

# An Update on Multidrug Resistant Gram Negative Bacteria

Jesse T. Jacob, MD

Georgia EIP Conference

March 11, 2016

No Disclosures

# 2011-2015 Case Definition

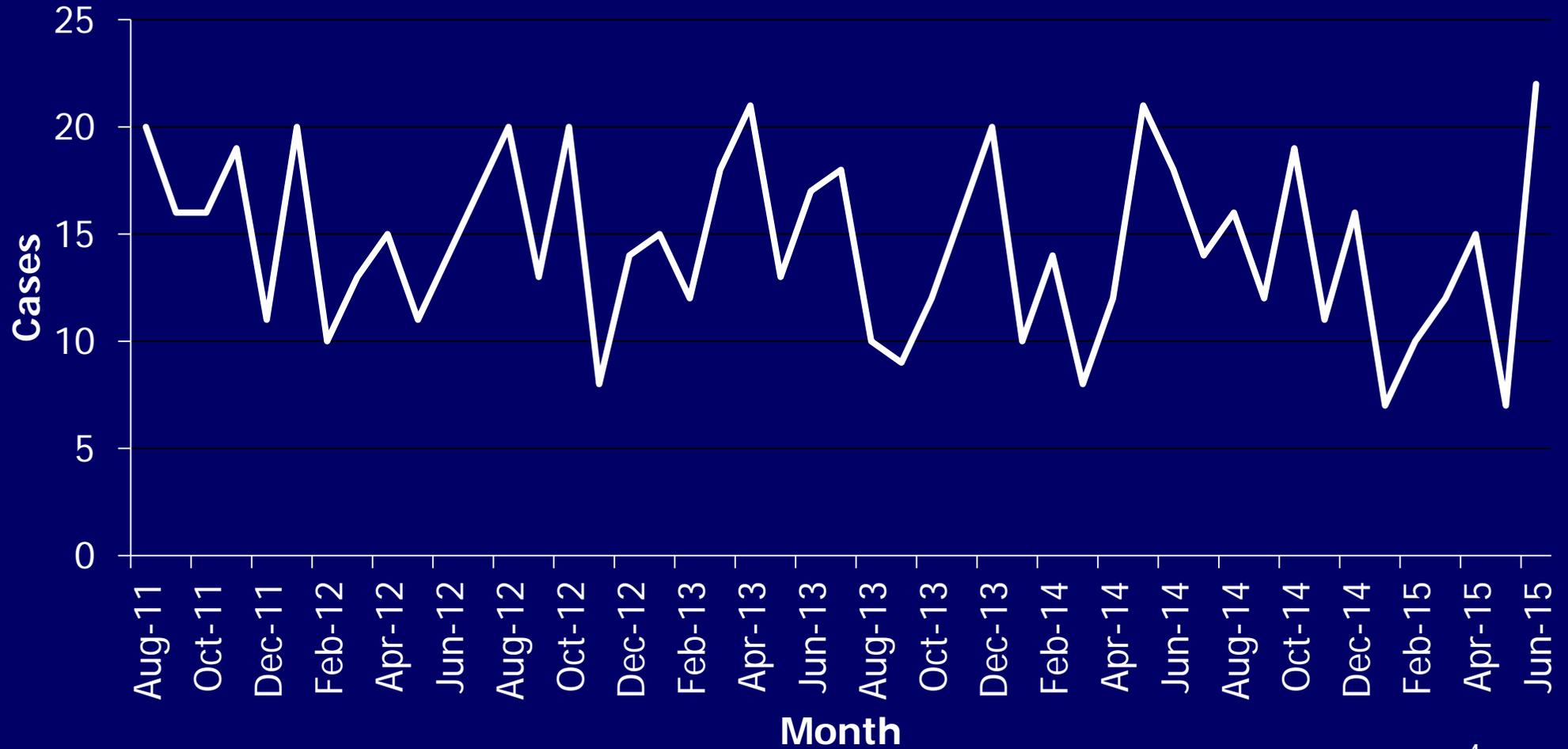
| Category  | Organism   | Carbapenem susceptibility phenotype   |
|---|--|---|
| <b>Carbapenem-nonsusceptible Enterobacteriaceae</b>             | <i>Escherichia coli</i><br><i>Klebsiella pneumoniae</i><br><i>Klebsiella oxytoca</i><br><i>Enterobacter cloacae</i><br><i>Enterobacter aerogenes</i> | <b>Intermediate or resistant to:</b><br>Imipenem (MIC >1),<br>Meropenem (MIC >1),<br>or Doripenem (MIC >1)<br><br><b>AND resistant to:</b><br>Ceftazidime (MIC >8),<br>Ceftriaxone (MIC >2),<br>and Cefotaxime (MIC >2) |
| <b>Carbapenem-nonsusceptible <i>Acinetobacter baumannii</i></b> | <i>Acinetobacter baumannii</i><br><i>Acinetobacter baumannii</i> complex<br><i>Acinetobacter calcoaceticus-baumannii</i> complex                     | <b>Intermediate or resistant to:</b><br>Imipenem (MIC >4),<br>Meropenem (MIC >4),<br>or Doripenem (MIC >1)  |

