Wisconsin State Laboratory of Hygiene

UNIVERSITY OF WISCONSIN–MADISON

Infectious Disease Case Studies: What's Lurking Out There?

ASCLS-WI State Convention

April 14, 2016

Case Study #2

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An Astute Clinical Laboratory…

- December 29, 2015 the Wisconsin Division of Public Health (WDPH) receives a call from a clinical laboratory in SE WI reporting three cases of sepsis caused by an unusual pathogen

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…And a Robust State-wide HAI Surveillance Program

- By Jan 4, 2016, three more clinical laboratories had reported cases of sepsis from this unusual pathogen to WDPH
- WDPH requested submission of all isolates to the Wisconsin State Laboratory of Hygiene for molecular subtyping by pulsed field gel electrophoresis (PFGE)
- CDC HAI Program contacted by WDPH
- WDPH issued a state-wide press release

Early in the Outbreak

- Multiple clinical laboratories have identified this uncommon pathogen as *Chryseobacterium meningosepticum*/ *Elizabethkingia meningoseptica*
- All cases had some type of health care exposure
- All cases had underlying medical condition(s)
- AST results reveal multiple drug resistance
  - Cephalosporins
  - Carbapenems

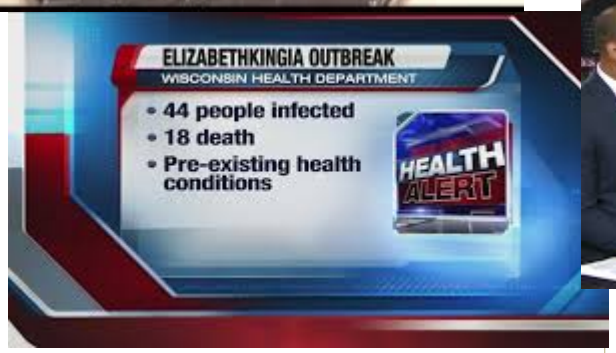
Elizabethkingia- Multi-drug Resistance

- Naturally resistant to beta-lactams, carbapenems, monobactams, aminoglycosides, tetracycline and polymyxins (metallobetalactamase carbapenemase and ESBL among other mechanisms)
- Broth microdilution gold standard (lower error rates than disk diffusion or E Test)
- CLSI interpretive criteria not well established for *Elizabethkingia* species.

Elizabethkingia Infections- Clinical Presentation

- Majority of patients have been >65 years of age and have underlying health issues
- Clinical presentation (presenting symptom):
  - Shortness of breath (41%)
  - Weakness (41%)
  - Fever (32%)
  - Cough (29%)
  - Altered mental status (20%)
- Blood was first positive specimen type in 88% of cases- High mortality initially (>40%)

