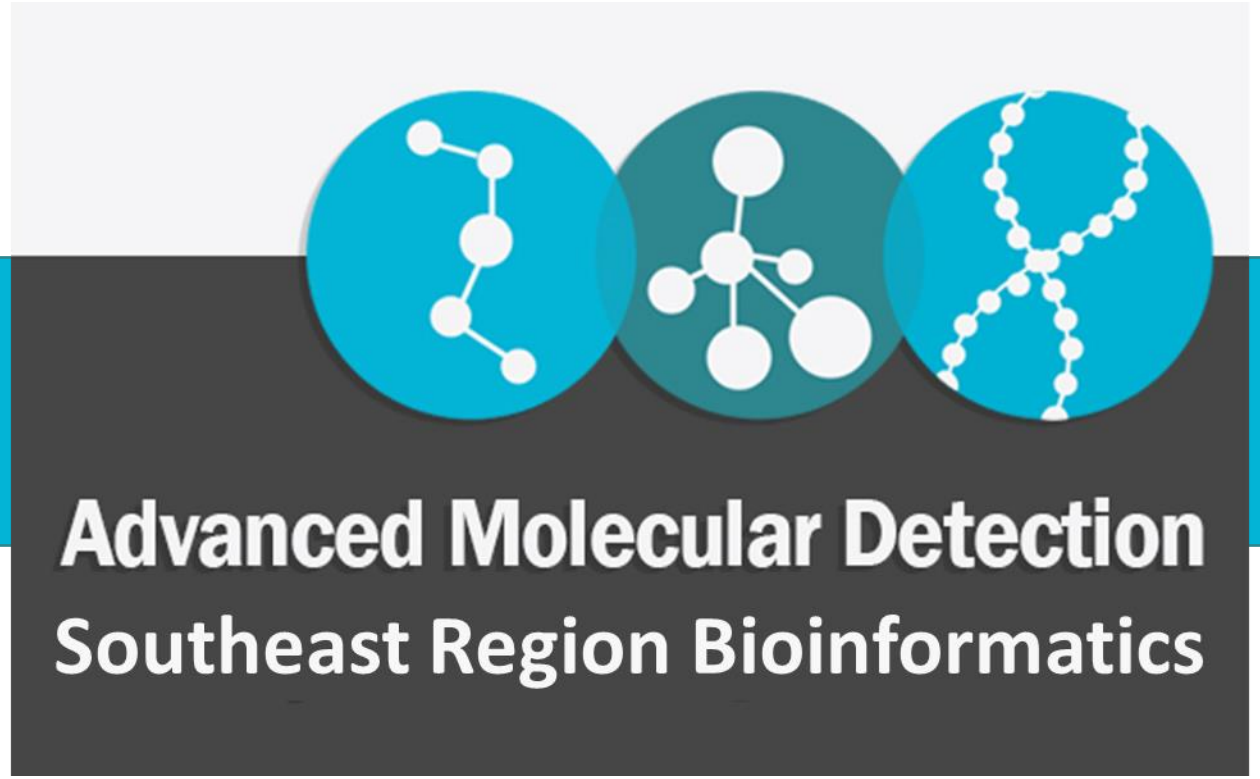

AMD Southeast Region Genomic Epidemiology Training
Case Studies
4/2/24

Case Studies

1. Carbapenem-Resistant *Psuedomonas 1eruginosa* (CRPA) in Tennessee
2. Dengue in Florida
3. *Neisseria meningitidis* in Florida

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Carbapenem-Resistant *Pseudomonas aeruginosa* outbreak in Tennessee, 2017-2022

https://www.dhs.wisconsin.gov/disease/carbapenem-resistant-pseudomonas-aeruginosa.htm

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Carbapenem-Resistant *Pseudomonas aeruginosa* (CRPA)

- *Pseudomonas aeruginosa* is a gram-negative bacterium commonly implicated in healthcare-associated infections (HAIs)
- Can cause a variety of health problems including, but not limited to, pneumonia, sepsis, urinary tract infections, and wound infections
- Carbapenems are heavy hitter antibiotics for multi-drug resistant infections
  - CRPA is resistant to Carbapenems at a minimum
  - Some CRPAs are resistant to all antibiotics, called carbapenemase-producing CRPA
- Transmitted person to person via contact
  - CRPA thrives in the presence of water, aka sinks and toilets

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Verona Integron-encoded Metallo-betalactamase-producing Carbapenem-Resistant *Pseudomonas aeruginosa* (VIM-CRPA)

- Has genetic elements that inactivate carbapenems and most other beta-lactam antibiotics
- Most frequently identified carbapenemase in the US and the world
- Multidrug resistant
- “Serious threat” according to the CDC 2019 Antibiotic Resistance Threat Report
- Loves water, will form persistent biofilms in plumbing

