Case Studies: Public Health Laboratories Respond to Threats
A Case of Four Wheeling Botulism in Minnesota

Moe Sullivan
Minnesota Department of Health
Public Health Laboratory Division
Infectious Disease Laboratory Section
Organism

- *Clostridium botulinum*
  - Gram positive
  - Obligate anaerobic bacillus
  - Spores
    - Ubiquitous
    - Resistant to heat, light, drying and radiation
# Neurotoxins

- Seven different types: A through G
  - All cause flaccid paralysis
  - Only a few nanograms can cause illness
  - Different types affect different species

<table>
<thead>
<tr>
<th>Neurotoxin</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
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<td>Cattle</td>
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<td>Dogs</td>
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<td>Mink &amp; Ferret</td>
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</tbody>
</table>
Human Disease

• Three forms
  – Infants <1 (most common form in US)
  – Foodborne (most common from home-canned foods)
    – Wound (spore enters wound in skin)
• All forms fatal and a medical emergency
• Incubation period: 12-36 hours
Adult Clinical Signs

• Nausea, vomiting, diarrhea
• Double vision
• Difficulty speaking or swallowing
• Descending weakness or paralysis
  – Shoulders to arms to thighs to calves
• Symmetrical flaccid paralysis
• Respiratory muscle paralysis
Infant Clinical Signs

- Constipation
- Lethargy
- Poor feeding
- Weak cry
- Bulbar palsies
- Failure to thrive
Botulism in Minnesota

1999-2016

- 15 cases infant botulism
  - 10 toxin type B
  - 3 toxin type A
- 2 cases foodborne botulism (type A)
- 1 cases of wound botulism (type A)

C. botulism in Minnesota

Toxin Type A

Toxin Type B
**Clostridium botulinum testing at MDH**

NOTE: Since 2013, all toxin A has been A silent B by PCR
LRN testing of botulism in Minnesota

- **PCR**
  - Toxin Type A, B, C, D, E, F and G
- **ELISA (food and environmental only)**
  - Toxin Type A, B, E and F
- **Mouse Bioassay**
  - Toxin Type A, B, and F
- **Future: MALDI**
LRN Testing

• Complicated
  – Not all labs can do MBA
  – Limited sample types
  – ELISA assay only good for two weeks
  – PCR testing

• Algorithm

• Fussy!
Case A

- 12 YO Male
- August 9 ATV accident
  - Surgically repaired shoulder and scalp
  - Discharged August 11
- August 16
  - Difficulty swallowing
  - Weak and altered speech
  - Taken to ER – normal chest and head CT
Case A

• August 17
  – Transferred to Children’s in Minneapolis
  – “looked septic”
  – Pus in wound on shoulder
  – Intubated
  – Reactive left pupil, but right pupil was difficult to assess because eye was swollen shut
  – Suspect ptosis in that eye
Case A

- Physician thinks of botulism, but defiantly not the classic presentation
- Patient did NOT have paralysis but did have progressive weakness
- Shoulder grew Enterobacter
- 8/21 CDC consult on case and Anti-toxin released
Summary of MDH testing of Case A

• Received 6 samples/isolates
  – Serum (low volume) only enough for MBA
    • MBA inconclusive (one B mouse didn’t die)
  – Second Serum
    • MBA positive for Toxin Type A
  – Isolated colony (called submitter to have them send isolate to MDH)
    • PCR positive for Toxin Type A silent B
    • Confirmed as Toxin Type A by ELISA
Case B

• 5 month old boy
• 1/8/16 onset of mild, nondescript symptoms
• 1/12/16 seen at pediatrician for:
  – Lethargy
  – Muted cry
  – Constipation
  – suspect URI- given supportive care and prune juice
Case B

• 1/15/16 seen by pediatrician for Well Child visit
  – Hoarse cry
  – Mild congestion
  – CBC normal

• Pediatrician visit
  – Continued lethargy and constipation
  – Infant “seems floppier
  – Congestion and hoarse voice resolved
  – Referred to Neuro
    • Neuro suspects botulism
    • Sends back to primary for stool culture
Summary of MDH testing of Case B

• MDH receives stool 2/13
  – Toxin Type B detected by MBA, PCR and ELISA
• California does NOT release BabyBIG
• 17th case of outpatient infant botulism documented
Select Agent Reporting

- Form 4 for Identification
  - Toxin
  - Isolate
- Timing of reporting
- Amended reports
Form 4 for Case A

• Complicated reporting

15. Comments / Notes:
A total of 3 samples were tested for botulinum neurotoxin by mouse bioassay.
1. 2015317440/H13647 (sample) was tested by mouse bioassay 8/21/15 but results were inconclusive. Disposed of on 8/26/15.
2. 2015317752/F70002 (sample) identified on 8/25/15 and disposed of 8/26/15
3. 2015317762/W31810 (isolate) identified 9/16/15 and disposed of 9/16/15.

3 additional isolates were sent by the submitter and tested by MDH for informational purposes. All were positive for botulinum neorotoxins by ELISA but were not confirmed by mouse bioassay. 2015318582/T43777, 2015318583/S76666, and 2015318584/S76662 were identified as isolates on 9/23/15 (see additional amended Form 4).
On a Side Note

- **Francisella tularensis**
  - 2015
    - 4 animals
    - 4 humans
  - 2016
    - 3 animals

- **Brucella species**
  - 2015
    - 15 Brucella (4 MN residents and 7 from foreign clients)
  - 2016
    - 3 Brucella (all from foreign clients)

This means lots of Form 4’s for the Select Agent program
QUESTIONS?

Thank You!!!