

# **Antimicrobial Resistance:** Healthcare Facilities and Health Departments Working Together

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# Antibiotic Resistance

- Antibiotics - critical public health tool since the discovery of penicillin
- The emergence of drug resistance in bacteria - reversing advancements of the past 80 years
  - Drug choices are increasingly limited, expensive, and nonexistent



# Antibiotic Resistance Threats, 2013



Estimated number of illnesses and deaths caused by antibiotic-resistance\*



**2,049,442** illnesses



**23,000** deaths

<https://www.cdc.gov/drugresistance/threat-report-2013/>

# Factors Leading to Antibiotic Resistance

- The **use of antibiotics** is the single most important factor leading to antibiotic resistance around the world
- Antibiotics are among the **most commonly prescribed drugs** used in human medicine
  - Up to 50% of all the antibiotics prescribed for people are not needed or are not optimally effective as prescribed (wrong drug, wrong dose, wrong duration)
- Pew and CDC report that **30% of antibiotics prescribed** in outpatient settings in United States **are unnecessary**

# The Cost of Antibiotic Resistance

- Antibiotic-resistant infections:
  - Require prolonged and/or costlier treatments
  - Extend hospital stays
  - Necessitate additional doctor visits and healthcare use
  - Result in greater disability and death compared with infections that are easily treatable with antibiotics
- Total economic cost of antibiotic resistance to the U.S. economy:
  - Estimates vary but have ranged as high as \$20 billion in excess direct healthcare costs
  - Additional costs to society for lost productivity as high as \$35 billion a year (2008 dollars)



## How Antibiotic Resistance Happens

1.

Lots of germs.  
A few are drug resistant.



2.

Antibiotics kill  
bacteria causing the illness,  
as well as good bacteria  
protecting the body from  
infection.



3.

The drug-resistant  
bacteria are now allowed to  
grow and take over.



4.

Some bacteria give  
their drug-resistance to  
other bacteria, causing  
more problems.



# Antibiotic Resistance Threats

- CDC conducted an assessment and categorized the threat level of each bacteria as urgent, serious, or concerning
- Threats were assessed using seven factors:
  - Clinical impact
  - Economic impact
  - Incidence
  - 10-year projection of incidence
  - Transmissibility
  - Availability of effective antibiotics
  - Barriers to prevention
- Focused on domestic impact

# Concerning Pathogens

HAZARD LEVEL

**CONCERNING**



These are bacteria for which the threat of antibiotic resistance is low, and/or there are multiple therapeutic options for resistant infections. These bacterial pathogens cause severe illness. Threats in this category require monitoring and in some cases rapid incident or outbreak response.

- VRSA
- Erythromycin-resistant *Streptococcus* Group A
- Clindamycin-resistant *Streptococcus* Group B



# Serious Pathogens

HAZARD LEVEL

**SERIOUS**



These are significant antibiotic-resistant threats. For varying reasons (e.g., low or declining domestic incidence or reasonable availability of therapeutic agents), they are not considered urgent, but these threats will worsen and may become urgent without ongoing public health monitoring and prevention activities.

- MDR *Acinetobacter*
- ESBLs
- VRE
- MDR *Pseudomonas*
- MRSA
- MDR and XDR TB

# Urgent Pathogens

HAZARD LEVEL

**URGENT**



These are high-consequence antibiotic-resistant threats because of significant risks identified across several criteria. These threats may not be currently widespread but have the potential to become so and require urgent public health attention to identify infections and to limit transmission.

- *Clostridium difficile*
- CRE
- Drug-resistant *Neisseria gonorrhoeae* (cephalosporin resistance)

# Running Out of Drugs!

- Gram-negative pathogens are particularly worrisome - becoming resistant to nearly all drugs that would be considered for treatment.
  - This is true as well, but not to the same extent, for some of the gram-positive infections (e.g., *Staphylococcus* and *Enterococcus*).
- The most serious gram-negative infections are healthcare-associated and the most common pathogens
  - Enterobacteriaceae, *Pseudomonas aeruginosa*, and *Acinetobacter*
- Treating infections of either pan-resistant or nearly pan-resistant gram-negative microorganisms
  - Increasingly common challenge in many hospitals