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Chan et al. 2023

Public Health Policies and Prevention

- Starting in 2017, clinical labs in TN asked to (voluntarily) submit CRPA samples to TN PHL (Public Health Laboratory) for Whole-Genome Sequencing (WGS)
- 20 VIM-CRPAs were identified by WGS between Nov 2017 and Aug 2022
- Epi review revealed that 8 cases were associated with one single room in an ICU
- Cases were diagnosed by:
  - 1 - Screening for Carbapenemase-Producing Organisms (CPO)s at a skilled nursing facility for part of a separate outbreak investigation
  - 3 - Routine admission screening at a long-term hospital
  - 3 - CPO ICU discharge screening
  - 1 - Clinical culture

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Chan et al. 2023

Genetic Relatedness

Source	Case A	Case B	Case D	Case F	Case G	Room X_HW	Room X_Bath
Case A	-	6	0	3	4	8	9
Case B	6	-	6	9	10	4	5
Case D	0	6	-	3	4	8	9
Case F	3	9	3	-	7	11	12
Case G	4	10	4	7	-	13	13
Room X_HW	8	4	8	11	13	-	7
Room X_Bath	9	5	9	12	13	7	-

- Samples from bathroom and handwashing sink drains grew VIM-CRPA ST253
- In this outbreak, 0-13 SNP differences were considered highly related
  - # of SNP difference deemed related differs by organism and outbreak

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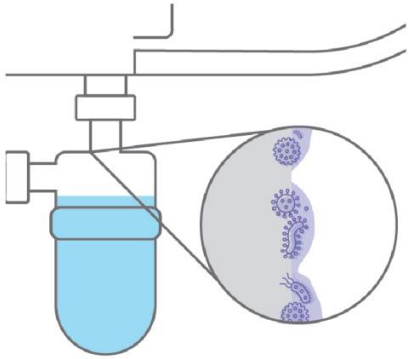
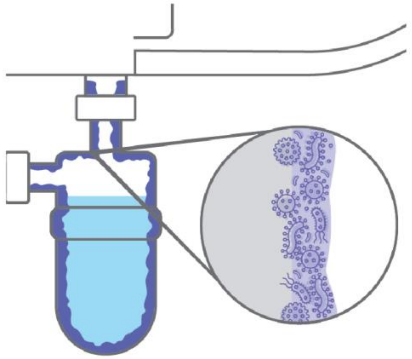
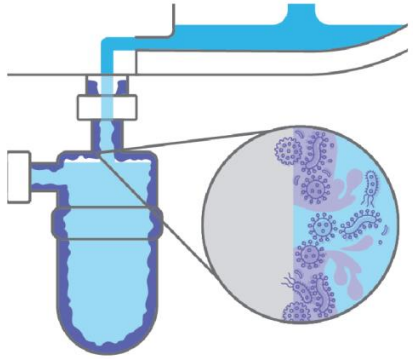
The Culprit: Biofilm in the Drains



Bacteria multiply and secrete substances that form a protective biofilm, which cannot be penetrated by traditional disinfectants (at lower concentrations).



Free-floating bacteria attach to the surface of the drain.



Running water causes splashback that transfers bacteria to the clinical environment, healthcare workers and patients.

- Acute Care Hospital (ACH), Intensive Care Unit (ICU), Room X
  - Samples from bathroom and handwashing sink drains grew VIM-CRPA ST253
  - WGS determined strain to be highly related to patients
- Sinks in Room Y and a hallway sink also grew VIM-CRPA
  - WGS determined it to be different and unrelated, non-carbapenemase producing strains ST235 and ST315

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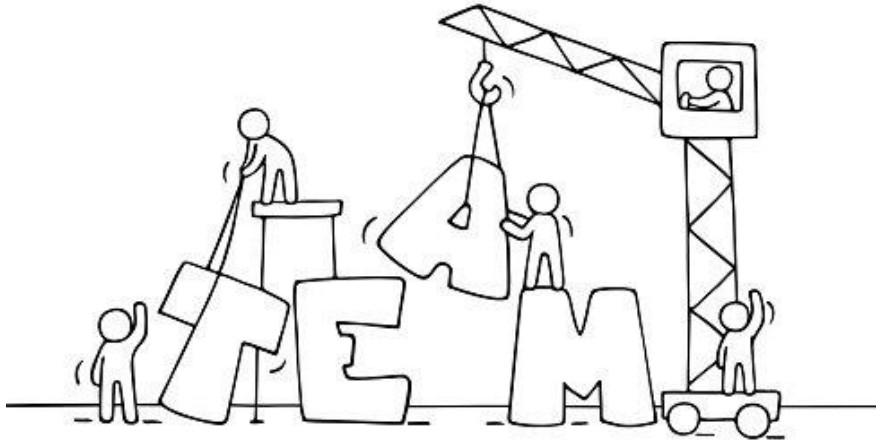
Benefits of WGS and Epi

- Epis identified the hospital and the ICU as hotspots for VIM-CRPA
- WGS determined that Room X was the cause of the outbreak, not room Y
- WGS showed that cases over two years were all related
  - Epis investigated and found biofilm in sinks
  - Epis implemented procedures to remedy the situation



