Multi-Drug Resistant Organisms: a Primer on CRE/CP-CRE, *C. auris*, ESBL & CRAB

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Learning Objectives

- Understand what is an MDRO
- Review antibiotics and bacterial resistance
- Identify sources of MDRO's
- Review bacterial resistance mechanisms
- Identify Current CDC MDRO threat levels
- COVID-19 impact on U.S. MDRO's
- Review ESBL, CRE, CRAB and C.auris
- Learn about next steps to mitigation

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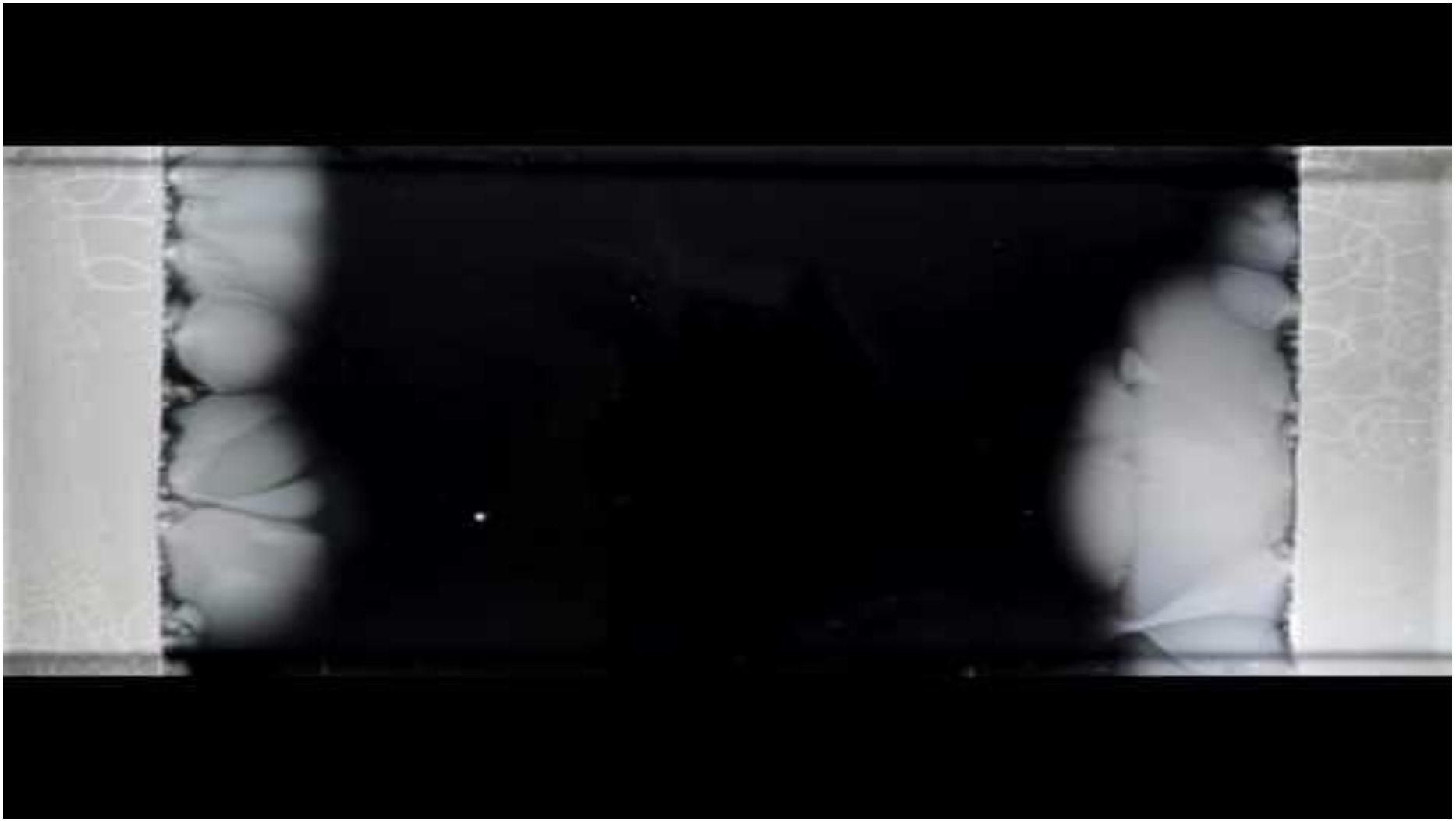
Setting the Table



https://www.youtube.com/watch?v=pIVk4NVIUh8

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What is a MDRO

MDRO Definition:

- For epidemiologic purposes, MDROs are defined as microorganisms, predominantly bacteria, that are resistant to one or more classes of antimicrobial agents.
- Multi-Drug-Resistant-Organism

Common Examples

- Methicillin-Resistant *Staphylococcus aureus* (MRSA)
- Vancomycin-Resistant *Enterococcus* (VRE)
- Extended Spectrum Beta-Lactamases (ESBL)
- Carbapenem-Resistant Enterobacterales (CRE)

Antibiotics and Resistance

- Penicillin was discovered in 1928 by Alexander Fleming
  - First resistance identified in 1940 in *Staphylococcus*
- Penicillin became commercially available in 1943
- After the discovery of each new antibiotic, there is acknowledgement of resistance alongside the discovery
- Bacteria know how to fight back, and they do so very quickly and efficiently

Bacterial Resistance Timeline

Antibiotic Approved or Released	Year Released	Resistant Germ Identified	Year Identified
Penicillin	1941	Penicillin-resistant *Staphylococcus aureus*[20, 21]	1942
		Penicillin-resistant *Streptococcus pneumoniae*[9,10]	1967
		Penicillinase-producing *Neisseria gonorrhoeae*[11]	1976
Vancomycin	1958	Plasmid-mediated vancomycin-resistant *Enterococcus faecium*[12,13]	1988
		Vancomycin-resistant *Staphylococcus aureus*[14]	2002
Amphotericin B	1959	Amphotericin B-resistant *Candida auris*[15]	2016
Methicillin	1960	Methicillin-resistant *Staphylococcus aureus*[16]	1960
Extended-spectrum cephalosporins	1980 (Cefotaxime)	Extended-spectrum beta-lactamase- producing *Escherichia coli*[17]	1983
Azithromycin	1980	Azithromycin-resistant *Neisseria gonorrhoeae*[18]	2011
Imipenem	1985	*Klebsiella pneumoniae* carbapenemase (KPC)-producing *Klebsiella pneumoniae*[19]	1996
Ciprofloxacin	1987	Ciprofloxacin-resistant *Neisseria gonorrhoeae*[20]	2007
Fluconazole	1990 (FDA approved)	Fluconazole-resistant *Candida*[21]	1988
Caspofungin	2001	Caspofungin-resistant *Candida*[22]	2004
Daptomycin	2003	Daptomycin-resistant methicillin-resistant *Staphylococcus aureus*[23]	2004
Ceftazidime-avibactam	2015	Ceftazidime-avibactam-resistant KPC-producing *Klebsiella pneumoniae*[24]	2015

https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf

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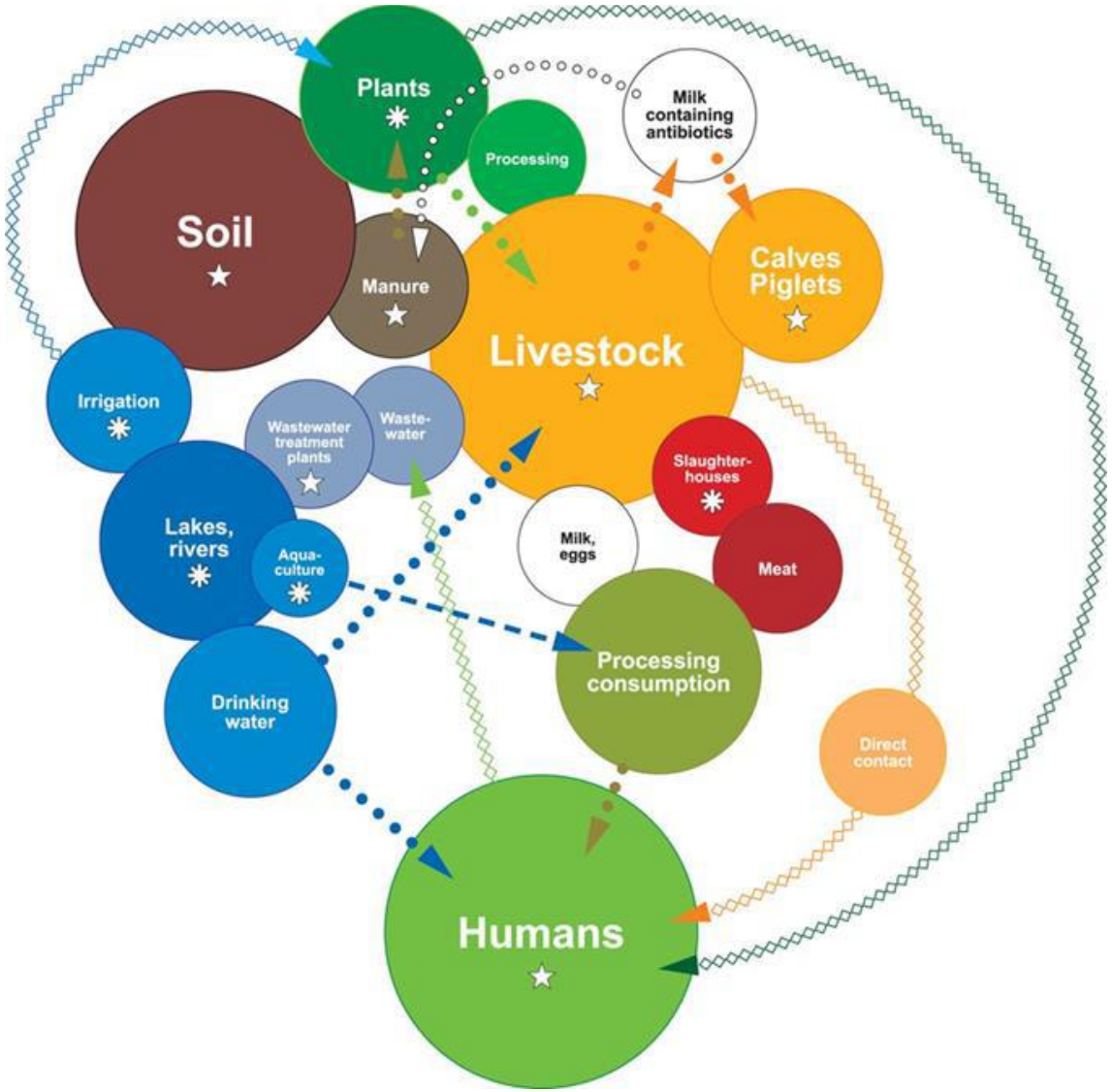
Where do MDRO's Come From? (page 1)

Reservoirs

- Food sources
- Agricultural animals and plants
- Companion animals
- Water / Soil
- Plumbing – drains (biofilms)



Thanner et al. mBIO 2016.