**Specimens: urine and normally sterile sites**

**Patients: HD3 resident**

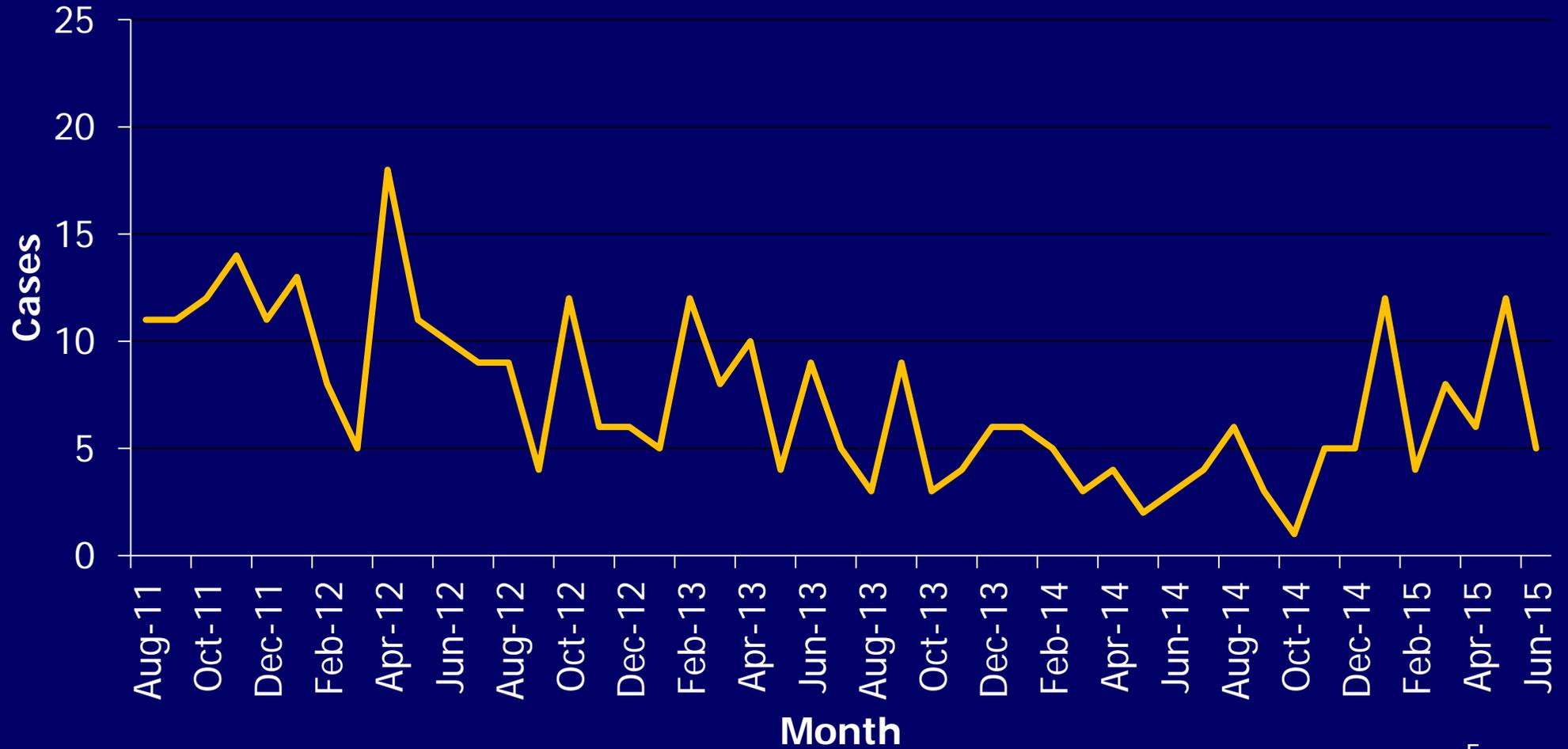
# CRE

## Atlanta, Aug 2011– Jun 2015



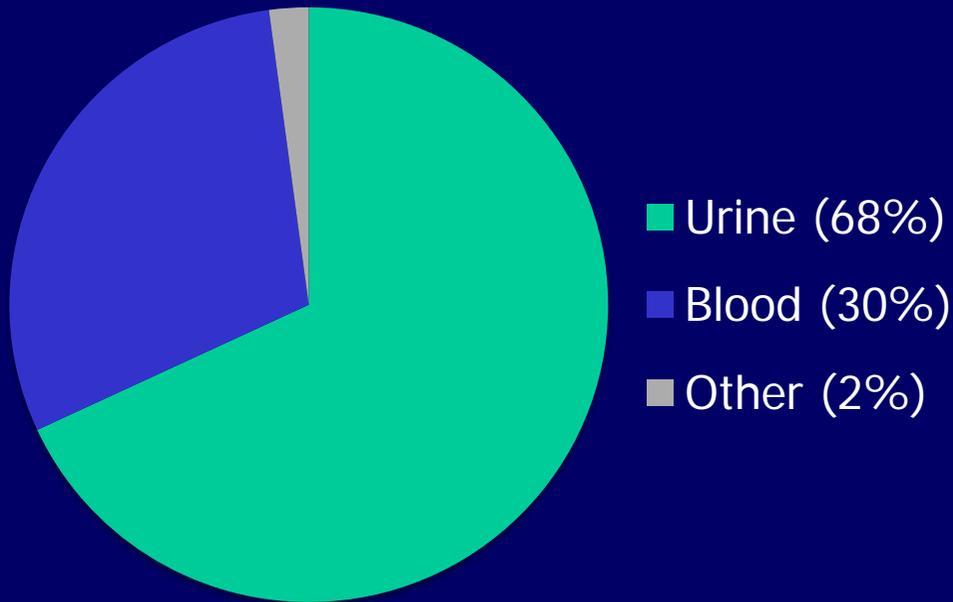
# CRAB

## Atlanta, Aug 2011 – Jun 2015

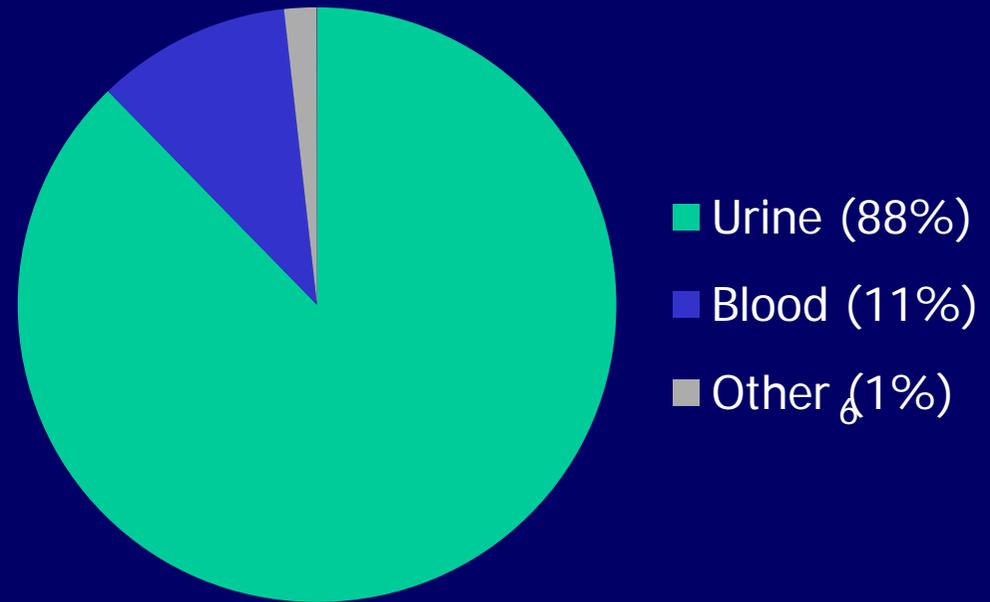


# Source and Organism, Georgia, 2014

**Acinetobacter, n=47**

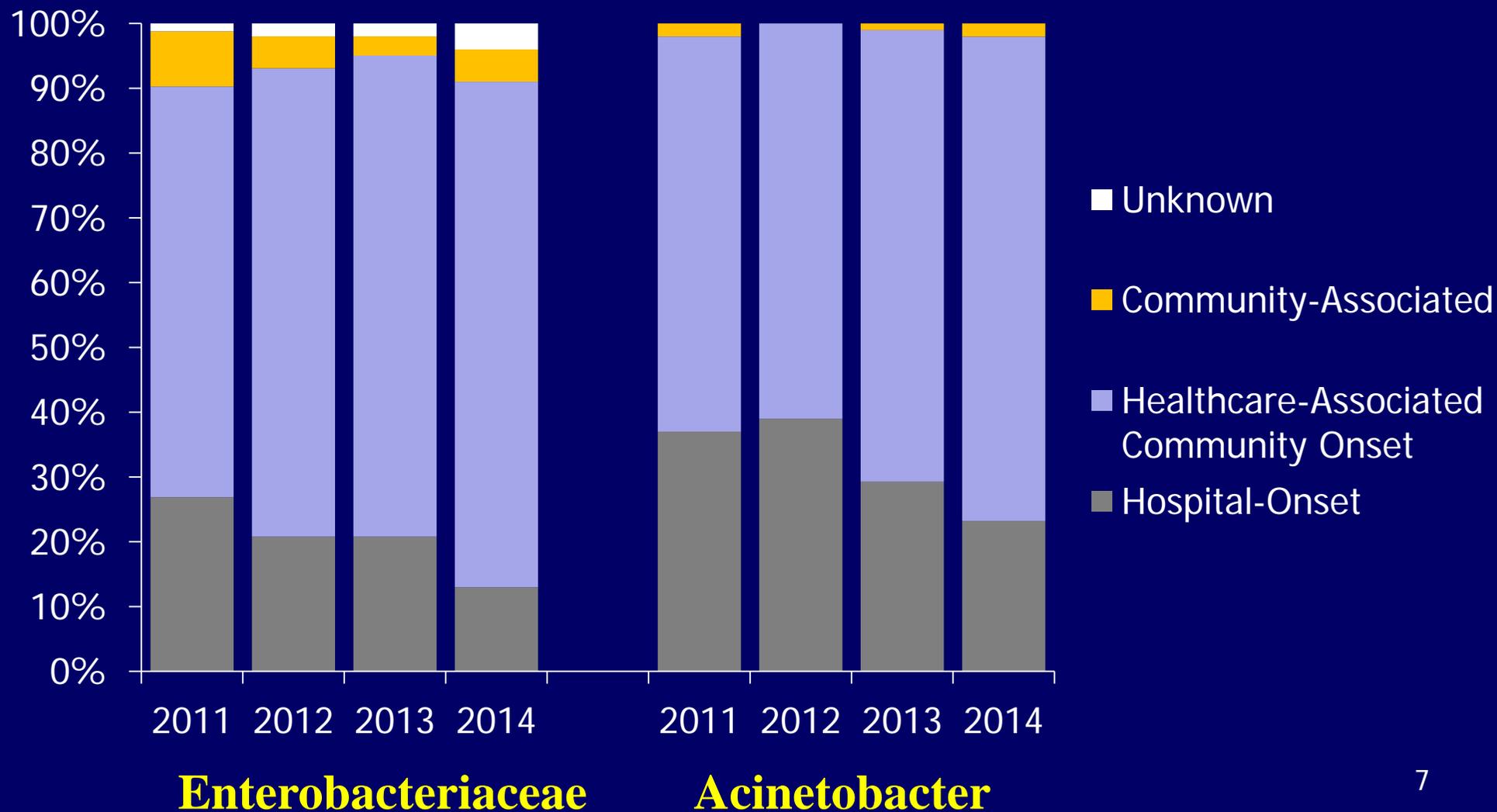


**Enterobacteriaceae, n=171**



**4 other sources: 2 pleural, 1 synovial fluid, 1 bone**

# Time of Onset of CRE, Georgia Aug 2011 – Dec 2014



# CRE in 7 EIPs, 2012-2013

## Organism Distribution

| Emerging Infections Program Site | Total No. | CRE Organism or Isolate, No. (%) |                                     |                         |                              |                           |
|----------------------------------|-----------|----------------------------------|-------------------------------------|-------------------------|------------------------------|---------------------------|
|                                  |           | <i>Enterobacter aerogenes</i>    | <i>Enterobacter cloacae</i> Complex | <i>Escherichia coli</i> | <i>Klebsiella pneumoniae</i> | <i>Klebsiella oxytoca</i> |
| Colorado <sup>b</sup>            | 27        | 7 (25.9)                         | 10 (37.0)                           | 3 (11.1)                | 7 (25.9)                     | 0                         |