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https://www.freeimages.com/premium-clipart/sketch-of-teamwork-with-working-little-people-4952038

2019 Dengue Epi Investigation in Florida

https://www.cdc.gov/dengue/index.html

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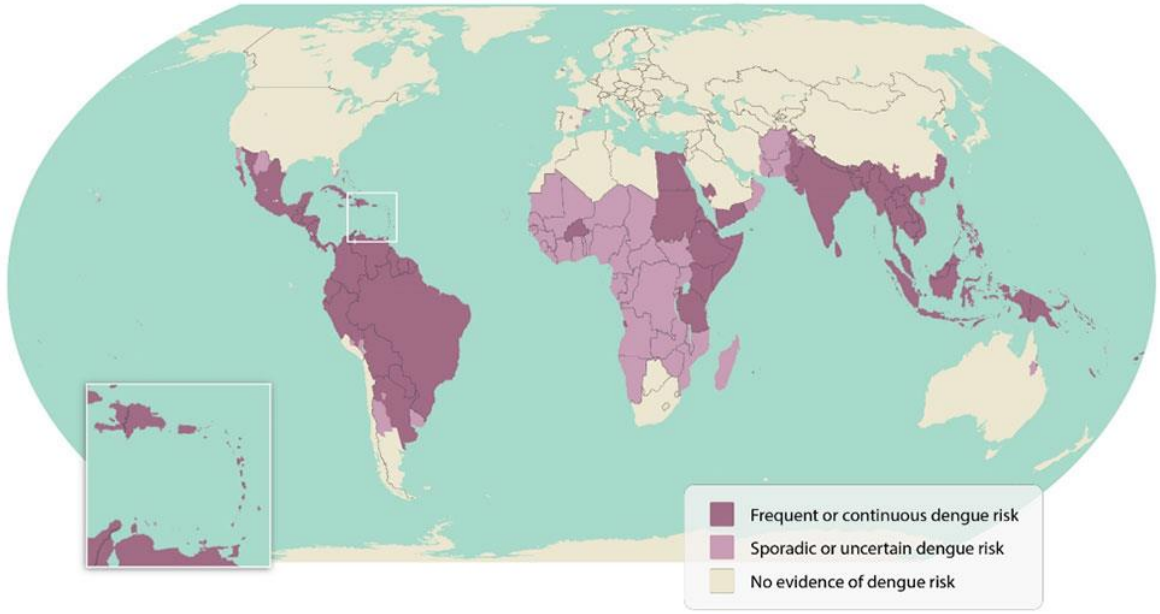
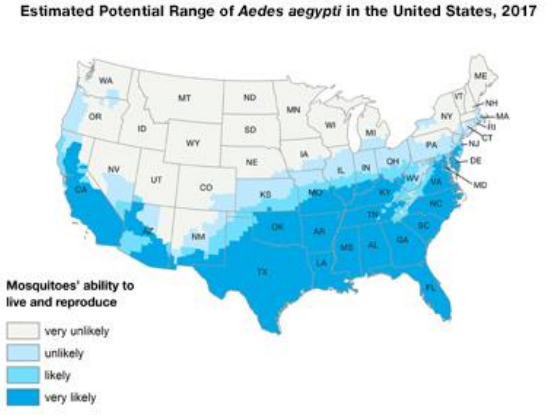
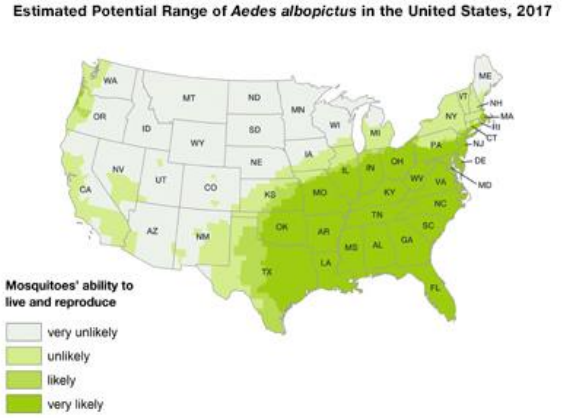
Dengue

- Dengue virus, an arbovirus, is spread to people via two types of *Aedes* mosquitoes
- ~4 billion people live in areas at risk for Dengue
- ~100 million people get sick from Dengue every year, about ¼ of the people infected
  - ~40,000 people die from Dengue every year