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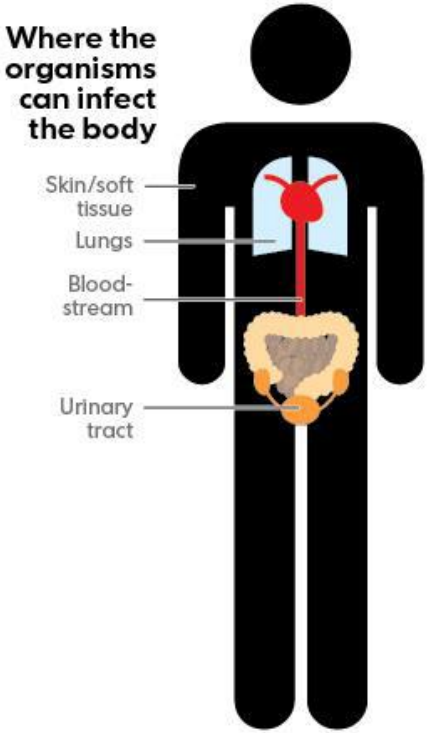
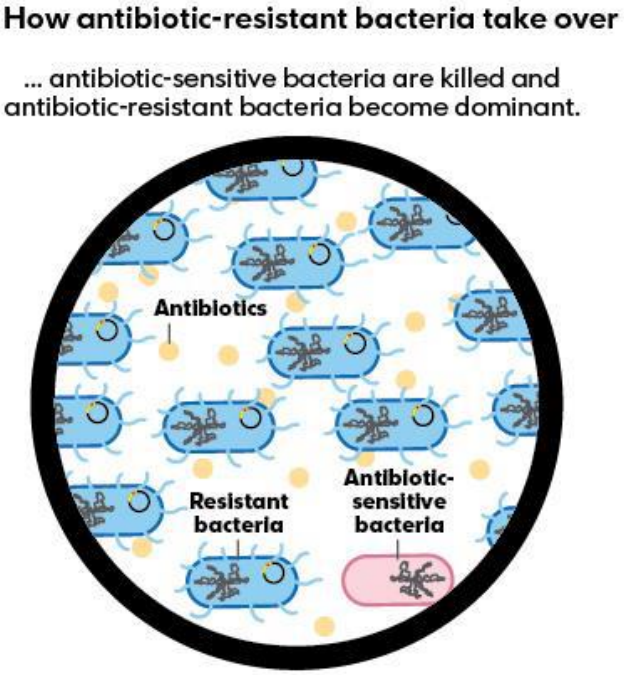
Where do MDRO's Come From? (page 2)

Reservoirs

- Asymptomatic carriers – transmission or environmental contamination
- Selected during treatment: not just the infection, but entire microbiome
- Topical antibiotics & colistin resistance





Thanner et al. mBIO 2016.

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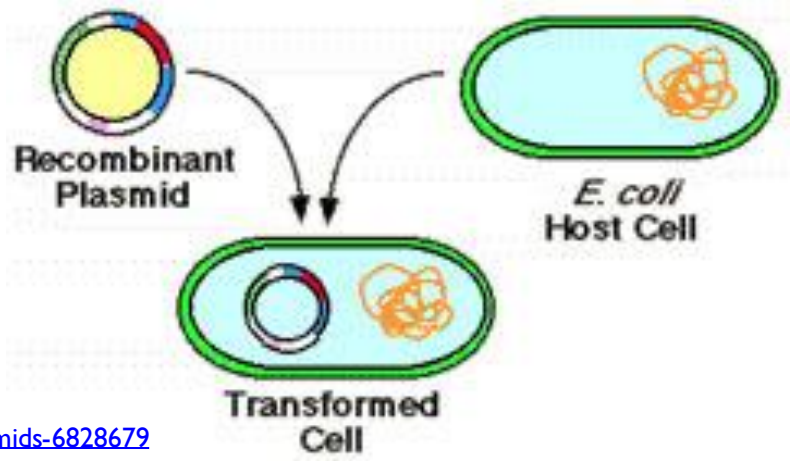
Bacterial Resistance to Antimicrobials

- Resistance is not new or unexpected, it's a natural phenomenon associated with DNA replication/transcription errors
- Three fundamental mechanisms of antimicrobial resistance. All DNA based.
  1. Enzymatic degradation of antibacterial drugs
  2. Alteration of bacterial proteins that are antimicrobial targets
  3. Changes in membrane permeability to antibiotics

Plasmid Mediated Resistance

- Plasmids harbor genes coding for antibiotic resistance and virulence factors.
- This allow bacteria to survive a hostile environment, and resist treatment.
- Examples:
  - *Pseudomonas aeruginosa* can become more mucoid
  - *K. pneumonia* with a KPC enzyme can resist most antibiotics
- Most CRE's are resistant due to having a plasmid



https://www.slideshare.net/doctorrao/plasmids-6828679

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CDC Serious Threats

Serious Threats

These germs are public health threats that require prompt and sustained action:

DRUG-RESISTANT
CAMPYLOBACTER

DRUG-RESISTANT
CANDIDA

ESBL-PRODUCING
ENTEROBACTERIACEAE

VANCOMYCIN-RESISTANT
ENTEROCOCCI

MULTIDRUG-RESISTANT
PSEUDOMONAS AERUGINOSA

DRUG-RESISTANT
NONTYPHOIDAL *SALMONELLA*

DRUG-RESISTANT
***SALMONELLA* SEROTYPE TYPHI**

DRUG-RESISTANT
SHIGELLA

METHICILLIN-RESISTANT
STAPHYLOCOCCUS AUREUS

DRUG-RESISTANT
STREPTOCOCCUS PNEUMONIAE

DRUG-RESISTANT
TUBERCULOSIS

https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf

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CDC Urgent Threats

https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf

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COVID-19 U.S. Impact on Antimicrobial Resistance

Serious Threats Impact

- Antifungal-resistant *Candida*, overall 12% increase, and 26% increase of Hospital-onset cases
- ESBL's, overall 10% increase in cases and 32% increase in Hospital –onset cases
- *Pseudomonas aeruginosa* counts stable, but saw a 32% increase in Hospital-onset cases

https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf

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COVID-19 U.S. Impact on Antimicrobial Resistance

Urgent Threat Impact:

- Carbapenem-resistant *Acinetobacter,* overall 35% increase, and 78% in Hospital-onset cases
- *C. auris*, 60% increase in cases to 754 cases in 2022. Newest report is now 3,270 cases, as 200% increase
- Carbapenem-resistant Enterobacterales, overall stable, but 35% increase in Hospital-onset cases

https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf
https://www.acpjournals.org/doi/10.7326/M22-3469

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Extended-Spectrum Beta-Lactamase (ESBL) Enterobacterales

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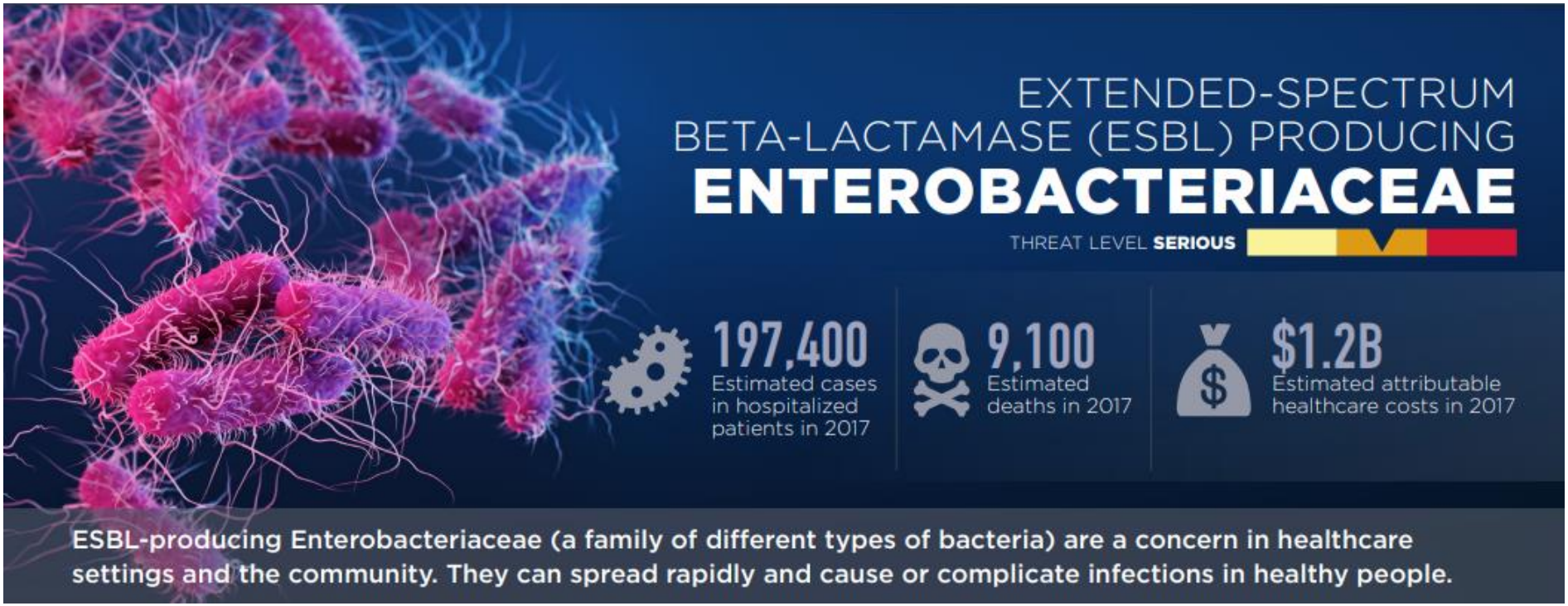
What is a ESBL?

- Some Enterobacterales can produce enzymes called extended-spectrum beta-lactamases (ESBLs). ESBL enzymes break down and destroy some commonly used antibiotics, including penicillins and cephalosporins, and make these drugs ineffective for treating infections