| Georgia                          | 356       | 22 (6.2)                         | 38 (10.7)                           | 56 (15.7)               | 235 (66.0)                   | 5 (1.4)                   |
| Maryland <sup>b</sup>            | 92        | 8 (8.7)                          | 6 (6.5)                             | 9 (9.8)                 | 69 (75.0)                    | 0                         |
| Minnesota                        | 71        | 29 (40.8)                        | 16 (22.5)                           | 10 (14.1)               | 16 (22.5)                    | 0                         |
| New Mexico <sup>b</sup>          | 6         | 2 (33.3)                         | 0                                   | 3 (50.0)                | 1 (16.7)                     | 0                         |
| New York <sup>b</sup>            | 27        | 3 (11.1)                         | 2 (7.4)                             | 5 (18.5)                | 17 (63.0)                    | 0                         |
| Oregon                           | 20        | 4 (20.0)                         | 7 (35.0)                            | 3 (15.0)                | 6 (30.0)                     | 0                         |
| Total                            | 599       | 75 (12.5)                        | 79 (13.2)                           | 89 (14.9)               | 351 (58.6)                   | 5 (0.8)                   |

# CRE in 7 EIPs, 2012-2013

## Carbapenemase Production

| Emerging Infections Program Site | Total No. | Isolates Submitted for Carbapenemase Testing | No. of Carbapenemase-Producing Isolates/Total No. of Isolates Submitted for Testing (%) <sup>a</sup> |
|----------------------------------|-----------|--|--|
| Colorado <sup>b</sup>            | 27        | 16 (59.3)                                    | 5/16 (31.3)  |
| Georgia                          | 356       | 75 (21.1)                                    | 48/75 (64.0)   |
| Maryland <sup>b</sup>            | 92        | 17 (18.5)                                    | 13/17 (76.5)   |
| Minnesota                        | 71        | 58 (81.7)                                    | 17/58 (29.3)   |
| New Mexico <sup>b</sup>          | 6         | <sup>c</sup>                                 | <sup>c</sup>   |
| New York <sup>b</sup>            | 27        | 9 (33.3)                                     | 5/9 (55.6)   |
| Oregon                           | 20        | 13 (65.0)                                    | 2/13 (15.4)  |
| Total                            | 599       | 188 (31.4)                                   | 90/188 (47.9)  |

# CRE in 7 EIPs, 2012-2013

## Incidence Rates

| Emerging Infections Program Site | Incident CRE Cases <sup>a</sup> |      |  |      |
|----------------------------------|---------------------------------|------|--|------|
|                                  | No. of Cases                    |      | Crude Annual Incidence Rate/100 000 Population |      |
|                                  | 2012 <sup>b</sup>               | 2013 | 2012 <sup>b</sup>                              | 2013 |
| Colorado                         |                                 | 27   |  | 1.05 |
| Georgia                          | 175                             | 181  | 4.58   | 4.68 |
| Maryland                         |                                 | 92   |  | 4.80 |
| Minnesota                        | 31                              | 40   | 1.82   | 2.32 |
| New Mexico                       |                                 | 6    |  | 0.89 |
| New York                         |                                 | 27   |  | 3.60 |
| Oregon                           | 6                               | 14   | 0.35   | 0.82 |
| Total                            | 212                             | 387  | 2.94   | 2.93 |