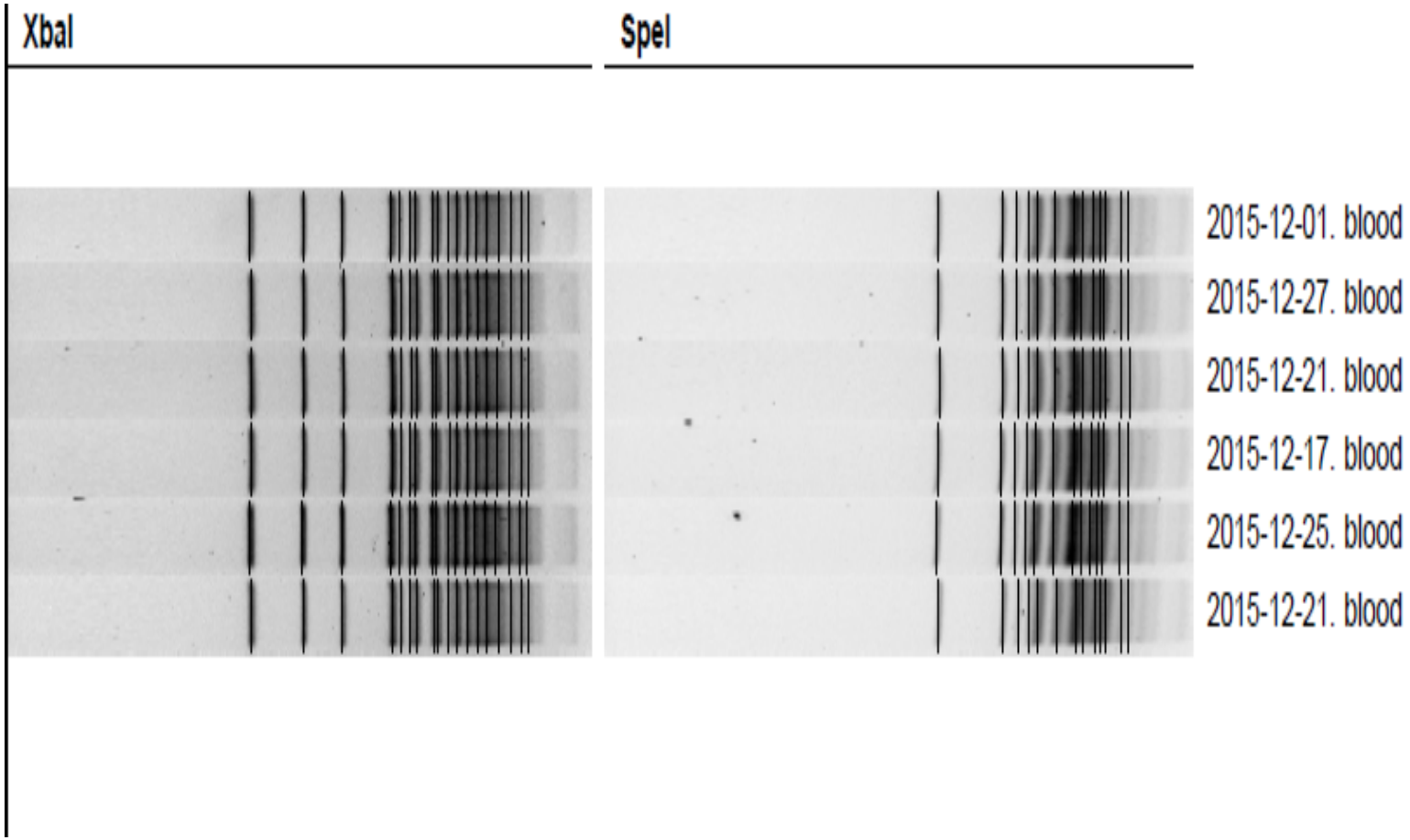
Elizabethkingia Outbreak- Media Coverage



WSLH Lab Testing

- The pathogens were identified by MALDI-TOF as *Elizabethkingia meningoseptica*
- Phenotypically, the Gram Negative bacilli were oxidase +, glucose oxidizers, urea -, indole +w, non-pigmented and non-motile
- 16s rRNA sequencing identified the organisms as *Elizabethkingia meningoseptica/ miricola*
- PFGE subtyping was performed to determine their genetic relatedness (“DNA fingerprint”)

PFGE Subtyping Results



CDC HAI Program Notified

- Because an apparent outbreak of sepsis caused by a rare bacteria was discovered, the CDC Healthcare-Acquired Infections Program offered WI lab and epi assistance
- A series of teleconference calls began to begin to attempt to identify the source of the outbreak
- CDC requested submission of all isolates to their laboratories for further studies

Additional Support for Finding the Outbreak Source

- Centers for Disease Control and Prevention sent multiple Epi-Aid and Epidemiology Infectious Disease (EID) Officers to WI to aid in the investigation
- EID Officers and Epi-Aid staff have been performing case interviews and site visits for clinical specimen, medical product and environmental sample collection

