Epidemiology of *Haemophilus influenzae* serotype a, an emerging pathogen in Alaska 2000-2015

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Disclosure

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• I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation
Overview

• Surveillance of invasive *Haemophilus influenzae* serotype a (Hia) in Alaska
  – Background
  – Characterize invasive Hia cases
  – Describe initial clinical presentation
  – Determine the incidence of invasive Hia disease in Alaska
  – Assess relatedness by molecular typing

• Study looking at severity of disease with invasive Hia

• Future directions and the possibility of an Hia vaccine
**Haemophilus influenzae**

- Gram-negative bacteria
- Colonizes the oral pharynx
- Clinical illness
  - Meningitis, epiglotitis, pneumonia, cellulitis, bacteremia, septic arthritis
- Polysaccharide capsule
  - 6 capsular types (a-f)
Background

- High rates of invasive Hia disease have been reported from the Navajo and White Mountain Apache in the Southwest US, Northern Canada and Alaska
- It has been sporadically reported from other countries over the past 40 years
Global Epidemiology

Figure 2: Geographical distribution of invasive *Haemophilus influenzae* serotype a disease

*Data from the *Haemophilus influenzae* multilocus sequence typing database.*
Haemophilus influenzae in Alaska
Invasive Hib Disease, Children Aged <5 Years, Alaska, 1980-2015

Hib Vaccine
Methods

- **Case definition of invasive Hia:**
  - Illness in a surveillance area resident with isolation of *Haemophilus influenzae* serotype a from a normally sterile site

- **Surveillance for invasive Hia is done by CDC’s Arctic Investigations Program (AIP):**
  - Collect clinical, demographic, laboratory information on all cases
  - Isolate sent to AIP for confirmation, serotyping, antimicrobial resistance testing
International Circumpolar Surveillance (ICS) Network

Regions Covered by ICS

- USA (Alaska)
- CANADA
- GREENLAND
- SVALBARD
- FINLAND
- DENMARK
- ICELAND
- NORWAY
- SWEDEN

Reference Lab

Contributing Lab
Invasive Disease Caused by Hia Alaska, 2000-2016

Alaska
N = 54
Number of Hia cases in yellow

- YK Delta: 44
- Interior Region: 1
- Anchorage Region: 2
- Yukon: 7
- Northwest Territory: 1
- Nunavut: 2
- N. Quebec: 1
- N. Labrador: 1

USA

Canada
Anchorage Region: 44 cases
Interior Region: 1 case
Yukon: 7 cases
Northwest Territory: Few cases
Nunavut: Lots of cases
YK Delta: Very few cases
N. Quebec: Some cases
N. Labrador: Cases
# Characteristics of Persons with Invasive Hia 2000-2016

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Alaska</th>
<th>N=54</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age (range)</td>
<td>0.8 year (0.3-76.8 years)</td>
<td></td>
</tr>
<tr>
<td>Gender (male)</td>
<td>35 (65%)</td>
<td></td>
</tr>
<tr>
<td>Indigenous</td>
<td>47 (87%)</td>
<td></td>
</tr>
<tr>
<td>Age appropriately vaccinated for Hib</td>
<td>44 (96%)</td>
<td></td>
</tr>
<tr>
<td>Hospitalization</td>
<td>46 (85%)</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>5 (9%)</td>
<td></td>
</tr>
</tbody>
</table>
### Hia Clinical Illness* in Children < 5 Years
### Alaska

<table>
<thead>
<tr>
<th>Illness</th>
<th>Alaska</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=49</td>
</tr>
<tr>
<td>Meningitis</td>
<td>20 (41%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>15 (31%)</td>
</tr>
<tr>
<td>Septic Arthritis</td>
<td>8 (16%)</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>9 (18%)</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Other**</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

*Cases may have multiple illnesses associated with Hia infection
**Other includes empyema, osteomyelitis, pericarditis and ‘other’
Severity of Invasive Hia Disease in Alaska children < 10 years of age, 2002-2014
N = 36

- Invasive Hia disease frequently led to death or disability
  - 25% died or had sequelae 1 year after illness
  - 11% Case fatality
    - 21% Case fatality if meningitis or no localized source
- 32% required hospital transfer
- 78% required air transport
- 36% required ICU or died before admission
- 14% had sequelae ≥1 year after the clinical episode: hemiparesis and speech or hearing loss
Annualized Incidence* of Invasive Hia Disease, Alaska, 2000-2016

<table>
<thead>
<tr>
<th></th>
<th># cases</th>
<th>Rate (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Ages</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>54</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5 (0-1.3)</td>
</tr>
<tr>
<td><strong>&lt; 2 years</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>44</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13.6 (0-36.6)</td>
</tr>
<tr>
<td><strong>&lt; 2 years Indigenous</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>42</td>
</tr>
<tr>
<td></td>
<td></td>
<td>40.9 (0-129.2)</td>
</tr>
</tbody>
</table>

* Rate is per 100,000 persons
Hia Strain Typing by PFGE

Dice (Opt:2.00%) (Tot 1.5%-1.5%) (H>0.0% S>0.0%) [0.0%-100.0%]

SmalPFGE

Nunavut N=9
Nunavut N=6
NWT N=3
Yukon N=1
AK Cluster N=5
AK N=5
Sequence Type Results for Hia Strains, Alaska Children < 5 Years
2002-2016

N = 44
Conclusions I

• Hia incidence is highest among
  – Children < 2 years of age
  – Indigenous people

• Majority of cases in 2 Arctic regions
  – Western Alaska, USA
  – Eastern Canada

• N Canadian & Alaskan isolates appear highly related
Conclusions II

- Hia is now the leading cause of encapsulated invasive *H. influenzae* disease in the North American Arctic
- Continued surveillance for invasive Hi disease is needed
- An Hia vaccine for Indigenous children of the North American is needed
Work on Development of an Hia Conjugate Vaccine has begun

- Late 2013: Formation of a Joint US (Alaska) and Canada workgroup on Hia

- Members:
  - CDC Alaska
  - Public Health Agency of Canada
  - The National Research Council (NRC) of Canada
Current Activities of the Joint Alaska and Canada Workgroup on Hia

• Characterize invasive Hia epidemiology in Alaska and N Canada
• Characterize Hia data from the US and other parts of the world
• Discussions with Utah and specific groups in the Southwest about their Hia data
Hia Conjugate Vaccine Development

- Colleagues at NRC in Canada have created a vaccine by conjugating Hia polysaccharide to 2 different carrier proteins (CRM-197, protein D)
- Injected into mice and rabbits
- Shown to be immunogenic and bactericidal
Next Steps

• Work with a government or private industry lab to produce an Hia conjugate vaccine for clinical trials
  – Considering use of OMP or tetanus toxoid protein
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• John Spika
• Shalini Desai
Haemophilus influenzae Cases by Serotype in Alaska, 2000-2016

N=130*
70% non-b
53% Hia

*141 non-typeable
What We Know About Invasive Disease with Hia (cont)

• Hia incidence is highest among
  – Children < 5 years of age
  – Indigenous children < 5

• Clinical presentation is similar to invasive Hib in the pre-vaccine era

• Invasive Hia causes severe disease and results in serious long-term sequelae in children
Clinical Response to cases of invasive Hia in the North American Arctic

• Cases are treated in a timely manner
• Some prophylaxis of close contacts
  – Despite no official recommendations for this
    • No evidence of invasive Hia case clusters
• Case control study of Hia
  – Non specific risk factors found