https://www.cdc.gov/drugresistance/pdf/threats-report/esbl-508.pdf

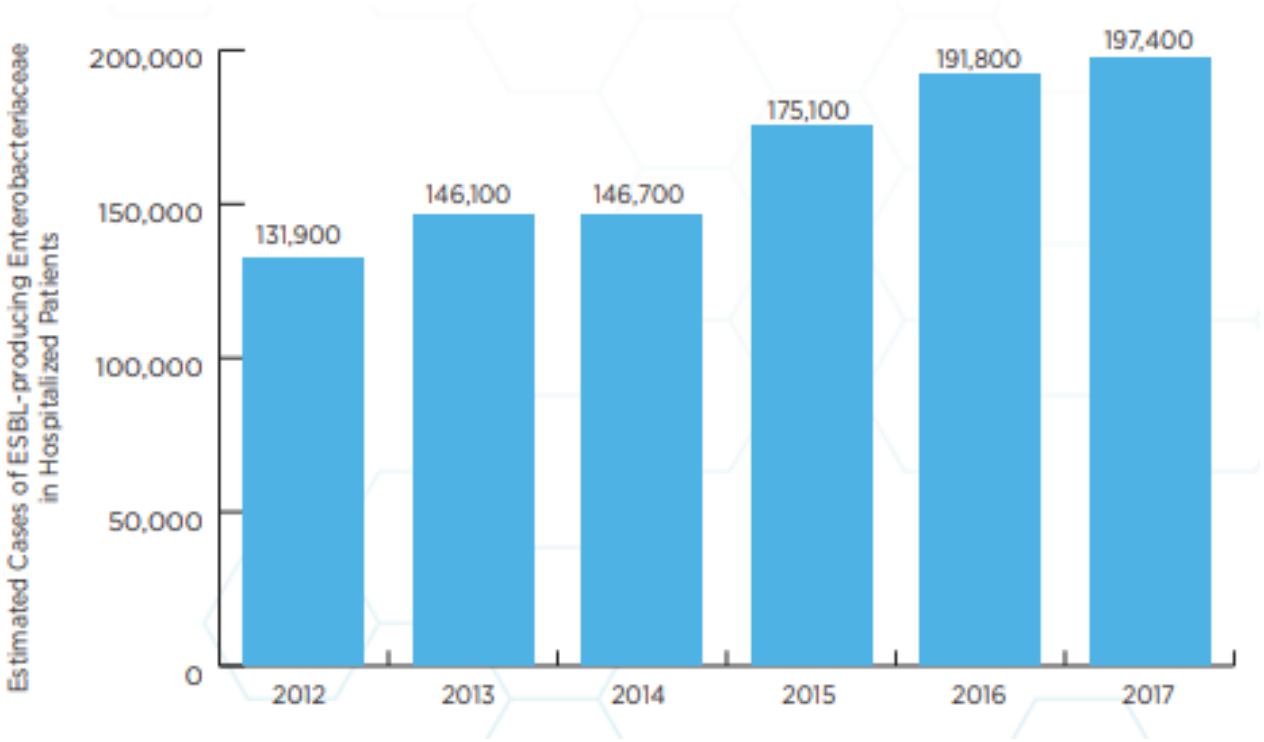
Why are ESBL Bacteria Considered Epidemiologically Important?

- ESBL-producing Enterobacteriaceae often cause infections in otherwise healthy people. About one-quarter of patients with these infection had no known underlying health conditions.
- Antibiotic options to treat ESBL-producing Enterobacteriaceae infections are limited. Healthcare providers often have to use intravenous (IV) carbapenem antibiotics to treat infections that used to be treated with oral antibiotics.

https://www.cdc.gov/drugresistance/pdf/threats-report/esbl-508.pdf

Current CDC ESBL Statistics

- CDC and partners are working to assess and address why cases of ESBL-producing Enterobacteriaceae have increased since 2012.



https://www.cdc.gov/drugresistance/pdf/threats-report/esbl-508.pdf

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ESBL Identification

- Standard microbiology testing, for organisms with susceptibilities
- ESBL will show resistance to 1st, 2nd and 3rd generation cephalosporin's

Enterobacterales (*E. coli, K. pneumoniae, K. oxytoca, or P. mirabilis* only):

	Ceftriaxone, Cefotaxime, or Ceftazidime	**Cefoxitin**	**Cefepime**	**Presumed Beta-lactamase**	**Beta-lactam treatment options**
Susceptibility	I or R	I or R	S	AmpC	Cefepime or carbapenems
Susceptibility	I or R	I or R	I or R	AmpC and ESBL	Carbapenems
Susceptibility	I or R	S	S	ESBL	Carbapenems

https://www.idstewardship.com/5-important-things-know-extended-spectrum-beta-lactamases-esbl-insights-clinical-microbiologist/

How to Test for ESBL

The Microbiology lab is your new best friend!

- Platforms your lab might have for susceptibilities
  - Automated susceptibilities testing (AST)
  - Kirby-Bauer disk diffusion
  - E-tests
  - Molecular testing, looking for CTX-M gene

ESBL Example

Escherichia coli

AUTOMATED SUSCEPTIBILITY	Breakpoint	S.I.R.
Amikacin	<=4 ug/mL	Susceptible
Amoxicillin/Clavulanic	4/2 ug/mL	Susceptible
Ampicillin	<=2 ug/mL	Susceptible
Ampicillin/Sulbactam	2/1 ug/mL	Susceptible
Aztreonam	<=1 ug/mL	Susceptible
Cefazolin	<=1 ug/mL	Susceptible
Cefepime	<=0.5 ug/mL	Susceptible
Ceftazidime	<=0.5 ug/mL	Susceptible
Ceftriaxone	<=0.5 ug/mL	Susceptible
Cefuroxime	<=4 ug/mL	Susceptible
Ciprofloxacin	<=0.5 ug/mL	Susceptible
Ertapenem	<=0.125 ug/mL	Susceptible
Gentamicin	<=1 ug/mL	Susceptible
Imipenem	<=0.25 ug/mL	Susceptible
Levofloxacin	<=1 ug/mL	Susceptible
Meropenem	<=0.125 ug/mL	Susceptible
Moxifloxacin	<=1 ug/mL	Susceptible
Piperacillin/Tazobactam	<=2/4 ug/mL	Susceptible
Tetracycline	<=1 ug/mL	Susceptible
Tobramycin	1 ug/mL	Susceptible
Trimethoprim/Sulfamethoxazole	1/19 ug/mL	Susceptible

Escherichia coli (ESBL)

AUTOMATED SUSCEPTIBILITY	Breakpoint	S.I.R.
Amikacin	<=4 ug/mL	Susceptible
Amoxicillin/Clavulanic	4/2 ug/mL	Susceptible
Ampicillin	>16 ug/mL	**Resistant**
Ampicillin/Sulbactam	16/8 ug/mL	Intermediate
Aztreonam	>16 ug/mL	**Resistant**
Cefazolin	>32 ug/mL	**Resistant**
Cefepime	>16 ug/mL	**Resistant**
Ceftazidime	16 ug/mL	**Resistant**
Ceftriaxone	>32 ug/mL	**Resistant**
Cefuroxime	>16 ug/mL	**Resistant**
Ciprofloxacin	>2 ug/mL	**Resistant**
Ertapenem	<=0.125 ug/mL	Susceptible
Gentamicin	<=1 ug/mL	Susceptible
Imipenem	<=0.25 ug/mL	Susceptible
Levofloxacin	>4 ug/mL	**Resistant**
Meropenem	<=0.125 ug/mL	Susceptible
Moxifloxacin	>4 ug/mL	**Resistant**
Piperacillin/Tazobactam	<=2/4 ug/mL	Susceptible
Tetracycline	>8 ug/mL	**Resistant**
Tobramycin	1 ug/mL	Susceptible
Trimethoprim/Sulfamethoxazole	<=0.5/9.5 ug/ml	Susceptible

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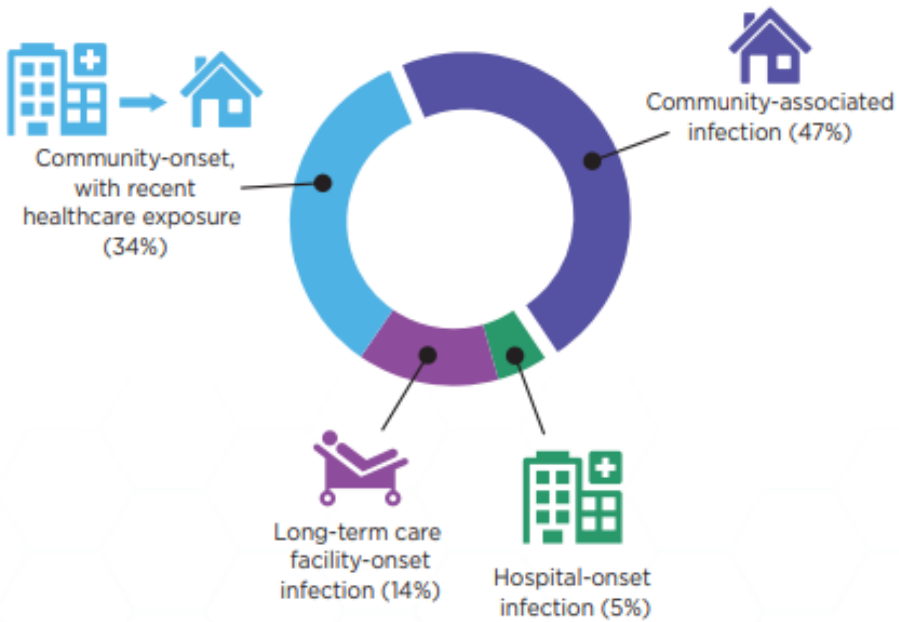
How Common are ESBL Infections?

- Almost half of ESBL-producing Enterobacteriaceae infections occur in people who have not had recent inpatient healthcare exposure or an invasive medical procedure. These infections are called community-associated infections



Data shows infections by epidemiological classification (the setting where patients most likely got the infection based on clinical information).

https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf

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Who is Most Likely to get a ESBL Infection?

- These infections most commonly occur in people with exposure to healthcare, including those in hospitals and nursing homes. However, unlike many other resistant germs, ESBL-producing Enterobacterales can also cause infections in otherwise healthy people who have not been recently been in healthcare settings. In healthy people, this often means urinary tract infections.
- ESBL germs have also been identified in people returning to the United States after traveling abroad, especially to places where these germs are more commonly found.

https://www.cdc.gov/hai/organisms/ESBL.html

Carbapenem-resistant Enterobacterales (CRE)

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What is a CRE or CP-CRE?

Enterobacterales that test resistant to at least one of the carbapenem antibiotics or produce a carbapenemase (an enzyme that can make them resistant to carbapenem antibiotics) are called CRE

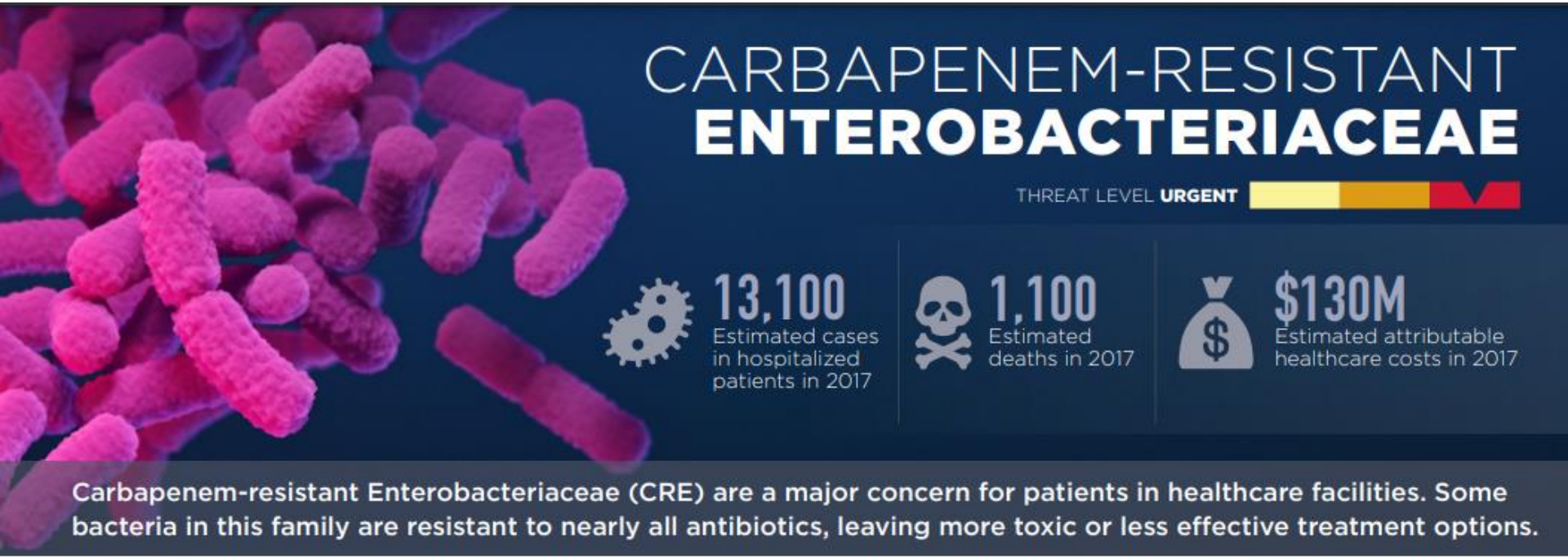
Common Plasmids:

- *K. pneumoniae* carbapenemase (KPC)
- New Delhi Metallo-beta-lactamase (NDM)
- Verona Integron-Encoded Metallo-beta-lactamase (VIM)
- Imipenemase (IMP)
- Oxacillinase-48 (OXA-48)

Carbapenem Antibiotics

- Doripenem
- Ertapenem
- Imipenem
- Meropenem

https://www.cdc.gov/hai/organisms/cre/index.html



In the United States, CRE are generally associated with healthcare settings, and approximately 30% of CRE carry a carbapenemase. These carbapenemase genes are often on mobile genetic elements, which can be easily shared between bacteria, leading to the rapid spread of resistance

https://www.cdc.gov/drugresistance/pdf/threats-report/CRE-508.pdf

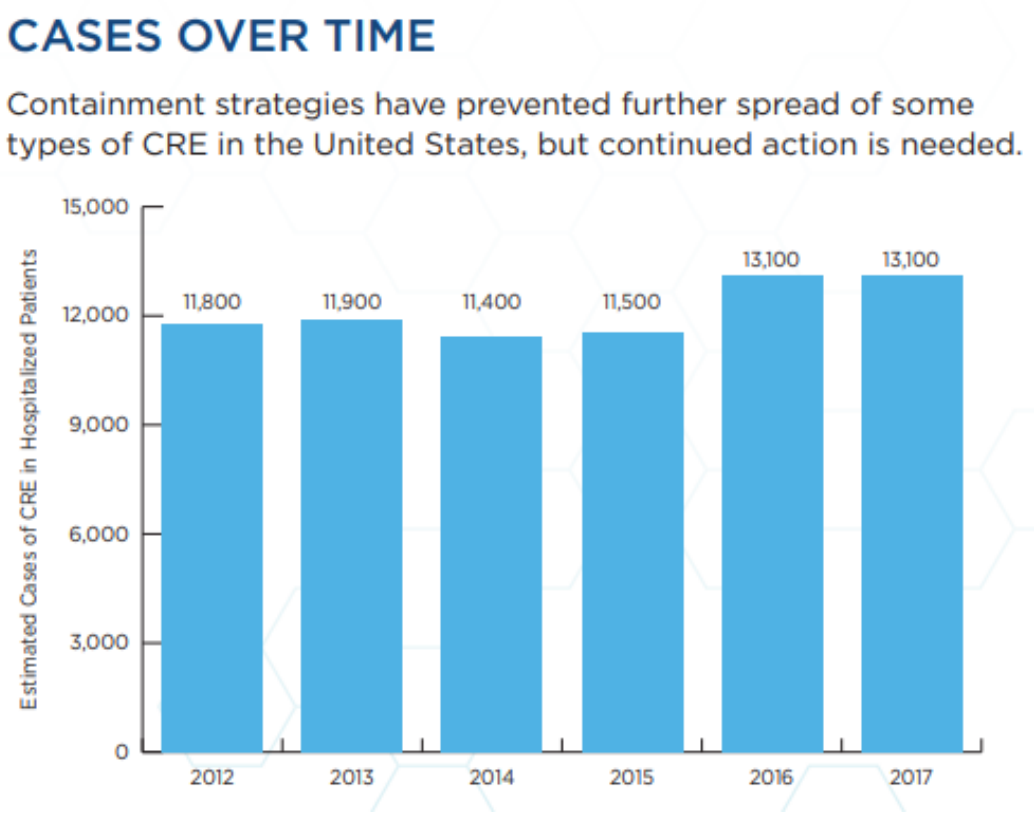
Why are CP-CRE Considered Epidemiologically Important?

- CRE organisms are often resistant to multiple classes of antibiotics, substantially limiting treatment options.
- Infections caused by these organisms are associated with high mortality rates among hospitalized patients, up to 50% in some studies.
- Many CRE produce carbapenemases, which can be transmitted from Enterobacterales to other germs, facilitating spread of resistance.
- Enterobacterales are a common cause of infections in both community and healthcare settings. Although CRE is currently primarily associated with inpatient healthcare settings, it has the potential to spread to community settings.

https://www.cdc.gov/hai/organisms/cre/cre-clinicians.html

Current CDC CRE Statistics

- Containment strategies have prevented further spread of some types of CRE in the United States, but continued action is needed.



https://www.cdc.gov/drugresistance/pdf/threats-report/CRE-508.pdf

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CRE and Carbapenemase Identification

CRE Identification

- Enterobacterales that test resistant to at least one of the carbapenem antibiotics on microbiology sensitivity report

Carbapenemase Identification

- Phenotypic tests for carbapenemase production
- Molecular assay for the presence of a carbapenemase gene

https://www.cdc.gov/hai/organisms/cre/technical-info.html#:~:text=Types%20of%20CRE-,How%20does%20CDC%20define%20CRE%3F,carbapenem%20antibiotics)%20are%20called%20CRE.

CRE Example

Escherichia coli

AUTOMATED SUSCEPTIBILITY	DISK DIFFUSION	Breakpoint	S.I.R.
Amikacin		16 ug/mL	Susceptible
Amoxicillin/Clavulanic		>16/8 ug/mL	**Resistant**
Ampicillin		>16 ug/mL	**Resistant**
Ampicillin/Sulbactam		>16/8 ug/mL	**Resistant**
Aztreonam		<=1 ug/mL	Susceptible
Cefazolin		>32 ug/mL	**Resistant**
Cefepime		>16 ug/mL	**Resistant**
Ceftazidime		>16 ug/mL	**Resistant**
Ceftriaxone		>32 ug/mL	**Resistant**
Cefuroxime		>16 ug/mL	**Resistant**
Ciprofloxacin		>2 ug/mL	**Resistant**
Doripenem	**Resistant**		
Ertapenem	**Resistant**		
Gentamicin		2 ug/mL	Susceptible
Imipenem	**Resistant**		
Levofloxacin		>4 ug/mL	**Resistant**
Meropenem	**Resistant**		
Nitrofurantoin		>64 ug/mL	**Resistant**
Piperacillin/Tazobactam		>64/4 ug/mL	**Resistant**
Tetracycline		>8 ug/mL	**Resistant**
Tobramycin		>8 ug/mL	**Resistant**
Trimethoprim/Sulfamethoxazole		<=0.5/9.5 ug/ml	Susceptible

PCR Testing	NDM-1

How to Test for CRE

- Clinical laboratories can perform phenotypic tests for carbapenemase production (e.g., CarbaNP, mCIM, and mCIM with eCIM) or molecular assays for the presence of a carbapenemase gene
- Carbapenemase testing is available through the AR Lab Network. This testing includes phenotypic testing for carbapenemase activity and molecular identification of the five carbapenemases most frequently identified in CRE: KPC, NDM, VIM, OXA-48-type, and IMP

https://www.cdc.gov/hai/organisms/cre/technical-info.html#Common

How Common are CRE Infections?

- In 2017, CRE caused an estimated 13,100 infections in hospitalized patients, and 1,100 estimated deaths in the United States [Source: 2019 AR Threats Report].
- NDM, VIM, and IMP are less commonly identified in CRE in the United States relative to KPC. Since the AR Lab Network began testing in 2017, only about 10% of carbapenemases identified have been metallo-β-lactamases (MBLs).

https://www.cdc.gov/hai/organisms/cre/cre-clinicians.html

Who is Most Likely to get a CRE Infection?

- Healthy people usually do not get CRE infections—
- Patients in hospitals and long-term care facilities like skilled nursing facilities and long-term acute care hospitals.
- Patients whose care requires devices like ventilators (breathing machines), urinary (bladder) catheters, or intravenous (vein) catheters
- Patients who are taking long courses of certain antibiotics
- Patients with weakened immune systems
- Healthcare-related risk factors include requiring help with most activities of daily living, like toileting and bathing, exposure to an intensive care unit, and mechanical ventilation.
- Several antibiotics have been associated with getting CRE, including carbapenems, cephalosporins, fluoroquinolones, and vancomycin.

https://www.cdc.gov/hai/organisms/cre/cre-clinicians.html

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What Can Clinicians do to Prevent CRE Transmission?

- Know if patients with CRE are admitted to your facility and stay aware of CRE infection rates in your facility.
- When you transfer a patient with CRE, use an inter-facility transfer form to alert the receiving facility during the transition of care.
- Ask if a patient has received medical care somewhere else, including another facility or other countries.
- Screen patients who have had an overnight stay in a healthcare facility outside the United States in the prior 6 months for the presence of carbapenemase-producing CRE. Free admission screening is available through the AR Lab Network. Contact your HAI coordinator for more information on accessing AR Lab Network testing.
- Whenever possible, place patients currently or previously colonized or infected with CRE in a private room with a bathroom and dedicate noncritical equipment (e.g., stethoscope, blood pressure cuff) to CRE patients.
- Wear a gown and gloves when caring for patients with CRE.

https://www.cdc.gov/hai/organisms/cre/cre-clinicians.html

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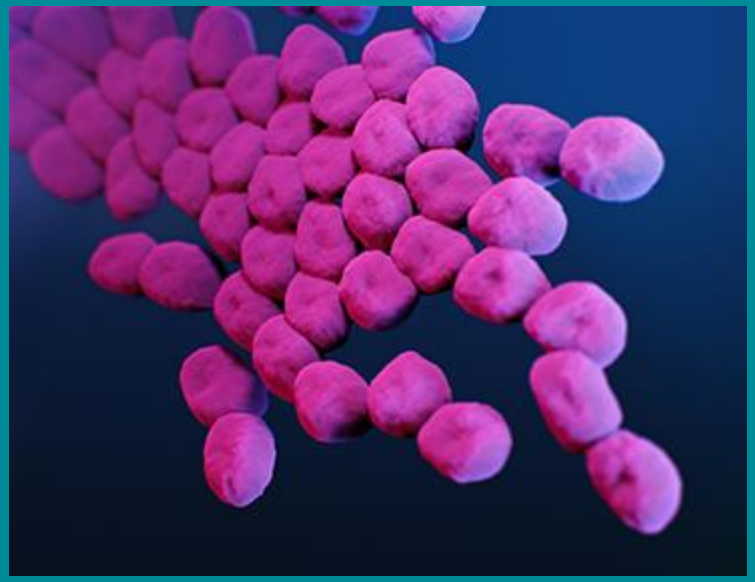
What Can Clinicians do to Prevent CRE Transmission?

