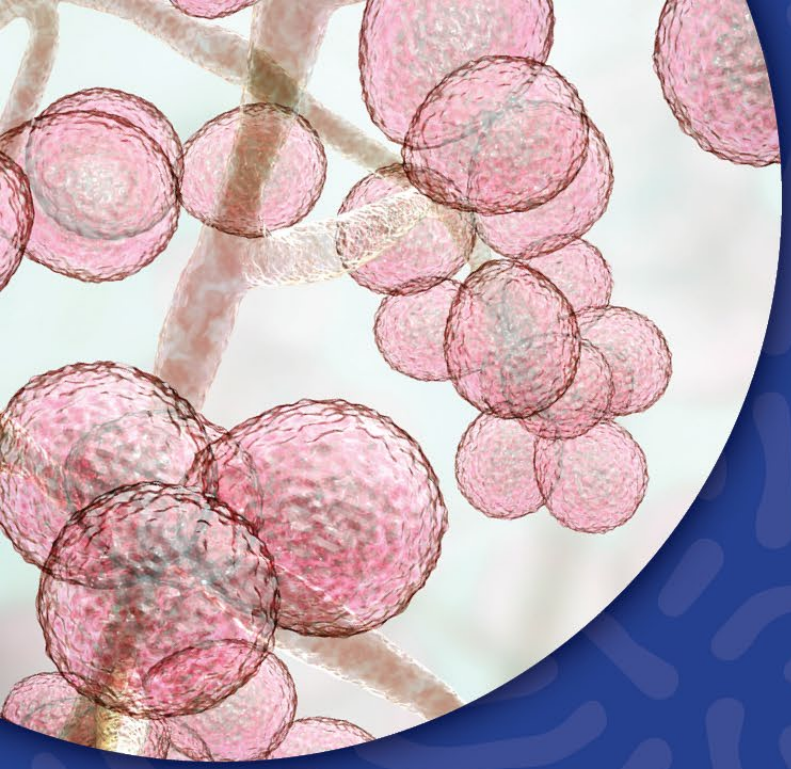
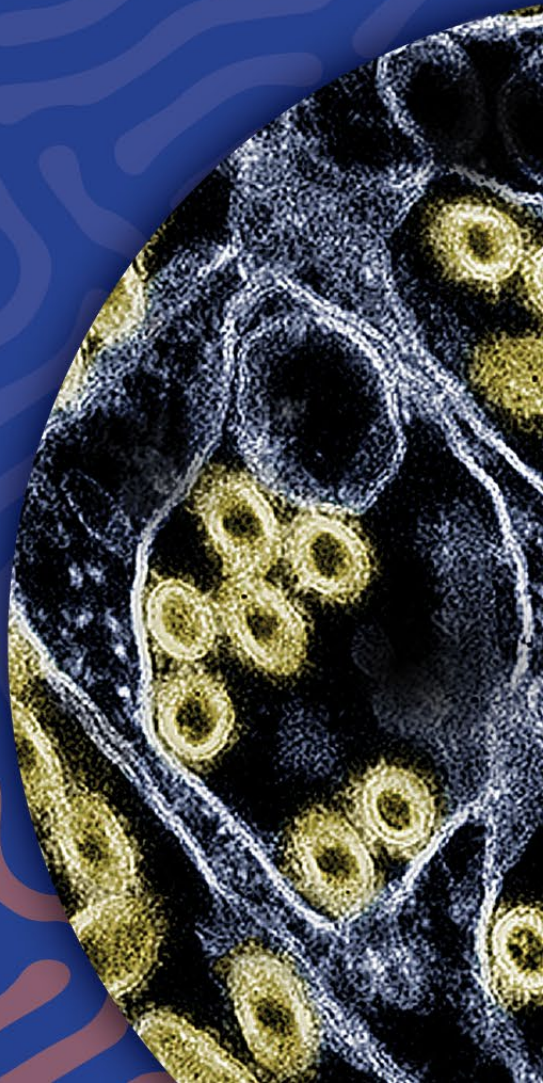


ID LAB CON

APHL

2025

#IDLabCon



Hot Topics in AMR

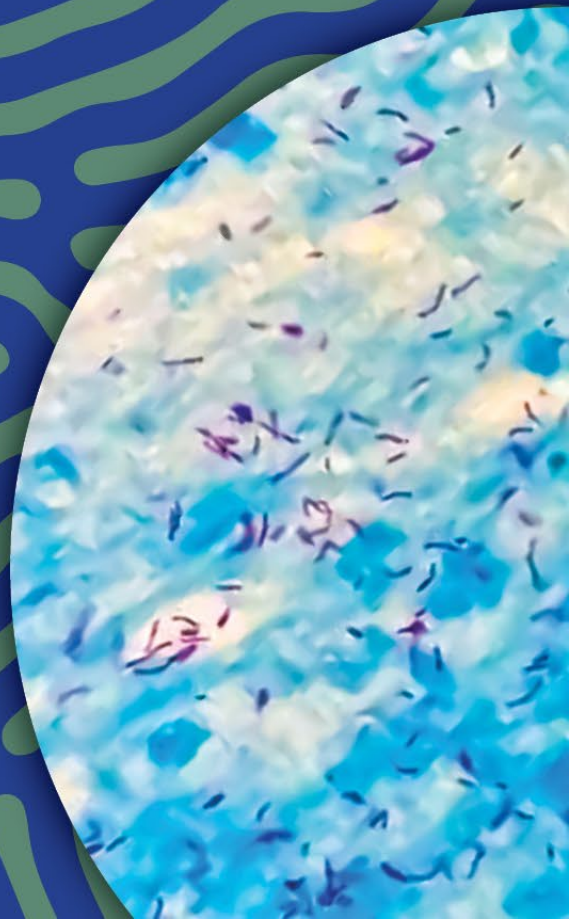
Romney Humphries
Paula Snippes Vagnone

#IDLabCon

Disclosures:

Romney Humphries

Paula Snippes Vagnone:
No Disclosures



#IDLabCon

Case 1

Case 1.

69-year old man, complicated past medical history

- Chronic respiratory failure, long-term ventilation and *K. pneumoniae* (KPC+) colonization
- Long term care facility resident
- Admitted to hospital, due to new onset respiratory distress and sepsis
- Started on ceftazidime-avibactam, vancomycin and micafungin

#IDLabCon

Respiratory culture

- Moderate growth *K. pneumoniae* (KPC+)
- Moderate growth yeast*

Urine culture

- 50,000 CFU/mL *Candida* spp.*

Blood culture

- No growth

*yeast not identified per laboratory SOP

Case 1, continued

- Blood cultures repeated on day 4 due to ongoing fever:
  - Molecular test detects *Candida auris*
  - AST performed (Sensititre, Thermofisher Scientific):

Antifungal	MIC (µg/mL)	Interpretation
Fluconazole	64 µg/mL	NI
Amphotericin B	0.25 µg/mL	NI
Micafungin	0.06 µg/mL	NI

NI, no interpretation.

"CDC tentative interpretations suggest fluconazole resistance in this *C.auris*."

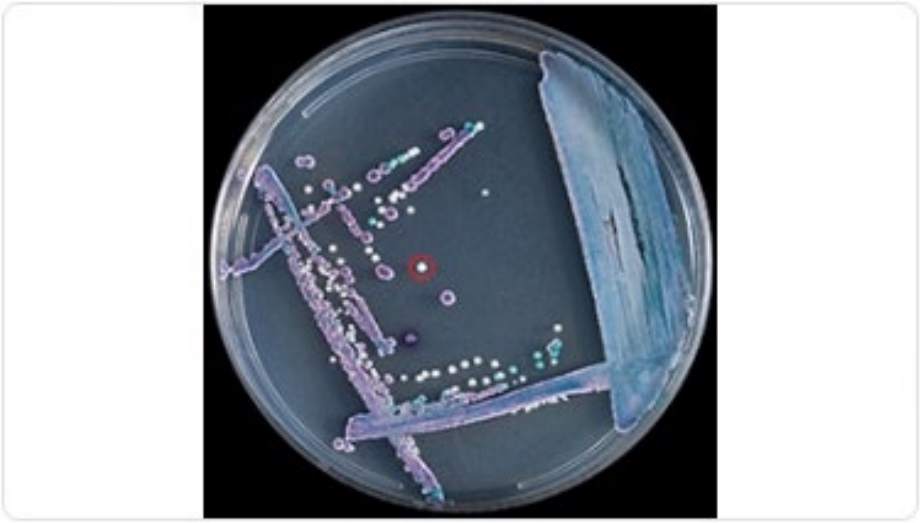
- Micafungin dose increased to 150 mg daily
- Central catheters removed
- Despite interventions, patient succumbed to multi-organ failure

Questions from this case...

- When should we identify *Candida spp.?*
  - Respiratory cultures?
  - Urine cultures?
- When should we perform antimicrobial susceptibility testing for *C. auris*?
- How should we perform antimicrobial susceptibility testing for *C. auris*?
- How can we help infection prevention screen for *C. auris* among other patients?

Candida auris

- Clinical impact:
  - Patients with multiple or prolonged health care or indwelling devices (incl. ventilation)
  - High rate of mortality associated with candidemia (29-65%)
  - Long hospital and ICU stays



Identification: MALDI-TOF is your best bet!

- MALDI-TOF FDA-cleared databases
  - Bruker Biotyper CA system library Version Claim 4
  - VITEK MALDI-TOF IVD v3.2
- CHROMagar: white or pink, some may be red or purple
- Molecular tests
  - ePlex BCID-FP Panel (Roche)
  - Biofire BCID2 (bioMérieux)

Phenotypic methods often mis-ID *C. auris*

ID method	Organism C. auris may be misidentified as…
Vitek2 YST (pre-version 8.01)	Candida haemulonii Candida duobushhaemulonii
API 20C	Rhodoturula glutinis Candida sake
API ID 32C	Candida intermedia Candida sake Saccharomyces kluyveri
BD Phoenix ID system	Candida haemulonii Candida catenulate
Microscan	Candida famata Candida guilliermondii Candida lusitaniae Candida parapsilosis
RapidID Yeast Plus	Candida parapsilosis

https://www.cdc.gov/candida-auris/hcp/laboratories/identification-of-c-auris.html

When should we identify a yeast?

- Add Paula's information

- Sterile Site: YES!
- Urine cultures: *Candida* in urine cultures often not needed[1]
  - Especially below 10^4 CFU/mL[2]
- Respiratory cultures: *Candida* colonize respiratory tract of ~50% of healthy humans. Treatment rarely indicated.[1] ID and AFST are generally not required.[2]

WHEN TO CONSIDER RULING OUT *C. auris* in non-sterile sites

1. Increase in *Candida* from urine/respiratory specimens for a hospital unit may prompt identification
2. Clinical or Infection Prevention team requests identification of yeast in these specimens
3. *Candida* growing from patient with *C. auris* identified in blood or other sterile site

1. Pappas. 2015. Clinical Practice Guideline for Management of Candidiaisis: 2016 Update by IDSA. CID 62:e1-50
2. Clinical Microbiology Procedures Handbook, 4th Ed.

When identification of yeast in non-sterile sites should be considered for Infection Prevention

- When a **case of *C. auris* infection or colonization has been detected** in the facility:
  - Implement yeast ID for at least **1 month** until no evidence of transmission.
- When a **patient has had an overnight stay** in a healthcare facility **outside of the United States** or in a **state with documented cases** and/or transmission.

Typically, directed by hospital epidemiology / infection prevention.

Approximately ½ of clinical cases in the U.S. have been from bloodstream, rest from non-invasive sites

How about AST?

- No clinical breakpoints by CLSI, EUCAST
- CDC has published “tentative” breakpoints:
  - NOTE: clinical response should be used to determine treatment efficacy, NOT a resistant MIC alone.

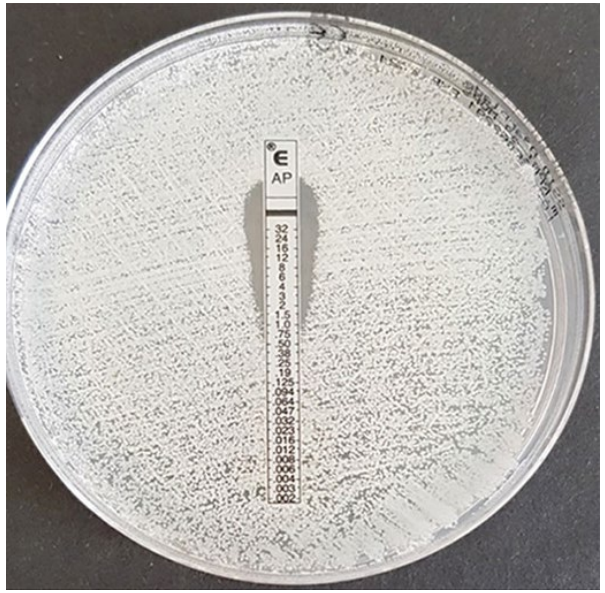
Antifungal agent	CDC Tentative “R”	Notes
Fluconazole	≥32 µg/mL	Associated with mutation to Erg11 gene
Amphotericin B	≥2 µg/mL	PK/PD in mouse model supports ≤1 µg/mL as “S”
Anidulafungin	≥4 µg/mL	Based on modal MIC distributions
Caspofungin	≥2 µg/mL	
Micafungin	≥4 µg/mL	

https://www.cdc.gov/candida-auris/hcp/laboratories/antifungal-susceptibility-testing.html

Typical Resistance Profile

- USA Data, CDC:

Year or Region	Fluconazole	Amphotericin B	Echinocandins*
2020 (n=1294)	85.7%	25.6%	1.2%
West (n=556)	99.5%	3.1%	0.2%



*echinocandins include:

Caspofungin

Micafungin

Anidulafungin

- Resistance to echinocandins low
  - Resistance may develop on treatment
  - May occur in outbreak setting
- Amphotericin B – careful!
  - Sensititre YeastOne has higher MICs than CLSI reference[1]
  - Vitek2 may over-call resistance[2]
  - Gradient diffusion can be highly variable, by inoculation method[3]
  - Modal MIC is very close to breakpoint = high risk of errors[3]

1. Siopi et al.2023 Microbiol Spectr Article e0443122
2. Kathuria et al. 2015. J Clin Microbiol 53:1823
3. Arendrup et al. 2025. Clin Microbiol Infect 31:108

C. auris: Antifungal Susceptibility Testing – Discrepant Results

Anomaly: Voriconazole MIC is higher than fluconazole MIC for any *Candida* species, or a result where an isoate is voriconazole resistant but fluconazole susceptible

Example	Species	VOR	AND	CAS	FZ	IZ	IVU	PZ	MF	AMB
	C.tropicalis	2	0.03	0.12	0.125	0.06	0.12	0.06	0.12	0.25

A voriconazole MIC should not be higher than fluconazole and isolates should not be voriconazole resistant but fluconazole susceptible. Could be trailing growth. **Retest the isolate.**

Anomaly: One echinocandin low when the others are high, any species

Example		VOR	AND	CAS	FZ	IZ	IVU	PZ	MF	AMB
	C. glabrata	0.125	2	4	4	0.06	0.125	0.06	0.008	1

When one echinocandin is very low and the others are resistant (well above the BP, not borderline), this is an anomaly. If one is low and the others are higher but susceptible, that is OK. **All three echinocandins should be retested.**

C. auris: Antifungal Susceptibility Testing – Discrepant Results

***Anomaly: C. parapsilosis* with only caspofungin M IC being high**

Example		VOR	AND	CAS	FZ	IZ	IVU	PZ	MF	AMB
	C. parapsilosis	<0.008	1	16	0.25	0.008	0.004	0.008	0.5	0.75

When the caspofungin MIC is high and the other echinocandins are low, this is often the Eagle effect. Look for a dimunition of growth in the middle wells. If this is seen, ignore the caspofungin MIC. Anidulafungin and micafungin can serve a surrogate marker for caspofungin. **Consider retesting all three echinocandins.**

Anomaly: Discrepant results between intraconazole and posaconazole, any *Candida* species

		VOR	AND	CAS	FZ	IZ	IVU	PZ	MF	AMB
	C. tropicalis	0.008	0.06	0.03	0.125	0.03	1	4	0.008	0.75

As these two drugs have a similar structure, there should be good correlation between them (MIC within 1-2 dilutions). **If the results are discrepant, retest.**

Candida auris

Paula Snippes Vagnone

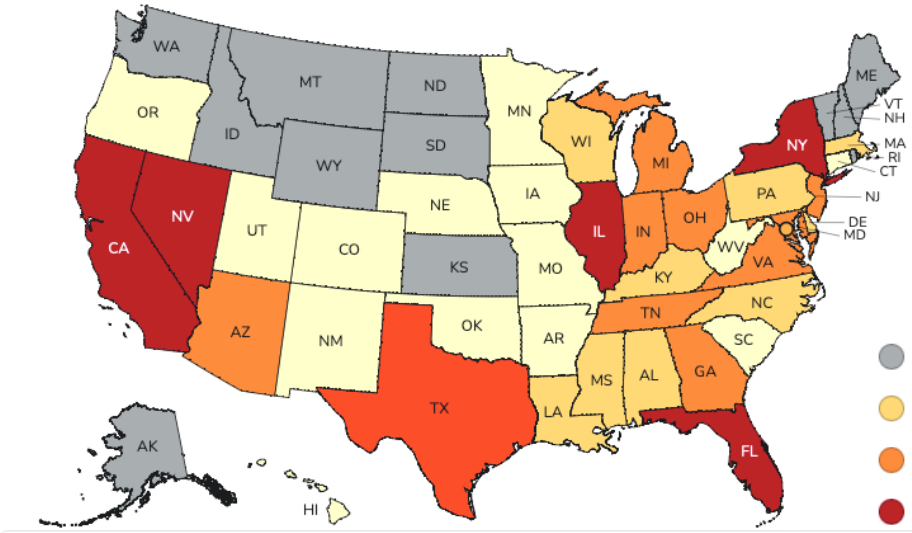
#IDLabCon

Candida auris

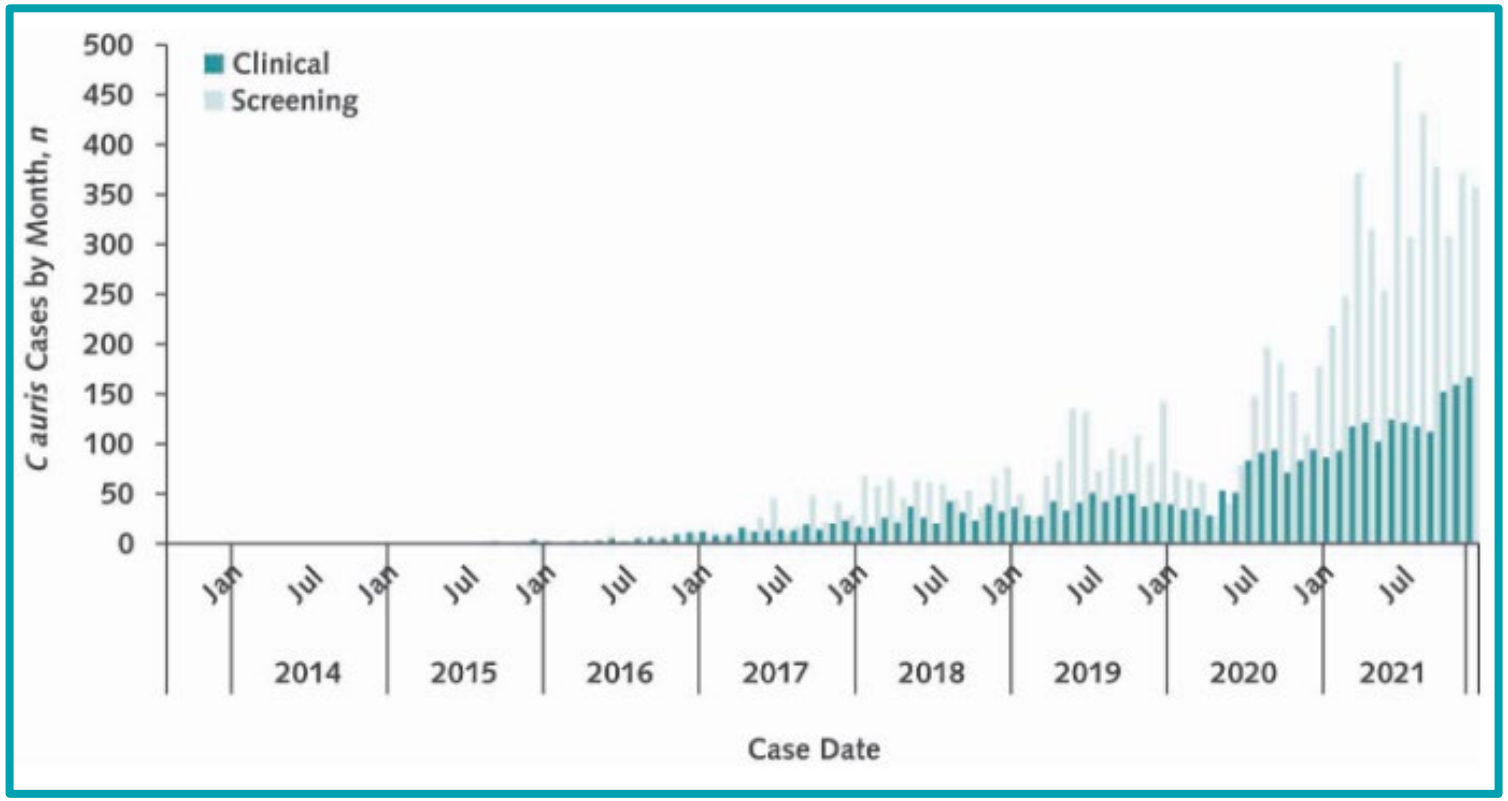
Epidemiology:

- First reported in US: 2016
- Now in >50% of US States
- Spread via healthcare

- High year-over-year increase in cases reported to CDC



Clinical and screening *C. auris* cases reported to CDC: 2013-2020

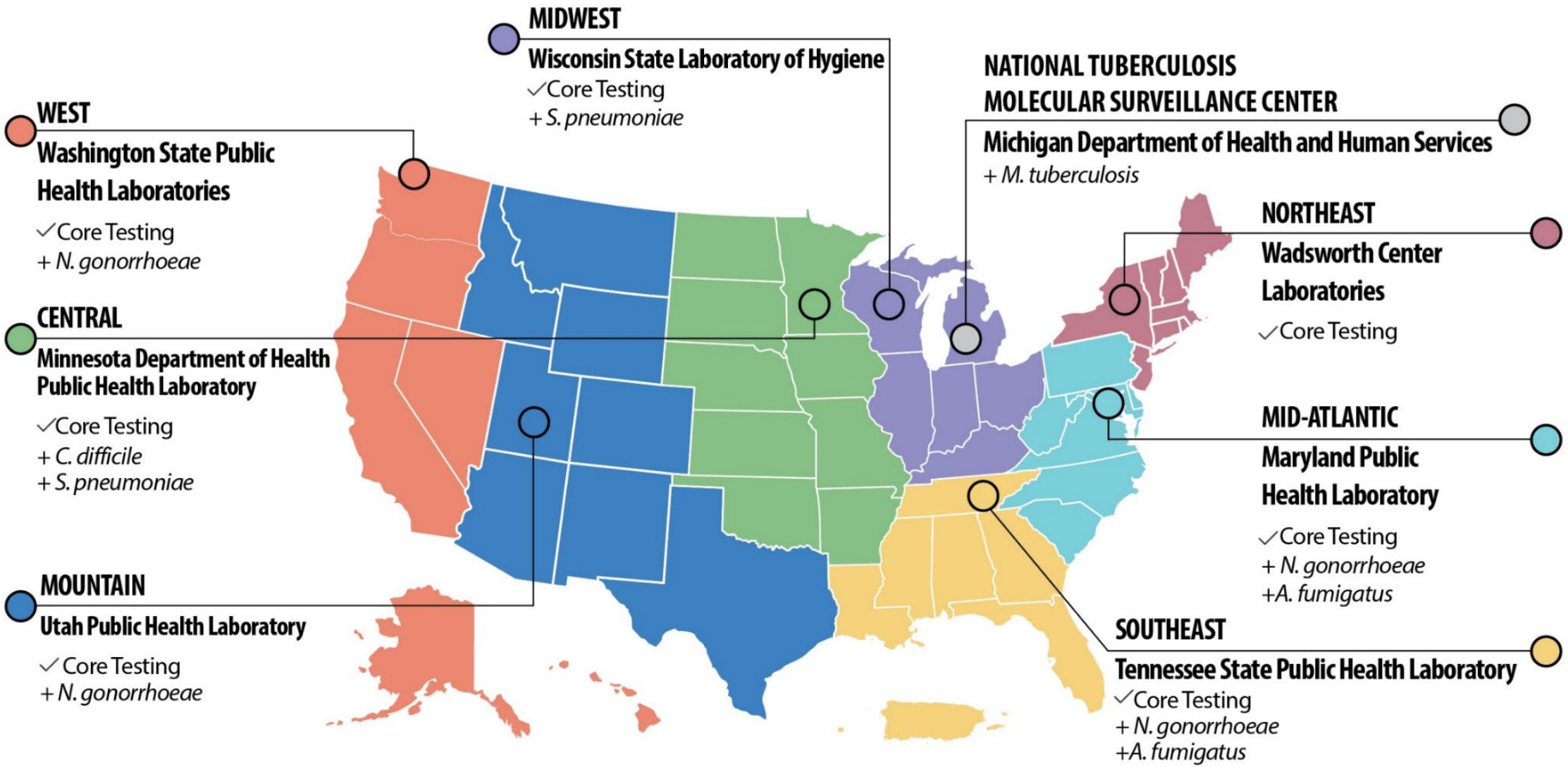


https://www.cdc.gov/candida-auris/tracking-c-auris/index.html

Lyman et al. Annals Internal Med. 2023 176:4

#IDLabCon

AR Lab Network Regional Labs



https://www.cdc.gov/drugresistance/laboratories/AR-lab-network-testing-details.html

AR Lab Network Regional Lab – *Candida auris*

- Confirm identification of isolates submitted from clinical and public health labs

Culture positive isolates

ID/confirm ID
(Bruker MALDI-TOF)

Antifungal Susceptibility Testing (AFST)
Microbroth dilution

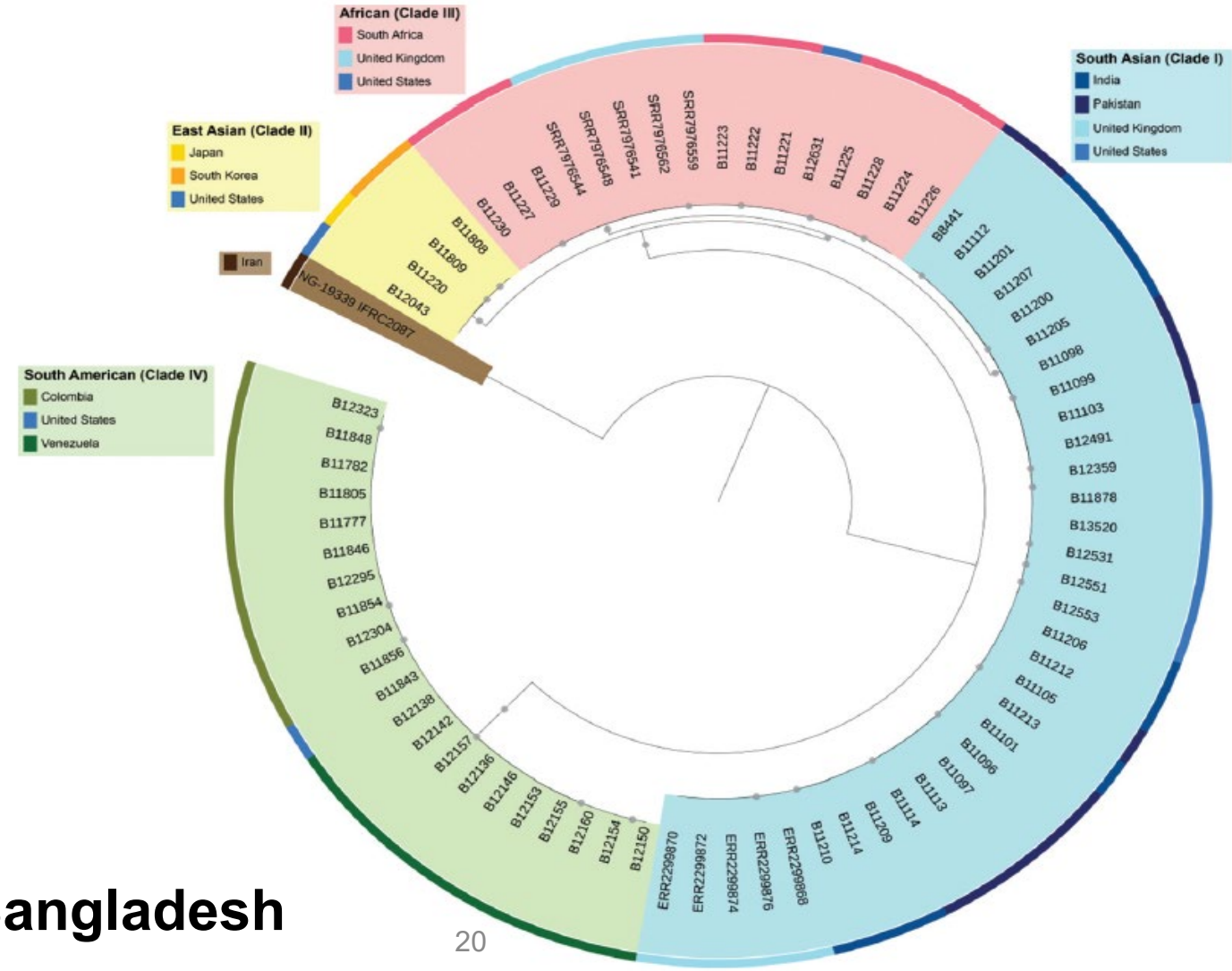
Amphotericin B
Anidulafungin
~~Caspofungin~~
Micafungin
Fluconazole
Isavuconazole
Itraconazole
Posaconazole
Voriconazole
Ibrexafungerp

Perform WGS MycoSNP

#IDLabCon

C. auris WGS

- **Clades** help to understand relatedness of organisms
- **5 major clades (reported)**
  - **Clade I (South Asian)**
    - Higher rates of resistance
  - **Clade II (East Asian)**
  - **Clade III (African)**
  - **Clade IV (South American)**
  - **Clade V (Iran)**
  - ***Clade VI – recently ID'd - Bangladesh**



C. auris: Clade Designation and Associated Resistance

TABLE 1

Frequency of antifungal drug resistance among *Candida auris* isolates by clade

Clade (*n*)	Frequency (%) of antifungal drug resistance in isolates (*n*)					
	Susceptible	Fluconazole resistant	Amphotericin B resistant	Micafungin resistant	MDR[a]	XDR[b]
Clade I (118[c])	3 (4)	97 (114)	47 (54)	6 (7)	45 (53)	3 (4)
Clade II (7)	86 (6)	14 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Clade III (51)	2 (1)	98 (50)	0 (0)	8 (4)	8 (4)	0 (0)
Clade IV (120)	31 (37)	59 (71)	11 (13)	9 (11)	10 (12)	0 (0)
Total (296)	16 (48)	80 (236)	23 (67)	7 (22)	23 (69)	1 (4)

[a]MDR, multidrug resistance to two major antifungal classes.

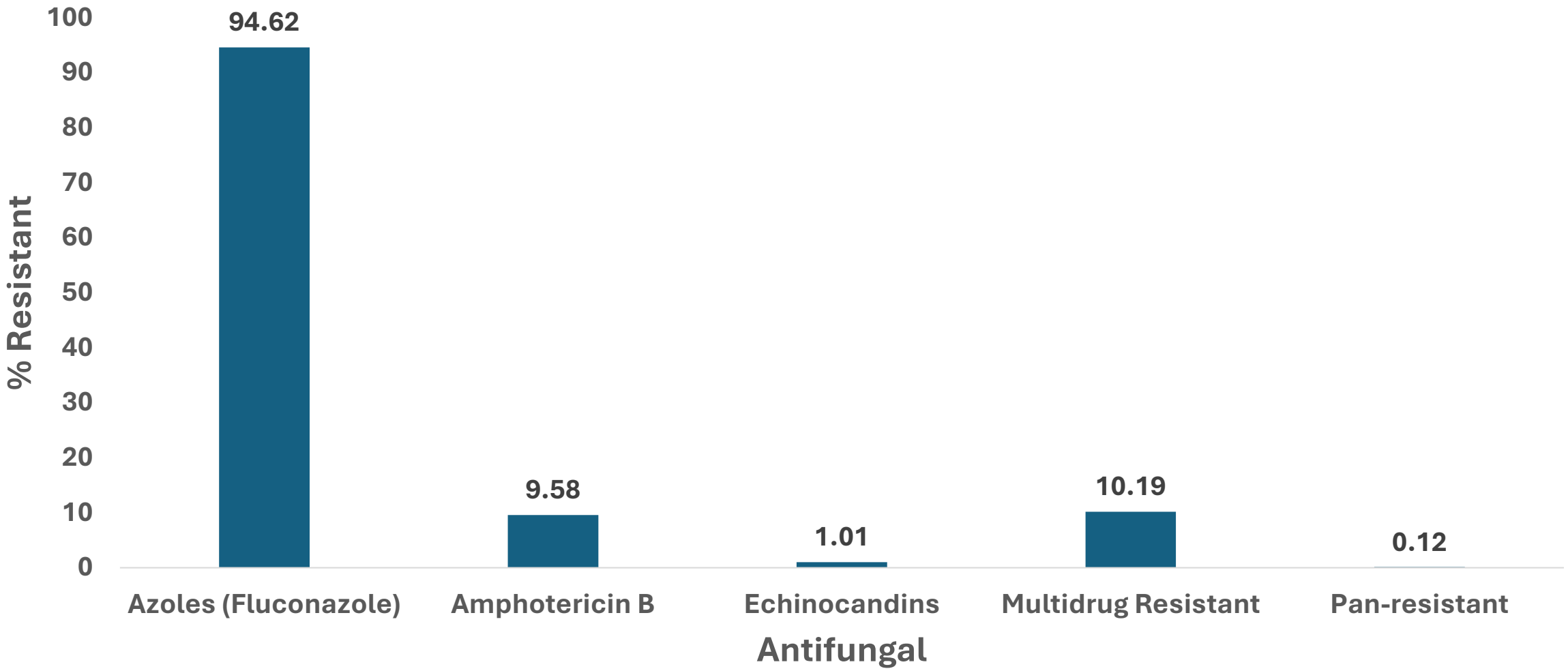
[b]XDR, extensive drug resistance to three major antifungal classes.

[c]Complete AFST data for 8 of the 126 clade I isolates were missing.

- **Clade I** - Higher rates of multi-drug resistance
- **Clade III** – higher frequency of fluconazole resistance

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7188998/

Candida auris Resistant in 2022



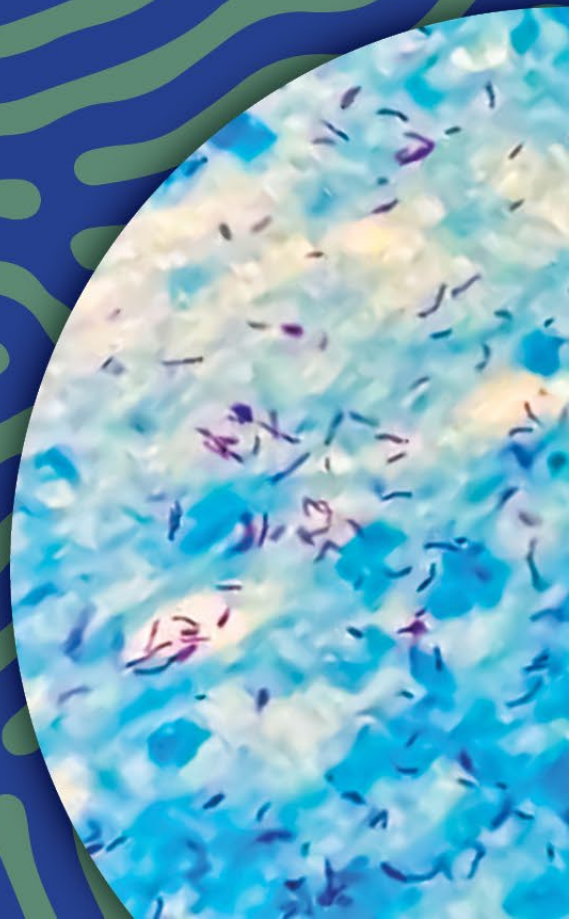
Multidrug resistant includes pan resistant cases
5 pan resistant cases were tested among specimen collected in 2022
4073 specimens were tested for resistance to at least 1 antifungal drug

Why do Screening for Candida auris?

- Avoid colonization turning into infection

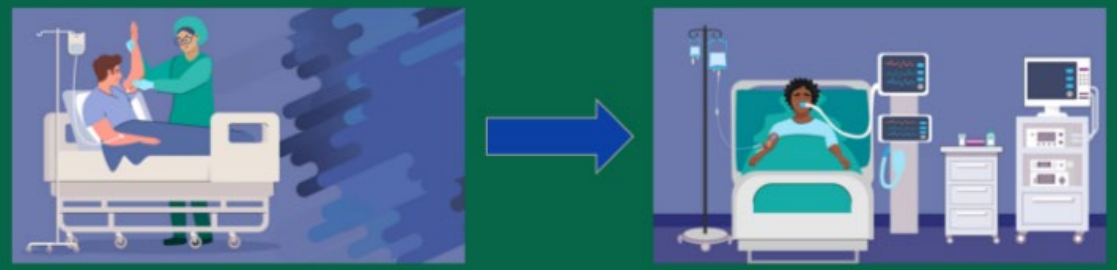
- Understand a transmission event

- Containing the spread



C. auris: Screening – Avoid Colonization to Infection

In the United States, **7.3%** of reported *Candida auris* screening cases had a **subsequent clinical case**.



Screening-to-clinical cases were **significantly** more likely to have screening specimens identified at **long-term acute care hospitals** and clinical specimens identified from **blood sources**.

Identifying facility type and specimen source associated with screening-to-clinical *Candida auris* patients in the United States, 2015-2022

Anna D. Baker, MPH, Malavika Rajeev, PhD, Jason Massey, PhD, Sophie Jones, PhD, and Meghan M. Lyman, MD
Centers for Disease Control and Prevention (CDC), National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Foodborne, Waterborne, and Environmental Diseases (DFWED), Mycotic Diseases Branch (MDB)

Why should screening be performed?

C. auris: Response – Screening to Contain Spread

- **Transmission can occur from colonized patients**
  - Identifying colonized patients or residents allows for implementation of infection control measures
- **In outbreak situations:**
  - Determine the scope of the outbreak
  - Determine if interventions are effective and if the outbreak is over through repeat testing
- **Screening available through AR Lab Network and results are available in timely manner to understand and stop further transmission**

C. auris: Response – Colonization Screening

- Axilla/groin swab (e.g. Eswab) collected by facility nursing staff
- Shipped to ARLN Regional Lab for testing
  - No cost to facility or patient
  - PCR for *Candida auris*
    - PCR positives reflex to culture
  - WGS in outbreak or cluster situations
- Screening results available within 2 days, often sooner

C. auris: Response – Colonization Screening

- Some Larger labs have implemented *C. auris* screening
- Simplexa® *C. auris* Direct PCR (Diasorin) – FDA approved
- Important to culture PCR positive specimens to obtain an isolate for WGS or AFST, if appropriate

C. auris: Case Study

- Patient A had a fall while vacationing in Tokyo and was hospitalized for several days prior to transfer to an acute care hospital (ACH) in US for hip surgery.
- Was admitted to transitional care unit 4 days ago
- A urine culture was ordered during the acute care stay.
- A health department HAI epidemiologist calls the transitional care facility with a report of a positive *C. auris* urine culture.

C. auris: Case Study

- What should the transitional care facility do?
- What about the acute care facility?
- Recommendations:
  - Colonization screening, potential contacts
  - Review products used for cleaning/disinfection (e.g. EPA List P products)
  - Implement Enhanced Barrier Precautions

Your Public Health HAI programs and AR Lab Network Labs can help

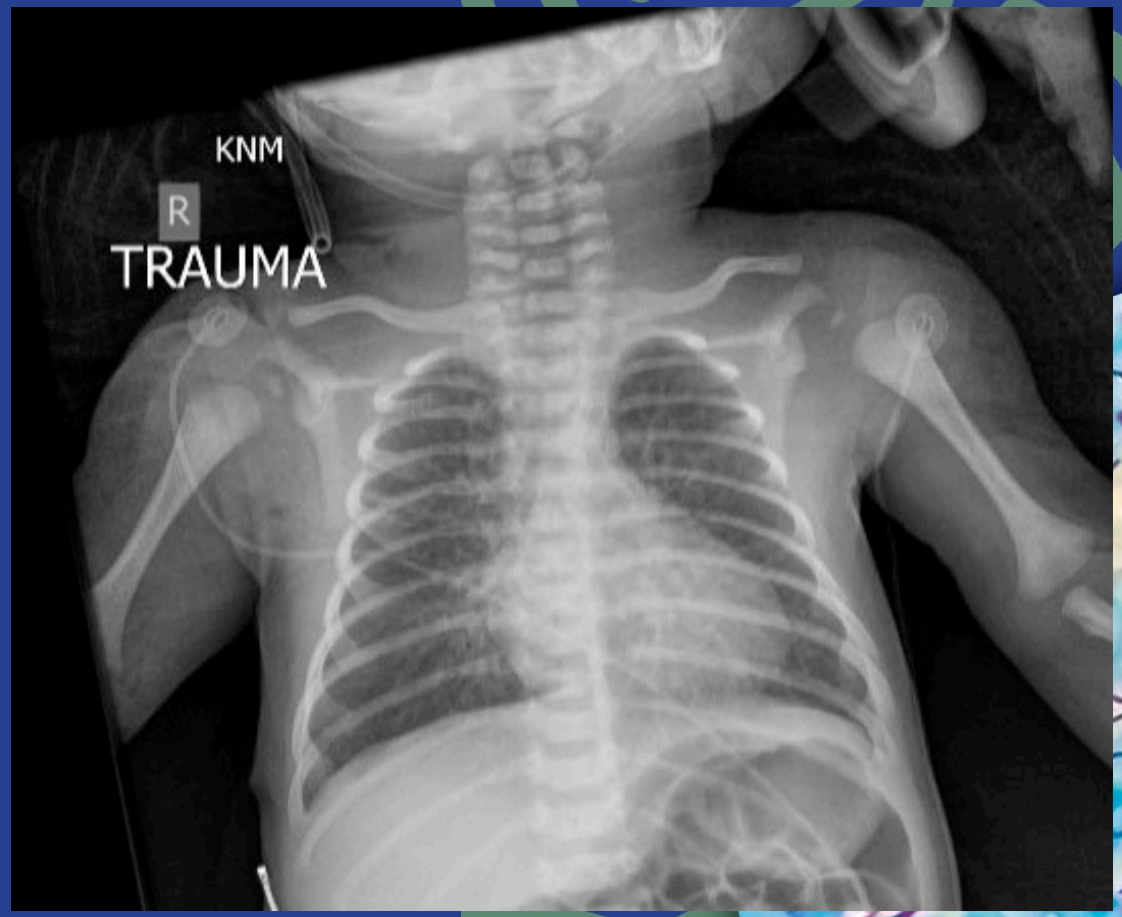
#IDLabCon

#IDLabCon

Case 2

Case 2.