| <b>Collection Location</b>                 |                |
|--|----------------|
| Short-stay acute care hospital             | 198/584 (33.9) |
| Outside acute care hospital                | 386/584 (66.1) |
| Outpatient setting or emergency department | 253/386 (65.5) |
| Long-term care facility                    | 104/386 (26.9) |
| Long-term acute care facility              | 29/386 (7.5)   |
| <b>Culture Source</b>                      |                |
| Urine                                      | 520/599 (86.8) |
| Blood <sup>a</sup>                         | 68/599 (11.4)  |
| Peritoneal fluid                           | 8/599 (1.3)    |
| Pleural fluid                              | 3/599 (0.5)    |
| Other normally sterile sites               | 7/599 (1.2)    |
| <b>Infection Types</b>                     |                |
| Lower urinary tract infection              | 392/559 (70.0) |
| Bacteremia                                 | 68/559 (12.2)  |
| Septic shock                               | 17/559 (3.0)   |
| Pneumonia                                  | 16/559 (2.9)   |
| Other infection types <sup>b</sup>         | 47/559 (8.4)   |

## Health Care Exposures During Prior Year

|   |                |
|---|----------------|
| Acute care hospitalization                                | 399/531 (75.1) |
| Resident of a long-term care facility                     | 259/531 (48.8) |
| Admission to a long-term acute care hospital <sup>c</sup> | 42/318 (13.2)  |
| Inpatient or outpatient surgery                           | 194/531 (36.5) |
| Current maintenance dialysis                              | 60/531 (11.3)  |
| Indwelling device (2 calendar days prior to culture)      | 382/525 (72.8) |
| Urinary catheter  | 285/382 (74.6) |
| Central venous catheter                                   | 163/382 (42.7) |
| Gastrostomy or jejunostomy tube                           | 151/382 (39.2) |
| Trachoestomy  | 120/382 (31.4) |
| Other device  | 81/382 (21.2)  |

# 2011-2015 Case Definition

| Category  | Organism   | Carbapenem susceptibility phenotype   |
|---|--|---|
| <b>Carbapenem-nonsusceptible Enterobacteriaceae</b> | <i>Escherichia coli</i><br><i>Klebsiella pneumoniae</i><br><i>Klebsiella oxytoca</i><br><i>Enterobacter cloacae</i><br><i>Enterobacter aerogenes</i> | <b>Intermediate or resistant to:</b><br>Imipenem (MIC >1),<br>Meropenem (MIC >1),<br>or Doripenem (MIC >1)<br><br><b>AND resistant to:</b><br>Ceftazidime (MIC >8),<br>Ceftriaxone (MIC >2),<br>and Cefotaxime (MIC >2) |

**Specimens: urine and normally sterile sites**

**Patients: HD3 resident**

# 2016 Case Definition

| Category  | Organism   | Carbapenem susceptibility phenotype   |
|---|--|---|
| <b>Carbapenem-nonsusceptible Enterobacteriaceae</b> | <i>Escherichia coli</i><br><i>Klebsiella pneumoniae</i><br><i>Klebsiella oxytoca</i><br><i>Enterobacter cloacae</i><br><i>Enterobacter aerogenes</i> | <b>Intermediate or resistant to:</b><br>Imipenem (MIC >4 2),<br>Meropenem (MIC >4 2),<br>Doripenem (MIC >4 2)<br><b>or Ertapenem (MIC &gt;1)</b><br><b>AND resistant to:</b><br><del>Ceftazidime (MIC &gt;8),</del><br><del>Ceftriaxone (MIC &gt;2),</del><br><del>and Cefotaxime (MIC &gt;2)</del> |