**What are we doing in Michigan?**

# MDHHS SHARP Unit, Bureau of Labs, and Michigan Antibiotic Resistance Reduction Coalition (MARR)

- Prevent healthcare associated infections (e.g., CDI, CRE, MRSA)
- Enhance HAI/AR detection and response infrastructure, establish AR expertise in HAI/AR programs
- Increase state laboratory capacity for CRE testing
- Establish regional laboratories as a national resource for AR testing and characterization
- Promote appropriate antibiotic use
  - Community Outreach

# Antimicrobial Stewardship Activities in MI

- **Antimicrobial Stewardship Subcommittee – Allison Murad**
  - MDHHS Antibiotic Use and Resistance Module in NHSN
    - Promoting usage and facility implementation and validation
  - MDHHS Communities of Care Initiative
    - Enrolling acute care, long-term acute care and long-term care working together on AMS

# **Antimicrobial Stewardship Activities in MI**

- **Antimicrobial Stewardship Subcommittee – Allison Murad**
  - Michigan Pharmacists Association (MPA)/Michigan Society of Health-System Pharmacists (MSHP) Antibiotic Stewardship Task Force
    - Looking to survey ambulatory clinics regarding AMS projects
  - Pew/CDC Inpatient Antibiotic Prescribing project
    - Aims to reach a national goal for reducing inappropriate use

# **Antimicrobial Stewardship Activities in MI**

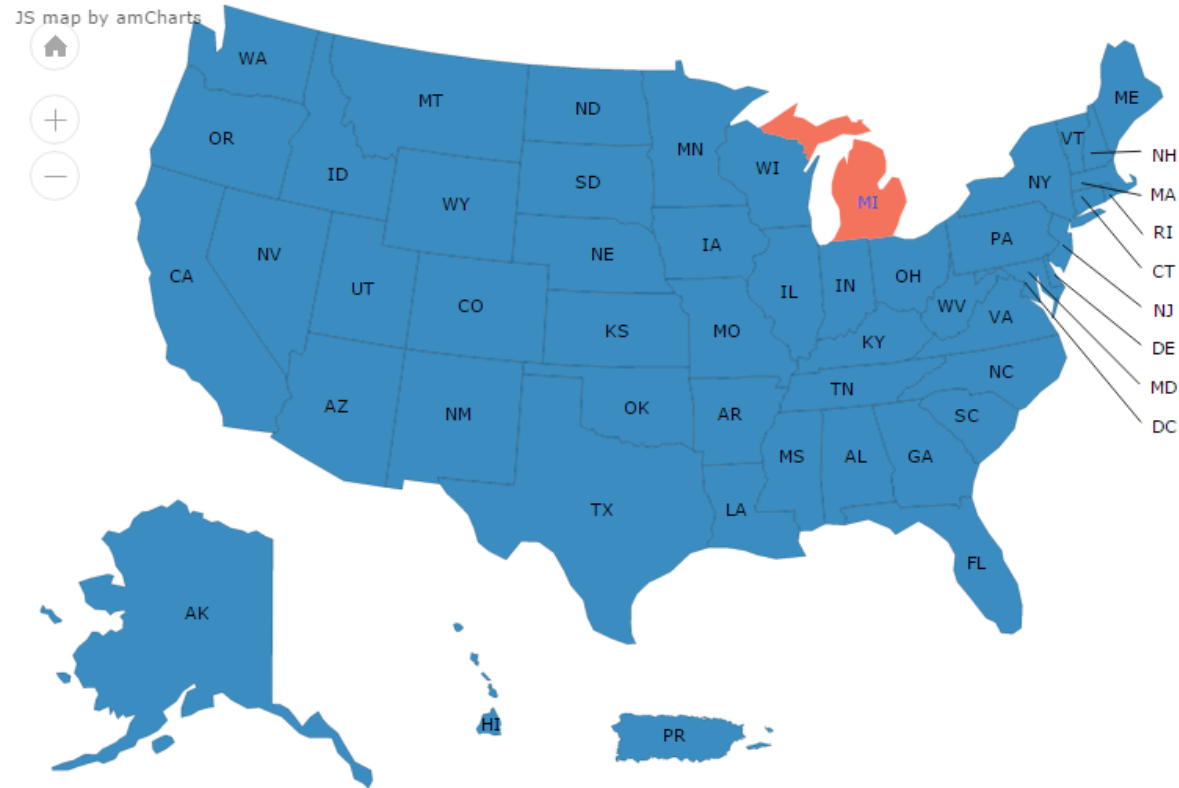
- **Antimicrobial Stewardship Subcommittee – Allison Murad**
  - Ferris State
    - Community Stewardship Initiative to determine/quantify antibiotics prescribed and appropriateness of prescriptions in ambulatory care sites
  - MPRO
    - Nursing home initiative
  - Michigan Antibiotic Resistance Reduction (MARR) Coalition
    - Working with dental associations to reduce antibiotic prescribing
  - Michigan Health and Hospital Association (MHA)
    - Working on Hospital Improvement and Innovation Network (HIIN)