- Perform hand hygiene—use alcohol-based hand rub or wash hands with soap and water before and after contact with patient or their environment.
- Make sure labs immediately alert clinical and infection prevention staff when CRE are identified. If your laboratory does not perform testing for carbapenemases, talk to your HAI coordinator about getting isolates tested through the AR Laboratory Network.
- Prescribe and use antibiotics appropriately.
- Discontinue devices like urinary catheters as soon as no longer necessary.
- When a patient with an unusual type of carbapenemase-producing CRE is identified in your facility, work with public health to prevent spread, including following guidance to assess for ongoing transmission.

https://www.cdc.gov/hai/organisms/cre/cre-clinicians.html

Carbapenem-Resistant *Acinetobacter baumannii* (CRAB)



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What is a CRAB?

- *Acinetobacter* is a group of bacteria (germs) commonly found in the environment, like in soil and water. While there are many types, the most common cause of infections is *Acinetobacter baumannii*, which accounts for most Acinetobacter infections in humans
- When resistant to multiple antibiotics, they're multidrug resistant
- Carbapenem-resistant *Acinetobacter* are usually multidrug-resistant.
- *Acinetobacter baumannii* can cause infections in the blood, urinary tract, and lungs (pneumonia), or in wounds in other parts of the body. It can also "colonize" or live in a patient without causing infections or symptoms, especially in respiratory secretions (sputum) or open wounds.

https://www.cdc.gov/hai/organisms/acinetobacter.html

https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf

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Why are CRAB Considered Epidemiologically Important?

- Carbapenem-resistant *Acinetobacter* cause pneumonia and wound, bloodstream, and urinary tract infections. These infections tend to occur in patients in intensive care units.
- Carbapenem-resistant *Acinetobacter* can carry mobile genetic elements that are easily shared between bacteria. Some can make a carbapenemase enzyme, which makes carbapenem antibiotics ineffective and rapidly spreads resistance that destroys these important drugs.
- Some *Acinetobacter* are resistant to nearly all antibiotics and few new drugs are in development.

https://arpsp.cdc.gov/story/cra-urgent-public-health-threat

Why are CRAB Considered Epidemiologically Important?

- Treatment options for infections caused by carbapenem-resistant *Acinetobacter baumannii* are extremely limited. There are few new drugs in development.

PERCENT OF GERMS THAT TESTED NON-SUSCEPTIBLE (NOT SENSITIVE) TO OTHER TYPES OF ANTIBIOTICS

Select Antibiotics	2013	2014	2015	2016	2017
Any fluoroquinolone	98%	93%	97%	92%	89%
Any extended-spectrum β-lactam	80%	75%	81%	79%	75%
Ampicillin/sulbactam	62%	62%	59%	64%	61%
Trimethoprim/ sulfamethoxazole	84%	74%	81%	77%	66%

Germs refer to isolates (pure samples of germs) from eight of CDC's Emerging Infections Program sites. See Technical Appendix for antibiotic susceptibilities details.

https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf

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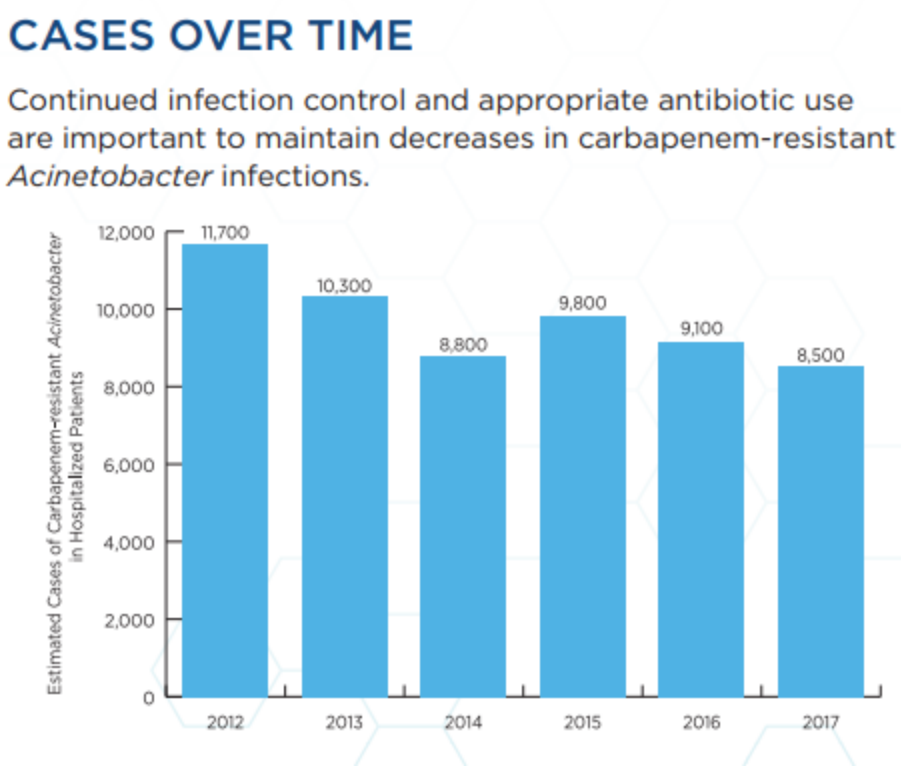
Current CDC CRAB Statistics

- In 2017, carbapenem-resistant *Acinetobacter* caused an estimated 8,500 infections in hospitalized patients and 700 estimated deaths in the United States.



https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf

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CRAB Identification

- Standard microbiology identification and sensitivities
- Molecular testing to look for a carbapanemase gene

How to Test for CRAB

- Testing in the Antibiotic Resistance Laboratory Network (AR Lab Network) during 2019 found that carbapenemase genes were detected in 83% of CRA isolates tested. These carbapenemase gene-positive CRA (CP-CRA) are divided into two categories based on the type of gene present:
  - Most CP-CRA possess genes for carbapenemases that have been specifically identified among *Acinetobacter* species. These more common genes make OXA-23-like, OXA-24/40-like and OXA-58-like oxacillinases. Because these genes were detected frequently, they are not targeted for routine molecular testing.
  - A small proportion of CP-CRA possessed mobile genes that encode carbapenemases (KPC, IMP, NDM, VIM, OXA-48-like) found often in other gram-negative bacteria, such as Enterobacterales. These genes are amplifying the problem of resistance and are targeted for further molecular testing.

https://arpsp.cdc.gov/story/cra-urgent-public-health-threat

Who is Most Likely to get a CRAB Infection?

- *Acinetobacter* infections typically occur in people in healthcare settings. People most at risk include patients in hospitals, especially those who:
  - are on breathing machines (ventilators)
  - have devices such as catheters
  - have open wounds from surgery
  - are in intensive care units
  - have prolonged hospital stays
- In the United States, *Acinetobacter* infections rarely occur outside of healthcare settings. However, people who have weakened immune systems, chronic lung disease, or diabetes may be more susceptible.

https://arpsp.cdc.gov/story/cra-urgent-public-health-threat

How are CRAB Germs Spread or Transmitted?

- *Acinetobacter* can live for long periods of time on environmental surfaces and shared equipment if they are not properly cleaned.
- The germs can spread from one person to another through contact with these contaminated surfaces or equipment or though person to person spread, often via contaminated hands

https://www.cdc.gov/hai/organisms/acinetobacter.html

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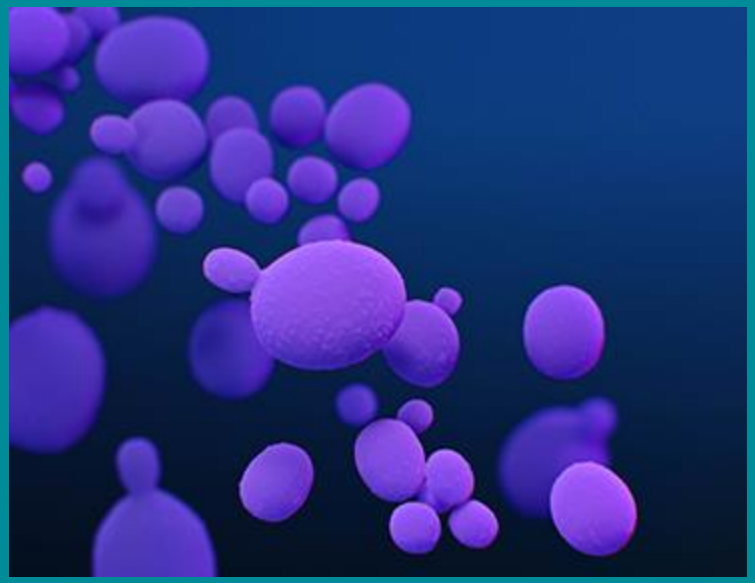
What Can Clinicians do to Prevent CRAB Transmission?

- When available, house patients infected or colonized with CRAB in single patient rooms. If the number of single patient rooms is limited, reserve these rooms for patients with highest risk for transmission (e.g., incontinence).
- Use gown and gloves (e.g., Contact Precautions in Acute Care settings and Enhanced Barrier Precautions in long-term care settings for patients/residents who are infected or colonized with CRA). Consider empiric use of these precautions for patients transferred from high-risk settings.
- Review facility infection prevention and control practices and provide staff with feedback, particularly for:
  - Hand hygiene adherence
  - Personal protective equipment donning and doffing and adherence
  - Environmental cleaning and disinfection

https://arpsp.cdc.gov/story/cra-urgent-public-health-threat

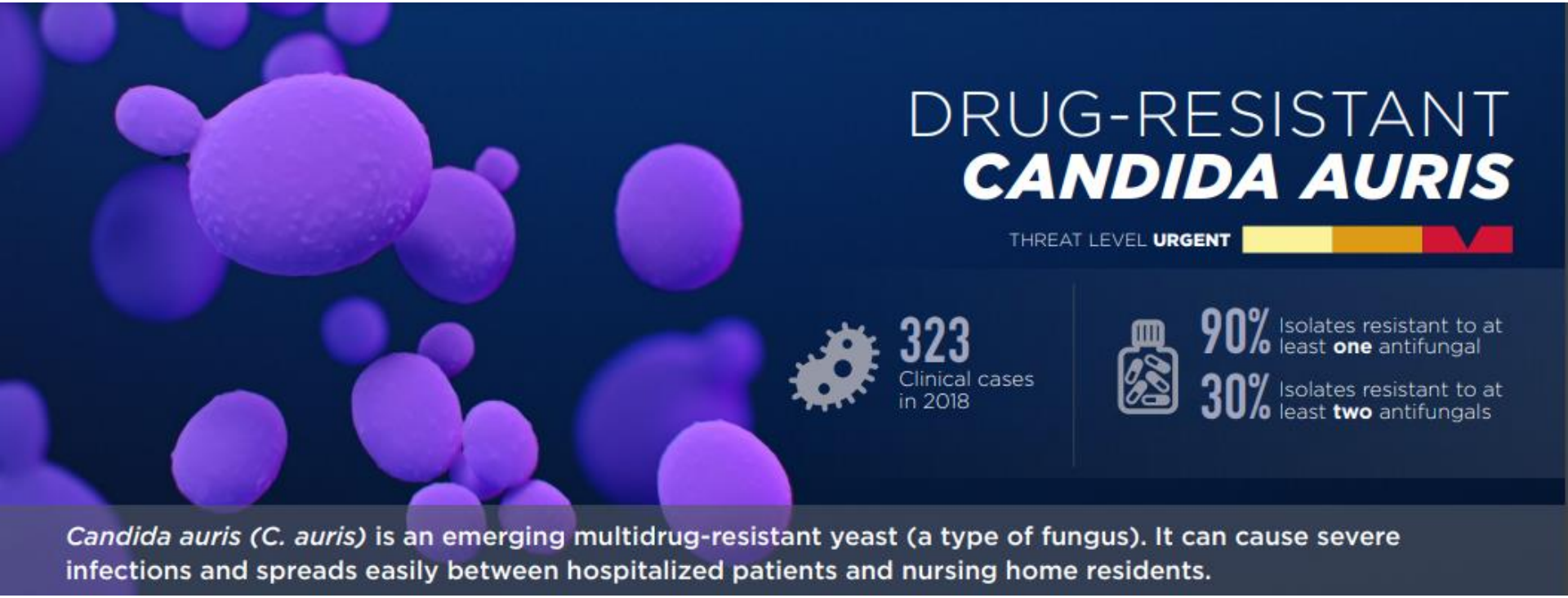
Candida auris



What is a *Candia auris*?

