A Royal Mystery in Wisconsin

Weird Science: Interesting and Unusual Cases in Public Health Laboratories

2018 APHL Annual Meeting
Pasadena, CA
June 3, 2018
The Mystery Begins

• WI State Division of Public Health (WDPH), Healthcare Acquired Infections (HAI) Program, is notified of six cases of invasive bacterial disease, with 3 deaths, in SE WI

• Patients in two counties; seen at two healthcare systems

• WDPH promptly notifies WSLH staff about the cluster of illnesses and asks what the lab needs and what laboratory test support the lab can offer
Discussion Point #1

• What information would you like to know from the clinical laboratories about this cluster of illnesses?
Clinical Laboratory Results

- **Gram stain:** Gram negative bacilli
- **ID:** *Chryseobacterium meningosepticum* (low confidence)
- **AST results:** Limited, but indicated MDR
- **PFGE subtyping:** One lab; 3 isolates appear to match one another
Discussion Point #2

• What laboratory testing would you offer to the state Division of Health epidemiologists?
Laboratory Results- WSLH

- **Gram Stain:** Gram negative bacilli
- **Oxidase:** Positive
- **Catalase:** Positive
- **Motility:** Nonmotile
- **Urea:** Negative
- **MacConkey Agar:** No to poor growth
- **MALDI-TOF Protein Profile (Bruker):** *Elizabethkingia meningoseptica*
- **PFGE subtyping:** 6/7 isolates tested appear indistinguishable
PFGE Subtyping Results-WSLH
Isolates Sent to CDC for Further Testing

- Broth Microdilution AST
- Confirmation of Identification
  - MALDI-TOF, 16S/rpoB sequencing, biochems
- Whole genome sequencing (WGS)
CDC Testing

- Special Pathogens Branch Reference Laboratory (SPBRL)
- https://www.cdc.gov/ncezid/dhcpp/bacterial

Special Bacteriology Reference Laboratory (SBRL)

Laboratory Activities

The Special Bacteriology Reference Laboratory (SBRL) provides reference services for the following unusual, rare, or novel Gram-positive or Gram-negative bacteria:

- Aerobic Actinomycetes (E.g., Nocardia spp., Streptomyces spp.)
- Fastidious bacteria (E.g., Capnocytophaga spp.)
- Gram-positive rods (E.g., Corynebacterium spp. EXCEPT C. diphtheria)
- Gram-negative non-fermentative rods (E.g., Stenotrophomonas spp.)

SBRL is comprised of three laboratory units (Actinomycetes Unit, Unusual Pathogens Unit, and Genomics Unit) that collaborate closely to provide state-of-the-art reference identification of these bacteria. Note that SBRL does not provide services for select agents (e.g., Bacillus anthracis, Brucella species, Burkholderia mallei, Burkholderia pseudomallei), anaerobic bacteria, or culture-negative specimens derived from putative bacterial infections.
MicrobeNet

- Online database of rare and unusual pathogens characterized by CDC (>2000 bacteria and >400 fungi)
- Contains nucleic acid sequence information, AR profiles, conventional biochem profiles and MALDI-TOF protein profiles and protocols
- https://www.cdc.gov/microbenet/index.html
• **Identification:** *Elizabethkingia anophelis*
  - MALDI-TOF
  - 16S/rpoB Sequencing
  - Conventional methods

• **AST:** R to β-lactams (incl. carbapenems and cephalosporins), tetracycline, aminoglycosides and polymyxins

• **WGS:** Isolates linked by PFGE subtyping were highly related; isolates not linked by PFGE remained unrelated
Alert to WI Healthcare providers

State of Wisconsin
Department of Health Services

Scott Walker, Governor
Kitty Rhoades, Secretary

For Immediate Release
March 2, 2016

Contact: Jennifer Miller
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Wisconsin Department of Health Services (DHS) Investigates Bacterial Bloodstream Infections

MADISON- The Wisconsin Department of Health Services (DHS), Division of Public Health (DPH) is currently investigating an outbreak of bloodstream infections caused by bacteria called Elizabethkingia.
Tapping into Resources

- Emerging Infections Network (EIN)
- CDC
  - MicrobeNet
  - Special Pathogens Reference Branch
  - EPI-Aid -> Epidemic Intelligence Officers
- Healthcare systems
  - Clinicians
  - Infection Prevention personnel
  - Laboratorians
Emerging Infections Network - EIN

- Provider-based emerging infections sentinel network started in 1995 by IDSA with grant funding from CDC
- Resource intended to help detect new/unusual clinical events, connect public and clinical health officials, aid in the gathering of information on emerging diseases and develop methods for info gathering

https://ein.idsociety.org/
E. anophelis Investigation - Next Steps

• Look at 5 year history of Flavobacterium, Chryseobacterium and Elizabethkingia in WI
• Ask WI clinical laboratories to submit isolates of Elizabethkingia species, Flavobacterium/Chryseobacterium meningosepticum or unidentified catalase- and oxidase-positive GNR with MDR antimicrobial resistance pattern to WSLH for further testing
Five Year History

