Times they are changing’: Shifts in the epidemiology of *Haemophilus influenzae*

Colorado Children’s’ Immunization Coalition Provider Education
December 14, 2017
Today’s talk:

Background- what we do as epidemiologists at CDPHE

Epidemiology of *Haemophilus influenzae* in the US and CO

Results of a “time to serotype” analysis
Learning objectives:

Be familiar with the role of the state public health department

Describe changes in epidemiology of H flu pre vs. post vaccine era

Know where serotyping is performed
Vaccine-preventable disease unit

Part of the Communicable Disease Branch at CDPHE

We do:

Surveillance - counting sick people, mostly

Technical assistance - helping generalist epidemiologists, health care providers, members of the public

Surge capacity and coordination
“This is a second opinion. At first, I thought you had something else.”
Nomenclature and numbers

*Haemophilus influenzae* is a cause of *bacterial infections* that are often severe, particularly among infants.

First described in 1892 during an outbreak of influenza.

Given the name *Haemophilus* by Winslow, et al. in 1920.

Not until 1933 that was established that influenza was caused by a virus and that *H. influenzae* was a cause of secondary infection.
H flu may be encapsulated (typeable) or unencapsulated (nontypeable)

-6 capsular antigens (a-f)
-unencapsulated lacks expression of capsular antigens
H. influenzae (Hi) Serotypes

- Encapsulated
  - Type b (Hib)
  - Type non-b (a, c, d, e, f)

- Unencapsulated
  - Nontypeable (NT)
Nomenclature and numbers

Not all H flu is Hib!

- 91 cases of invasive H flu in 2015, only 2 were Hib
- No cases of Hib in 2016 or 2017 YTD

Type b, Hib, the most well-known and feared type of H flu

Only Hib may require disease control intervention
Nomenclature and numbers

Invasive disease

Determined by a positive culture or PCR from a normally sterile site - blood, spinal fluid, etc.

Non-invasive disease

Localized infection in a non-sterile site that is “open” to the environment - skin, lung, etc.

Invasive Hi is reportable in Colorado
Epidemiology

Gram-negative coccobaccilus

Reservoir: upper respiratory tract

Transmission: person-to-person, respiratory droplets or contact with discharges from the nose/throat of infected person;

in neonates- aspiration of amniotic fluid or contact with genital tract secretions containing the organism
H flu disease

In the pre-vaccine era:

Type b responsible for 95% of invasive disease

Nontypeable strains are a common cause of ear infections in children and bronchitis in adults

Post-vaccine era:

Nontypeable strains a common cause of invasive Hi disease; generally thought to be less virulent
Incidence* of Invasive Hib Disease, 1990-2010

*rate per 100,000 children <5 years of age

Incidence* by Age Group

*Rate per 100,000 population, prevaccine era

Haemophilus influenzae type b 1986

Haemophilus influenzae type b clinical features, pre-vaccine

- Epiglottitis: 17%
- Meningitis: 50%
- Pneumonia: 15%
- Osteomyelitis: 2%
- Arthritis: 8%
- Cellulitis: 6%
- Bacteremia: 2%

Source: CDC Pinkbook
Hib Vaccines

Polysaccharide

- Available 1985-1988
- Age-dependent immune response; not effective <18 months of age
- No booster response

Polysaccharide conjugate

- Stimulates T-dependent immunity
- Enhanced Ab production, esp. in young children
- Booster response with repeat doses
Hib vaccines

Hib Conjugate Vaccines

PRP-T: ActHIB, Pentacel, Hiberix (booster dose only) MenHibrix

PRP-OMP: PedvaxHIB, COMVAX

Currently no vaccines for non-b H flu
Hib vaccines

Immunogenicity and efficacy

95%+ infants develop protective Ab levels after primary series

Clinical efficacy estimates at 95-100%

Effective in those at increased risk for invasive disease*
**Surveillance data sources**

Reportable conditions in Colorado - routine surveillance/investigation

CDC funded Emerging Infections Program (EIP) Active Bacterial Core Surveillance

- enhanced surveillance in 5 county metro area; 10 sites nationally

- lab and epi data matched

- 1st Hib vaccine, polysaccharide, kids >18 months
- 2nd Hib vaccine, conjugate, kids >18 months
- Conjugate Hib vaccines licensed for infants >2 months

450 H flu cases reported 2010-2015:
- 308 (68.4%) non-typable
- 119 (26.4%) serotypes a,c,d,e, or f
- 14 (3.1%) unknown
- 9 (2.0%) serotype b
  - 3 (33.3%) were <5 years old
Reported Cases of Invasive *Haemophilus influenzae* by serotype, Colorado, 2007 - 2016