- 4-day old female, found not breathing by mom
- Mom had limited prenatal care
- Exam: bilateral purulent conjunctivitis with conjunctival lesion
- X-ray: interstitial fluid in lungs
- Started on ampicillin + gentamicin and acyclovir
  - ID consulted, cefotaxime added



Case 2, continued

- CSF:
  - Glucose, 90
  - Protein, 161
  - 6 nucleated cells
- Eye discharge:
  - Gram-negative diplococci
  - *Neisseria gonorrhoeae*
- Tracheal aspirate:
  - *Light growth N. gonorrhoeae*

Pediatric infectious diseases:

"Can we perform antimicrobial susceptibility?"

Treatment expanded: ceftriaxone, azithromycin

AST for *N. gonorrhoeae*

AST Indications[1]

- Suspected gonorrhea treatment failure
- Outbreak of drug-resistant gonorrhea
- Disseminated gonococcal infections

CLSI M100 Tier 1 agents to consider testing[2]

- Azithromycin
- Ceftriaxone
- Cefixime
- Ciprofloxacin
- Tetracycline

- Methods:
  - Disk diffusion
  - Gradient diffusion
  - Agar dilution
- Media: GC test agar +1% IsoVitaleX
- Most clinical laboratories do not perform testing
- Some labs perform a nitrocefin beta-lactamase test – but this is not indicated

1. Workowski et al. MMWR Recomm Rep. 2021 70:1-187
2. CLSI. 2025. M100, Table 1F, page 44

Beta-lactam resistance in *N. gonorrhoeae*

Determinant	Mechanism	Affected antimicrobials	Detected by nitrocefin test?	Notes
penA mutation	PBP2 target alternation	Penicillins (low level)	No	First emerged 1946
mtrR mutation	Efflux		No	
porB1b mutation	Reduce influx		No	
ponA mutation	PBP1 target alteration		No	
TEM-1, TEM-135*	Hydrolysis of penicillin	Penicillins (high level)	Yes	1976, likely from *H. parainfluenzae*
penA mosaic allele	Altered PBP2 target	Ceftriaxone Cefixime	No	Early 2000s

- **Nitrocefin test of little value ….**

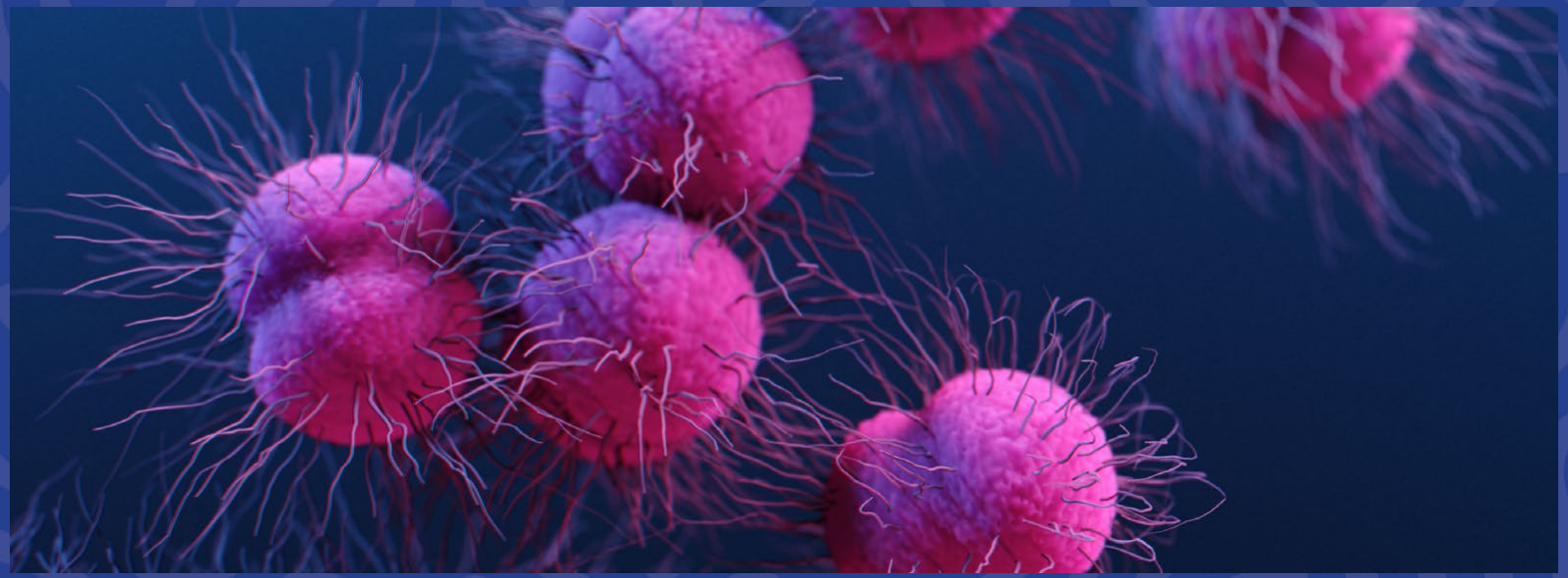
*TEM-135 is a single nucleotide mutation away from becoming an ESBL

Unemo and Shafer 2015 CMR

Case 2. Final laboratory report

- Isolate sent to Tennessee Department of Health
- Agar Dilution
  - Cefixime, 0.015 ug/mL S
  - Ceftriaxone, 0.008 ug/mL S
  - Azithromycin, 1 ug/mL S

Baby recovers well, discharged to grandparents



ID LAB CON
APHL 2025

#IDLabCon

Neisseria gonorrhoeae

Paula

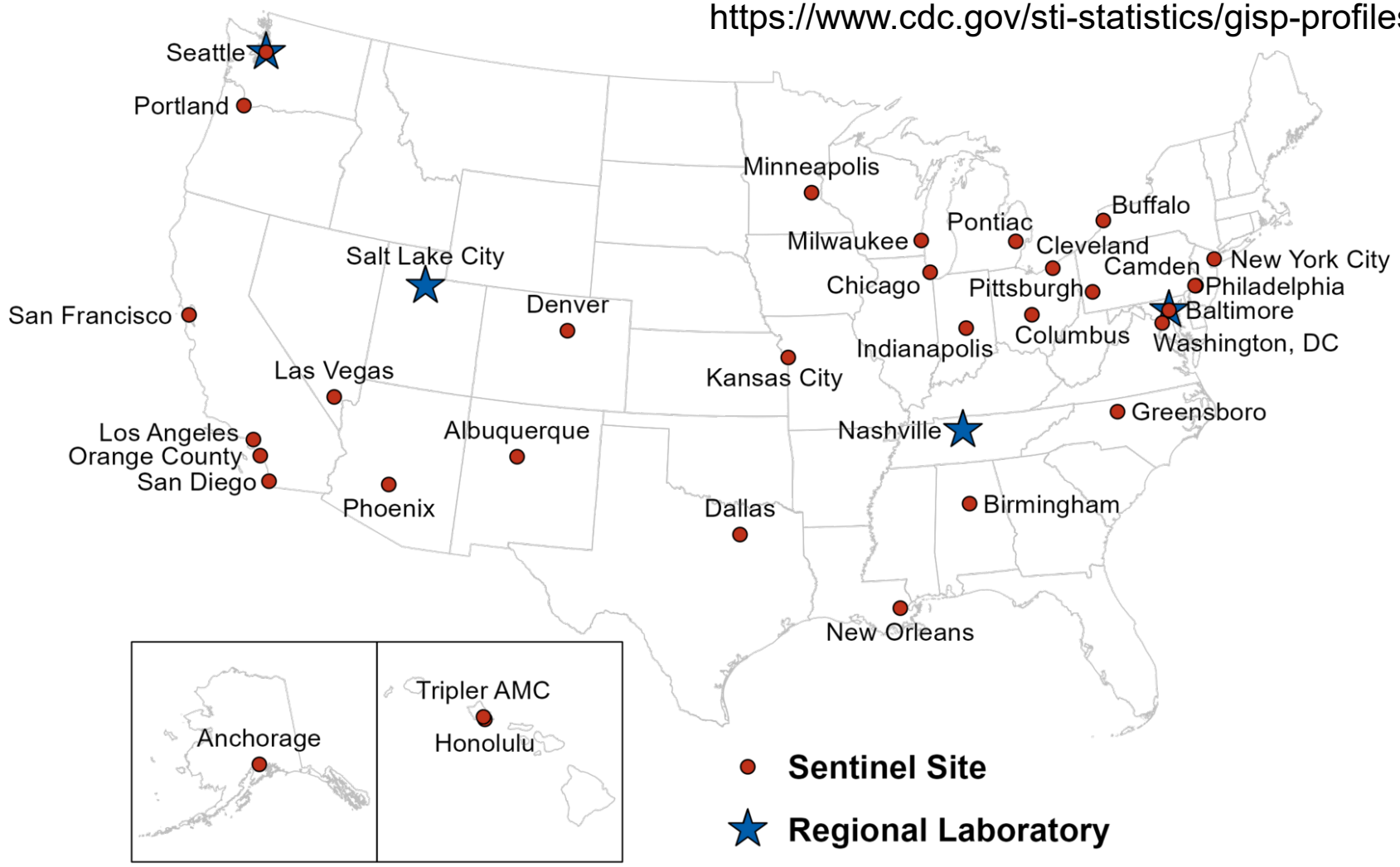
CDC Surveillance Programs for GC

- **GISP – Gonococcal Isolate Surveillance Project**
  - Established in 1986 to monitor trends in antimicrobial susceptibilities of GC strains in the US in order to establish an evidence-based rationale for selection of gonococcal therapies.
- **SURRG - Strengthening the United States Response to Resistant Gonorrhea**
  - a collaborative effort initiated in 2016 emphasizing rapid detection and response to drug-resistant gonorrhea in eight areas around the country.

Need to culture an organism in order to do further characterization

STD clinics affiliated with 32 state or city health departments contributed 3,684 gonococcal isolates to GISP in 2022. Of these 32 sites, 10 current sites have participated continuously since 1987

https://www.cdc.gov/sti-statistics/gisp-profiles/index.html

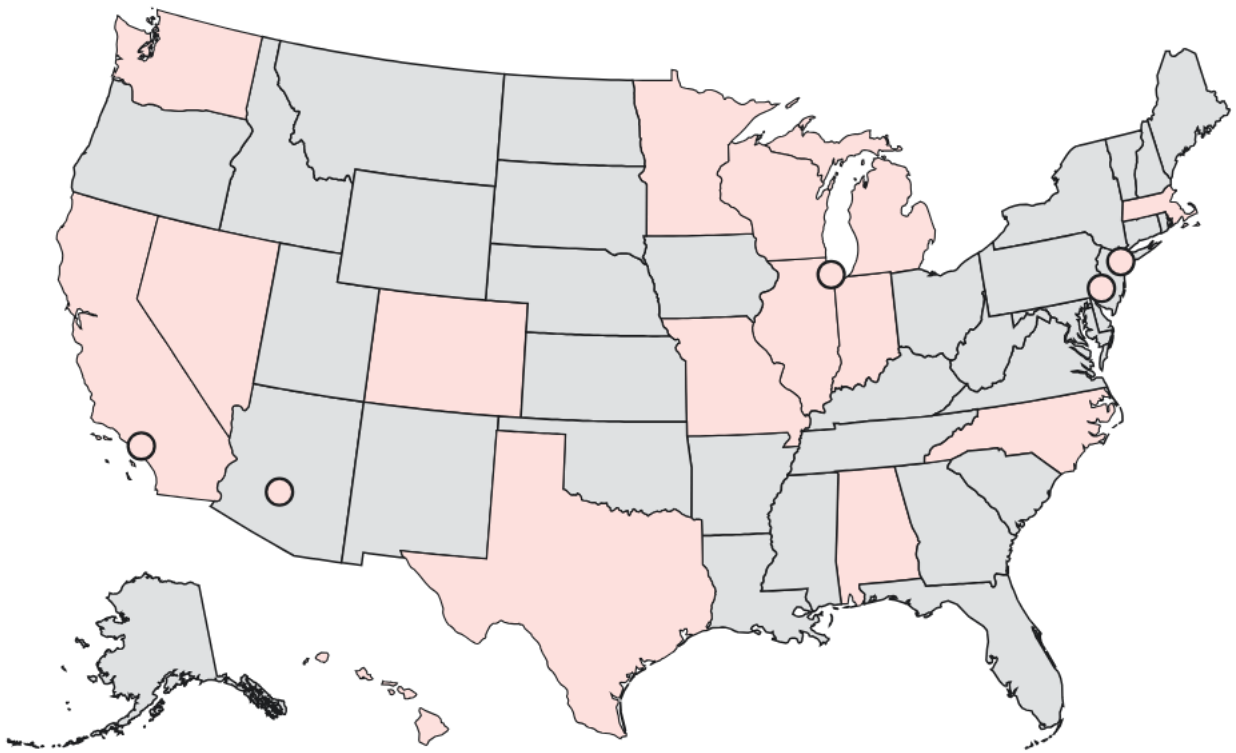


Map showing 2022 GISP Clinical Sites and Regional Laboratories

CDC Surveillance Programs for GC

- **CARGOS - Combatting Antimicrobial Resistant Gonorrhea and Other STIs**
  - Allows CDC and state and local health departments to monitor trends in antimicrobial-resistant (AR) gonorrhea and other STIs in the U.S.
  - Intended to strengthen state and local capacity to rapidly detect and respond to threats of resistance.

In the first year of the project, CDC has awarded a total of $6.5 million to the following recipients:

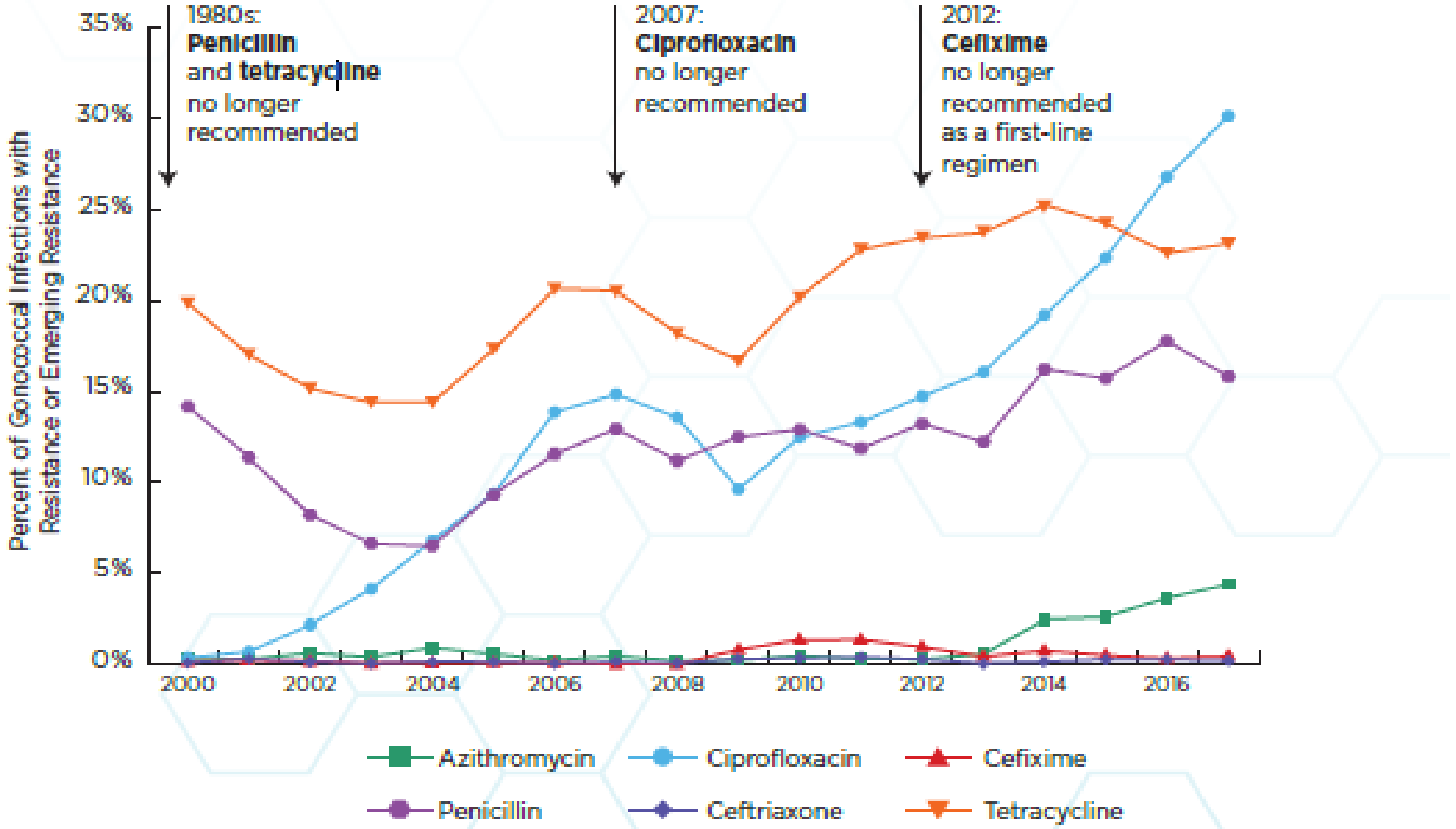


CARGOS

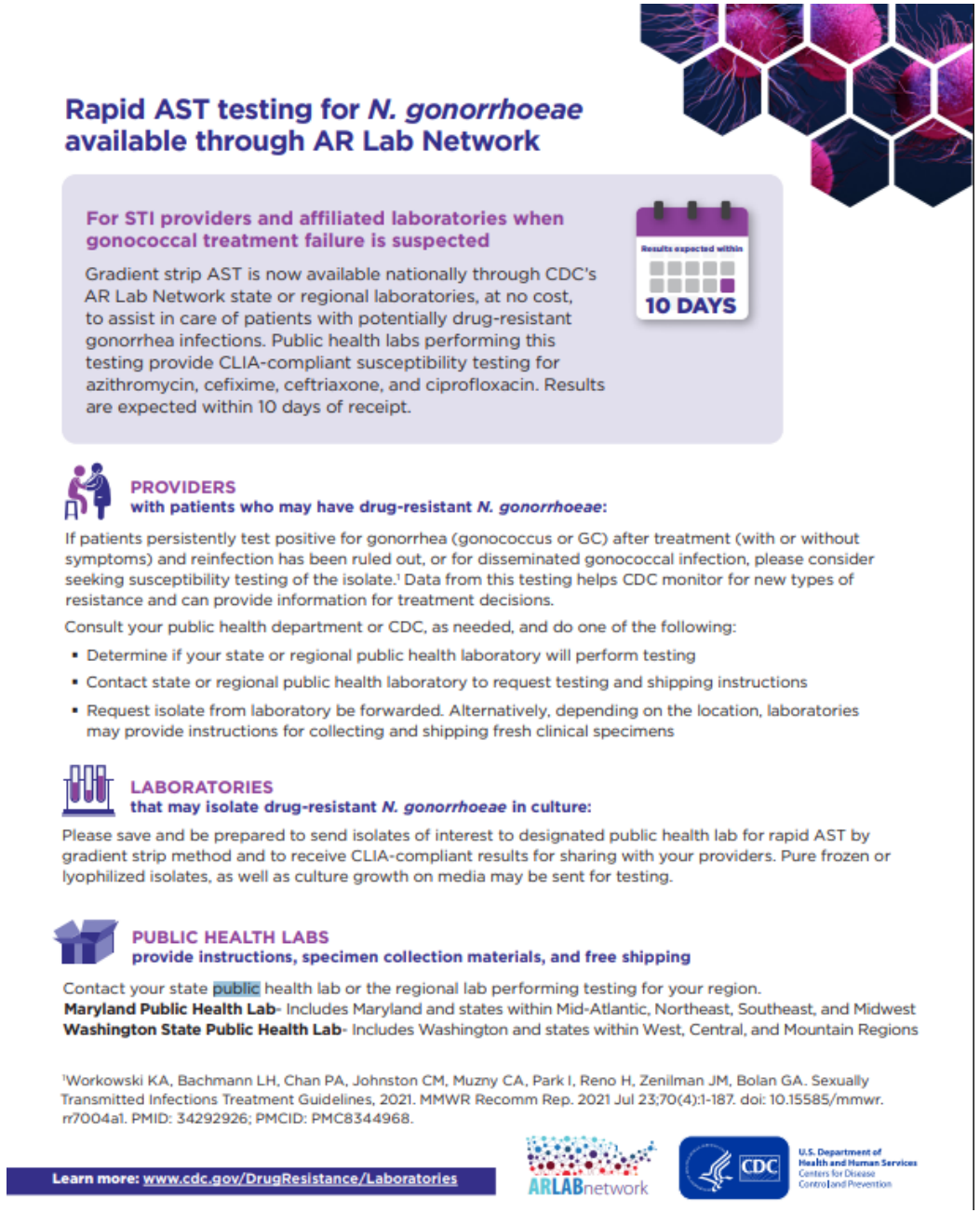
- *N. gonorrhoeae* isolates are collected monthly from up to the first 25 men with symptomatic gonococcal urethritis seeking care at participating STD clinics. 2nd year – also collect pharyngeal swabs from men and women
- Isolates are shipped from participating clinics to the regional laboratories participating in the Antimicrobial Resistance (AR) Lab Network for Agar dilution AST
- In 2022, isolates were tested to determine MICs for penicillin, tetracycline, ceftriaxone, cefixime, ciprofloxacin, azithromycin, and gentamicin.
- Clinical, demographic, and lab data are compiled and analyzed at CDC for public use.

