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Summary

• Background
• Objectives
• Methods
• Results
• Conclusions
Haemophilus influenzae (Hi)

- Gram negative bacteria
- Colonizes oropharynx
- Clinical illnesses
  - Meningitis, epiglottitis, pneumonia, cellulitis, bacteremia, septic arthritis, otitis media
- Encapsulated
  - Six serotypes (a - f)
- Non-encapsulated (non-typeable)
- Vaccine for Hib
Haemophilus influenzae in Alaska

- CDC’s Arctic Investigations Program (AIP) has conducted surveillance of invasive Hi disease in Alaska since 1980
- Hib disease rates in Alaska were some of highest in the world prior to vaccine
- Post vaccine, Hib disease declined >90%
- Hi disease caused by other serotypes and non-typeable organisms continues to occur
Background

• Increases in disease caused by non-typeable Hi organisms have been seen in other studies
  – US
    • In premature infants and older children with certain risk factors
    • In adults with chronic disease
    • Associated with increased mortality in elderly
  – Other countries
    • In premature infants and older children with certain risk factors
Objectives

- Characterize the epidemiology of non-typeable Hi (NT-Hi) in Alaska
- Determine the incidence of NT-Hi
- Describe the clinical presentation
- Characterize antimicrobial susceptibilities
Methods

• Case definition: invasive Hi
  – Isolate from normally sterile site drawn from a surveillance region resident
• Isolates forwarded to AIP by clinical labs
• Serotyping
  – Slide agglutination with PCR confirmation
  – NT-Hi identified by a negative test for serotypes a-f
• Antimicrobial resistance testing
• Clinical and demographic information
• Laboratory quality control program
Results, 1980-2016

• 1,318 total invasive Hi cases reported
  – 1,108 isolates received and serotyped
    • 222 (17%) were NT-Hi

• Rates of disease caused by NT-Hi
  – 0.98/100,000 (1980-2016)
  – 0.6/100,000 (1980-1984)
  – 1.5/100,000 (2010-2016)
  – Significant increase (p<0.001)
Number of Invasive Hi Serotypes by Year, Alaska, 1980-2016
Rate of Invasive NT-Hi by Time Period, Alaska, 1980-2016

Cases per 100,000

Years


p for trend < 0.001
## Overall Characterization of NT Hi

<table>
<thead>
<tr>
<th></th>
<th>AK Native (n=77)</th>
<th>Non-Native (n=145)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (% male)</td>
<td>57%</td>
<td>46%</td>
</tr>
<tr>
<td>Median Age (min-max)</td>
<td>34.3 (0-92.7)</td>
<td>59.3 (0-101.1)</td>
</tr>
<tr>
<td>Overall Rates*</td>
<td>1.9**</td>
<td>0.8</td>
</tr>
</tbody>
</table>

*Rates per 100,000 persons

**AK Native vs non-Native rates p value < 0.001
Rate of Invasive NT-Hi, by Race, Alaska, 1980-2016

AK Native p for trend = 0.001
Non-Native p for trend = 0.003
Age Distribution – NT Hi

Numbers above bars = number of cases

Age (Years)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>AK Native</th>
<th>Non-Native</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2</td>
<td>24</td>
<td>17</td>
</tr>
<tr>
<td>2-19</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>20-39</td>
<td>12</td>
<td>23</td>
</tr>
<tr>
<td>40-59</td>
<td>12</td>
<td>26</td>
</tr>
<tr>
<td>60+</td>
<td>24</td>
<td>71</td>
</tr>
</tbody>
</table>
Clinical Presentation – NT Hi
Pneumonia – NT Hi

- 111/222 cases (50%)
- Occurred in all age groups
- Since 2000, among adults (> 35) chronic lung disease most common risk factor
  - AK Native – 50%
  - Non-Native – 46%
Case Fatality Ratios – NT Hi

<table>
<thead>
<tr>
<th></th>
<th>Overall Deaths/Total Cases (%)</th>
<th>AK Native Deaths/Total Cases (%)</th>
<th>Non-Native Deaths/Total Cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Ages</strong></td>
<td>45/222 (20%)</td>
<td>15/77 (19%)</td>
<td>30/145 (21%)*</td>
</tr>
<tr>
<td><strong>&lt; 5</strong></td>
<td>8/48 (17%)</td>
<td>6/27 (22%)</td>
<td>2/21 (10%)</td>
</tr>
<tr>
<td><strong>45 +</strong></td>
<td>33/129 (26%)</td>
<td>8/35 (23%)</td>
<td>26/94 (28%)</td>
</tr>
</tbody>
</table>

p values not significant for any AK Native/non-Native comparison

*Outcome unknown in 4 cases
Antimicrobial Susceptibilities – NT Hi

- Susceptible to:
  - Ceftriaxone 100%
  - Chloramphenicol 100%
  - Cotrimoxazole 82%
  - Ampicillin 79%
Limitations

- Small number of cases
- Early surveillance focused on Hib cases
- Diagnostic practices may not be consistent across regions
- Risk factor data not collected consistently

Arctic Investigations Program
Conclusions

- NT-Hi rates have increased significantly over time in Alaska
- Overall disease rates are higher in AK Native persons than non-Native persons
- Proportionally more cases in older persons in non-Natives and young children in AK Natives
- Chronic lung disease is a common risk factor associated with NT-Hi pneumonia cases
- CFRs are high
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The findings and conclusions in this presentation have not been formally disseminated by the Centers for Disease Control and Prevention (CDC) and should not be construed to represent any CDC determination or policy.
Invasive Hib Disease, Children Aged <5 Years, Alaska, 1980 - 2014

Proportion of Invasive Hi Serotypes by Year, Alaska, 1980-2015