CDC Lab Testing- Cont'd

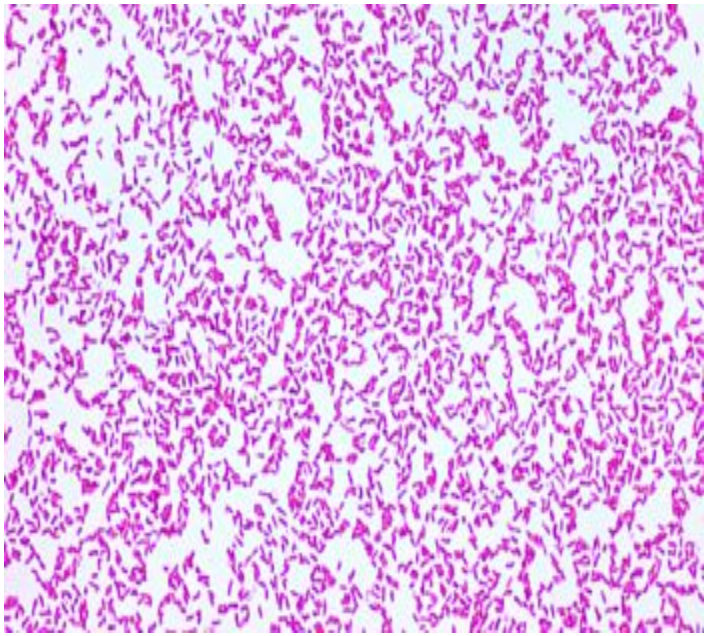
- Environmental and product testing
  - No recovery of *E. anophelis* from environmental or unopened product at this time; more testing in progress

CDC Lab Testing

- MALDI-TOF identification
  - Identification of *E. anophelis*; not *E. meningoseptica*
- Optical Mapping
  - Confirmed WSLH PFGE subtyping results; isolates cluster with one another
- Whole Genome Sequencing (WGS)
  - Results pending at this time
- Antimicrobial Susceptibility Testing
  - Broth Microdilution; confirmed MDR

Elizabethkingia anophelis

CDC



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Elizabethkingia anophelis

- Gram Negative bacillus; first isolated from the midgut of an *Anopheles* mosquito in 2011
- Environmental organism; commonly found in soils, water but not normally found as human microflora
- Associated with meningitis and septicemia in infants and immunosuppressed
- May be confused with other organisms (*Sphingobacterium*, *Aeromonas)*
- Resistant to multiple antimicrobials

E. anophelis- Antimicrobial Susceptibility Testing

Suspected Agent: **Elizabethkingia meningoseptica**

Final Identification: **Elizabethkingia anophelis**

ANTIMICROBIC	MIC (mg/mL)	INTERPRETATION
Ciprofloxacin	2	
Doxycycline	2	
Levofloxacin	2	
Minocycline	0.25	
Moxifloxacin	0.5	
Piperacillin-tazobactam	>128/4	
Rifampin	<=0.5	
Trimethoprim-sulfamethoxazole	<=0.5/9.5	
Vancomycin	16	

BROTH MIC MEDIUM: Cation Adjusted Mueller-Hinton Broth (CAMHB)

Comments:

If no interpretation is indicated, there are no approved breakpoints or they are under investigation.