EMERGING ANTIBIOTIC RESISTANCE

Gonorrhea rapidly develops resistance to antibiotics--ceftriaxone is the last recommended treatment.



http://www.cdc.gov/DrugResistance/Biggest-Threats.html



Rapid AST testing for *N. gonorrhoeae* available through AR Lab Network

For STI providers and affiliated laboratories when gonococcal treatment failure is suspected

Gradient strip AST is now available nationally through CDC's AR Lab Network state or regional laboratories, at no cost, to assist in care of patients with potentially drug-resistant gonorrhea infections. Public health labs performing this testing provide CLIA-compliant susceptibility testing for azithromycin, cefixime, ceftriaxone, and ciprofloxacin. Results are expected within 10 days of receipt.

Results expected within
10 DAYS

PROVIDERS
with patients who may have drug-resistant *N. gonorrhoeae*:

If patients persistently test positive for gonorrhea (gonococcus or GC) after treatment (with or without symptoms) and reinfection has been ruled out, or for disseminated gonococcal infection, please consider seeking susceptibility testing of the isolate.[1] Data from this testing helps CDC monitor for new types of resistance and can provide information for treatment decisions.

Consult your public health department or CDC, as needed, and do one of the following:

- Determine if your state or regional public health laboratory will perform testing
- Contact state or regional public health laboratory to request testing and shipping instructions
- Request isolate from laboratory be forwarded. Alternatively, depending on the location, laboratories may provide instructions for collecting and shipping fresh clinical specimens

LABORATORIES
that may isolate drug-resistant *N. gonorrhoeae* in culture:

Please save and be prepared to send isolates of interest to designated public health lab for rapid AST by gradient strip method and to receive CLIA-compliant results for sharing with your providers. Pure frozen or lyophilized isolates, as well as culture growth on media may be sent for testing.

PUBLIC HEALTH LABS
provide instructions, specimen collection materials, and free shipping

Contact your state public health lab or the regional lab performing testing for your region.
Maryland Public Health Lab- Includes Maryland and states within Mid-Atlantic, Northeast, Southeast, and Midwest
Washington State Public Health Lab- Includes Washington and states within West, Central, and Mountain Regions

[1]Workowski KA, Bachmann LH, Chan PA, Johnston CM, Muzny CA, Park I, Reno H, Zenilman JM, Bolan GA. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. 2021 Jul 23;70(4):1-187. doi: 10.15585/mmwr.rr7004a1. PMID: 34292926; PMCID: PMC8344968.

Learn more: www.cdc.gov/DrugResistance/Laboratories

ARLABnetwork

CDC U.S. Department of Health and Human Services Centers for Disease Control and Prevention

Where can I get AST?

- **CLIA validated gradient strip AST is available nationally through CDC's AR Lab Network, at no cost.**
- 21 PHLs are doing the testing
- To assist in care of patients with potentially drug-resistant gonorrhea infections
- Test for azithromycin, cefixime, ceftriaxone, and ciprofloxacin
- Results are expected within 10 days of receipt

https://www.cdc.gov/antimicrobial-resistance-laboratory-networks/media/pdfs/NG-GradientStripAST-FS-508.pdf

Pan-resistant GC – 2023 - Massachusetts

Patient presented to a primary care clinic with symptoms of urethritis. GC was isolated from a clinical specimen. The Massachusetts State Lab identified a concerning susceptibility pattern and sent isolates to CDC for further testing.

Box 1: Minimum Inhibitory Concentrations (MIC) by Agar Dilution of the Massachusetts Gonococcal Isolate of Concern

Drug	MIC	Susceptible	Intermediate Resistance	
Ceftriaxone	1.0 µg/mL	≤ 0.25 µg/mL	UD^	NS
Cefixime	> 1.0 µg/mL	≤ 0.25 µg/mL	UD^	NS
Azithromycin	2.0 µg/mL	≤ 1.0 µg/mL	UD^	NS
Ciprofloxacin	16.0 µg/mL	≤ 0.06 µg/mL	0.12–0.5 µg/mL	R
Tetracycline	2.0 µg/mL	≤ 0.25 µg/mL	0.5–1.0 µg/mL	R
Gentamicin	8 µg/mL	UD^	UD^	NS
Penicillin	32.0 µg/mL	≤ 0.06 µg/mL	0.12–1.0 µg/mL	R

^UD: undefined

https://archive.cdc.gov/www_cdc_gov/std/dstdp/dcl/2023-01-19-bachmann-amr-gonorrhea.htm

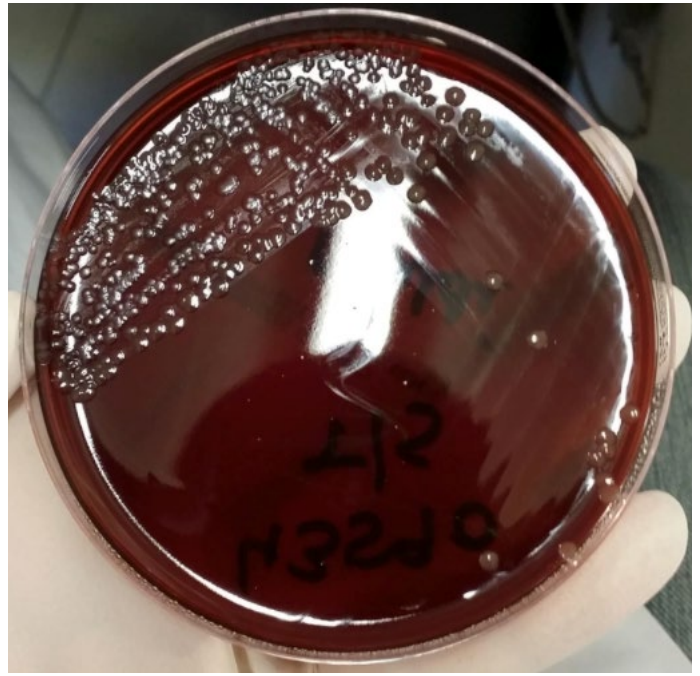
Pan-resistant GC – 2023 - Massachusetts

- Subsequently found 2 isolates in the same patient, and an additional case.
- Follow-up testing performed by CDC's STD Laboratory
  - identified the *penA60* allele, previously associated with ceftriaxone non-susceptiblity
- This is the first case of documented resistance to 6 of the 7 drugs tested on the standard GISP panel
- The second and third identified gonococcal cases in the US with the *penA60* allele.
- The first *penA60* allele was identified in Las Vegas, NV in December 2019.

Case 2.1

- 33 year old man with 4 days urethral discharge
- CT, NG tests negative
- Symptoms persist, urine culture sent which grows

N. meningitidis



Meningococcal urethritis

- Emerging STI among heterosexual men
- Associated with U.S. N. meningitidis urethritis clade US_NmUC
- Unencapsulated, with virulence factors that allow growth in anaerobic conditions & to avoid host immune response
- Rarely cause invasive disease, and only in immunocompromised
- Treatment: like for gonococcal urethritis

Burns and Rhoads J Clin Microbiol. 2022 60:e00575-22.

AST for *N. meningitidis*

Treatment

- Ceftriaxone or cefotaxime
  - Ampicillin or penicillin if isolate is “S”
- Chemoprophylaxis:
  - Rifampin, ceftriaxone or ciprofloxacin

AST indications (not always needed)

- Serious infection (blood, CSF other sterile sites)
- May be useful when deciding prophylaxis

Methods:

- Disk diffusion
- Gradient diffusion*, broth microdilution

- Media: MHA with 5% sheep blood; CAMHB+LHB
- Most clinical laboratories do not perform testing
- Nitrocefin test **not validated, resistance for penicillin usually due to PBP modification**
- USE CAUTION – test in a BSC

*Etest used by PHL, Liofilchem strip performance reasonable (Jonsson 2018 APMIS. 126:822)

Biosafety Precautions when working with *N. meningitidis*

- High risk of aerosolization in laboratory with invasive isolates
  - Infection of microbiologists documented from reading plates or subculturing on bench
- Isolates from respiratory source are in general less pathogenic and lower risk
- Precautions:
  - Vaccination (BOTH quadrivalent and Meningococcus B) – note, not 100% effective
  - Post-exposure prophylaxis (e.g., if manipulated cultures outside BSC)
  - Perform all procedures in a class II BSC
    - Splash guards, masks are not validated protective measures

MMWR. 2002 51;141

Sejvar et al. 2005 JCM 43:4811

AST options for *N. meningitidis*

Disk diffusion

- Not validated for penicillin due to errors[1]

Gradient diffusion

- Good agreement with reference MIC[1,2]

Reference Lab

- Time to results for clinical isolates long
- Ensure you clearly label to avoid exposures!

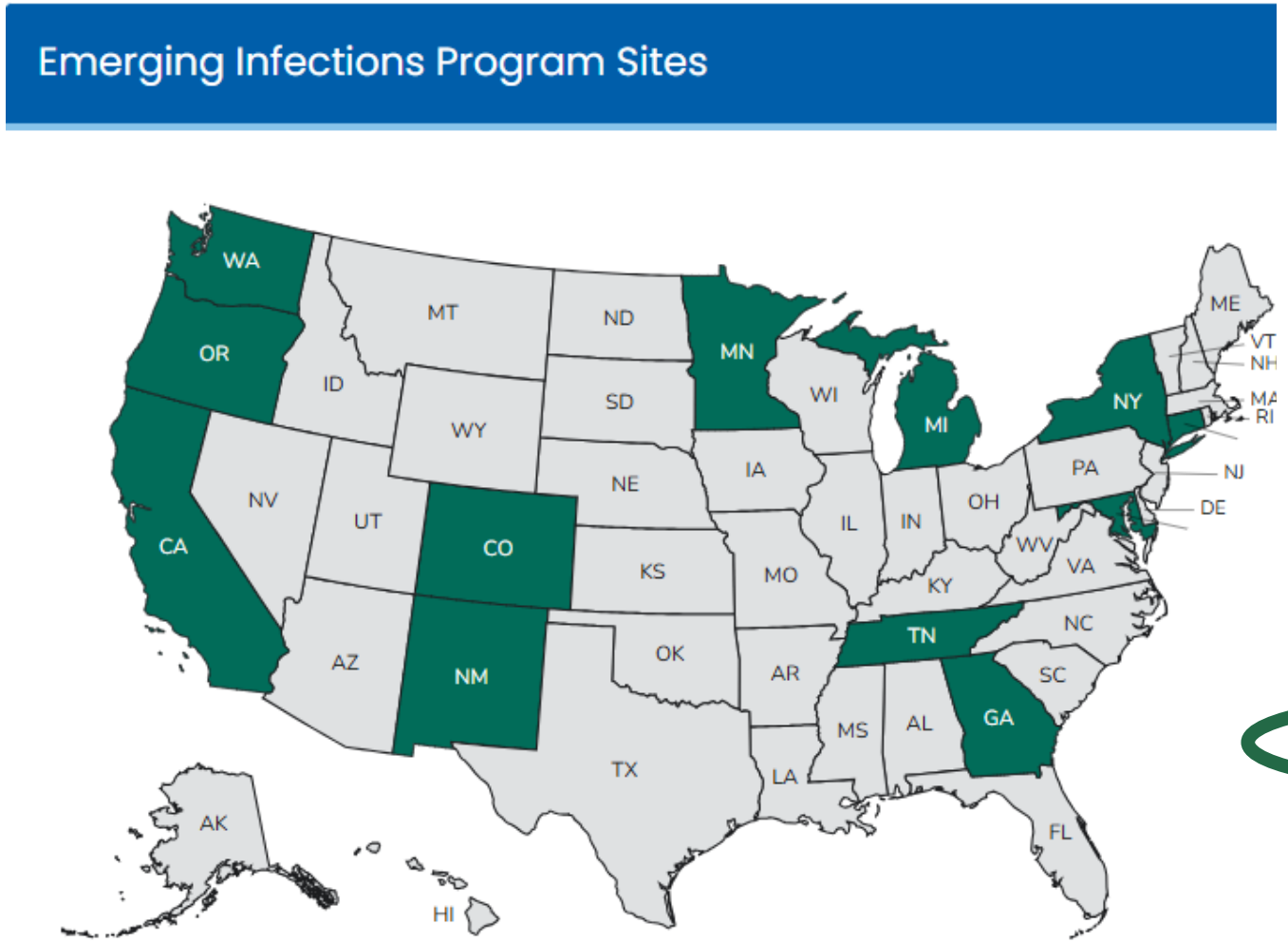
1. Jorgensen et al 2006. JCM 44:1744; 2. Marshall et al. 1997. Diagn Microbiol Infect Dis. 27:93 3. Daher 2002. Diagn Microbiol Infec Dis 43:119.

#IDLabCon

Neisseria meningitidis

Paula

CDC's Surveillance for *Neisseria meningitidis*



Overview

Emerging Infections Program (EIP) activities focus on surveillance, applied research, and flexible and enhanced responses to emerging issues. These efforts generate reliable incidence estimates and provide critical information on risk factors, spectrum of disease, and intervention impact.

ABCs

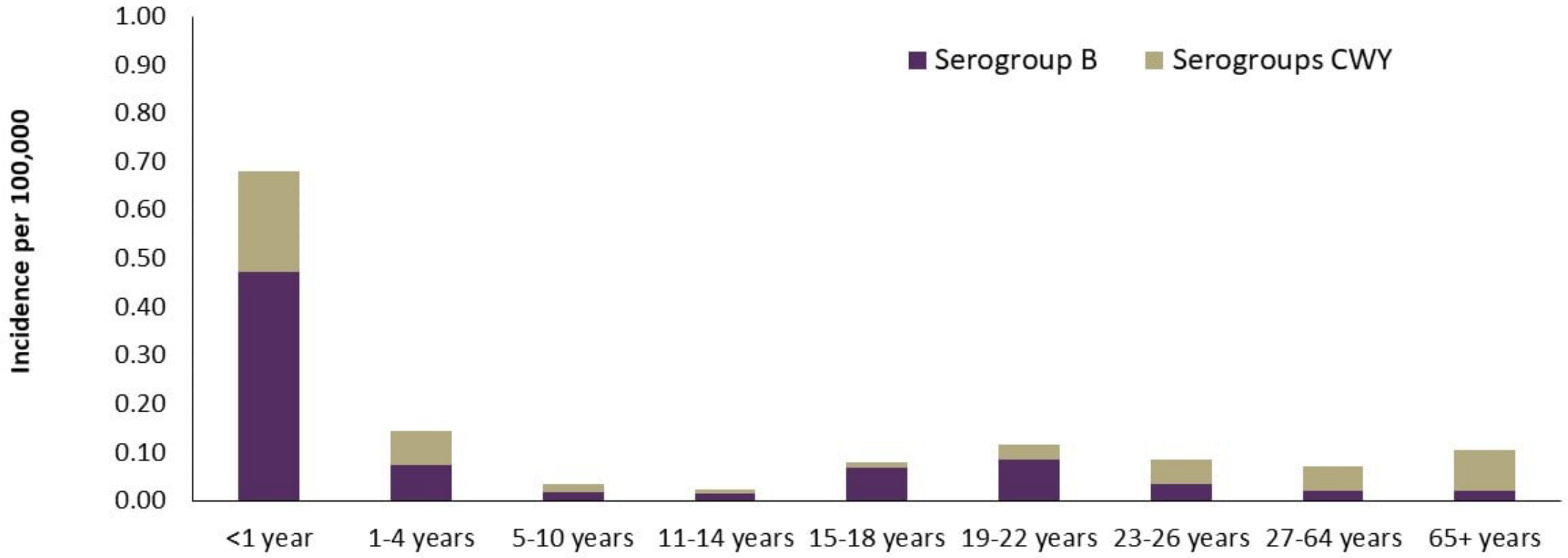
Active Bacterial Core surveillance (ABCs) is a laboratory- and population-based surveillance system for five bacterial pathogens:

- group A *Streptococcus*
- group B *Streptococcus*
- *Haemophilus influenzae*
- *Neisseria meningitidis*
- *Streptococcus pneumoniae*

ABCs provides estimates of invasive disease burden and trends for these pathogens. ABCs also monitors changes in antimicrobial resistance and other characteristics through collection of bacterial isolates and demographic and clinical data.

2nd - The National Notifiable Diseases Surveillance System (NNDSS)

Meningococcal incidence by serogroup* and age-group, 2013–2022



* Unknown serogroup (12%) and other serogroups (9%) excluded

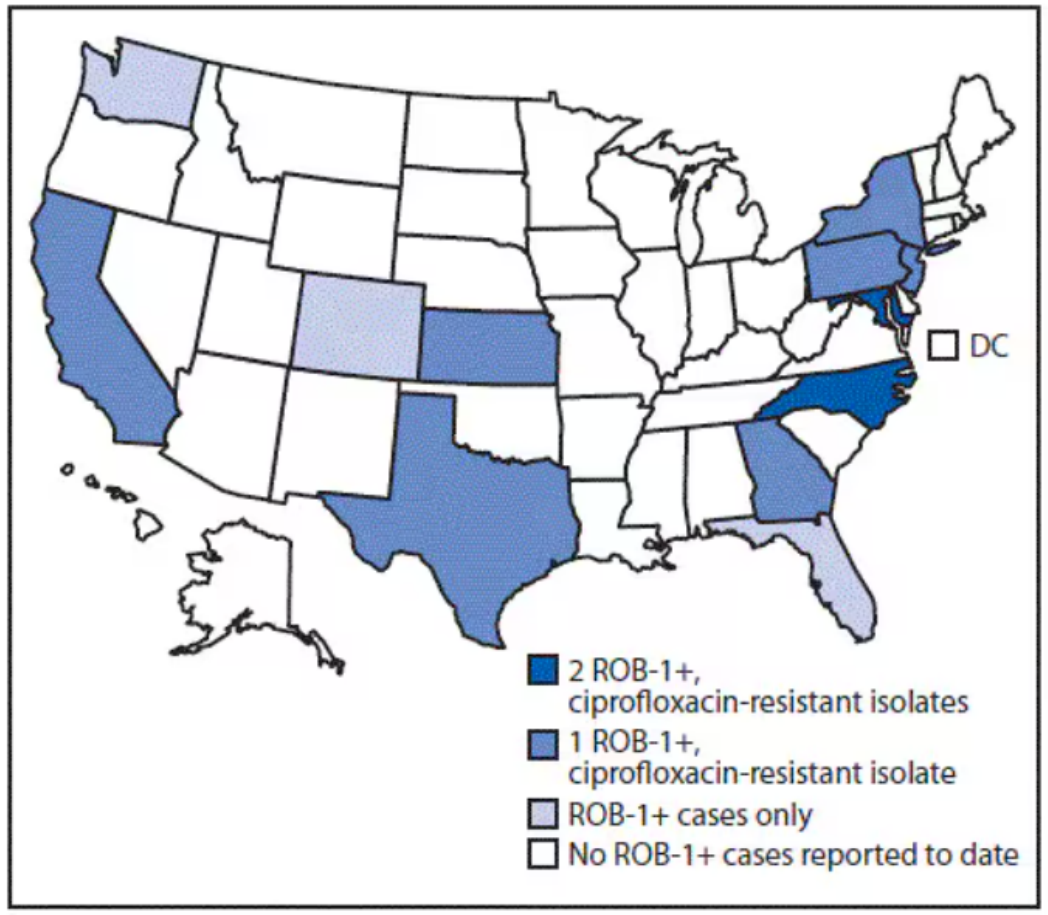
SOURCE: CDC; National Notifiable Diseases Surveillance System with additional serogroup data from Active Bacterial Core surveillance and state health departments

Detection of Ciprofloxacin-Resistant, β-Lactamase–Producing *Neisseria meningitidis* Serogroup Y Isolates — United States, 2019–2020

Weekly / June 19, 2020 / 69(24);735–739

- During 2019–2020, 11 meningococcal isolates from U.S. patients had isolates containing a $bla_{\text{ROB-1}}$ β-lactamase gene associated with penicillin resistance and mutations associated with ciprofloxacin resistance.
- An additional 22 cases reported during 2013–2020 contained $bla_{\text{ROB-1}}$ but did not have mutations associated with ciprofloxacin resistance.