![Bar chart showing cases by year and serotype](chart.png)
Cases of Invasive *H. influenzae* Serotype b (Hib) by Age Group and Report Year, Colorado, 2010-2016
Incidence of *H. influenzae*, United States, 1994-2015

ABCs cases from 1999-2015 and estimated to the U.S. population
Estimated U.S. incidence of *H. influenzae* by age group and serotype, 2010-2015

Among <1 year olds:
- 46% cases <1 month
- 67% of NT cases <1 month
### Change in incidence of *H. influenzae* serotypes, United States, 2003-2008 vs. 2009-2014

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*Average annual incidence for the time period*
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*MacNeil et al. QD 2011; **Average annual incidence for the time period
Estimated U.S. incidence of non-b *H. influenzae* by age group and serotype, 2010-2015
**Haemophilus influenzae** clinical syndromes, 2015, Active Bacterial Core Surveillance

- **64, 65%**: Pneumonia w/obacteremia
- **27, 27%**: Bacteremia w/o focus
- **8, 8%**: Meningitis
Pre-vaccine era vs. post

- Meningitis 50%
- Pneumonia 15%
- Osteomyelitis 2%
- Arthritis 8%
- Cellulitis 6%
- Bacteremia 2%

2015

- Bacteremia w/o focus 27%
- Pneumonia w/obacteremia 65%
- Meningitis 8%
Total *H. influenzae* case fatality by age group, 2010-2015

- Overall CFR=14.8
- <1 year olds: 8.8%
- 1-4: 3.6%
- 5-17: 2.5%
- 18-34: 8.6%
- 35-49: 8.5%
- 50-64: 13.7%
- 65+: 19.8%
Clinical syndromes of *H. influenzae* by serotype, 2009-2014
Risk factors for Hib

**Exposure factors**

- Household crowding/large household size
- Child care attendance
- Low SES, low parental education levels
- School-aged sibling

**Host factors**

- Race/ethnicity (Hispanic and AI/AN- may be confounded by SES)
- Chronic disease
- Gender (possibly)- risk higher for males
Protective factors

For infants less than 6 months of age:

Breastfeeding

Passive acquisition of maternal Ab
How serotype is determined

Isolates forwarded from clinical or commercial labs to CDPHE lab

CDPHE lab:

- PCR to confirm species
- PCR to determine serotype
- Confirm serotype with anti-sera agglutination (and morphology)
Time to serotype

Serotyping of H flu isolates only available at state public health laboratory

Requested data on all specimens serotyped in 2015

Matched to CEDRS cases (disease surveillance database)

Looked at all reports and metro vs. non-metro (Adams, Arapahoe, Denver, Douglas, Jefferson) reports
Time-to-serotype for *Haemophilus influenzae* specimens, Colorado (all counties), 2015

- Report to serotype: Mean time 3.5 days, Median time 3.2 days
- Report to receipt: Mean time 1.8 days, Median time 1.5 days
- Receipt to serotype: Mean time 1.2 days, Median time 1.2 days
- Collect to serotype: Mean time 5.5 days, Median time 5.5 days
- Collect to report: Mean time 3.0 days, Median time 2.8 days

n=88
Metro vs. non-metro

Median time-to-serotype for *Haemophilus influenzae* specimens, Colorado (2015)
When you are notified of a case of Hi, do you:

- Contact the case and find out if there are close contacts at risk for Hib
- Contact the case only if they are likely to have Hib based on age, clinical illness, etc
- Contact the case only if isolate is confirmed to be serotype b at CDPHE lab
- Other *

* Both "Other" responses specified
Take home messages

Hib is rare and not clinically distinct from other invasive H flu in the post-vaccine era

Non-typeable H flu has increased, causes most invasive infections

Hia is emerging as a cause of severe Hi invasive disease

National guidelines don’t specify an approach to the time between reporting and serotype

Surveillance tracks clinical and epidemiological changes of H flu in post-vaccination era
Thank you! And Thanks to:

Our LPHA and lab partners

Lisa Miller

Meghan Barnes

Emily Travanty

Amanda Reiff

Karen Edge

Questions?
Resources


**Prophylaxis criteria**

If any household contact (4 hrs day for prev 7 days) meets any of below criteria, prophylaxis recommended for all household contacts of Hib case, except pregnant women:

- <12 months of age and has not completed the Hib primary vaccine series
  - OR
- Immunocompromised child, regardless of Hib immunization status
  - OR
- Contact is <4 years of age and unimmunized or incompletely immunized for Hib.
Incidence of *H. influenzae* serotypes, United States, 1999-2015

ABCs cases from 1999-2015 and estimated to the U.S. population