- *Candida auris* (*C. auris*) is an emerging multidrug-resistant yeast (a type of fungus). It can cause severe infections and spreads easily between hospitalized patients and nursing home residents.
- First identified in 2009 in Asia
- More than 1 in 3 patients with invasive *C. auris* infection (for example, an infection that affects the blood, heart, or brain) die

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



https://www.cdc.gov/drugresistance/pdf/threats-report/candida-auris-508.pdf

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Why are *C.auris* Considered Epidemiologically Important?

CDC is concerned about *C. auris* for three main reasons:

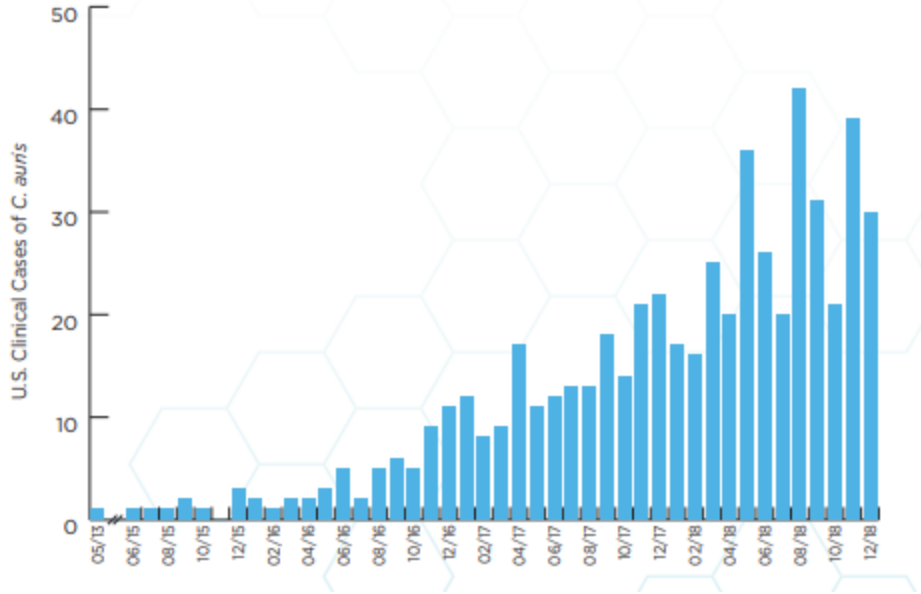
- It is often multidrug-resistant, meaning that it is resistant to multiple antifungal drugs commonly used to treat *Candida* infections.
- It is difficult to identify with standard laboratory methods, and it can be misidentified in labs without specific technology. Misidentification may lead to inappropriate management.
- It has caused outbreaks in healthcare settings. For this reason, it is important to quickly identify *C. auris* in a hospitalized patient so that healthcare facilities can take special precautions to stop its spread.

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

Current CDC *C.auris* Statistics

CASES OVER TIME

C. auris began spreading in the United States in 2015. Reported cases increased 318% in 2018 when compared to the average number of cases reported in 2015 to 2017.



- In 2021, cases reached a count of 3,270 with an active infection and 7,413 that showed the fungus was present but hadn't caused an infection. Infection counts were up 95% over the previous year, and the fungus showed up on screenings three times as often. The number of cases resistant to medication also tripled

https://www.cdc.gov/drugresistance/pdf/threats-report/candida-auris-508.pdf
https://www.acpjournals.org/doi/10.7326/M22-3469

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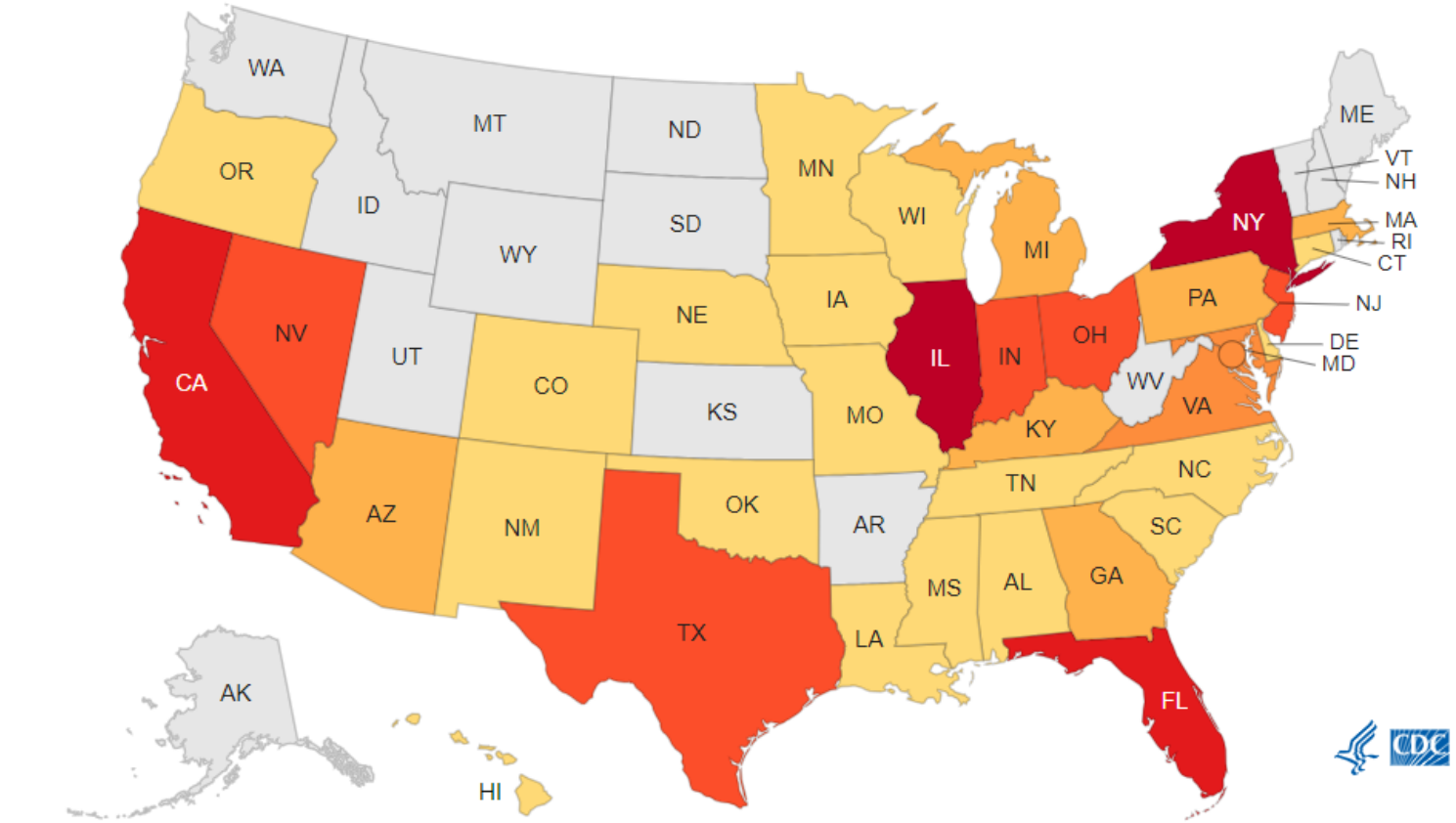

Number of *C. auris* clinical cases through December 31, 2022

There have been 5,654 clinical cases and 13,163 screening cases since 2013.

- 0 clincial cases and at least 1 screening case
- 1 to 10
- 11 to 50
- 51 to 100
- 101 to 500
- 501 to 1000
- 1001 or more

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

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C.auris Identification

It is difficult to identify.

- *C. auris* can be misidentified as a number of different organisms when using traditional phenotypic methods for yeast identification such as VITEK 2 YST, API 20C, BD Phoenix yeast identification system, and MicroScan

https://www.cdc.gov/fungal/candida-auris/identification.html

When to suspect *C. auris*

Identification Method	Organism *C. auris* can be misidentified as
Vitek 2 YST*	*Candida haemulonii* *Candida duobushaemulonii*
API 20C	*Rhodotorula glutinis* (characteristic red color not present) *Candida sake*
API ID 32C	*Candida intermedia* *Candida sake* *Saccharomyces kluyveri*
BD Phoenix yeast identification system	*Candida haemulonii* *Candida catenulata*
MicroScan	*Candida famata* *Candida guilliermondii*** *Candida lusitaniae*** *Candida parapsilosis***
RapID Yeast Plus	*Candida parapsilosis***

https://www.cdc.gov/fungal/candida-auris/identification.html

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How to Test for *C. auris*

- Diagnostic devices based on matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) can differentiate *C. auris* from other *Candida* species, but not all the reference databases included in MALDI-TOF devices allow for detection
- Molecular methods based on sequencing the D1-D2 region of the 28s rDNA or the Internal Transcribed Region (ITS) of rDNA also can identify *C. auris*
- The GenMark ePlex Blood Culture Identification Fungal Pathogen (BCID-FP) Panel and BioFire FilmArray BCID2 have been FDA approved as molecular tests for *C. auris* identification in positive blood cultures
- AR Lab Network

https://www.cdc.gov/fungal/candida-auris/identification.html

How Common are *C. auris* Infections?

- In 2019 CDC reported 476 clinical cases
- 2015 to 2017 saw a 318% increase in reported cases
- 754 estimated cases in 2020
- 3270 estimated cases in 2021

Case counts continue to rise quickly, along with colonization screening cases.

While not a common as a ESBL, or CRE, *C. auris* is rising the fastest among the CDC urgent threats

https://www.cdc.gov/media/releases/2023/p0320-cauris.html

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Who is Most Likely to get a *C. auris* Infection?

- People who are very sick with invasive medical devices
- Long or frequent stays in Hospitals and Long-term-care facilities and nursing homes
- Long term antibiotic use or antifungals
- People who weakened immune systems
- Patients who received medical care in foreign countries

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

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How are *C. auris* Spread or Transmitted?