FIGURE 2. Meningococcal disease cases with clonal complex 23 Neisseria meningitidis isolates (N = 33) with a *bla*$_{ROB-1}$ β-lactamase enzyme gene* alone or in combination with a ciprofloxacin resistance–associated mutation, by state — United States, 2013–2020 * Conferring resistance to penicillins.



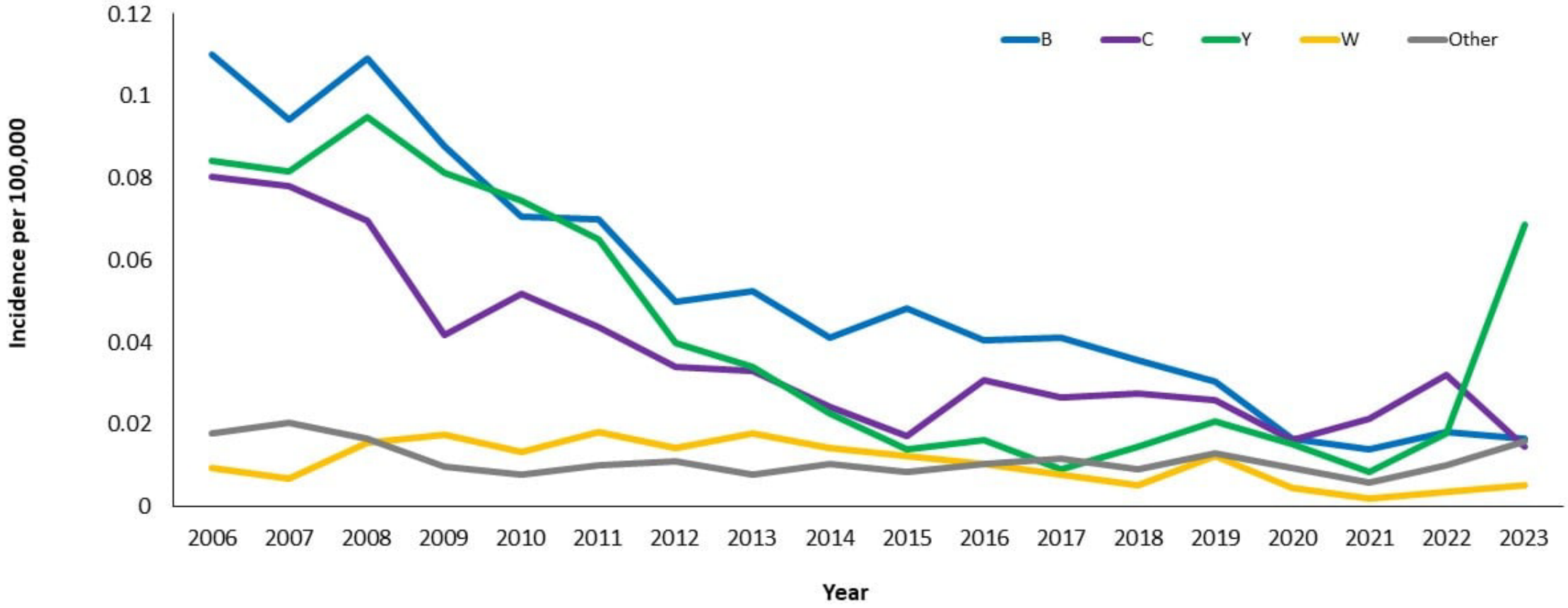
Abbreviation: DC = District of Columbia.

McNamara LA, Potts C, Blain AE, et al. Detection of Ciprofloxacin-Resistant, β-Lactamase–Producing *Neisseria meningitidis* Serogroup Y Isolates — United States, 2019–2020. MMWR Morb Mortal Wkly Rep 2020;69:735–739. DOI: http://dx.doi.org/10.15585/mmwr.mm6924a2

Neisseria meningitidis Disease Trends Since 2021

- U.S. cases of meningococcal disease have increased sharply since 2021 and now exceed pre-pandemic levels. In 2023, **438** confirmed and probable cases were reported. This is the **largest number** of U.S. meningococcal disease cases reported **since 2013**.
- *Neisseria meningitidis* serogroup Y drives much of this recent increase.
- **People disproportionately affected** by the increase include:
  - People between the ages of 30 and 60 years
  - Black or African American people
  - Adults with HIV

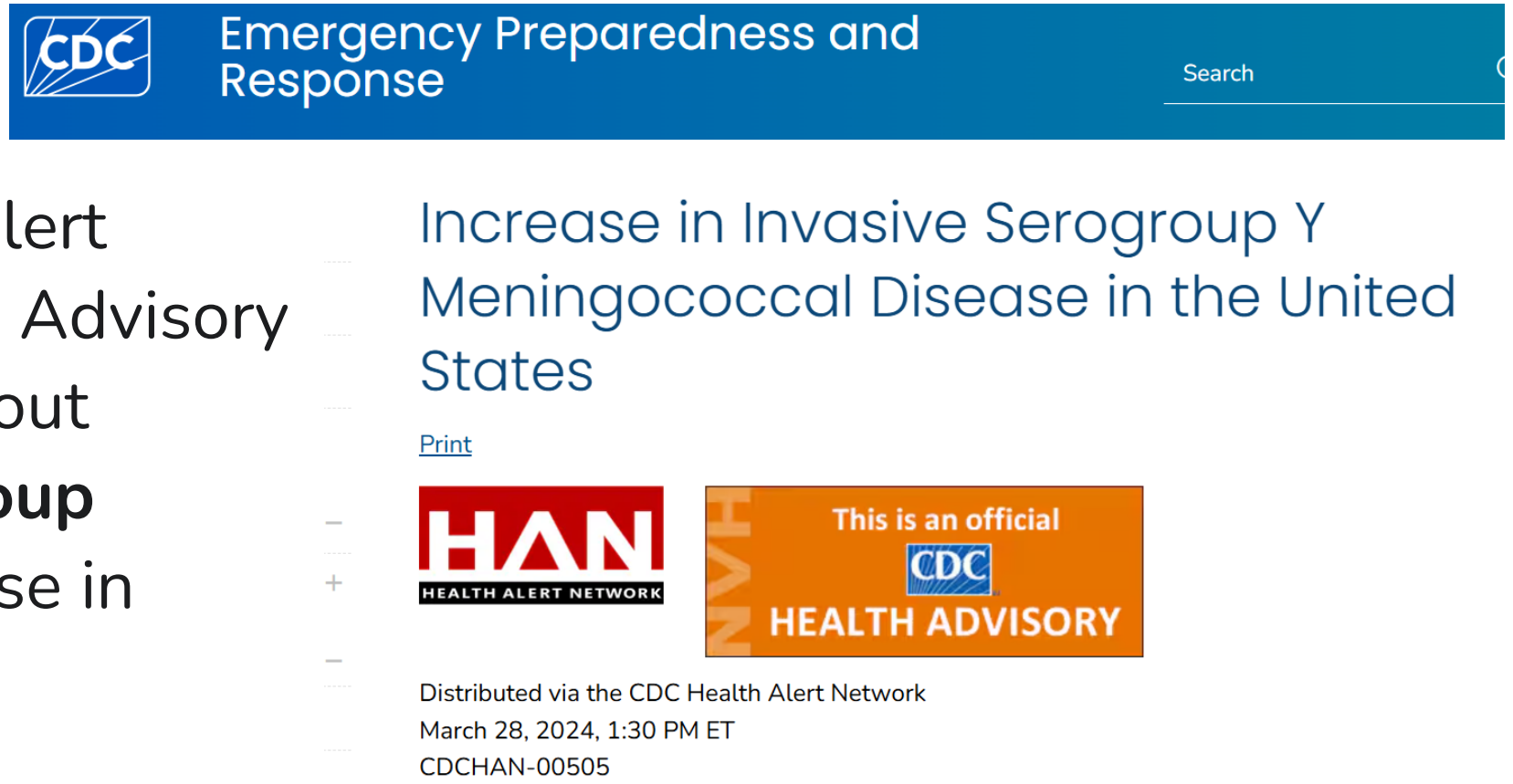
Trends in Meningococcal Disease Incidence by Serogroup – United States, 2006–2023*



Source: NNDSS data with additional serogroup data from Active Bacterial Core surveillance (ABCs) and state health departments
*2023 data are preliminary

Neisseria meningitidis serogroup Y

CDC issued a Health Alert Network (HAN) Health Advisory on March 28, 2024, about the **increase in serogroup Y** meningococcal disease in the **United States**.



https://www.cdc.gov/han/2024/han00505.html

#IDLabCon

ID LAB CON APHL 2025

Neisseria meningitidis serogroup Y

- A specific meningococcal strain, sequence type **(ST)1466**, is responsible for most (101 of 148, 68%) serogroup Y cases with available sequence type data that were reported across the United States in 2023.
- Most cases of invasive meningococcal disease caused by ST-1466 in 2023 had a **clinical presentation other than meningitis**: 64% presented with bacteremia, and at least 4% presented with septic arthritis.
- Serogroup Y ST-1466 isolates tested to date have been **susceptible to all first-line antibiotics** recommended for treatment and prophylaxis.

https://www.cdc.gov/han/2024/han00505.html

N. Meningitidis Treatment and Prophylaxis

- **Treatment:** Empirical therapy for suspected meningococcal disease is an extended-spectrum cephalosporin, such as cefotaxime or ceftriaxone.
- Treatment with penicillin or ampicillin requires susceptibility testing.

- **Prophylaxis:** typically ciprofloxacin, ceftriaxone, rifampin
- Expands to azithromycin in place of ciprofloxacin when two or more **ciprofloxacin-resistant** meningococcal disease cases that account for ≥20% of all cases are reported in a local catchment area during a 12-month period.

VPD Reference Centers

Bacterial Pathogens

Detection and Serogroup/serotype

- *Haemophilus influenzae*
- *Neisseria meningitidis*

Detection

- *Bordetella pertussis*

https://www.aphl.org/aboutAPHL/publications/Documents/VPD-Reference-Guide.pdf#search=vpd%20reference%20centers

Testing Available at VPD RCs

Bacterial Pathogen Testing

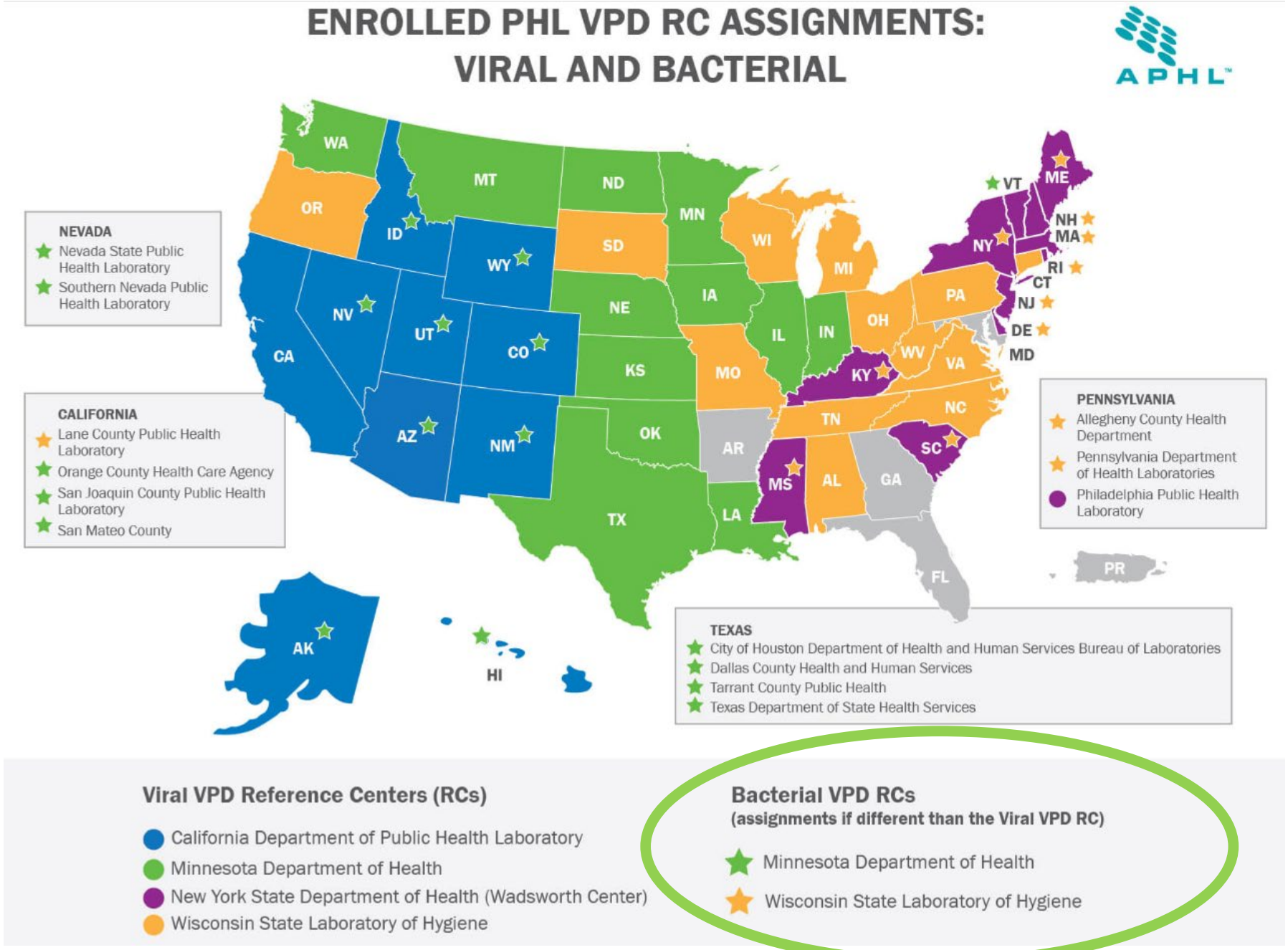
VPD RC laboratories that provide bacterial pathogen testing perform: PCR for detection, serotyping/serogrouping and culture.

Pathogen	PCR	Serotyping/ Grouping	Maximum Turnaround Time (# of Business Days)		Location(s)/ Network
			PCR	Serotyping/ Grouping	
B. pertussis *	Yes	N/A	2	N/A	**Minnesota Only**
H. influenzae	Yes	Yes	2	5	Both Bacterial RCs
N. meningitidis	Yes	Yes	2	5	Both Bacterial RCs
S. pneumoniae	Yes	Yes	2	5	**AR Lab Network**†

Viral Pathogen Testing

VPD RC laboratories that provide viral pathogen testing perform PCR and genotyping, which is conducted on all PCR-positive specimens unless otherwise indicated as part of larger outbreak.

Pathogen	PCR	Genotyping	Maximum Turnaround Time (# of Business Days)		Location(s)
			PCR	Genotyping	
Measles virus‡	Yes	Yes	2	10	All Viral RCs
Mumps virus	Yes	Yes	2	10	All Viral RCs
Rubella virus	Yes	Yes	2	10	All Viral RCs
Varicella-zoster virus	Yes	Yes	2	10	All Viral RCs
Enterovirus	Yes	Yes	Surveillance testing only, results not reported		All Viral RCs
MERS-CoV	Yes	N/A	2	N/A	**California & New York Only**



VPD Reference Center Testing Resources:

- Where to send specimen/isolate
- Bacterial/Viral pathogens tested
- Specimen types accepted
- Minimum volumes
- Shipping/storing conditions

Contact your public health lab for more info

https://www.aphl.org/aboutAPHL/publications/Documents/VPD-Reference-Guide.pdf#search=vpd%20reference%20centers

#IDLabCon

Case 3

Case 3: “Will”

- Influenza A infection on Fall break
- Mom notices rash all over body
- At hospital: rapid progression to septic shock
- Multiple cardiac arrests, requires advanced organ support
- Treated with cocktail of broad-spectrum antibiotics
- Necrosis of all 4 limbs, leading to amputation
- Laboratory diagnosis (day 4):

  Group A *Streptococcus (S. pyogenes*)

Stock photo

Increase in invasive Group A Streptocccus cases

> Euro Surveill. 2023 Jan;28(1):2200942. doi: 10.2807/1560-7917.ES.2023.28.1.2200942.

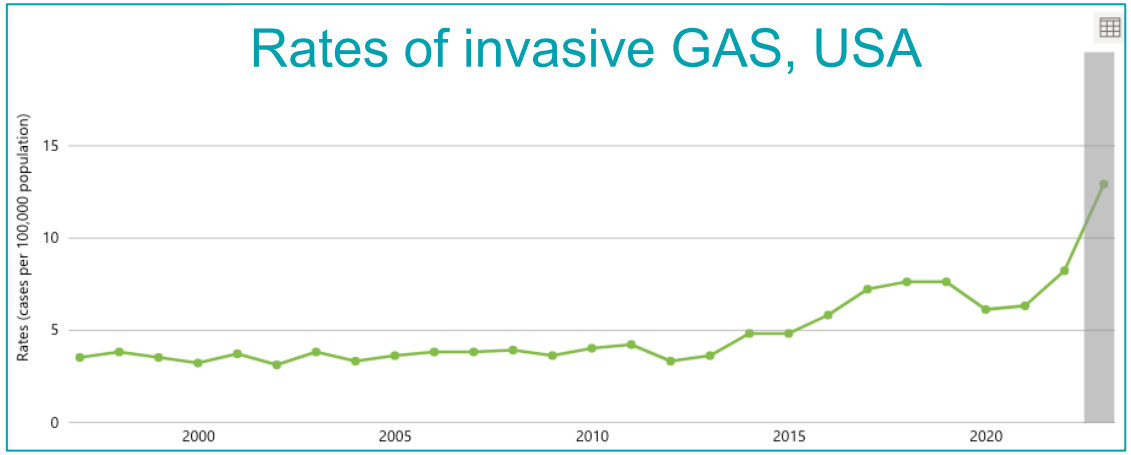
Increase in invasive group A streptococcal infection notifications, England, 2022

> Euro Surveill. 2023 Jan;28(1):2200941. doi: 10.2807/1560-7917.ES.2023.28.1.2200941.

Increase in invasive group A streptococcal (*Streptococcus pyogenes*) infections (iGAS) in young children in the Netherlands, 2022

> MMWR Morb Mortal Wkly Rep. 2023 Mar 10;72(10):265-267. doi: 10.15585/mmwr.mm7210a4.

Notes from the Field: Increase in Pediatric Invasive Group A Streptococcus Infections – Colorado and Minnesota, October–December 2022



https://www.cdc.gov/abcs/bact-facts/data-dashboard.html

- Change for VUMC antibiogram

Increase in invasive Group A *Streptocccus* cases

VUMC antibiogram data

Age group	Penicillin	Cefotaxime	Erythromycin	Clindamycin	Linezolid	Vancomycin
Pediatric	100	100	95	97	100	100
Adults	100	100	82	82	98	100

- Penicillin remains universally susceptible
- Treatment of invasive disease
  - Penicillin
  - + Clindamycin, reduces risk of necrotizing soft tissue infection
  - Linezolid alternative, no resistance to date[1]
- Penicillin allergy: clindamycin or azithromycin are alternatives

- Testing indications: serious infections OR penicillin allergies
  - Test erythromycin to predict azithromycin or clarithromycin[2]

1. Babiker et al. 2025 Lancet ID 25:265
2. CLSI M100 35th Ed. Table 2H-2, page 136

How about Group B *Streptococcus*?