# Antibiotic Resistance Investments

## Key Investments to Combat Antibiotic Resistance

\*Hover over and select state for more details



*This map represents CDC's largest funding categories for antibiotic resistance. It shows domestic, extramural funding that supports AR activities from multiple funding lines.*

<https://www.cdc.gov/arinvestments>

# AR Solutions *In Action*

CDC's Investments to Combat Antibiotic Resistance Threats Nationwide

FISCAL YEAR

2016

## MICHIGAN

# \$3,252,781

Funding for AR Activities  
Fiscal Year 2016



\$386,127

### HAI/AR DETECT AND RESPOND PROGRAMS

Quickly detect and then contain the spread of resistant infections, protecting patients from new resistance threats.



\$853,354

### HAI/AR PREVENTION PROGRAMS

Work with partners to prevent infection and contain spread of germs between patients and healthcare facilities, and increase antibiotic stewardship education, to protect patients.

## FUNDING TO STATE HEALTH DEPARTMENTS



\$452,159

### FOOD SAFETY

Projects protect communities by rapidly identifying drug-resistant foodborne bacteria to stop and solve outbreaks and improve prevention.

## FUNDING TO UNIVERSITIES & HEALTHCARE PARTNERS

### University of Michigan

#### Microbiome Assessment & Intervention



Determine how orthopedic surgery patients are impacted by antibiotics, \$304,683

Develop a diagnostic test to detect ESBL colonization and domination, \$336,339

#### Innovative Prevention & Tracking



Apply genome sequencing to understand spread of resistance within and between hospitals, \$399,788

Determine how improving hand hygiene could prevent patients from being colonized or infected with drug-resistant bacteria, \$520,271

**Surveillance of  
CRE and Novel Resistance Activity  
in Michigan**

# Carbapenem Resistant *Enterobacteriaceae*

- *Enterobacteriaceae* – enteric organisms, gram negative bacilli
- Carbapenems – class of broad-spectrum,  $\beta$ -lactam antibiotics
  - Agents of last resort – one of the few remaining effective therapies
- Pathogens responsible for urinary tract infections, bacteremia, pneumonia, wound infections

# Mechanisms of Carbapenem Resistance

1. Carbapenemases
2. Acquired resistance
3. Naturally imipenem-resistant *Enterobacteriaceae*

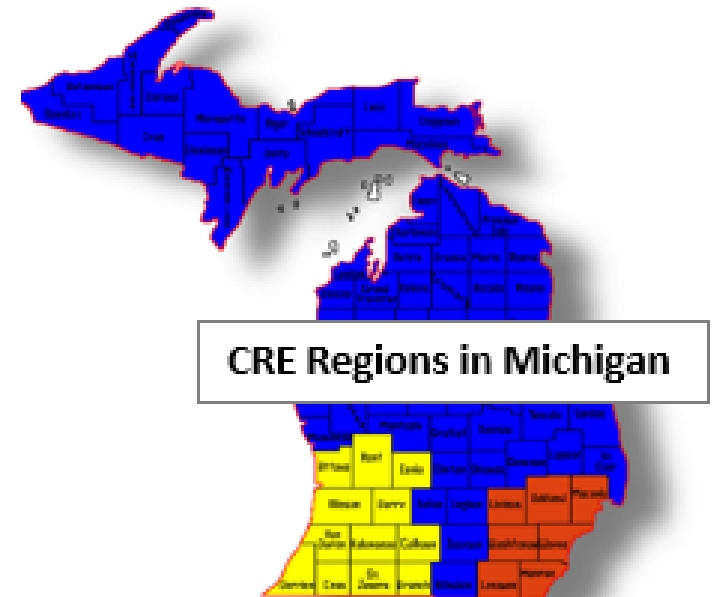
***Not all CRE are carbapenemase producers...***

