192 (59%); 2.3</td>
<td>64%</td>
</tr>
<tr>
<td>Northern</td>
<td>1357 (38%); 170</td>
<td>14 (4%); 1.3</td>
<td>9%</td>
</tr>
<tr>
<td>Southern</td>
<td>422 (12%); 22</td>
<td>102 (31%); 4.2</td>
<td>20%</td>
</tr>
<tr>
<td>Western</td>
<td>238 (7%); 44</td>
<td>20 (6%); 2.4</td>
<td>7%</td>
</tr>
<tr>
<td>Unknown</td>
<td>145 (4%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
</tbody>
</table>

*Regions: Central (Gila, Maricopa, Pinal Counties); Northern (Apache, Coconino, Navajo, Yavapai); Southern (Cochise, Graham, Greenlee, Pima, Santa Cruz); and Western (La Paz, Mohave, Yuma)
Risk factors or possible sources of infection

*Indicates difference between the time periods at p = 0.05 level, based on non-overlapping 95% confidence intervals for the Yes values for the risk factors.

Hepatitis A contact = Sexual or household contact of known hepatitis A case
MSM = Men who have sex with men (restricted to male cases)
IDU = Injecting drug user
Daycare = Child or employee in daycare center, nursery or preschool
Daycare contact = Household contact of child or employee in daycare center, nursery or preschool
Outbreak = Outbreak-associated (suspected of being part of common-source foodborne or waterborne outbreak)
Discussion

• Nearly 40-fold decline in incidence in Arizona:
  – 79 cases/100,000 in 1989 to 2.3 cases/100,000 in 2007
• Cyclic incidence has disappeared
• AZ approaching, though still above, national rates
• Anticipate that these rates will continue to decline, especially among children and young adults, as more of the population is vaccinated
Discussion: Shift in ages

- Biggest changes are in children:
  - Pre-vaccine: half of AZ and one-third of U.S. cases were age <15 years
  - Ten-fold decrease in incidence among children <15 years in AZ
    - Only 20% of cases are among children age <15 (2006-2007)
    - Incidence among children <10 years is lower than among adults
  - Vaccine coverage among 2-4 and 5-9 year olds in AZ rose fastest and stayed the highest
    - By 2000: 36% and 24% of AZ children in these age groups were vaccinated

- Mid-2000s, age burden shifted to adults (63% of AZ cases, 2006-2007)
Discussion: Racial/ethnic disparities

- Incidence has dropped substantially among all racial/ethnic groups
- Elimination of huge disparities between Native American and non-Hispanic White populations in Arizona (and nationally)
  - IHS vaccination policies have been successful
  - Earliest increases in AZ vaccination coverage among 2-4 and 5-9 year olds were in 2 counties with highest Native American populations
  - >30% of children in these 2 counties vaccinated by 2000
- Continued disparity between Hispanic and non-Hispanic White populations
  - 42% of 2006-2007 AZ cases are among Hispanic populations (25% of state population in 2000)
  - Rates among Hispanics double those among non-Hispanic Whites in 2006-2007
  - No comparison available for vaccination rates
Changes in regional burden within AZ

• Shift from Northern parts of state (high proportion of Native American population) to Southern parts of state (Mexican border)
  – Central region still has largest proportion of cases, along with 65% of the state’s population

• Southern part of state less affected by IHS policies & Maricopa childcare entry requirement
Why do current patterns persist?

• Southern region has larger Hispanic population
  – Increasing proportions in Hispanic population and Southern region likely measure the same thing
  – 50% of children in Southern region were Hispanic (2010), compared to 41% Central and 16% Northern
• Other studies have seen persisting higher morbidity among Hispanic populations
  – Possibly related to continued re-introduction of the virus from international travel
• Hepatitis A is not part of the routine childhood Mexican vaccination schedule
  – Hepatitis A incidence rates in Mexico have not changed substantially over 1995-2010 as they have in the U.S.
Changes in risk factors

• Shift from hepatitis A contact or child care association (1994-1995) to TRAVEL (2006-2007)
• Transmission appears largely interrupted in childcare setting
  – Likely highest vaccination rates due to age-based recommendations and Maricopa County entry requirement
• More than half of AZ cases traveled internationally in 2-6 weeks before illness (2006-2007).
  – Higher than reports from other studies (18-41%)
  – Nationally, Mexico & Central/South America represented 85% of U.S. cases reporting travel (2007)
  – Did not examine destinations for AZ cases, but these are likely travel sites for AZ residents
  – Travel-related cases likely to be sustained despite childhood vaccinations
Limitations

• Potential for changes in surveillance & investigations over 20-year period
• Passive surveillance system – potential for underreporting and missing data
• Risk factor data missing for many cases
• Reporting from federal facilities (including IHS) cannot be mandated under AZ rules
  – However: lab reporting, good partnerships, no significant changes known
Conclusions

• Dramatic decline in hepatitis A incidence in AZ
• Declines correspond with trends in hepatitis A vaccine implementation
• Epidemiology of the disease has changed greatly
  – Need to make sure that public health, clinical and public awareness all focused in the right place
• Continued increases in vaccination coverage in AZ and U.S. could lead to further changes in epidemiology
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