- Penicillin susceptibility remains nearly universal
  - Some elevated MICs reported due to mutation to PBP2x[1]
  - Vancomycin resistance reported due to van genes[2]
- VUMC, clindamycin resistance: 70%
- Shift in USA from causing disease in neonates to older diabetic patients
  - Primary bacteremia
  - Skin or soft tissue infection
  - Pneumonia
  - Urosepsis
  - Endocarditis
  - Osteomyelitis

Indications for testing:

- Sterile site infection
- Predominant on wound (e.g., diabetic foot)
- Prenatal screening, if penicillin allergy

Primary treatment: penicillin (ceftriaxone)
Penicillin allergy: ceftriaxone or vancomycin
Mild SSTI: fluoroquinolone, SXT
Simple cystitis: amoxicillin, nitrofurantoin
Antenatal prophylaxis: penicillin, clindamycin or vancomycin

#IDLabCon

1. McGuire et al. 2024. JAC 80:399; 2.Park et al. 2024 NEJM 370:885

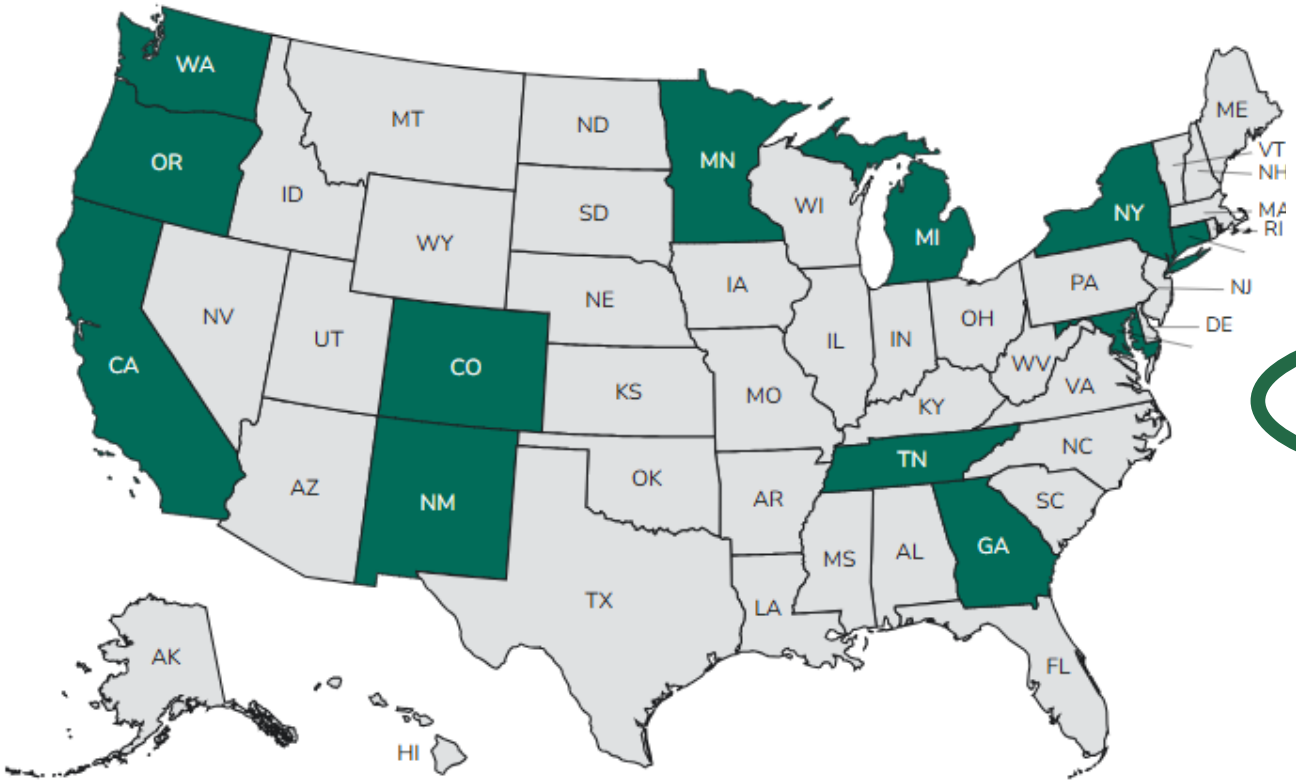
ID LAB CON
APHL 2025

#IDLabCon

Grp A and B Streptococus

CDC's Surveillance for *Neisseria meningitidis*

Emerging Infections Program Sites



Overview

Emerging Infections Program (EIP) activities focus on surveillance, applied research, and flexible and enhanced responses to emerging issues. These efforts generate reliable incidence estimates and provide critical information on risk factors, spectrum of disease, and intervention impact.

ABCs

Active Bacterial Core surveillance (ABCs) is a laboratory- and population-based surveillance system for five bacterial pathogens:

- group A *Streptococcus*
- group B *Streptococcus*
- *Haemophilus influenzae*
- *Neisseria meningitidis*
- *Streptococcus pneumoniae*

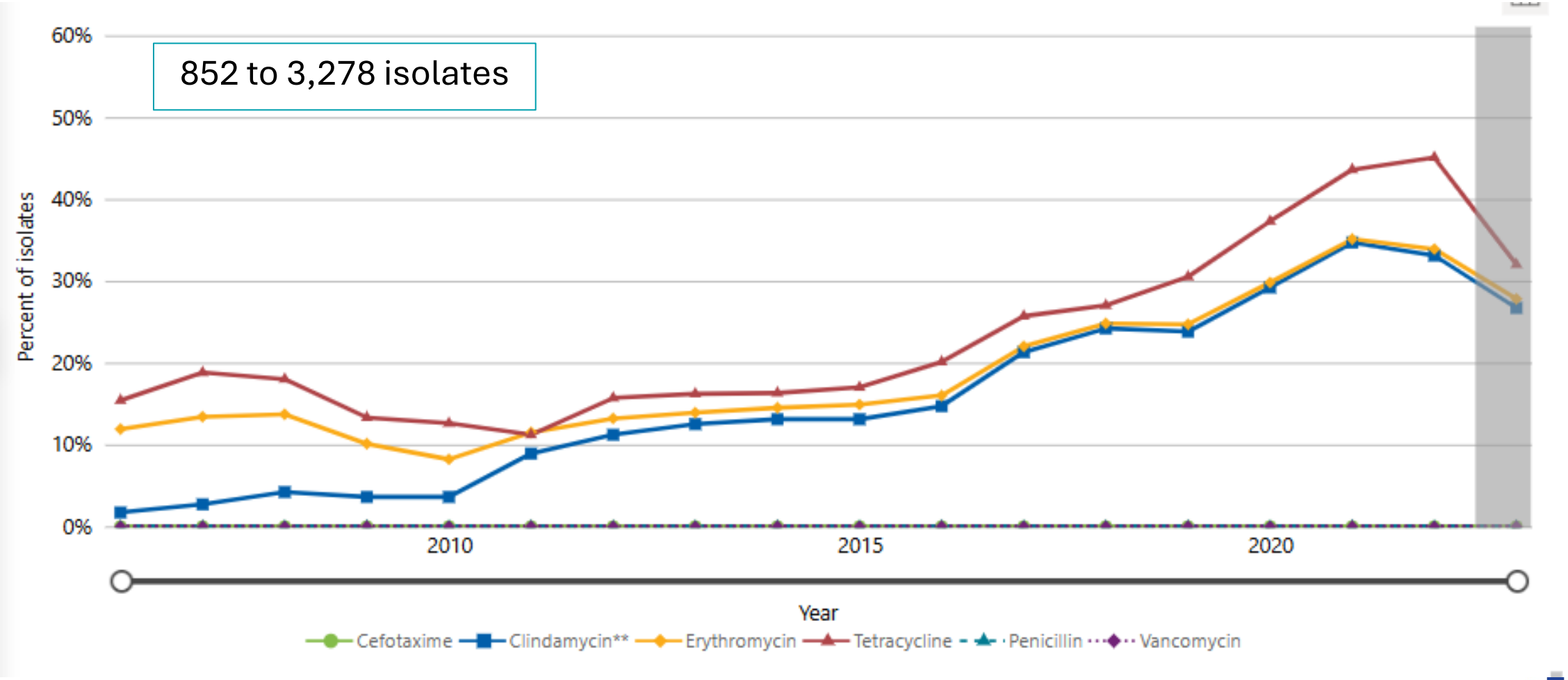
ABCs provides estimates of invasive disease burden and trends for these pathogens. ABCs also monitors changes in antimicrobial resistance and other characteristics through collection of bacterial isolates and demographic and clinical data.

2nd - The National Notifiable Diseases Surveillance System (NNDSS)

GAS – Nationwide Surveillance

- **Active Bacterial Core Surveillance (ABCs)**
  - Track invasive cases of disease
  - Track antibiotic resistance
- **National Notifiable Disease Surveillance System (NNDSS)**
  - Streptococcal Toxic Shock Syndrome (STSS) – only nationally notifiable disease caused by GAS

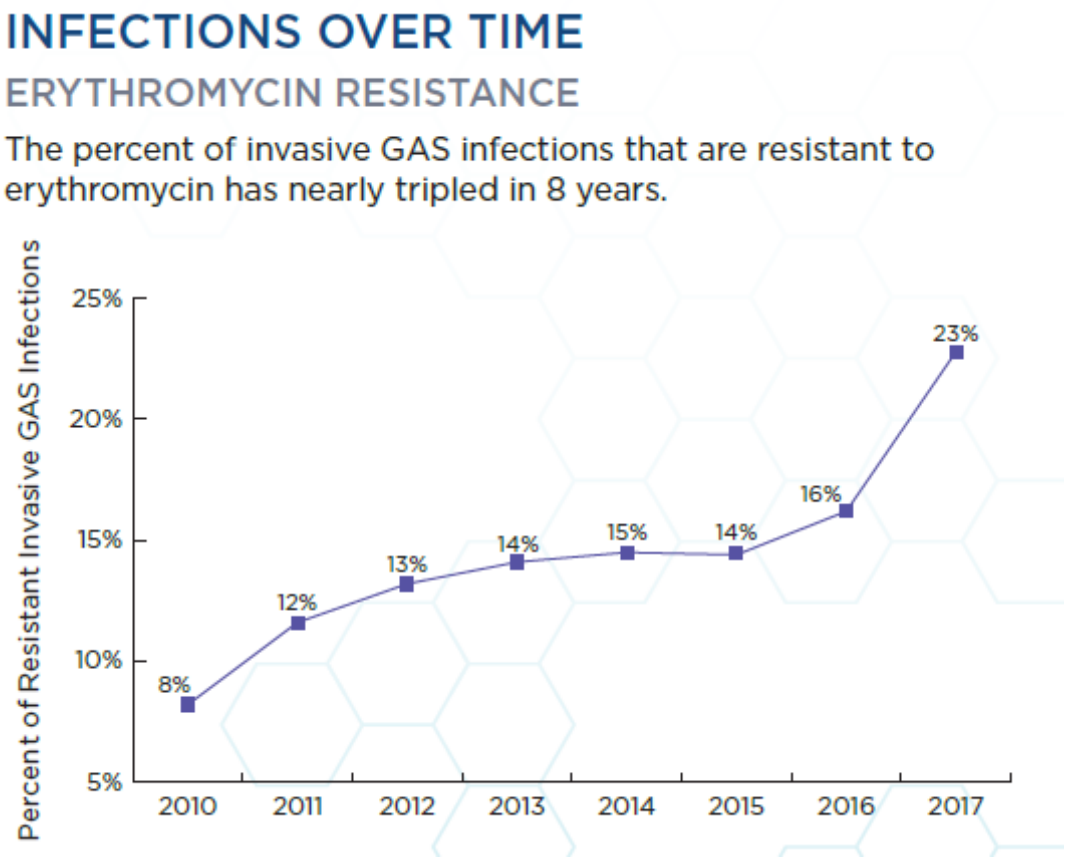
GAS - % of Invasive GAS Isolates Resistant to Select Antibiotics in ABCs Areas



https://www.cdc.gov/abcs/bact-facts/data-dashboard.html

GAS

- There's never been a report of a clinical isolate of group A strep bacteria that's resistant to penicillin or cephalosporins.
- Not resistant to the first line drugs to treat strep throat: Penicillin and Amoxicillin
- However, resistance to azithromycin, clarithromycin, and clindamycin is well known and varies geographically and temporally.



Group B Strep (GBS)

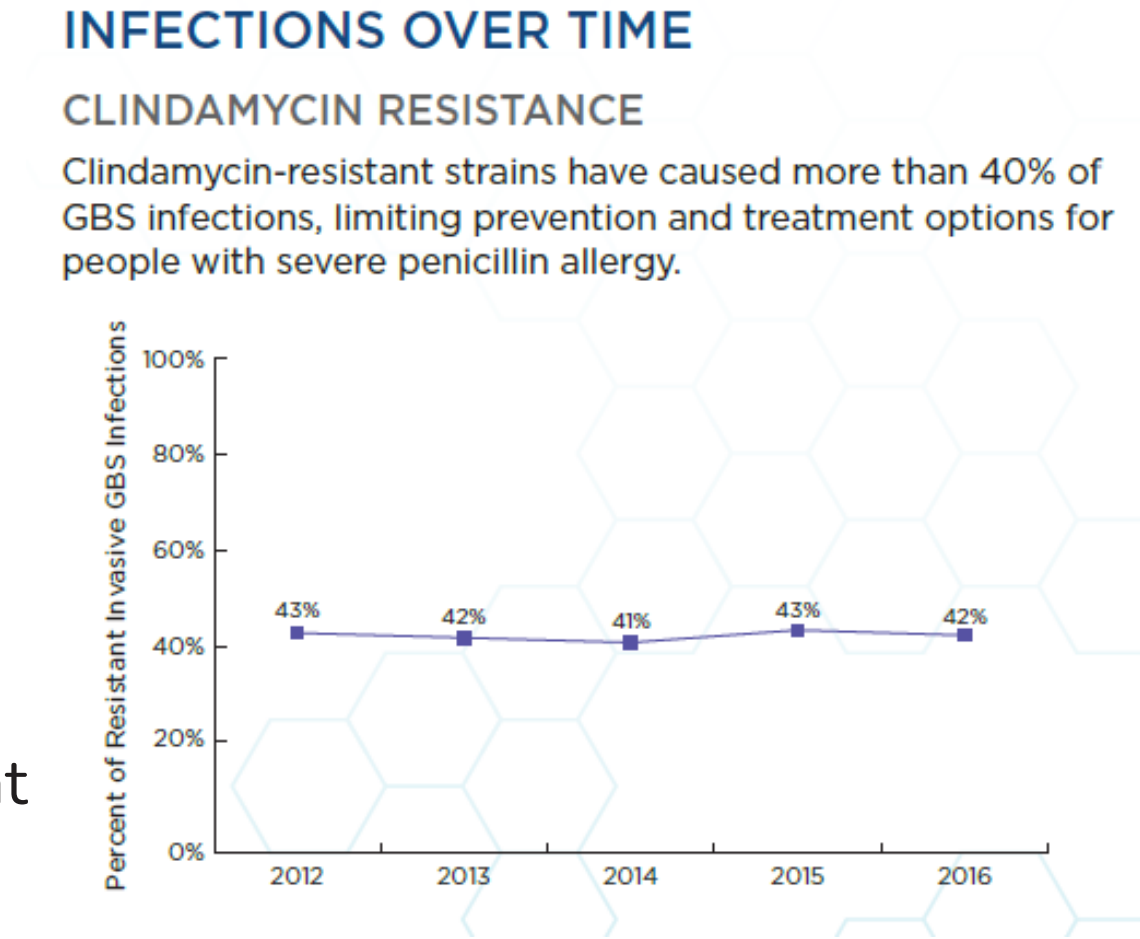
Active Bacterial Core Surveillance (ABCs)

- CDC conducts active surveillance for invasive group B *Streptococcus* disease.

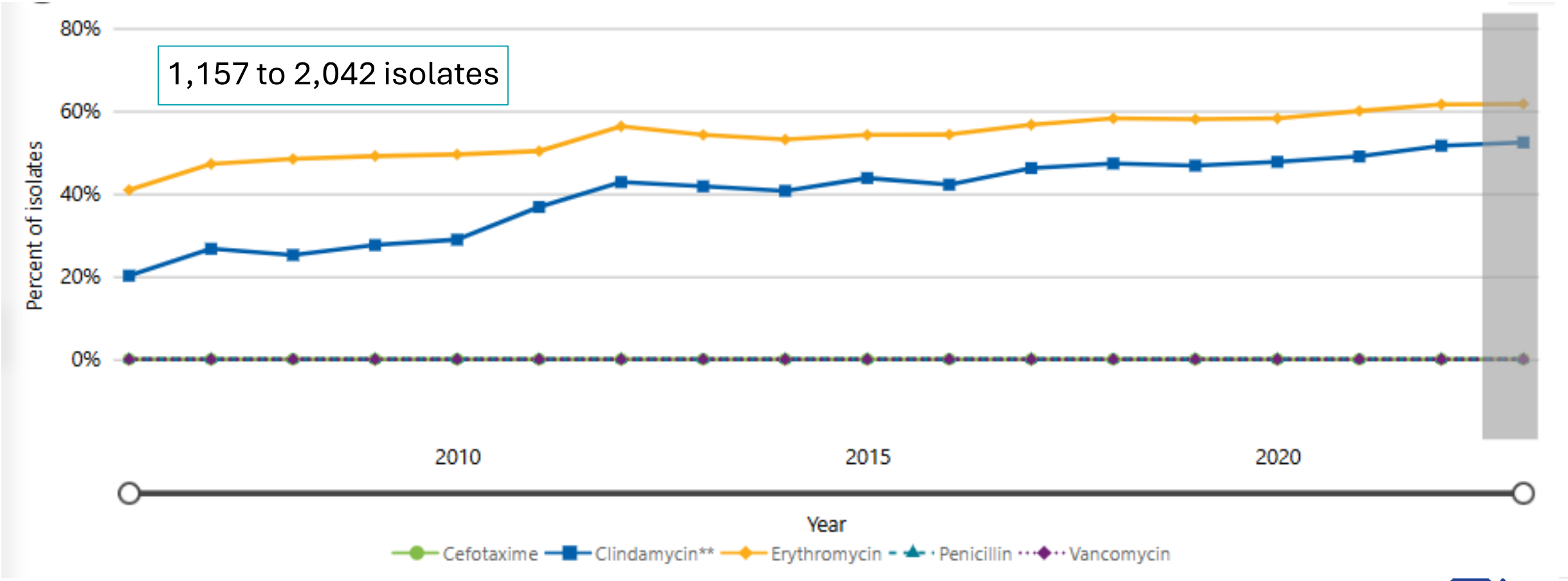
- GBS bacteria remain a leading cause of meningitis and bloodstream infections in newborns younger than 3 months old.

GBS

- Mothers can pass GBS to their infants during labor, threatening newborns with sepsis during the first week of life.
- When indicated, doctors give mothers antibiotics during labor to protect their newborns from GBS disease.
- Resistance to clindamycin limits treatment and prevention options for adults with severe penicillin allergy.



GBS – % of Invasive GBS Isolates Resistant to Select Antibiotics in ABCs Areas



https://www.cdc.gov/abcs/bact-facts/data-dashboard.html

#IDLabCon

Case 4

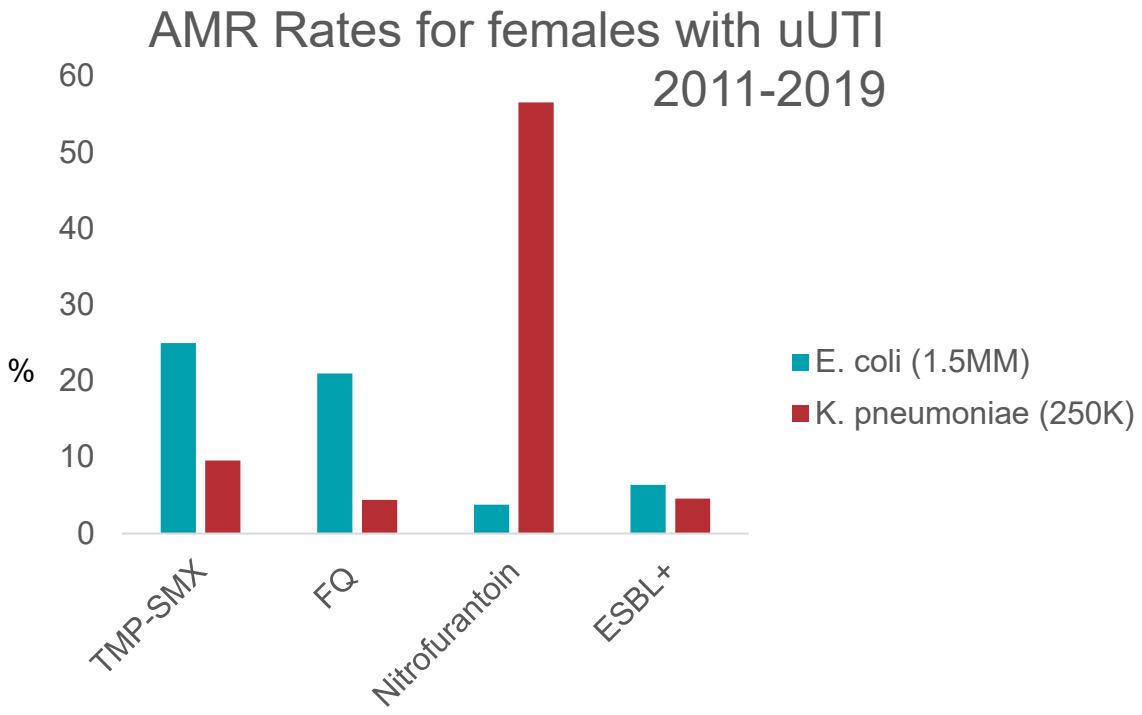
Case 4.

- 21 YO with pelvic pain and urinary frequency
- UA with reflex to culture ordered:
  - Urine LE: Positive
  - Urine Nitrite: Positive
  - Urine Blood: Trace
- Urine culture: >100,000 CFU/mL ***E. coli***

Antimicrobial agent	MIC (µg/mL)	
Amox/Clav	8/4	S
Ampicillin	>16	R
Amp/Sulbactam	8/4	S
Cefazolin	>16	R
Ceftriaxone	>32	R
Ciprofloxacin	>2	R
Ertapenem	≤0.25	S
Gentamicin	≤2	S
Levofloxacin	>4	R
Meropenem	≤0.25	S
Nitrofurantoin	≤16	S
Trimethoprim-sulfa	>2/38	R

Trends in Enterobacterales ESBLs

- Pre-1990: almost always nosocomial, TEM or SHV
- 1990s: CTX-M emerges & community-onset ESBLs
- 2000s: widespread R to FQ and TMP-SMX
- 2010s: doubling of ESBL rates in community



IDSA empiric rx for uncomplicated cystitis:

- Nitrofurantoin
- Trimeth-sulfa
- Fosfomycin

Culture usually only if recurrent

- No response in 48h
- Postmenopausal women

Kaye et al. 2021 CID 73:1992

Kaye et al. 2024. ARIC 13:21

Gupta et al. 2011 CID 52:e103

Do I need to do an ESBL confirmatory test?