# CRE and Novel Resistance Activity

- Carbapenemases:
  - *Klebsiella pneumoniae* carbapenemase (KPC)
  - New Delhi metallo- $\beta$ -lactamase (NDM)
  - Verona integron encoded metallo- $\beta$ -lactamase (VIM)
  - Imipenemase metallo- $\beta$ -lactamase (IMP)
  - Oxacillinase-48 (OXA-48)
- Other resistance elements:
  - Mobile colistin resistance (MCR)

# CRE Surveillance and Prevention Initiative

- Voluntarily reporting cases of *Klebsiella pneumoniae* and *Escherichia coli*
- Began September 2012
- 40 participating facilities over 3 phases



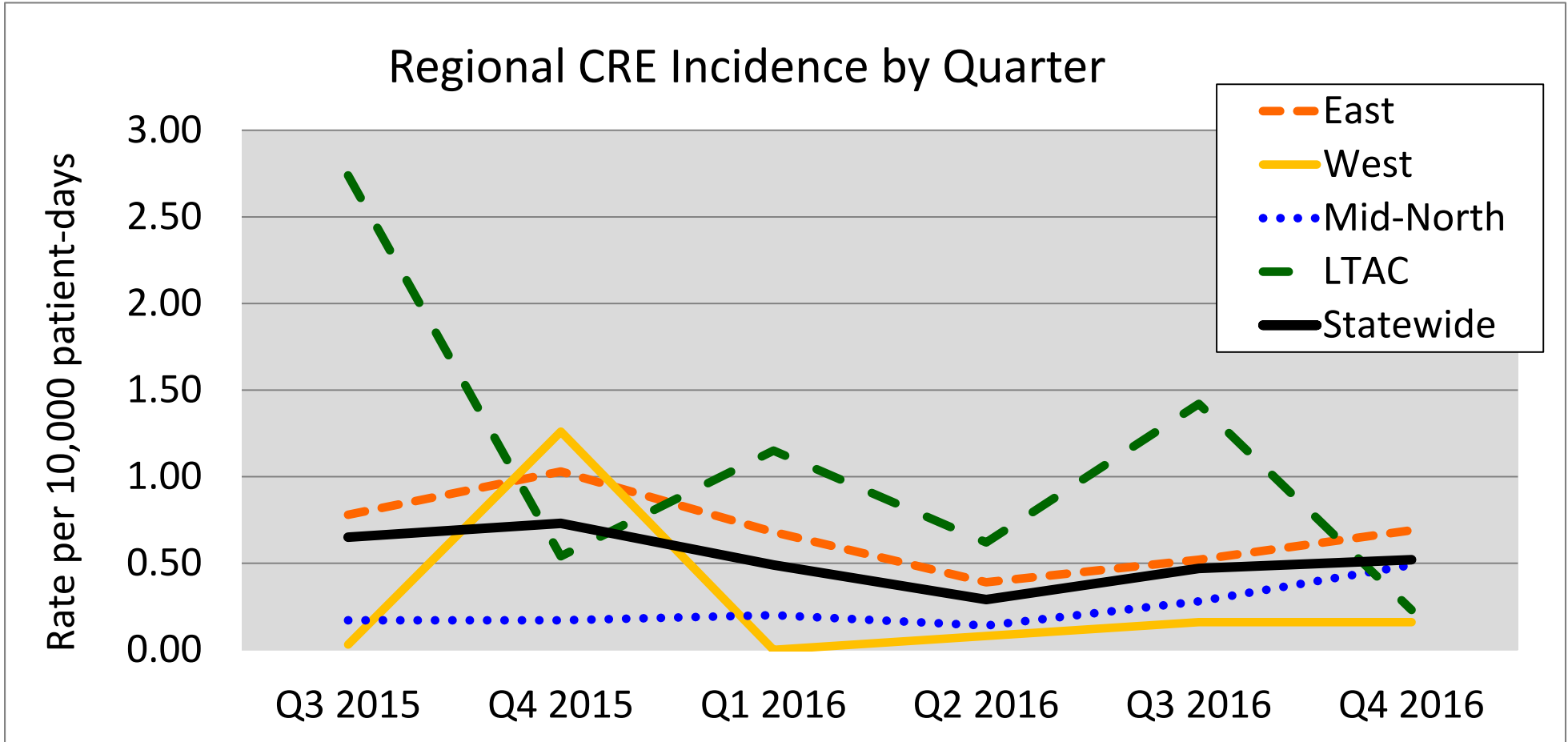


# CRE Surveillance and Prevention



Region	Number of Facilities	Q4 Total Events	Q4 Total Patient-days	Q4 Overall Rate per 10,000 Patient-days (Q3 2016 Overall Rate)
East	15	25	360,461	0.69 (0.52)
West	6	2	128,019	0.16 (0.16)
Mid-North	7	7	143,056	0.49 (0.28)
LTACs	12	1	43,450	0.23 (1.42)
Statewide	40	35	674,986	0.52 (0.47)