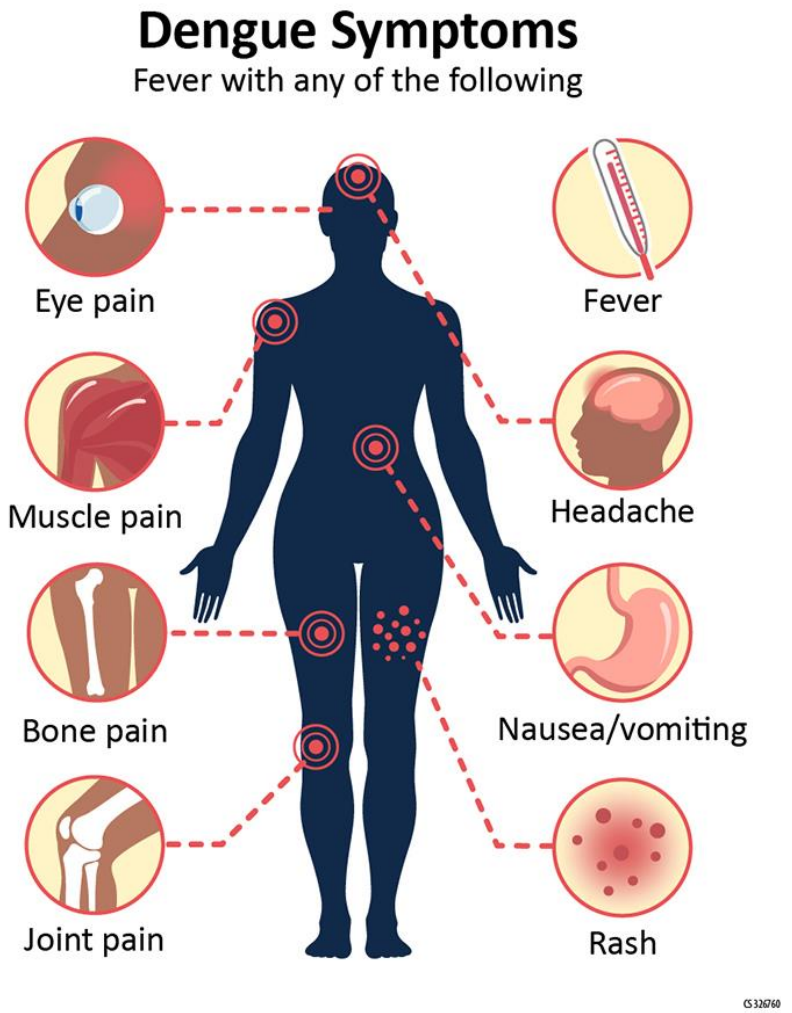




https://www.cdc.gov/dengue/about/index.html

Dengue

- Dengue was endemic in Florida until the 1930s (yay air conditioning!)
  - Most cases are now travel related
  - Most Dengue cases in Florida in 2019 were imported from Cuba
  - At least one local transmission case a year on average since 2009, usually more
- 4 serotypes, DENV-1 through 4
  - Immune to one serotype once you get, it but can get other



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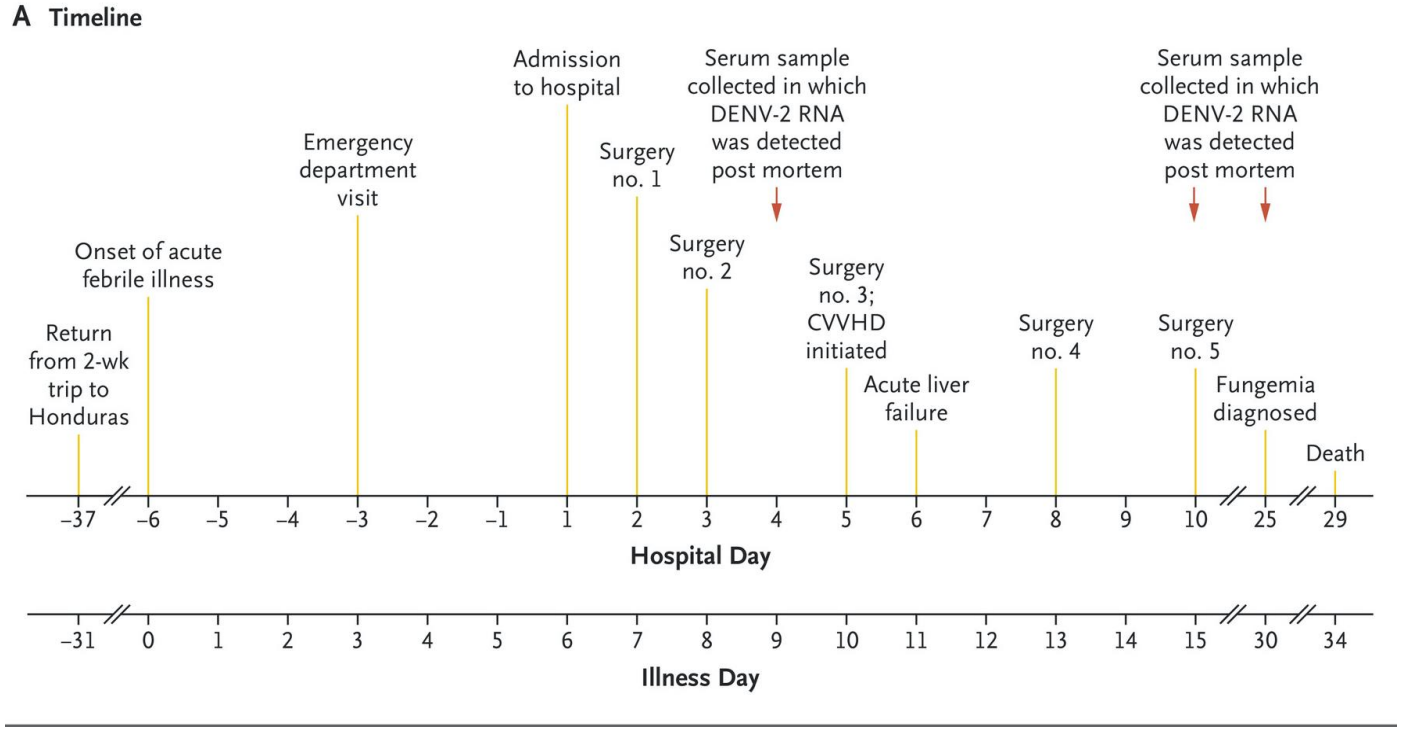
https://www.cdc.gov/dengue/about/index.html