- Useful for infection prevention
- Useful for epidemiology studies
- Increasingly, desire to use carbapenem if ESBL present

- No ESBL confirmatory test (except sequencing) is 100% accurate
- Many labs use ceftriaxone resistance as surrogate indicator
- Plasmid AmpC also important clinically
- Phenotypic tests only work for *E. coli, K. pneumoniae*, K.*oxytoca* and *P. mirabilis*

Options

For *E. coli*, *K. pneumoniae, K. oxytoca* and *P. mirabilis*

Option 1:

Add comment for ceftriaxone resistant isolates:

“ESBL probable in this isolate.”

Option 2:

If available on automated AST system, report ESBL confirmatory test result:

“ESBL confirmatory test positive.”

Option 3:

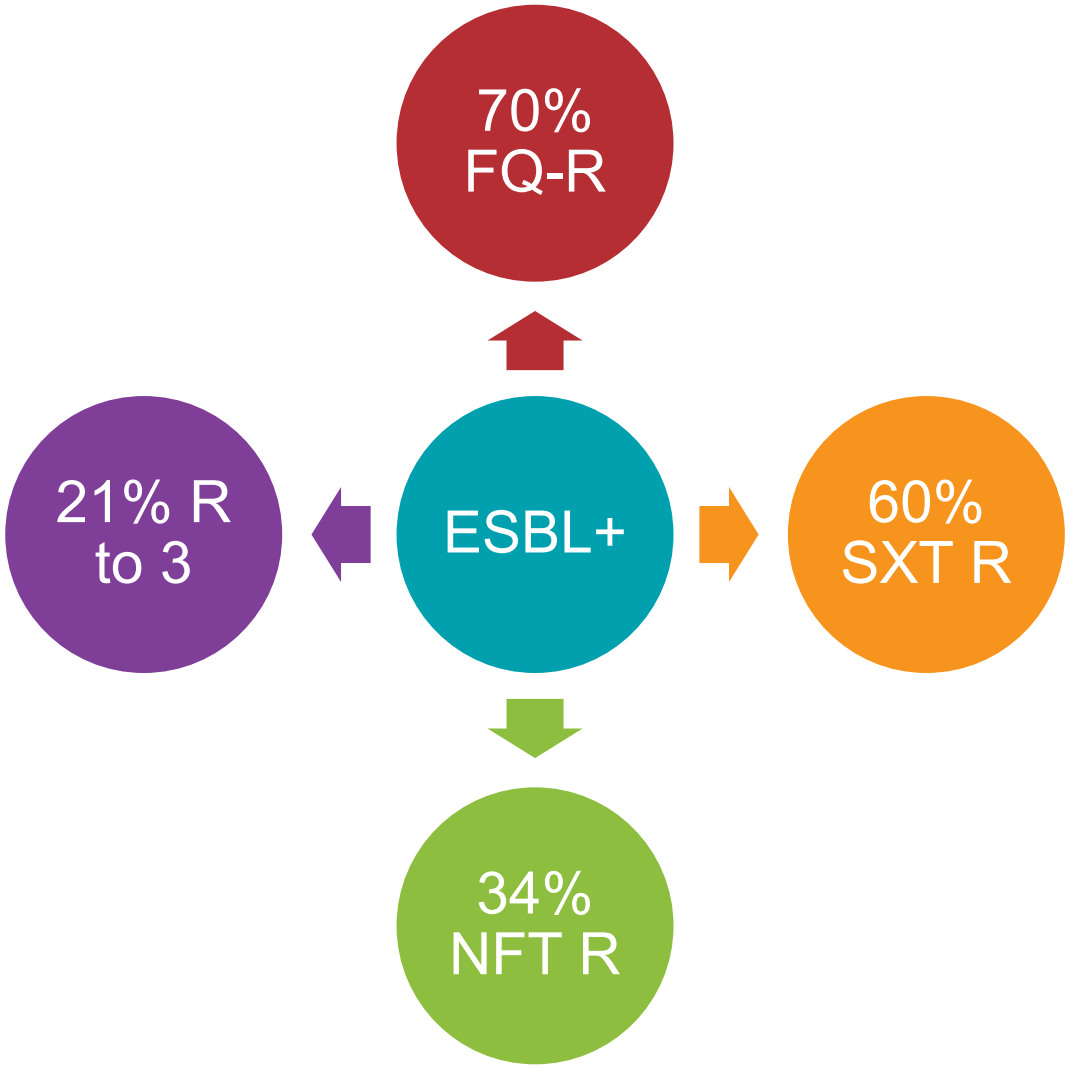
If automated AST expert system predicts phenotype, report:

“ESBL probable in this isolate.”

Additional considerations:

1. Many ASP recommend against use of piperacillin-tazobactam, ampicillin-sulbactam or amoxicillin-clavulanate for ESBL
2. For urinary tract infections, nitrofurantoin or fosfomycin may be options, or a fluoroquinolone, if “S”
3. Discuss reporting with ASP
4. Use current CLSI/FDA breakpoints regardless if you do an ESBL test!

Treatment options: ESBL uUTI

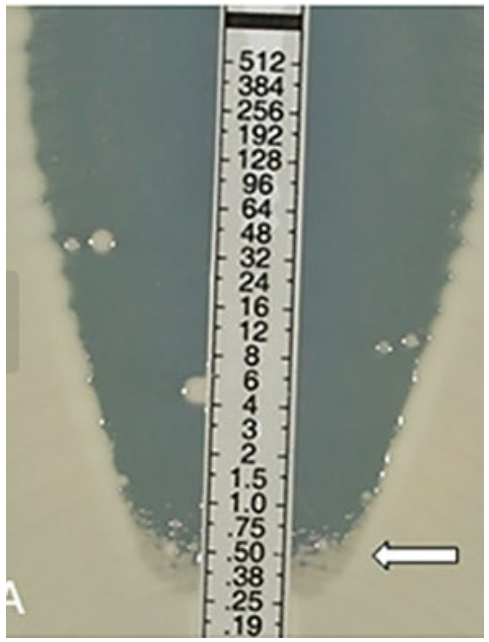


- Very few oral options for ESBL+[1]
  - 21% are resistant to FQ, SXT, and nitrofurantoin
  - Many patients with SXT allergy
  - Nitrofurantoin avoided for elderly
  - FQ avoided unless last option
- Fosfomycin active ESBL *E.coli*
  - Resistance documented, often in critically ill patients

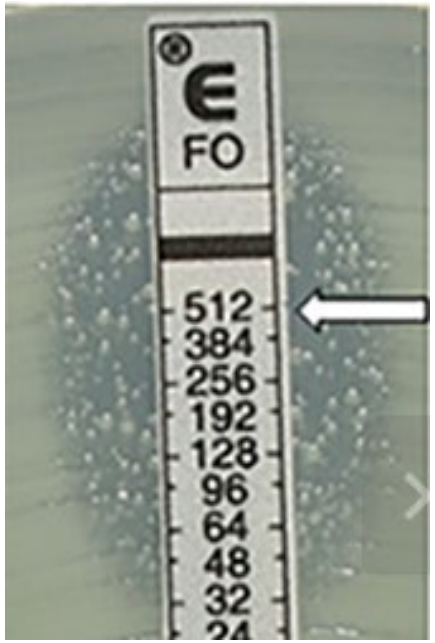
1. Dunne et al. BMC Infect Dis 22:194; 2. Dunne et al. CID. 2023 76:78
3. Puttagunta et al. 2025 OFID 12:Suppl 1

Fosfomycin testing

- Breakpoints only for *E. coli* and *E. faecalis*
  - Requires Glucose-6-Phosphate for testing E. coli[1]
- Agar dilution and disk diffusion are CLSI methods[1]
- New FDA-cleared Etest (FO) available, performs well with 99% categorical agreement vs. AD [2]



Ignore microcolonies…



Unless they fill the ellipse!

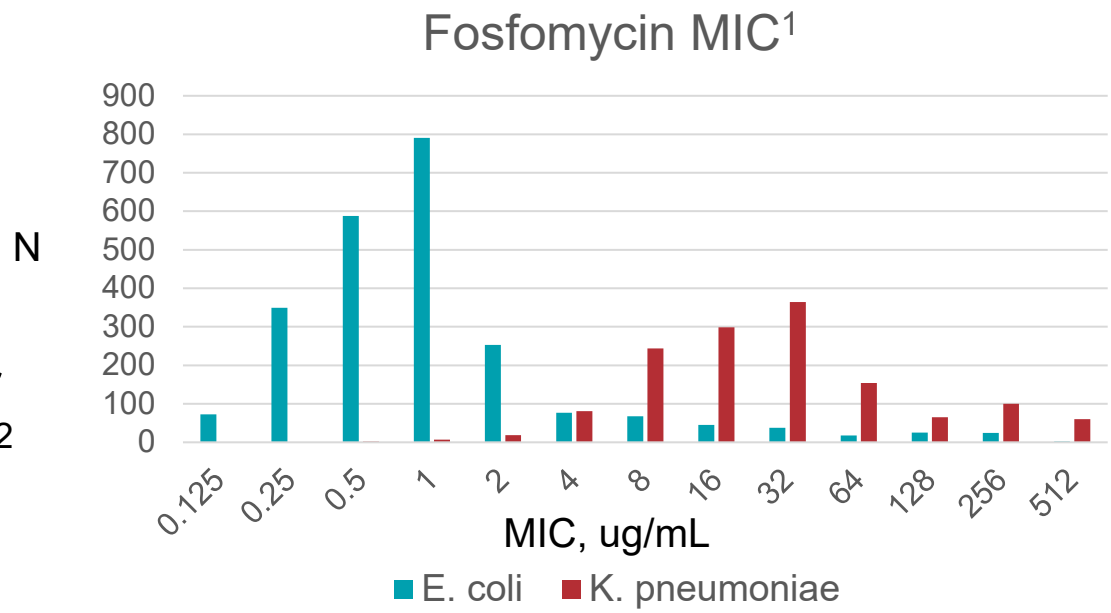
Disk diffusion:

CLSI, read inner, colony-free zone of inhibition!

1. CLSI 2025. M100
2. Goer et al. 2022 J Clin Microbiol 60:e00021-22

Fosfomycin testing: other Enterobacterales

- MIC distributions are very different from *E.coli*
- Oral fosfomycin breakpoints are ONLY for E. coli (both CLSI and EUCAST)
- IV fosfomycin available outside the USA
- EUCAST breakpoints for IV fosfomycin are only for *E. coli* and infections originating in the urinary tract[2]
- Resistance to fosfomycin:
  - Fosfomycin cleavage by FosA
  - modification of murA target
  - mutation of fosfomycin transporter
- No relationship between MIC and outcome for K. pneumoniae[3]



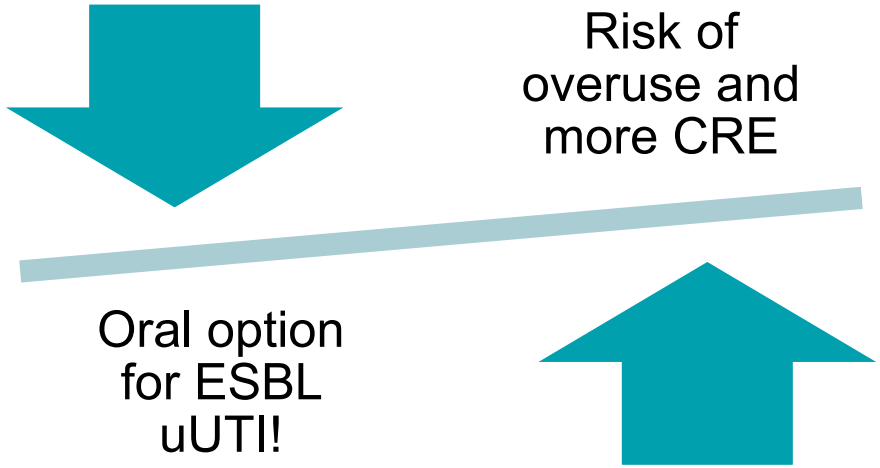
Most K. pneumoniae, K. aerogenes, P. aeruginosa and Enterobacter have FosA

Testing should not be performed!

1. EUCAST MIC Distributions
2. EUCAST v 15.0 breakpoint tables, www.eucast.org
3. Kaye et al. 2019. CID 69:045

Sulopenem

- *Sulopenem* is a new oral carbapenem approved in 2024
  - Similar to ertapenem in activity (including vs. ESBL and AmpC)
  - IV and Oral formulations
  - FDA indication: uUTI (not cUTI and pyelonephritis)
  - Failed to achieve primary endpoint vs. ertapenem[2]
  - Succeeded vs. ciprofloxacin in FQ-R infections and amoxicillin-clavulanate[3]



Talk to your ASP to see if sulopenem use is in discussion!

#IDLabCon

New antimicrobial agents!

Antimicrobials approved by FDA in last 2 years!

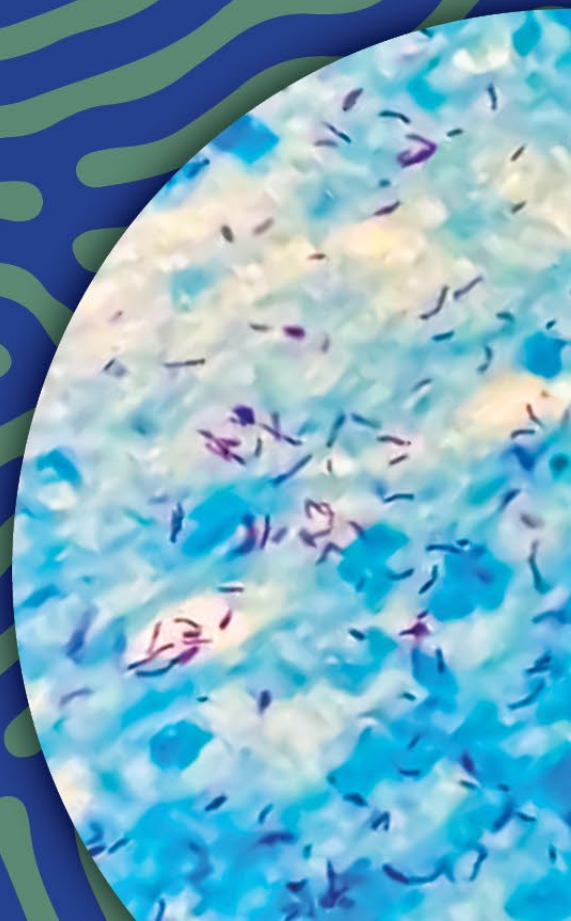
Generic Name	Trade Name	Indication(s)	Organism(s)	What makes it special
Aztreonam-avibactam	Emblaveo	Intra-abdominal infections	Enterobacterales	Activity vs. MBL
Cefepime enmetazobactam	Exblifep	cUTI	Enterobacterales and P. aeruginosa	Activity vs. ESBL
Ceftobiprole	Zevtera	S. aureus bacteremia, endocarditis Skin soft tissue infections Community bacterial pneumonia	Enterobacterales, S. aureus, S. pyogenes, S. pneumoniae, Hm	*S. aureus* coverage
Sulopenem	Orlynvah	uUTI	Enterobacterales	Oral carbapenem
Rezafungin	Rezzayo	Candidemia and invasive Candida	C. albicans, C. glabrata, C. tropicalis, C. parapsilosis	Long-acting echinocandin
Sulbactam-durlobactam	Xacduro	Hospital and ventilator pneumonia Serious CRAB infx	Acinetobacter baumannii	Activity vs. CRAB

FDA-cleared tests – March 17 2025

Generic Name	Disk	Gradient diffusion	Sensititre (ThermoFisher)	Automated
Aztreonam-avibactam	No	No	No	No
Cefepime enmetazobactam	No	No	No	No
Ceftobiprole	No	MTS (Liofilchem)	Yes	No
Sulopenem	No	No	No	No
Rezafungin	Hardy Oxoid	No	Yes	No
Sulbactam-durlobactam	Hardy Oxoid	Etest (bioMérieux)	Yes	No

So – what do I need to do?

1. Talk with your antibiotic stewardship team –
   - Are there discussions to bring these onto formulary?
   - Is AST routinely needed?
2. Investigate your testing options – if needed
   - Disks, Etest and Sensititre
   - Talk to your pharmaceutical rep – who is testing?
   - Talk to your contracted reference lab – are they testing?
3. Evaluate verification isolate options – if needed
   - LSI for Sulbactam-durlobactam and rezafungin (labspec.org)
   - Currently no AR Bank isolates for these…

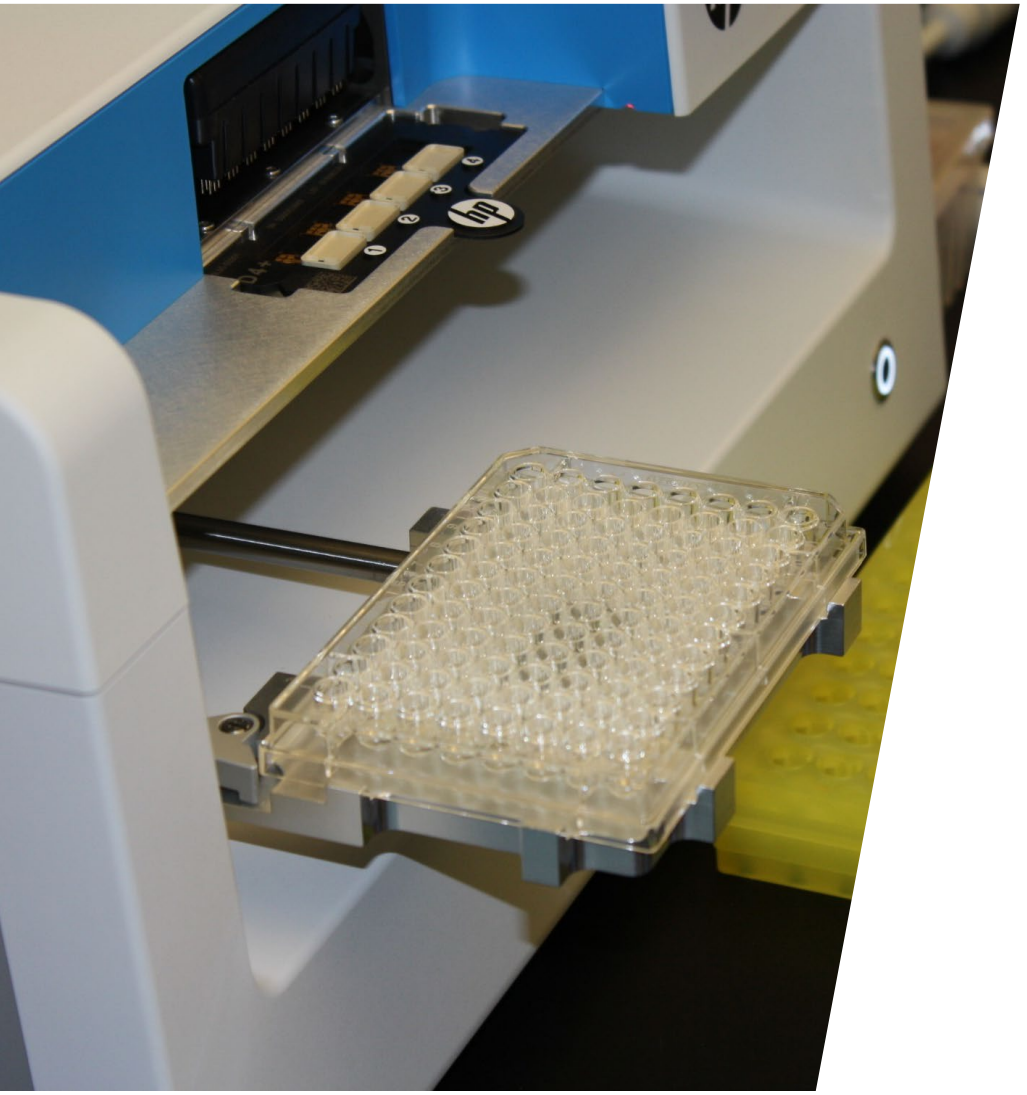


#IDLabCon

Expanded AST

Paula

Expanded AST – AR Lab Network Regional Labs



Expanded AST

To fill the gap between new drug approval and FDA-approved AST on commercial devices

7 AR Regional labs

Test and report:

- Aztreonam
- Ceftazidime/avibactam
- Aztreonam/avibactam

Enterobacterales only

Metallo-β-lactamase producer (NDM, IMP, VIM)

Expanded Antimicrobial Susceptibility Testing for Hard-to-Treat Infections

Antimicrobial susceptibility testing for Enterobacterales producing a metallo-beta-lactamase (MBL)

Clinicians and clinical and public health laboratories can request expanded antimicrobial susceptibility testing **(ExAST)** from CDC's Antibiotic Resistance Lab Network (AR Lab Network) to find potentially effective treatment options for their patients' most resistant infections.