- *C. auris* can spread in healthcare settings through contact with contaminated environmental surfaces or equipment, or from person to person.
- *C. auris* can be transmitted in healthcare settings and cause outbreaks
- It can colonize patients for many months
- It can persist in the environment and on surfaces
- Withstands some commonly used healthcare facility disinfectants

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

What Can Clinicians do to Prevent *C. auris* Transmission?

- Quickly identify any patient with colonization or active infection based on their risk factors, and implement precautions
- Adherence to hand hygiene
- Appropriate use of Transmission-Based Precautions based on setting
- Cleaning and disinfecting the patient care environment, daily and terminal cleaning using Products with EPA-registered claims for *C. auris* (List P)
- Use disposable equipment, or dedicated equipment
- Communicate patient *C. auris* status when patient transferred
- Screening for high-risk patients

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

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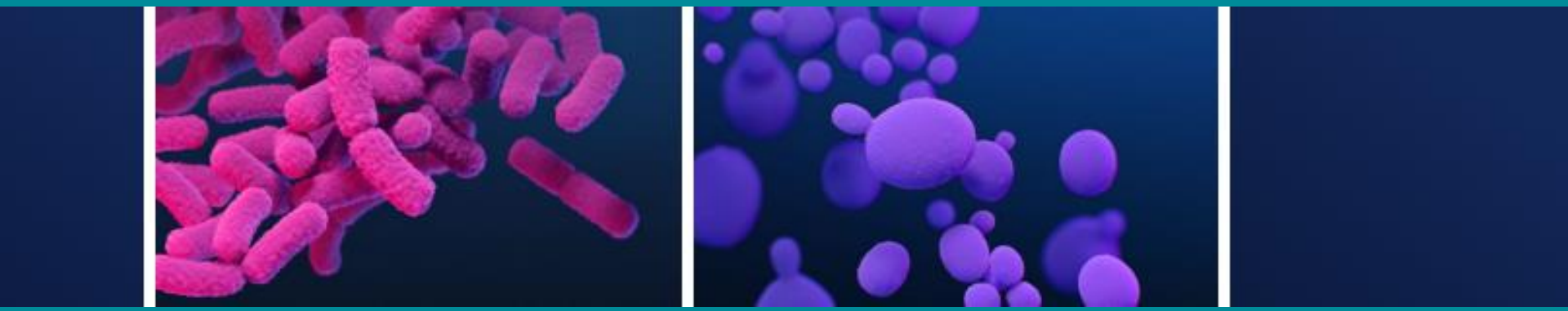
Addressing MDRO's: Next Steps



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Antimicrobial Resistance: 5 Things to Know

1. Antimicrobial resistance occurs when germs defeat the drugs designed to kill them, called antibiotics or antifungals.
2. Antimicrobial resistance can affect people at any stage of life. Infections caused by resistant germs are difficult—sometimes impossible—to treat.
3. You can take steps to reduce your risk of getting an infection.
4. Talk to your healthcare provider or veterinarian about whether antibiotics or antifungals are needed.
5. Tell your healthcare provider if you recently traveled to or received care in another country. Antimicrobial resistance has been found in all regions of the world.

https://www.cdc.gov/drugresistance/about/5-things-to-know.html#:~:text=Antimicrobial%20resistance%20occurs%20when%20germs,at%20any%20stage%20of%20life.

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MDRO Identified, Now What?

- Confirm if the patient has an active infection or is colonized, ensure the proper treatment course has been selected
- Place patient in transmission-based precautions or enhanced barrier precautions
- Look for other cases. Is this just one, or are there others?
- Report the case to public health as needed or required
- Ensure good hand hygiene practices are in place
- Ensure proper cleaning and disinfection is occurring

Hand Hygiene

Use an Alcohol-Based Hand Sanitizer

- Immediately before touching a patient
- Before performing an aseptic task (e.g., placing an indwelling device) or handling invasive medical devices
- Before moving from work on a soiled body site to a clean body site on the same patient
- After touching a patient or the patient's immediate environment
- After contact with blood, body fluids or contaminated surfaces
- Immediately after glove removal

Wash with Soap and Water

- When hands are visibly soiled
- After caring for a person with known or suspected infectious diarrhea
- After known or suspected exposure to spores (e.g. *B. anthracis*, *C difficile* outbreaks)

https://www.cdc.gov/handhygiene/providers/index.html

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Environmental Cleaning and Disinfection

- Environmental cleaning is part of Standard Precautions, which should be applied to all patients in all healthcare facilities.
- Clean with an EPA registered disinfectant with the proper/needed kill claims for the MDRO in question
- Clean high touch surfaces regularly
- Launder linens at high temperature
- Ensure staff are properly trained with competencies
- Audit cleaning processes to ensure compliance

https://www.cdc.gov/hai/prevent/resource-limited/index.html

PPE

Standard precautions say to use PPE as needed based on the risk of exposure

- Gloves
- Masks (ear loop, surgical, N-95)
- Gowns
- Eye protection (glasses, goggles, face shields)

- Follow correct donning and doffing sequences
- Always perform hand hygiene after removal of PPE

https://www.cdc.gov/hai/prevent/ppe.html

Standard Precautions

- Perform hand hygiene
- Use PPE whenever there is an expectation of possible exposure to infectious material
- Follow respiratory hygiene/cough etiquette principles
- Ensure proper patient placement
- Properly handle and clean and disinfect patient care equipment and instruments/devices
  - Clean and disinfect the environment appropriately
- Handle textiles and laundry carefully
- Follow safe injection practices
- Ensure healthcare worker safety including proper handling of needles and other sharps

https://www.cdc.gov/infectioncontrol/basics/standard-precautions.html

Transmission Based Precautions

Contact Precautions

- Patient placement
- Use needed PPE correctly
- Limit transport and movement of patients
- Use disposable or dedicated patient-care equipment
- Prioritize cleaning and disinfection of the rooms

Droplet Precautions

- Source control: put a mask on the patient
- Ensure appropriate patient placement
- Use PPE appropriately
- Limit transport and movements of patients

Airborne Precautions

- Source control
- Patient placement in Airborne Infection Isolation room (AIIR)
- Restrict susceptible healthcare personnel from entering room
- Use PPE appropriately
- Limit transport and movement of patients
- Immunize susceptible persons as soon as possible following unprotect contact

https://www.cdc.gov/infectioncontrol/basics/transmission-based-precautions.html

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Enhanced Barrier Precautions

- Enhanced Barrier Precautions (EBP) are an infection control intervention designed to reduce transmission of resistant organisms that employs targeted gown and glove use during high contact resident care activities.
- EBP may be indicated (when Contact Precautions do not otherwise apply) for residents with any of the following:
  - Wounds or indwelling medical devices, regardless of MDRO colonization status
  - Infection or colonization with an MDRO.

Examples of high-contact resident care activities requiring gown and glove use for ***Enhanced Barrier Precautions*** include:

- Dressing
- Bathing/showering
- Transferring
- Providing hygiene
- Changing linens
- Changing briefs or assisting with toileting
- Device care or use: central line, urinary catheter, feeding tube, tracheostomy/ventilator
- Wound care: any skin opening requiring a dressing

https://www.cdc.gov/hai/containment/PPE-Nursing-Homes.html

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Acute Care Setting Prevention

- Always follow Standard Precautions
- Implement Transmission Based Precautions based on organism
  - Contact Precautions (MDRO, ESBL, CRAB, CRE, C.auris)
  - Droplet Precautions (Respiratory viruses)
  - Airborne Precautions (TB, Chickenpox, Measles)

- Leave precautions in place until discharge, or per CDC Appendix A, or per internal policy guidance

Post Acute Care Setting Prevention

- Always follow Standard Precautions
- Enhanced Barrier Precautions for residents with MDRO infection or colonization
- Contact Precautions: All residents infected or colonized with MDRO in the following situations
  - Acute diarrhea, draining wounds, other site excretions or secretions that are unable to be covered or contained
  - For a limited time period as determined in consultation with public health authorities, on units or in facilities during the investigation of a suspected or confirmed MDRO outbreak
  - When otherwise directed by public health authorities
  - All residents who have another infection (e.g., *C. difficile*, norovirus, scabies) or condition for which Contact Precautions is recommended in Appendix A (Type and Duration of Precautions Recommended for Selected Infections and Conditions) of the CDC Guideline for Isolation Precautions

https://www.cdc.gov/hai/containment/PPE-Nursing-Homes.html

Outbreaks

- Healthcare Facility contacts Local Public Health for assistance
- Epidemiologist gathers initial information and provides consultation on case finding, lab testing and infection control
- Team works on-site and help gather additional information from interview, case/chart review, observations and environmental sampling as needed
- Analyze information to identify risk factors for infection and help develop control measures
- Recommend new or revised measure and steps to prevent more patients from becoming infected or harmed
- Health department and facility implement recommendations and check to ensure the control measures are working

https://www.cdc.gov/hai/pdfs/outbreaks/how-cdc-help-resolves-outbreaks-hc-facilities-508.pdf

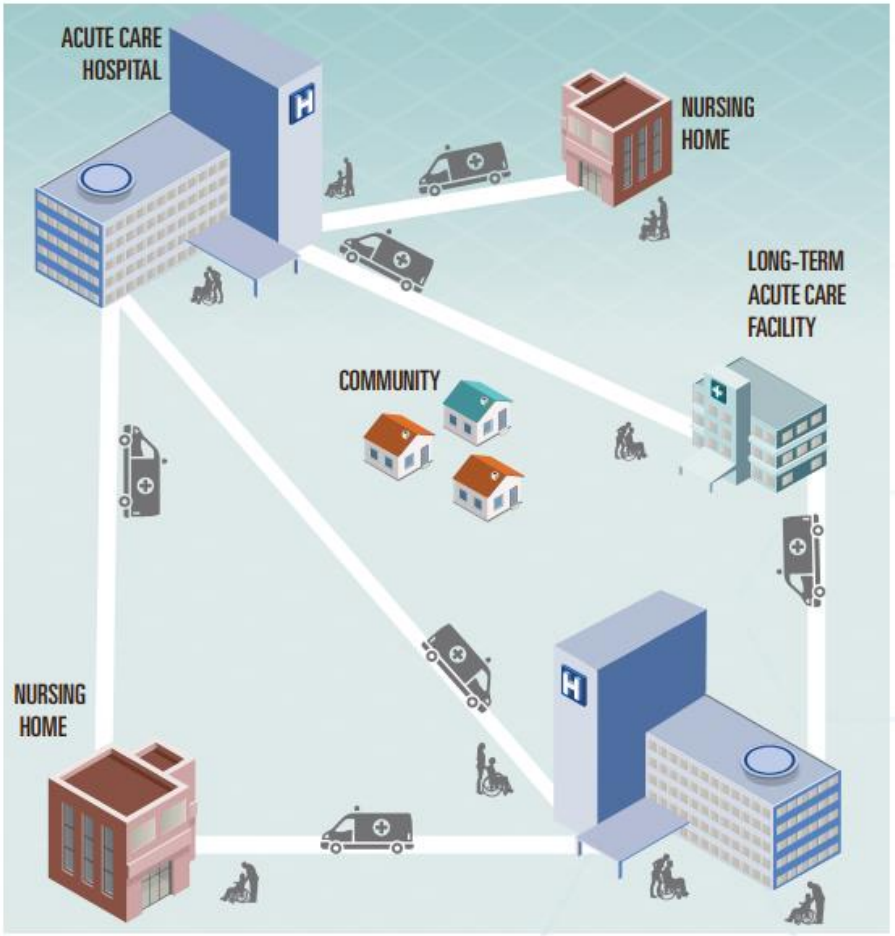
Individual Prevention

- Maintain good hygiene, wash hands regularly, maintain good health
- Proper use of antibiotics
- Clean your environment