Sharp et al. 2021.

2019 Case Study

- Woman in her 30s
  - Lived in Miami
  - Presented after being symptomatic for 7 days with fever, flank pain, and hypotension
  - Detected through extra testing as initial testing did not meet lab criteria for Dengue
- Acute cholecystitis
  - Gallbladder removed laparoscopically
- Patient died from hemorrhage and multiorgan failure
- DENV-2 identified postmortem



Sharp and Morrison et al. 2019. Thanks, Andrea!

2019 Case Study

- Epi investigation uncovered a trip to Honduras 5 weeks prior to symptom onset
  - Travel within the last 14 days would be expected for travel related Dengue
- 5 family members in household all tested negative for Dengue (all also traveled to Honduras)
- Sequencing revealed the strain of DENV-2 was highly related to Cuban strains
  - Was likely a case of local transmission after the strain was imported from Cuba
  - Sequencing allowed for the confirmation that it was not an atypical case acquired in Honduras

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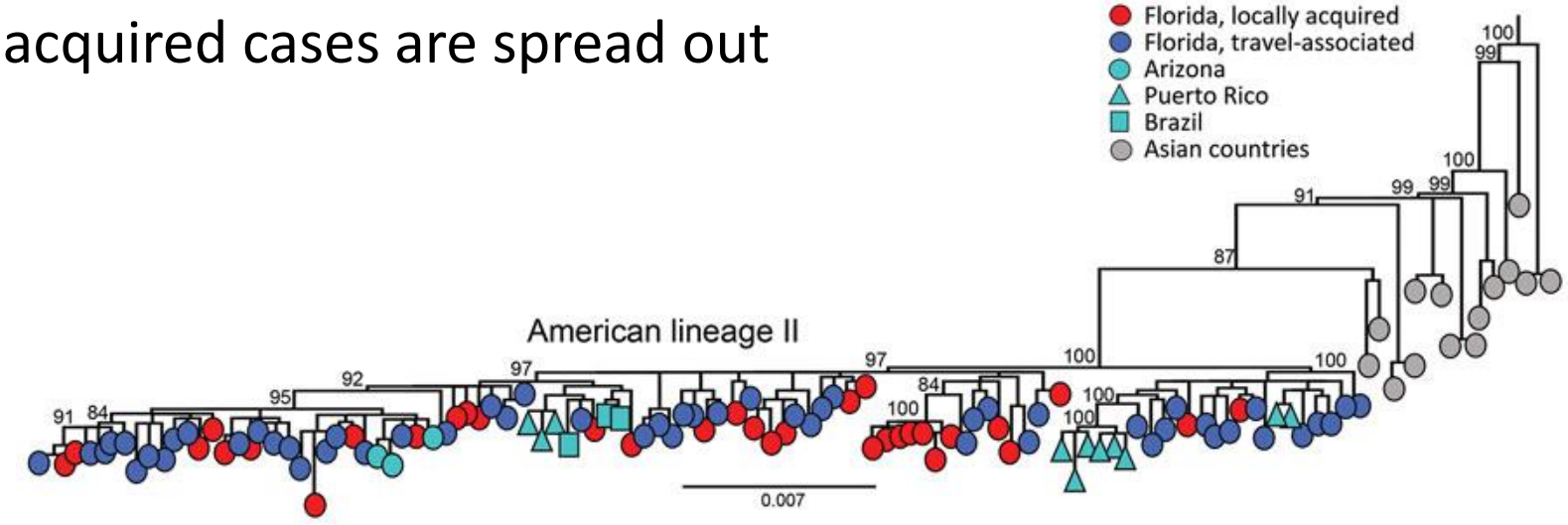
Sharp and Morrison et al. 2019. Thanks, Andrea!

