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Texas Department of State
Health Services

Mitigation of a Multiple Organism New Delhi metallo-beta-lactamase (NDM) Carbapenem-resistant Enterobacterales (CRE) Outbreak in North Texas

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Presentation Outline

- The threat of antimicrobial resistance
- Carbapenem-resistant Enterobacterales (CRE) & New Delhi metallo-beta-lactamase (NDM) background
- Initial case report
- Epidemiology surveillance
- Public health mitigation steps
- Whole genome sequencing of isolates

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The Threat of Antimicrobial Resistance

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Antimicrobial Resistance



- Bacteria, viruses, fungi, and parasites can change over time and become resistant to antimicrobials
- Antimicrobial-resistant organisms are harder to treat and can cause more severe illness/death

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Antimicrobial resistance and spread is caused by.....





- Using antimicrobials incorrectly
- Lack of standard treatment guidelines in other countries
- Spread in healthcare facilities
 - Poor infection control practices
 - Prolonged hospital stays and treatment courses

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Antimicrobial Resistance Lab Network Targeted Organisms




- Carbapenem-resistant Enterobacterales (CRE)
o.i.e., *E.coli*, *Klebsiella spp*, *Enterobacter spp*, *Providencia spp*, *Proteus spp*, *Morganella spp*, *Citrobacter spp*, *Serratia spp*.
- Carbapenem-resistant *Acinetobacter baumannii* (CRAB)
- Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA)
- *Candida spp*, including *Candida auris*



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Carbapenemases



- Some organisms produce enzymes called carbapenemases
- Carbapenemases inactivate antibiotics such as carbapenems and other β -lactams, which makes them ineffective to treat a patient
- Carbapenemases are often produced from genes located on transferable elements that can spread resistance easily from germ to germ and person to person

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Carbapenemase producing genes

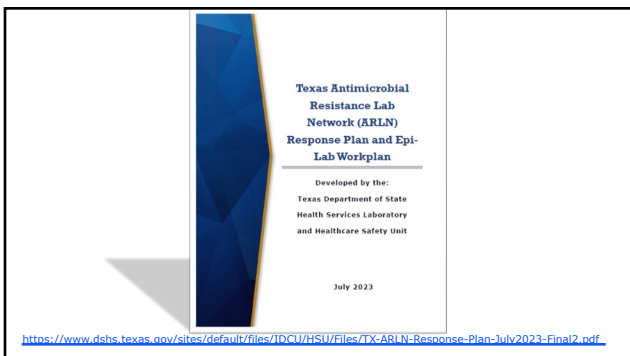


- **NDM** – New Delhi Metallo- β -lactamase
- **VIM** – Verona Integron-encoded Metallo- β -lactamase
- **IMP** – Imipenemase Metallo- β -lactamase
- **KPC** – *Klebsiella pneumoniae* carbapenemase
- **OXA** – Oxacillinase
(includes OXA-23, OXA-24/40, OXA-58, OXA-48)
- **mCIM+ /PCR negative** – positive for the presence of a carbapenemase, but specific gene unable to be identified

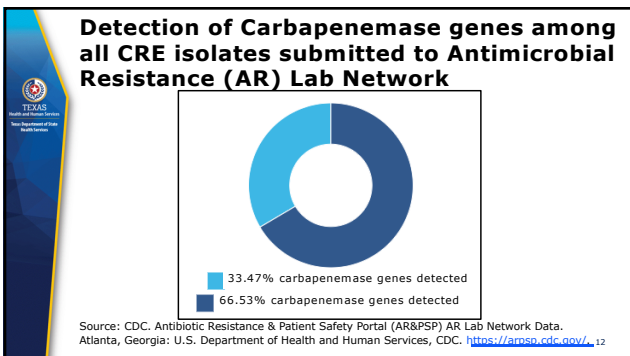
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NDM Cases in North Texas, January 2018 February 2023



A total of 117 specimens from patients in North Texas healthcare facilities were identified with NDM mechanism