Communication is Key

Patient Transfers Between Healthcare Locations

- Implement systems to designate patients known to be colonized or infected with a targeted MDRO and to notify receiving healthcare facilities and personnel prior to transfer of such patients within or between facilities



https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf
https://www.cdc.gov/infectioncontrol/guidelines/mdro/index.html

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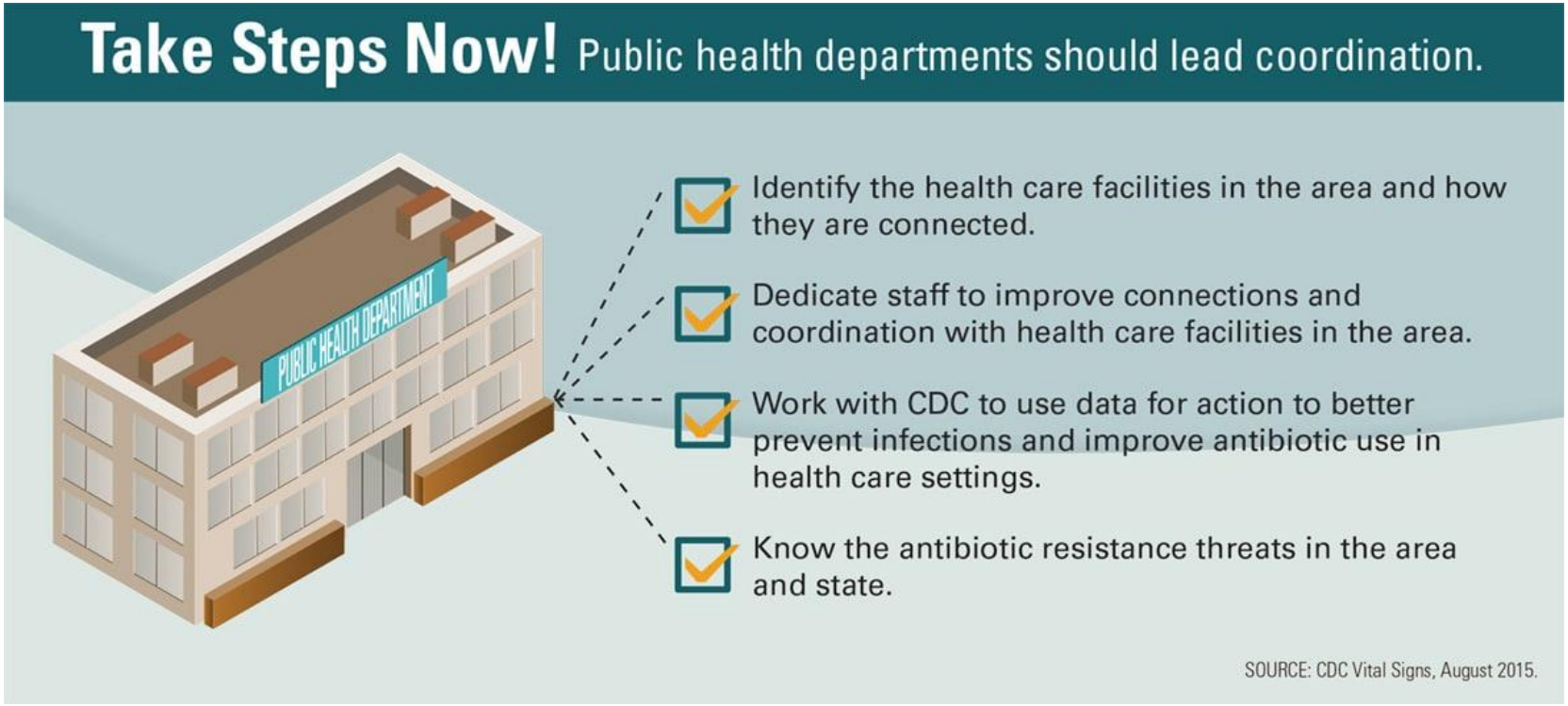
Public Health Departments and MDROs



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Public Health Departments

- Understand the prevalence or incidence of MDRO in their jurisdiction by performing some form of regional surveillance for these organisms.
- Increase awareness among healthcare facilities of the regional prevalence of MDRO and prevention strategies and initiatives.
- Provide a standardized form for facilities to use during patient transfers, especially between hospitals and long-term care facilities.
- Consider including MDRO infections on your state's Notifiable Diseases List.
- Include a range of facility types when developing regional MDRO prevention projects.
- Be a resource for healthcare facilities on appropriate infection prevention measures and antimicrobial stewardship

https://www.cdc.gov/hai/mdro-guides/prevention-strategy.html

What CDC is Doing: Investments and Action

Since 2016 Congress has appropriated $160 million in investments to for the CDC to fight antimicrobial resistance.

- State level funding
- Healthcare programs to reduce MDRO and HAI's
- Community actions (education, data, testing, research)
- Environmental Actions (water and soil)
- Food Supply Actions (lab capacity, innovation, data sharing)
- Global Action (collaborating with global partners, investing)
- Lab Capacity Action (expansion of testing and AR Lab Network)
- Innovative Action (research)

https://www.cdc.gov/drugresistance/solutions-initiative/index.html

CDC Antimicrobial Resistance Laboratory Network

CDC's Antimicrobial Resistance Laboratory Network (AR Lab Network), established in 2016, provides nationwide lab capacity to rapidly detect antimicrobial resistance and inform local responses to prevent spread and protect people. It closes the gap between local capabilities and the data needed to combat antimicrobial resistance in the U.S.

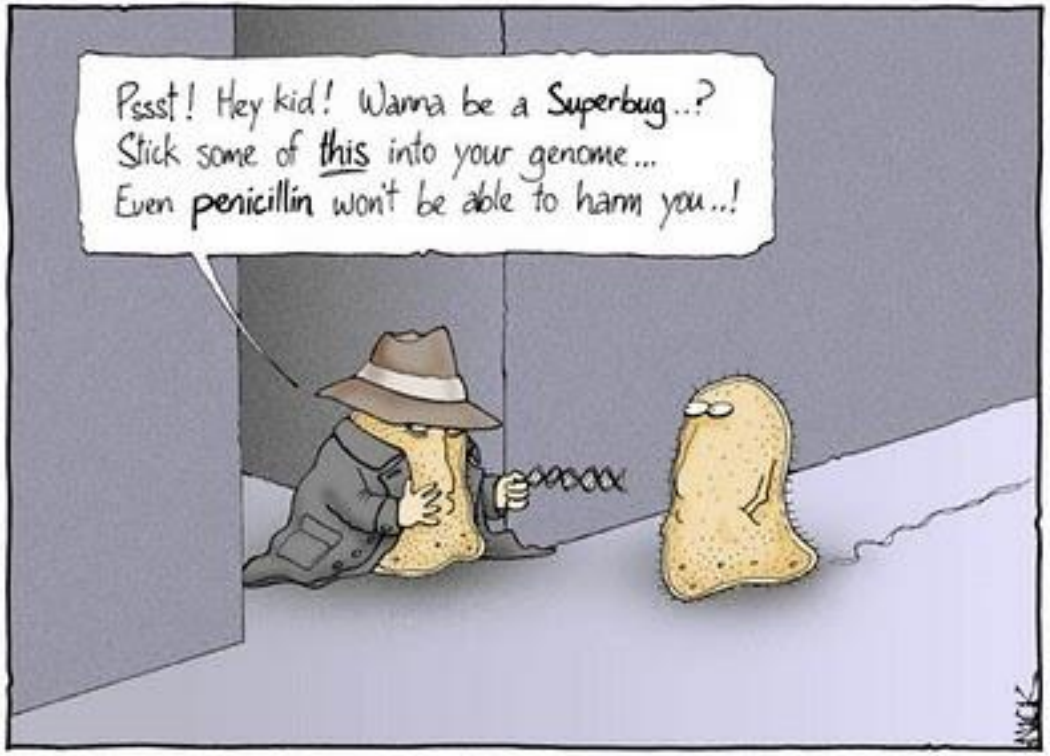
Core Testing by all regional labs

- Molecular testing to detect colonization of carbapenem-resistant Enterobacterales (CRE).
- Detection of new and emerging threats, like novel carbapenemase genes, and ability to detect changes in known threats, like methicillin resistant Staphylococcus aureus.
- Fungal susceptibility of Candida species to identify emerging resistance. Identification and colonization screening to detect and help prevent spread of Candida auris (C. auris).
- Perform expanded susceptibility testing to determine if new drugs or drug combinations will be effective to treat patients infected with especially rare resistant pathogens.
- Isolates may be used for the CDC and FDA AR Isolate Bank and WGS projects.

https://www.cdc.gov/drugresistance/ar-lab-networks/domestic.html

We have work to do!

Questions?



It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

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Resources

- CDC Antibiotic Resistance Threats in the U.S., 2019
- CDC COVID-19 U.S. Impact on Antimicrobial Resistance, Special Report 2022
- https://www.acpjournals.org/doi/10.7326/M22-3469
- https://www.cdc.gov/drugresistance/pdf/threats-report/esbl-508.pdf
- https://www.cdc.gov/hai/organisms/ESBL.html
- https://www.cdc.gov/hai/organisms/cre/index.html
- https://www.cdc.gov/drugresistance/pdf/threats-report/CRE-508.pdf
- https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf
- https://www.cdc.gov/hai/containment/PPE-Nursing-Homes.html
- https://www.cdc.gov/drugresistance/solutions-initiative/ar-lab-network.html
- https://www.cdc.gov/hai/organisms/acinetobacter.html
- https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf
- https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf
- CDC Homepage for AR Lab Network: https://www.cdc.gov/drugresistance/laboratories.html
- CDC Containment Strategy Guidelines for Multidrug-Resistant Organisms: https://www.cdc.gov/hai/containment/guidelines.html
- CDC Antibiotic Resistance Threats Report (2019): https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf
- Infection Preventionists Fact Sheet
- Laboratory Staff Fact Sheet
- Identification of *C. auris*
- Screening for *C. auris*
- https://www.cdc.gov/fungal/candida-auris/fact-sheets/c-auris-testing.html
- https://www.cdc.gov/fungal/candida-auris/c-auris-drug-resistant.html
- https://www.cdc.gov/fungal/candida-auris/index.html

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Additional Resources

- https://www.cdc.gov/hai/pdfs/mdro-guides/Health-Response-Contain-MDRO-H.pdf
- https://www.cdc.gov/hai/mdro-guides/prevention-strategy.html
- https://www.cdc.gov/drugresistance/ar-lab-networks/domestic.html
- https://www.cdc.gov/infectioncontrol/guidelines/mdro/index.html
- https://www.cdc.gov/drugresistance/biggest-threats.html
- https://www.cdc.gov/hai/outbreaks/index.html
- https://www.cdc.gov/hai/containment/PPE-Nursing-Homes.html
- https://www.cdc.gov/drugresistance/solutions-initiative/index.html

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