- Resistance to new drugs used for treatment of carbapenem-resistant Enterobacterales (CRE) has been identified, specifically to ceftazidime-avibactam, meropenem-vaborbactam, and imipenem-relebactam. However, these bacteria may be susceptible to the combination therapy ceftazidime-avibactam plus aztreonam, a combination of drugs that is an option in current IDSA guidance for treatment of serious infections caused by MBL-producing Enterobacterales.[1]
- Susceptibility testing is **CLIA-compliant** and is performed at **no cost**. **MIC results** will be reported within **3 business days** for treatment of ceftazidime-avibactam, aztreonam, and aztreonam-avibactam to help assess utility of combination therapy.

- **Southeast:** Tennessee Public Health Laboratory | ARLN.health@tn.gov
- **Mid-Atlantic:** Maryland Public Health Laboratory | MDPHLarln@maryland.gov
- **Northeast:** Wadsworth Center Labs | ARLNcoreNY@health.ny.gov
- **Midwest:** Wisconsin State Lab of Hygiene | wiARLN@slh.wisc.edu
- **West:** Washington State Public Health Labs | ARLN@doh.wa.gov
- **Central:** Minnesota Dept. of Health Public Health Lab | ARLNMN@state.mn.us
- **Mountain:** Utah Public Health Lab | ARLNUtah@udah.gov

1. Isolates to submit:

Hospital laboratories and clinicians are encouraged to submit Enterobacterales isolates that:

- Test "not susceptible" to all beta lactams tested, including ceftazidime-avibactam, meropenem-vaborbactam, or imipenem-relebactam. These may be MBL-producing isolates with few treatment options.

-OR-

- Enterobacterales that test positive for NDM, VIM, or IMP genes.

2. What is the testing process?

- Isolates will be tested to confirm carbapenem resistance, carbapenemase production, and to identify the presence of specific carbapenemase genes.
- Isolates meeting the inclusion criteria will be tested against ceftazidime-avibactam, aztreonam, and avibactam-aztreonam.
- AST turn-around time is 3 business days after receipt of isolate.

3. How do I request ExAST and receive results?

- Please email your AR Lab Network Regional Laboratory (see map) to request testing and submission instructions.
- Please provide prior laboratory testing results, including organism identification and AST.
- Please confirm that Infection Prevention and Infectious Diseases services are aware of this patient and isolate.

[1]Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of Extended-Spectrum β-lactamase Producing Enterobacterales (ESBL-E), Carbapenem-Resistant Enterobacterales (CRE), and Pseudomonas aeruginosa with Difficult-to-Treat Resistance (DTR-P. aeruginosa). Clin Infect Dis. 2021 Apr 8;72(7):e169-e183. doi: 10.1093/cid/ciaa1478. PMID: 33106864.

For more information on CDC's AR Lab Network, visit:
www.cdc.gov/drugresistance/laboratories.html

ARLABnetwork

CDC

U.S. Department of Health and Human Services
National Center for Emerging and Zoonotic Infectious Diseases

CS326608-A

ARLABnetwork

https://www.cdc.gov/antimicrobial-resistance-laboratory-networks/media/pdfs/drug-susceptibility-tests-P.pdf

#IDLabCon

APHL ID LAB CON 2025

AR Lab Network Tiered New Approach to AST

3 Tiers

- **Basic** – AST on CPOs – surveillance only
- **Standard** – AST on CPOs and CRE – surveillance only
- **Response** – Surveillance and Diagnostic (CLIA validated) AST
  - 7 AR Regional labs
  - TAT ≤ 3days from isolate receipt
  - Test and report:
  - Next funding cycle – August 2025

- **Response – Test and report**:
  - Carbapenems
  - Ceftazidime, ceftriaxone (or other 3GC), cefepime, and **cefiderocol**
  - **Ceftaz/avi, mero/vabor, imi/rel, ceftol/taz, sulbact/durlo,** pip/taz
  - Aztreonam
  - Tigecycline
  - Minocycline

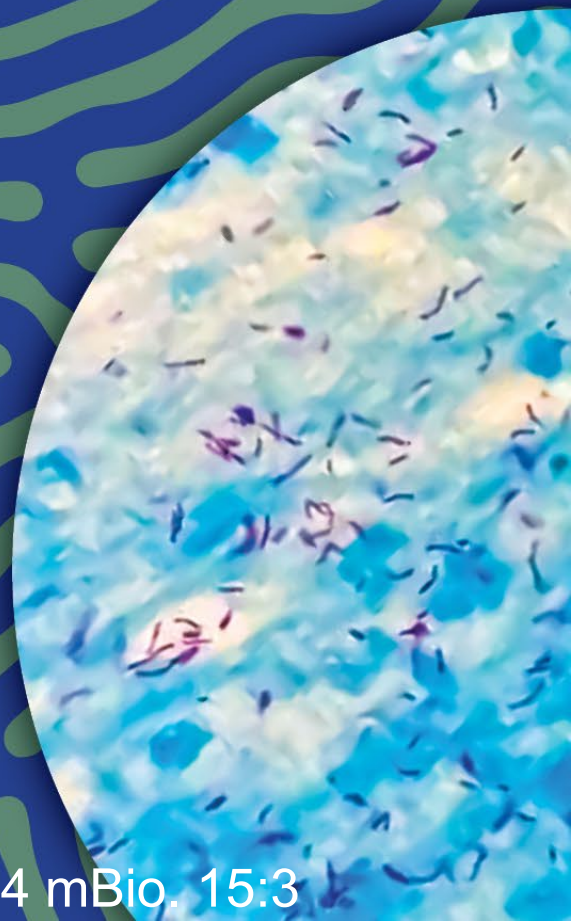
#IDLabCon

Case 5

57 year old with Sjogren's syndrome and immunosuppression
Recurrent *E. faecium* bloodstream infections over 6 years
no source of infection identified
Admitted and persistent bacteremia for 26 days, treated with

Daptomycin
Vancomycin
Ceftaroline + Daptomycin
Oritavancin

Tigecycline
Tedizolid
Doxycycline

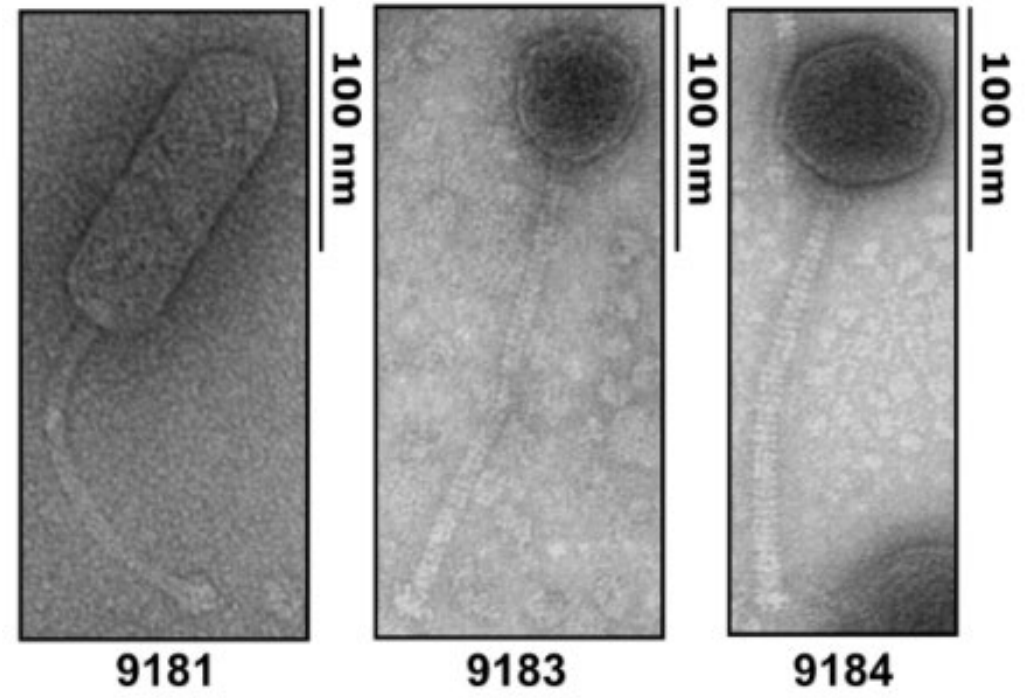


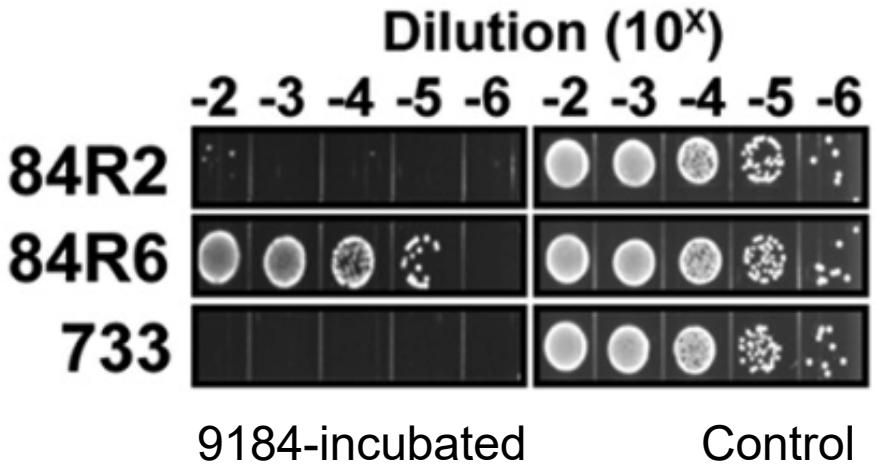
Patient referred for salvage phage therapy

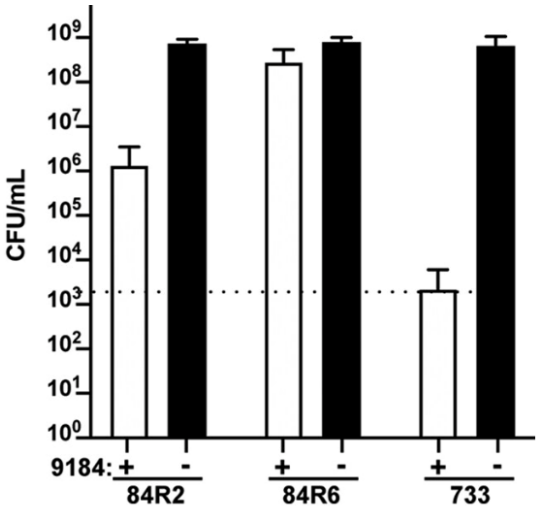
Stellfox et al. 2024 mBio. 15:3

Phage selection

- *E. faecium Siphoviridae* phage from raw sewage (prior studies)
  - Phage work on some, but not all clinical isolates of *E. faecium*
- *9184 confirmed to have lytic activity against patient's E. faecium*







Patient treated with $1x10^9$ PFU q 8h IV and PO

Bacteremia resolved within 24h

#IDLabCon

Canfield. 2021 AAC 65:00143-21

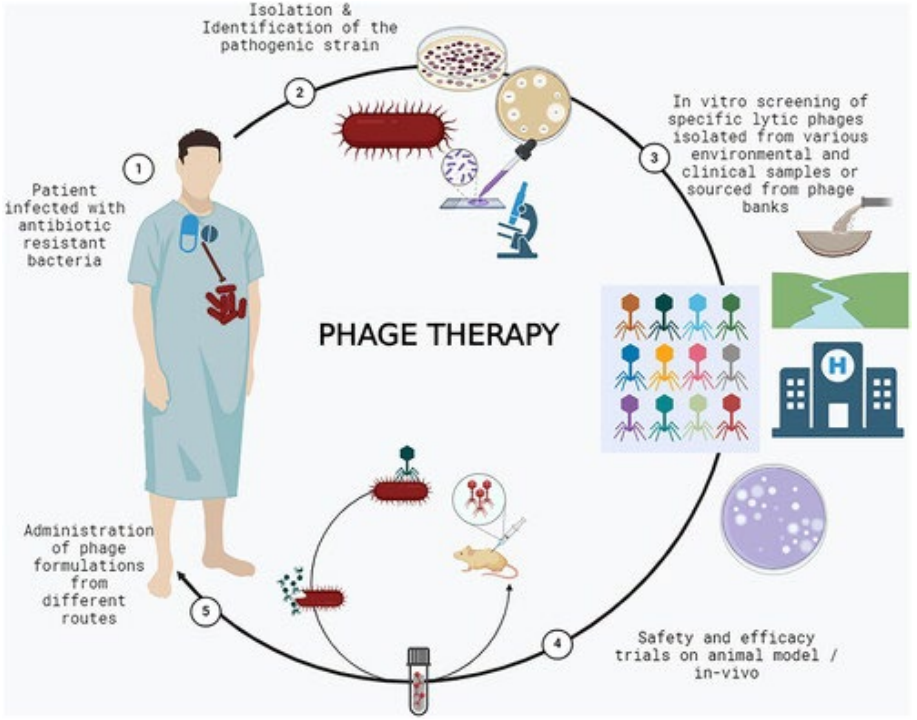
Case 5 continued....

- Bacteremia returned after 31 days of phage + daptomycin + vancomycin
  - Intermittent bacteremia over the next 2 months
- Second phage, Hi3 was added, and patient was bacteremia-free for 4 months
  - IV Antimicrobials were changed to oral doxycycline and tedizolid, along with 2x day phage
  - ~3 months later, bacteremia returned

- No resistance to antibiotics or phage were identified
- No antibodies detected to the phage before Hi3 was added
- Serum collected 27 days after starting Hi3 caused a ~100-fold reduction in phage activity = host neutralizing antibodies

Bacteriophage

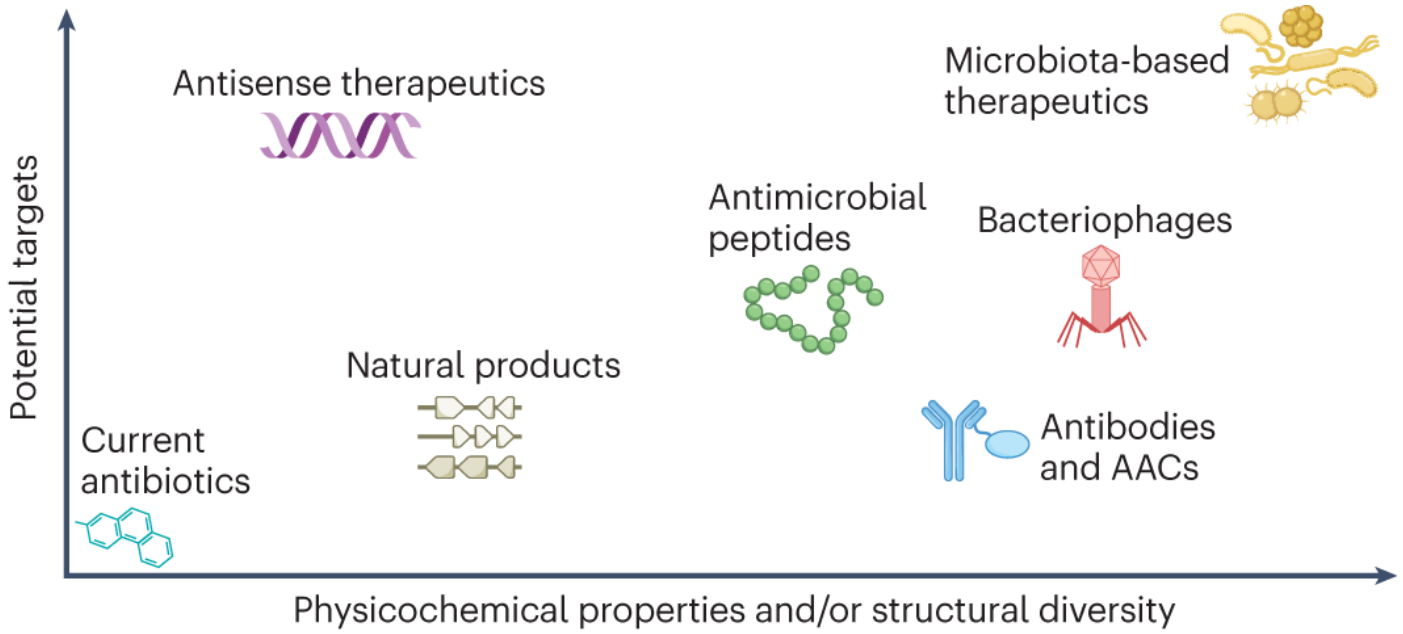
- Therapeutics:
  - Phage cocktail
    - Typical lytic phage, but give a cocktail to increase chance of active combo
  - Engineered phage
    - Modified fiber tails to ehanced binding capability to wide spectrum of bacteria
  - Genetic material delivery
    - E.g., delivery of CRISPR-Cas to trigger bacterial death
  - Phage-derived endolysins
    - Use directly without delivery by the phage



- Challenges:
  - Phages are strain-specific
  - More phage = increased immune reaction by host
  - Resistance can emerge quickly

Pal et al. Infect Dis. 56:785

Alternatives to antibiotics



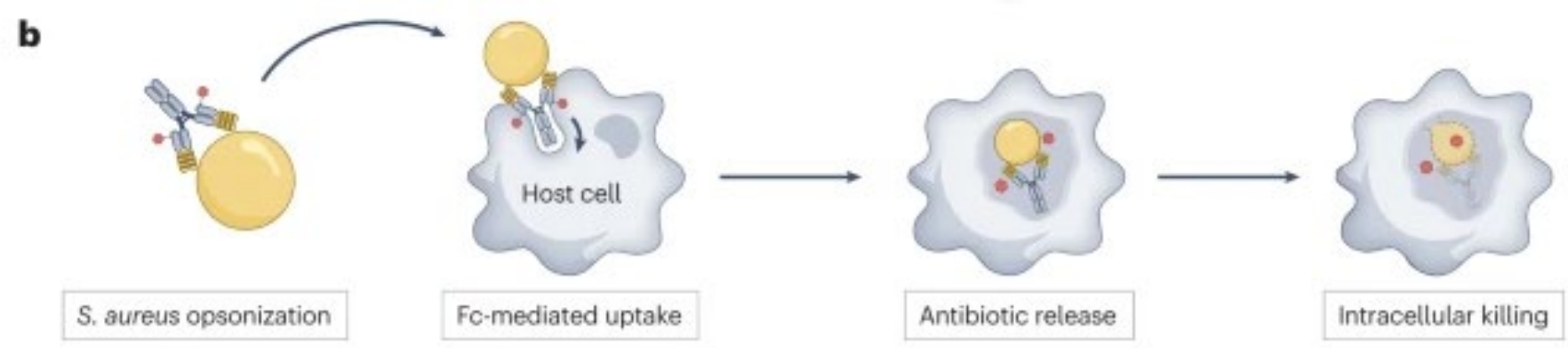
- Antimicrobial peptides
  - Naturally occurring
  - Include some existing antibiotics (colistin)
  - Limitation: host cell toxicity
- Antibodies (available now!)
  - Raxibacumab (anthrax anthrax protective antigen)
  - Obiltoxaximab (anthrax protective antigen)
  - Bezlotuxoumab (C. difficile toxin B)

AAC, antibody-antibiotic conjugate

McNair, Rutherford and Tan. 2024. Nat Rev Microbiol. 22:262

Example: Antibody-antibiotic conjugate

- DSTA4637A
- Antibody against S. aureus cell wall teichoic acid + rifampicin analogue dmDNA31
- Mode of action:



Mechanisms beyond killing: Future Rx

Antivirulence

E.g., sibofimloc (blocks *E. coli* adhesin FimH)

Antibiotic adjuvant

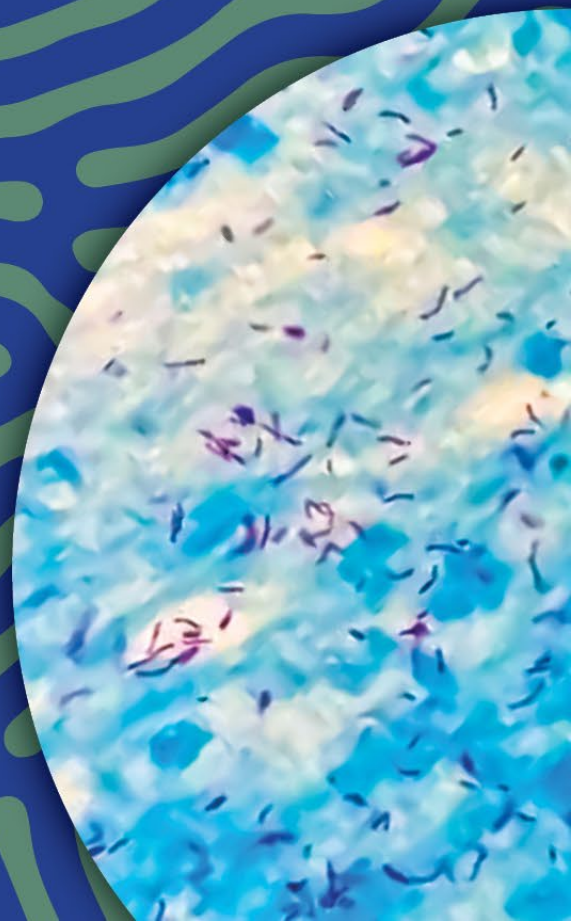
E.g., SPR741 (disrupts outer membrane)

Bacterial diversity

E.g., VE303 (Clostridia cocktail for treatment of C. difficile)

Vaccines

E.g., PCV20



THANK YOU!

Romney Humphries
romney.humphries@vumc.org

Paula Snippes Vagnone
paula.snippes@state.mn.us