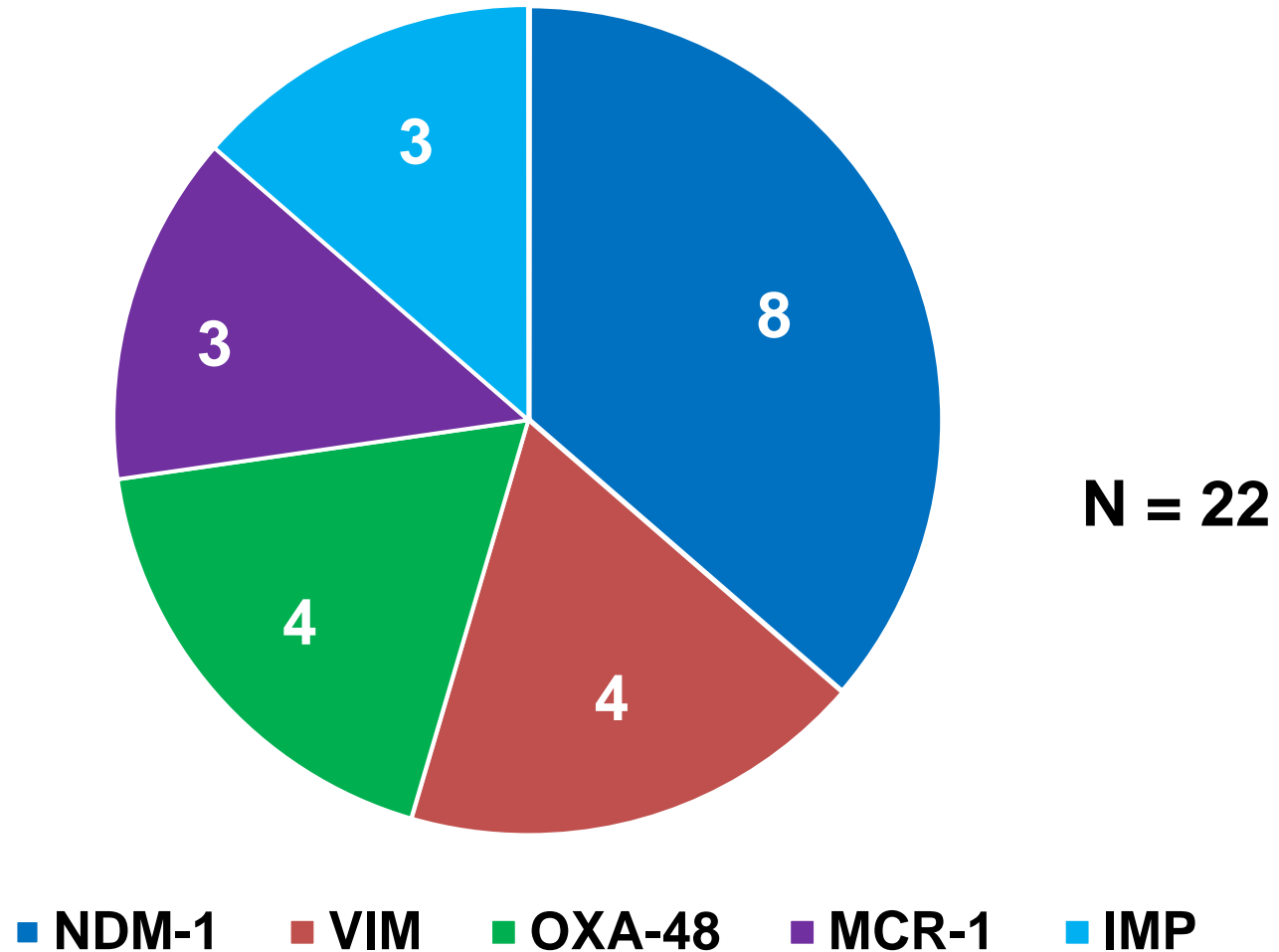
# CRE Surveillance and Prevention



# CRE / Novel Resistance Activity

- Michigan mostly detects KPC...
  - With new laboratory testing capabilities, we are detecting more novel carbapenemases and colistin resistance

# Novel Resistance Mechanisms 2014 to present



# NDM-1

- 175 reports in U.S. (uncommon)
- 8 reported in Michigan
  - 5 report travel (3 India, 1 Romania, and 1 Philippines)
- 1<sup>st</sup> worldwide report in Sweden 2008 (patient from India)
- NDM-1 not in a single species but in many unrelated species
  - Spread in the environment
- Frequent acquisition by *K. pneumoniae*, a typical nosocomial pathogen
  - Also by *E. coli* (community-acquired)
- Size of the reservoir—the Indian subcontinent has >1.4 billion people

# VIM

- 27 reported in the U.S. (rare)
- 4 cases reported in Michigan
  - 3 *Pseudomonas aeruginosa*
  - 1 *Enterobacter cloacae*
  - No travel reported - multiple healthcare exposures and comorbidities
- 1<sup>st</sup> reported in Greece 2002/2003 and then Korea and Taiwan

# IMP

- 14 reports in the U.S. (rare)
- 3 cases reported in Michigan
  - 2 *Enterobacter cloacae* species
  - 1 *Morganella morganii*
  - No reported travel – multiple healthcare exposures and comorbidities