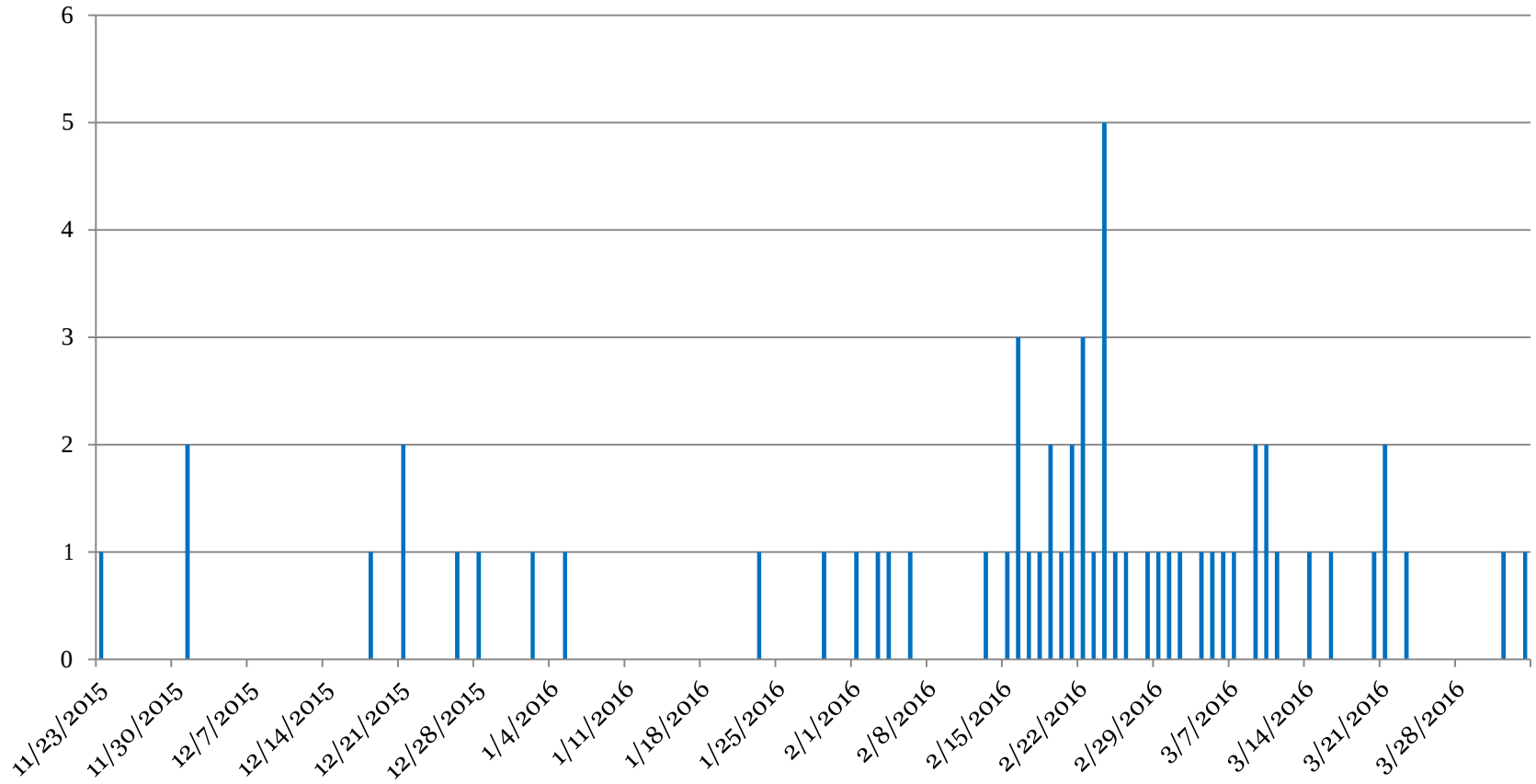
Not all antimicrobics are appropriate for treatment of infections at all anatomic sites.

The Outbreak Continues…

- CDC Special Pathogens Branch shares their MALDI-TOF *Elizabethkingia* library with WSLH
  - WSLH now able to accurately ID *E. anophelis* and rule out other *Elizabethkingia* species
- Cases continue to be identified across SE WI, with additional cases in MI and IL (1 case each)
- Mortality rate decreases; factor of early treatment with effective antimicrobial combinations?

E. anophelis Outbreak- Epi Curve

(# Cases vs Date collected)



Additional Support for Finding the Outbreak Source- Cont'd

SCOTT WALKER
OFFICE OF THE GOVERNOR

Governor Scott Walker Increases Support in the Fight Against Elizabethkingia

Approves nine project positions to assist in search to find the source of the potentially deadly bacteria

Friday, April 8, 2016 - Press Release

Madison – This week, Governor Scott Walker approved a plan for additional project positions at the Department of Health Services (DHS) to assist in the response and investigation of the *Elizabethkingia Anophelis* outbreak, as well as preparation and response to other current public health risks, including the Zika virus and an increase in Tuberculosis (TB) cases.

"Our team at DHS' Division of Public Health has been working aggressively to locate the source of *Elizabethkingia* outbreak since the first notification," Governor Walker said. "We need to make sure we have the resources to address the risk, and do whatever we can to keep Wisconsinites safe."

E. anophelis Outbreak Update- 4/11/16

- There are 59 WI cases and 1 case each from MI and IL
- There have been 18 deaths (31%) to this point
  - Unknown how many deaths attributed to infection (vs underlying condition(s) attribution)
- Twelve WI counties have at least one case
- There are four possible cases; epi-linked but no organism available for molecular subtyping

References

- WDPH Web Pages
  - https://www.dhs.wisconsin.gov/disease/elizabethkingia.htm
  - https://www.dhs.wisconsin.gov/hai/index.htm
- CDC Web Page
  - http://www.cdc.gov/elizabethkingia/index.html