Specimens: urine and normally sterile sites

Patients: HD3 resident

# CRE Definitions Study

**Table 1.** Summary of 11 phenotype-based definitions evaluated for reliability in identifying carbapenemase producers among carbapenem-resistant *Enterobacteriaceae*, United States, January 1, 2011–January 30, 2014\*

| Antimicrobial included                     | Study inclusion criteria | Definition† |    |    |   |   |   |   |     |     |    |    |
|--|--------------------------|-------------|----|----|---|---|---|---|-----|-----|----|----|
|  |                          | 1           | 2  | 3  | 4 | 5 | 6 | 7 | 8   | 9   | 10 | 11 |
| Any carbapenem‡                            | NS                       |             |    |    | R |   | R | R |     | NS§ | R  |    |
| Any carbapenem (without ertapenem)         |                          | NS          | NS | NS |   | R |   |   |     |     |    | NS |
| ≥2 carbapenems‡                            |                          |             |    |    |   |   |   |   | NS§ |     |    |    |
| All third-generation cephalosporins tested |                          |             | R  |    |   |   | R |   |     |     |    |    |
| Any third-generation cephalosporins tested |                          |             |    | R  |   |   |   | R |     |     |    |    |
| Cefepime                                   |                          |             |    |    |   |   |   |   |     | R   | R  | R  |

# CRE Definitions Study



**Table 3.** False-positive and selected false-negative results in a study evaluating phenotype-based definitions for reliability in identifying carbapenemase producers among carbapenem-resistant enterobacterial isolates from 6 US Emerging Infections Program sites, January 1, 2011–January 30, 2014

| Result                  | No. isolates/no. tested (%), by definition no., N = 307* |                  |                  |                   |                  |                   |                   |                  |                  |                  |                  |
|-------------------------|--|------------------|------------------|-------------------|------------------|-------------------|-------------------|------------------|------------------|------------------|------------------|
|                         | 1  | 2                | 3                | 4                 | 5                | 6                 | 7                 | 8                | 9                | 10               | 11               |
| False-positive          | 117/307<br>(38.1)  | 82/307<br>(26.7) | 91/307<br>(29.6) | 169/307<br>(55.0) | 57/307<br>(18.6) | 146/307<br>(47.6) | 153/307<br>(49.8) | 60/307<br>(19.5) | 37/307<br>(12.1) | 34/307<br>(11.1) | 17/307<br>(5.5)  |
| Selected false-negative | 12/307<br>(3.9)  | 15/307<br>(4.9)  | 13/307<br>(4.2)  | 2/307<br>(0.7)    | 17/307<br>(5.5)  | 7/307<br>(2.3)    | 4/307<br>(1.3)    | 27/307<br>(8.8)  | 85/307<br>(27.7) | 85/307<br>(27.7) | 85/307<br>(27.7) |

\*False-positive isolates are those meeting the definition but not found to produce a carbapenemase. Selected false-negative isolates were selected on the basis of nonsusceptibility to  $\geq 1$  carbapenem not meeting the definition but found to produce a carbapenemase. Definitions: 1, nonsusceptible to any

# CRE Definitions Study

---

| Result                  | 1                 | 2                | 3                | 4                 |
|-------------------------|-------------------|------------------|------------------|-------------------|
| False-positive          | 117/307<br>(38.1) | 82/307<br>(26.7) | 91/307<br>(29.6) | 169/307<br>(55.0) |
| Selected false-negative | 12/307<br>(3.9)   | 15/307<br>(4.9)  | 13/307<br>(4.2)  | 2/307<br>(0.7)    |

# CRE Definition Change

---

- Definition 4 (R to any carbapenem) used by
  - National Healthcare Safety Network
  - Council of State and Territorial Epidemiologists
- Public health interest in carbapenem-resistance, not carbapenemase-production

# CRE Lab Practices in Georgia

---

- Lab survey, Nov 2015
  - 14/24 labs use the modified Hodge test
  - No labs are doing PCR routinely
  - How many labs using 2010 or later CLSI breakpoints for CRE?
- Infection prevention
  - How many isolate for CRE?
  - How many screen for CRE?

# MULTIDRUG-RESISTANT PSEUDOMONAS AERUGINOSA



**6,700**

MULTIDRUG-RESISTANT  
PSEUDOMONAS  
INFECTIONS



**440**

DEATHS



**51,000**

PSEUDOMONAS  
INFECTIONS  
PER YEAR

THREAT LEVEL  
**SERIOUS**



This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

- ~8% of all infections in CDC surveillance (NHSN)
  - Pneumonia, surgical site, and bloodstream infections
  - 13% of severe infections are multidrug resistant
- Intrinsically resistant to many commonly used antibiotics via multiple resistance mechanisms