Organism	Number of Specimens
Carbapenem-resistant Enterobacterales (CRE)*	

*CRE organisms included: *Citrobacter freundii*, *E. coli*, *Enterobacter cloacae*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Klebsiella variicola*, and *Providencia rettgeri*


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History of NDM Cases within Tarrant County

- No reported cluster/outbreak of NDM CRE in the last five years.
- However, 11 sporadic cases between February 2018 to October 2021 without any epi-linkages.
- Breakdown of Cases by Specimen Source:
 - Urine = 6
 - Wound = 2
 - Tissue = 1
 - Sputum = 1
- Breakdown of Cases by Facility Type:
 - 6 Acute Care Hospitals
 - 4 Outpatient Clinics
 - 1 Long-Term Acute Care Facilities




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Current NDM Outbreak

- Started in May 2022.
- 1st alert date = 06/24/2022 with 3 cases
 - Overlap in admission periods noted in one acute care facility.
- As of February 2023, there were 35 cases reported.
- Collection Date Range = 05/14/2022 – 02/10/2023




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Demographic Breakdown of Cases

- Total = 35
- Gender
 - Male = 12
 - Female = 23
- Age
 - Median Age = 70 years old
 - Youngest Case = 24 years old
 - Oldest Case = 91 years old



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Breakdown by Organism

- 7 organisms isolated:

Organism	Number of Cases	Proportion of Cases (%)
<i>Klebsiella pneumoniae</i>	15	42.86
<i>Escherichia coli</i>	9	25.71
<i>Klebsiella varicola</i>	6	17.14
<i>Klebsiella oxytoca</i>	2	5.71
<i>Enterobacter cloacae</i> *	1	2.86

* *E. cloacae*, *E. asburiae*, and *C. amalonaticus* are typically not reportable CRE organisms, however, in the case of a mechanism, these organisms become reportable.




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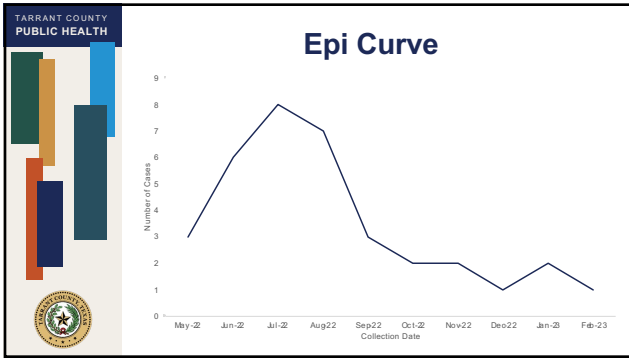
Breakdown by Specimen Source

- 9 specimen sources:

Organism	Number of Cases
Urine	22
Blood	4
Tissue	3
Tracheal Aspirate	2
Other (Aerobic, Bronchial Wash, Semen, Sputum)	4



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Breakdown of Cases by Facility Type



Facility Type	Number of Facility Type	Number of Cases	Proportion of Cases (%)
Acute Care Hospital	2	30	85.71
Long-Term Acute Care Facility	1	1	2.86
Nursing Home	1	1	2.86
Outpatient Clinic	2	2	5.71
Home Health Agency	1	1	2.86

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- Actions Taken- Retrospective Surveillance**
- Contact with the ordering facility of each case.
 - Thorough interview involving:
 - Admission history (hall/room locations, facilities transferred from)
 - Control measures implemented
 - Specialty Services (therapies, imaging, surgeries)
 - Invasive devices
 - Documentation of international travel
 - Antibiotic/antifungal therapy

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Key Findings

- Between May 2022 and August 2022, majority of the cases were identified from an acute care hospital.
- None of the cases reported had any roommates; analysis of transmission was focused on the halls/units of the facilities involved as opposed to the rooms of the cases.
- All patient histories in the medical record indicated no international travel in the previous 12 months.