- First detected in Japan 1991
- First report in the US was 2011
  - California pediatric ICU

# OXA-48

- 73 reports in the U.S. (uncommon)
- 4 cases reported in Michigan
  - 3 *Klebsiella pneumoniae*
  - 1 *E. coli*
    - 2 reported travel
- First detected in Turkey 2003
- First report in the US was 2012



# MCR-1

- 12 reports in U.S. (10 *E. coli* and 2 *Salmonella*)
- 3 cases reported in Michigan (all 3 *E. coli*)
- Not necessarily pan-resistant
  - Only 1 CP-CRE (NDM-1)
- 9 of 12 are travel-associated
  - 5 Asia, 3 Caribbean, 1 Europe
- Patients can be positive up to 4 months after initial culture
  - Concern for persistent colonization in urine
- Can potentially add colistin-resistance to isolates with already high levels of resistance
  - Further limiting or eliminating treatment options for patients

# How Do We Know This?

- Clinical lab/healthcare facility submits culture to MDHHS BOL
- BOL confirms organism ID, antimicrobial susceptibilities, phenotypic test (Neo-Rapid CARB) and PCR
  - PCR: KPC, NDM-1, VIM and OXA-48-like
  - Send isolates that are phenotypically positive / PCR negative or colistin-resistant to CDC
  - Notifies SHARP Unit
- CDC tests isolate
  - Send report if negative
  - Notifies SHARP Unit and BOL if positive