Sequencing Priorities for Investigations

- Confirm geographic origin of cases
  - Particularly important with many countries of import
- Examine linkages between local cases with each other
  - Is there one local transmission or many related cases
- Tree below is DENV-3 in Florida May 22-April 23
  - Locally acquired cases are spread out



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Jones et al. 2024

Benefits of WGS and Epi

- Sequencing data is used to link locally acquired cases to travel related cases
  - Epis investigate travel history and test all members of the infected's household
- Serum tests can distinguish between DENV-1 through 4, but sequencing is required for further detail
- Thank you, Andrea!

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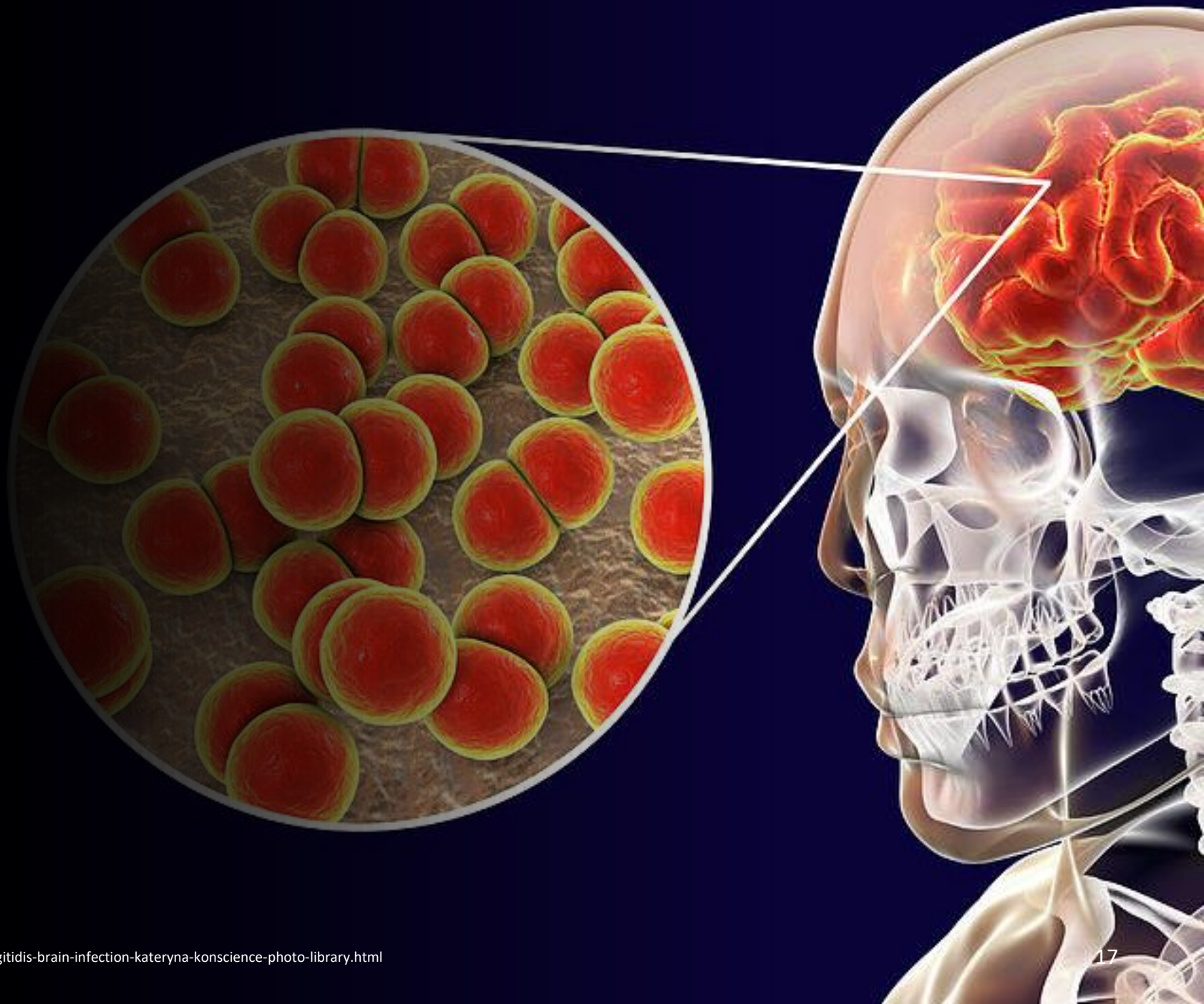
nasir1164 - Fotolia

Neisseria meningitidis outbreak in Florida, 2021-2023



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https://sciencephotogallery.com/featured/3-neisseria-meningitidis-brain-infection-kateryna-konscience-photo-library.html

Neisseria meningitidis (*N. men*)

- *N. men* is a gram-negative bacterium that can cause meningococcal disease
  - 2 most common meningococcal diseases are meningitis (infection of lining of brain and spinal cord) and bloodstream infection (septicemia)
  - Gram-negative bacteria are commonly resistant to antibiotics
- 10% of the population are carriers for *N. men*
  - They carry the bacteria (in the back of the nose and/or throat) without becoming sick
- *N. men* is spread via saliva or spit
  - Usually via coughing or kissing
  - Generally, not spread via casual or short contact