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Infection Control Guidance- General Containment

- Guidance provided to all facilities with NDM CRE cases.
 - Placing close contacts on isolation and contact precautions.
 - Giving specific recommendations on disinfecting rooms.
 - Cohorting patients in halls/units, when appropriate.

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Infection Control Guidance- Key Infection Control Issues

- While working with our facilities, we noted a few key issues including:
 - Non-compliance with hand hygiene and PPE among healthcare staff.
 - Inconsistent processes used for managing bath basins for pericare.
 - Failed sink assessments.
 - Disinfectants used were not on the approved disinfectant list for the various facilities.
 - Insufficient amount of audits for EVS, radiology, pharmacy, transport, and ancillary services.

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Infection Control Guidance- Overall Recommendations

- In addition to identifying infection control issues, we also wanted to provide education and recommendations on controlling the transmission of NDM CRE cases:
 - Reviewing and re-educating staff on PPE donning/doffing, hygienic practices with all staff.
 - Intra-facility education focused on raising awareness of NDM mechanism and the need to increase surveillance practices
 - Emphasis on paying attention to pericare- coherent processes for disinfection of invasive devices.
 - Increasing frequency of EVS, hand hygiene, and PPE audits.
 - Proper usage of disinfectants.

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Prospective Surveillance and Colonization Screening

- Requested all affected facilities to send *Klebsiella* and *E. coli* isolates to the DSHS lab, regardless of mechanism.
- Continue to watch for any unusual trends in MDRO prevalence in various units/halls.
- Colonization screening.
 - Not implemented within Tarrant County due to reluctance from providers as a result of the invasive nature of screening.
 - Chose to instead do prospective surveillance.
 - Implemented at a SNF within North Texas but outside Tarrant County.

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Whole Genome Sequencing

- Whole Genome Sequencing (WGS) is a lab testing method that reveals the complete DNA makeup of an organism, enabling laboratorians and epidemiologists to better understand differences within and between cases
- For AR related investigations, epidemiologists can combine epidemiology data, clinical data plus the WGS results to test hypotheses, determine the relatedness between cases, and infer possible causes of disease transmission

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Whole Genome Sequencing

• Single nucleotide polymorphism (SNP)

- A single DNA building block called a nucleotide, which is found in DNA between the genes
- Used to compare isolates; the smaller the SNP difference between two isolates, the more similar the isolates

• A phylogenetic tree is a diagram that shows the evolutionary descent of AR organisms

- The nodes of a tree represent each isolate
- The branches that connect the nodes are proportional in length to the number of SNPs that differ between the isolates

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Whole Genome Sequencing – *E. coli*

The phylogenetic tree for *E. coli* shows a root on the left. A branch leads to "Isolate for comparison". Another branch leads to a node that splits into "Isolate 1" and "Isolate 2". A final branch leads to "Isolate 3". The x-axis at the bottom is labeled with values 0.000, 0.002, 0.004, 0.006, 0.008, and 0.010.

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Whole Genome Sequencing – *K. variicola*

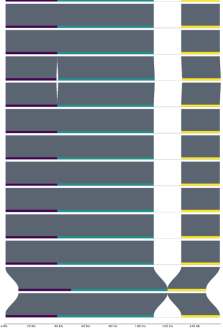
The phylogenetic tree for *K. variicola* shows a root on the left. A branch leads to "Isolate 11". Another branch leads to a node that splits into "Isolate for comparison" and "Isolate 10". A final branch leads to a node that splits into "Isolate 9" and "Isolate 8". A subsequent branch leads to a node that splits into "Isolate 7" and "Isolate 6". A final branch leads to a node that splits into "Isolate 5" and "Isolate 4". A subsequent branch leads to a node that splits into "Isolate 3" and "Isolate 2". A final branch leads to "Isolate 1". The x-axis at the bottom is labeled with values 0.000, 0.002, 0.004, 0.006, 0.008, and 0.010.

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Whole Genome Sequencing Results

- 13 total isolates
- Have same plasmid containing NDM-4




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Questions?

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