# *Pseudomonas* Surveillance Pilot

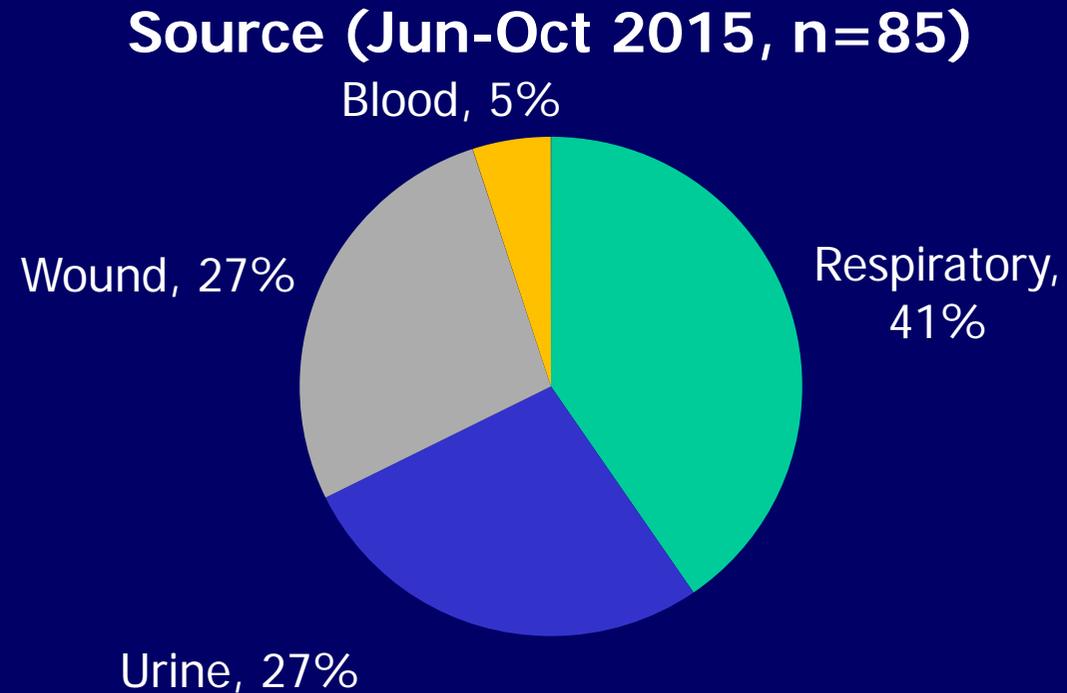
---

- Sentinel surveillance in two labs in HD3
- Case definition
  - Isolation of carbapenem resistant *P. aeruginosa* from any specimen source except stool, rectal, or nasal swabs.

# *Pseudomonas* Pilot Data from 2 Sentinel Sites in Georgia

---

| Month        | N          | Carbapenem Resistant |                |
|--------------|------------|----------------------|----------------|
| 6-2015       | 134        | 17                   | (12.7%)        |
| 7-2015       | 139        | 16                   | (11.5%)        |
| 8-2015       | 132        | 16                   | (12.1%)        |
| 9-2015       | 157        | 25                   | (15.9%)        |
| 10-2015      | 138        | 11                   | (8.0%)         |
| 11-2015      | 140        | 15                   | (10.7%)        |
| <b>TOTAL</b> | <b>840</b> | <b>100</b>           | <b>(11.9%)</b> |



# 2016 Case Definition

| Category  | Organism                      | Carbapenem susceptibility phenotype   |
|---|-------------------------------|---|
| Carbapenem-Resistant<br><i>Pseudomonas aeruginosa</i> | <i>Pseudomonas aeruginosa</i> | Resistant to:<br>Imipenem (MIC >4),<br>Meropenem (MIC >4),<br>or Doripenem (MIC >4) |

Specimens: to be determined

Patients: HD3 resident

- Tentatively starting July 2016
- No change to your workflow
- Please put any carbapenem-resistant organism in EIP bin
- Updates to queries (and alerts) coming soon

# Summary

---

- Georgia has a high but stable incidence of CRE compared to other regions in the US
- Most CRE associated with healthcare
- New surveillance definitions for CRE
  - Better sensitivity and alignment
  - No changes to your workflow
- New surveillance for carbapenem resistance in *Pseudomonas* to better define the problem

# Acknowledgements

---

- Chris Bower
- MuGSI Team in GA
  - Surveillance Officers
  - Labs, IPs
- THANK YOU!