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https://www.cdc.gov/meningococcal/about/causes-transmission.html

Neisseria meningitidis (*N. men*)

- Six subtypes of *N. men* cause most disease: A, B, C, W, X, and Y
  - B, C, and Y are the most common in the US
- MenACWY and MenB vaccines are available
  - Recommended for teens and preteens
  - 2-dose booster series recommended for people with HIV
  - Booster recommended for close contacts of someone with meningococcal disease

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https://www.cdc.gov/meningococcal/outbreaks/FL2022.html

2021-2023 Florida *N. men* outbreak

- At least 44 cases and 7 deaths
- Primarily affected the men who have sex with men (MSM) community
  - About half the cases were Hispanic men
  - Some cases also have HIV
- Serogroup C, ST11CC11 (sequence type, clonal type)
  - Able to link cases and identify antibiotic resistance genes

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https://www.cdc.gov/meningococcal/outbreaks/FL2022.html
https://wwwnc.cdc.gov/eid/article/30/4/23-1392_article

Epi and Sequencing Together

- Epi identified MSM community and specifically Hispanic MSM members are at high risk
- Sequencing linked cases by serogroup and clonal type
  - Constructed phylogenetic trees
- Able to launch targeted vaccination campaign

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Targeted Vaccination Campaign

- Recommended vaccination groups (18 yo+)
  - Men who have sex with men (MSM)
  - People living with HIV
  - Immunocompromised People
  - LGBTQ+ Community
  - People listed above who had a meningitis vaccine 5+ years ago

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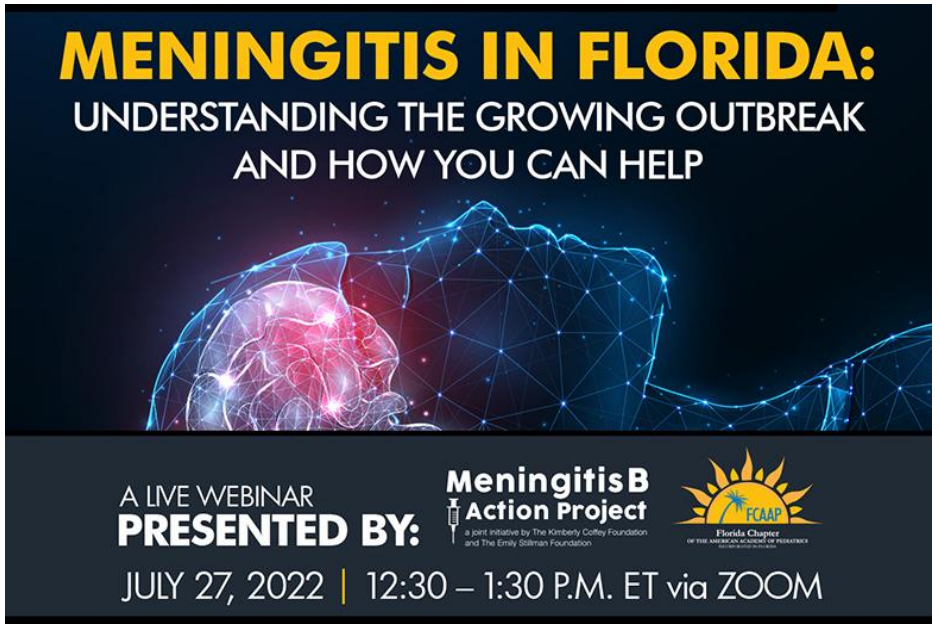
https://www.thepowertoprotect.org/vaccines/meningococcal.html

Targeted Vaccination Campaign

- 24-hour (free) vaccine drive at The Center (Orlando LGBTQ+ Support Clinic)
- Free vaccines at county health departments
- Florida Chapter American Academy of Pediatrics
- Local and national news



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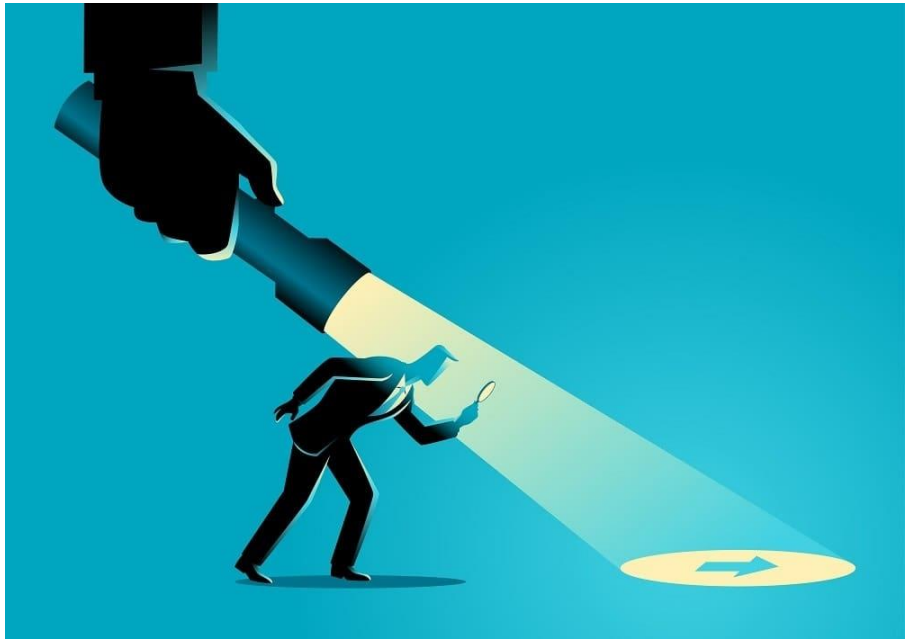
https://www.fcaap.org/posts/news/events/meningitis-in-florida-understanding-the-growing-outbreak-and-how-you-can-help/