Isolates of *Elizabethkingia* spp. from sterile sites, January 1, 2011—May 31, 2016, Wisconsin (n = 81)

- **Incidence = 0.24 cases/month**
  - n = 14
- **Incidence = 9.6 cases/month**
  - n = 67

*Elizabethkingia* isolate not available for testing
*Elizabethkingia* isolate non-outbreak strain
*Elizabethkingia anophelis* isolate outbreak strain

Culture collection date: month/year
Discussion Point #3

- WSLH Epidemiologists and CDC EIS officers worked to identify the source of the outbreak. To what source was the outbreak of *E. anophelis* finally linked?
  
  A. Contaminated food product
  B. Contaminated personal care product
  C. Contaminated healthcare product
  D. Environmental water
  E. None of the above; source was never found
Elizabethkingia and Similar Organisms- Issues to Consider

- Organisms are non-reportable; “fly under the public health radar”
  - Clinical laboratory partnership, communication to report anomalies important

- Identification databases (Vitek, Microscan, MALDI-TOF) are less-established than routine pathogens; inconsistent ID’s may result

- No established AST breakpoints to guide laboratorians and clinicians
**Rare Occurrence?**

**Multistate Outbreak of Fungal Meningitis and Other Infections**

October 30, 2015 further updates to the case counts are not anticipated at this time.

On October 30, 2015, CDC updated its web resources for patients and clinicians. Patients affected by tainted steroid injections from the New England Compounding Center continue to receive treatment for their infections and clinicians should continue to monitor patient recovery. All relevant materials for patients and clinicians concerning the multistate outbreak of fungal meningitis and other infections are located on this page.

**FDA updates on 2017 Burkholderia cepacia contamination**

**Update [10/27/2017]** FDA testing has identified *Burkholderia cepacia* in several bottles of Rugby Dioclo (docosyl ester sodium) oral liquid from lot No. 20351701 manufactured by PharmaTech LLC, Davie, Florida. The lot was collected by FDA in response to a 2017 multistate outbreak of *B. cepacia* complex (BCC) bacterial infections that affected at least eight patients in California and Maryland. Laboratory evidence from FDA and CDC indicates that PharmaTech's docosyl ester sodium product is the source of the BCC infections.

An outbreak in 2016 ([Drugs/DrugSafety/ucm511527.htm](https://www.fda.gov/Drugs/DrugSafety/ucm511527.htm)) included serious infections in 63 confirmed cases and 45 suspected cases in 12 states. These 2016 infections were also linked to contaminated product made by PharmaTech, as confirmed by CDC and FDA testing. An FDA investigation associated with the 2016 multistate outbreak identified BCC in more than 40 lots of oral liquid docosyl ester sodium manufactured by PharmaTech. The 2016 investigation also detected BCC in the water system used to manufacture the product.

**Multistate Outbreak of Burkholderia cepacia Complex Infections Associated with the Use of Medline Remedy Essentials No-Rinse Cleaning Foam**

**Update May 21, 2018**

CDC is collaborating with the Food and Drug Administration (FDA), state and local health departments, and healthcare facilities to investigate a recent outbreak of *Burkholderia cepacia* complex (Bcc) infections. As of May 21, 2018, CDC confirmed 15 cases of Bcc infections associated with use of Medline (Northfield, IL) Remedy Essentials No-Rinse Cleansing Foam. Seven infections were in patients in Pennsylvania, seven were in California, and one was in New Jersey. These patients were already hospitalized for acute conditions and acquired the infections while hospitalized.

As of May 8, 2018 FDA is advising ([https://www.fda.gov/Food/RecallsOutbreaksEmergencies/Outbreaks/ucm607082.htm](https://www.fda.gov/Food/RecallsOutbreaksEmergencies/Outbreaks/ucm607082.htm))
Where are we now?

- The source for the outbreak of *E. anophelis* in WI, MI and IL was never found
- Total case numbers for the outbreak:
  - 65 confirmed cases (63 WI, MI, IL)
  - 20 deaths (18 WI, MI, IL)
- Cases originated from 22 acute care facilities; 12 counties in SE WI
- WI clinical labs continue to submit isolates
  - 27 *Elizabethkingia* isolates subtyped by PFGE-no outbreak matches or new clusters found
WGS Findings

- Sequences shared in March 2016; multiple publications followed
- Mutated mutY gene discovered; lead to high rate of genetic mutations/variability
- Estimated that the initial outbreak strain originated ~ 1 yr prior to the discovery
Food for Thought...

- How often do outbreaks due to non-reportable organisms like *E. anophelis* actually occur?
- What is the true burden to the U.S. healthcare system and public health?
- How prepared is your jurisdiction to identify and respond to an outbreak such as this?
  - There are numerous local, state and national resources available to assist with public health instances such as this
Contact Information

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