**Healthcare Facilities  
and  
Local Health Departments**



**Working together on Antibiotic Resistance**

# New CDC Guidance

- Interim Guidance for Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (MDROs)
- <https://www.cdc.gov/hai/outbreaks/mdro/index.html>

# New CDC Guidance

- Goals of prompt response and containment:
  - Identify if transmission/dissemination is occurring
  - Identify the affected patients
  - Ensure appropriate control measures are promptly initiated/implemented to contain potential spread
  - Characterizing the organism or mechanism in order to guide further response actions, patient management, and future responses

# Working Together

- Healthcare facilities
  - Notified by SHARP Unit
  - Verify patient info
  - CRE data collection form
  - Check contact precautions
  - Assess screening recommendations
  - Coordinate additional testing
    - Screen or culture
  - Ensure adherence to infection control measures
- Local Health Departments
  - Notified by SHARP Unit
  - Contact the patient
  - Extended questionnaire
    - Food and travel history
  - Coordinate additional testing
    - Screen or culture
    - May include sample collection

# Example #1

- CDC notified SHARP on 2/3/17
  - Confirmed MCR-1 E. coli isolate from 70 y/o F – urine collected 12/8/16
  - SHARP notified the ACF
    - Seen at another ACF
    - *Salmonella* in November 2016
    - Cirrhosis, hepatic encephalopathy, liver transplant 11/23/16
    - Notes in her chart indicated travel to China 2 weeks in October
    - Patient was no longer at the ACF
  - Called Local Health Department for assistance
    - Extended questionnaire to interview patient
    - Possible screening cultures from index patient and close contacts/travel companions

# Example #1

- Healthcare facility
  - Track the patient through facility
    - Private rooms, shared equipment, procedures
  - Looked into future appointments to obtain screen
    - Outpatient setting
    - Index-patient only
    - Also ended up getting contact's screen
- Local Health Department
  - Prior relationship due to confirmed Salmonella
  - Interviewed patient
  - Obtained detailed food and travel exposure
  - Focus on the patient's husband for screen
    - Received swabs and were ready to collect!



## Example #2

- CDC notified SHARP on 4/5/17
  - Confirmed MCR-1 *E. coli* isolate from 22 y/o F – urine collected 3/8/17
  - SHARP notified the ACF
    - No significant medical history
    - Had an IUD placed 2/6/17 and diagnosed with UTI on 2/7/17 – treated with Macrobid
    - Return visit on 3/6/17 and called 3/8/17 with recurrence of UTI sx
    - Both travel screening questions were negative
  - Called Local Health Department for assistance
    - Notify them of patient in their jurisdiction
    - Extended questionnaire to interview the patient
    - Possible screening cultures from index patient and close contacts/travel companions

## Example #2

- Healthcare facility
  - Complete CRE data collection form
    - Confirm travel negative
  - Track the patient through facility
    - Private rooms, shared equipment, procedures
  - Looked into future appointments to obtain screen
    - None scheduled
- Local Health Department
  - Discussed investigation with LHD
  - MDHHS interviewed patient
  - Obtained detailed food and travel exposure
    - Travel to Mexico
    - Multiple food and water exposures

## Example #2

- Healthcare facility
  - ID Physician ordered culture for index patient
- Local Health Department
  - Discussed investigation with LHD
  - MDHHS interviewed patient
  - Obtained detailed food and travel exposure
    - Travel to Mexico
    - Multiple food and water exposures
    - Multiple travel companions!
      - Focus on close contact
- Campus Health Services
  - MDHHS arranged swabs to be sent
  - MDHHS coordinated with index patient to have contact go to clinic once swabs arrived
  - Training to clinic to complete/send BOL forms

# Summary Points

- Antibiotic resistance is threatening public health
- Healthcare facilities and health departments (state and local) will all play a critical role
- Not much is known on many of these novel resistance mechanisms
  - CDC is enthusiastic about collecting information
- Some investigations will be logistically-challenging!
  - Coordination will be difficult and complex
- Rapidly evolving approach
  - Each investigation has been different
  - Hard to create standardized protocol... working on it!

# Thank you

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