2021-2023 Florida *N. men* outbreak

- Vaccination campaign ended the outbreak!
- Epis and Lab still sequencing meningitis cases to monitor for new outbreaks
- Thanks, Labake!



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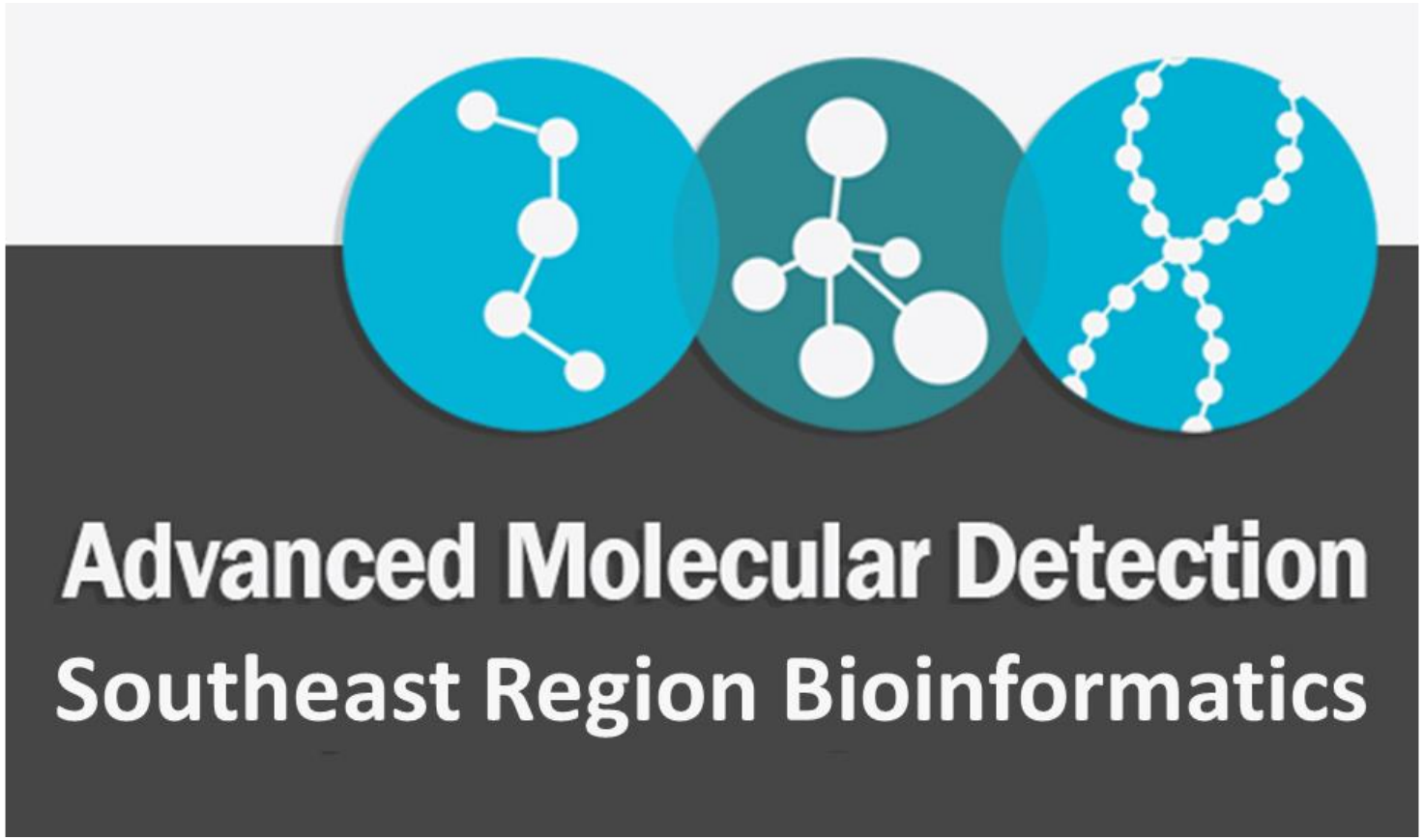

Questions?

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