Looking for the Bad Bugs in Wisconsin

David Warshauer, PhD, D(ABMM)
Deputy Director, Communicable Diseases
Wisconsin State Laboratory of Hygiene
Using a Proven Model for Antimicrobial Resistance Surveillance

- CDC
- Public Health Laboratories
- Clinical Laboratories
- Commercial Laboratories
- Research Laboratories

The LRN

- National Labs
- Reference Labs
- Sentinel Labs

definitive characterization
confirmatory testing
recognize, rule out, refer
Traditional *State* Partners in Public Health

- WSLH
- State Health Dept.
- Clinical Labs and Healthcare Facilities
- Local Health Depts.
- Clinicians
Role of Clinical Laboratories

- Submission of isolates
  - Voluntary
- Submission of AST results
- Reporting to public health

http://www.gru.edu/alliedhealth/mlirs/images/cls-program.jpg
Wisconsin Antimicrobial Resistance Surveillance

- NARMS
  - Salmonella
  - E. coli O157
  - Shigella
  - Listeria
  - Vibrio

- WSLH
  - Salmonella
  - S. pneumoniae

- Milwaukee City Lab/GISP
  - Neisseria gonorrhoeae

- State Antibiogram
  - Clinical Lab Data
Streptococcus Pneumoniae Susceptibilities 2010-2014 (Non-Meningitis Breakpoints)
Salmonella Antibiotic Resistance Surveillance
Non-typhoidal *Salmonella* isolates tested for antibiotic susceptibility at WSLH, 2003-2012

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Enteritidis</td>
<td>128</td>
<td>151</td>
<td>245</td>
<td>8</td>
<td>8</td>
<td>11</td>
<td>5</td>
<td>11</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Typhimurium</td>
<td>134</td>
<td>181</td>
<td>192</td>
<td>161</td>
<td>173</td>
<td>136</td>
<td>96</td>
<td>115</td>
<td>88</td>
<td>106</td>
</tr>
<tr>
<td>Newport</td>
<td>106</td>
<td>81</td>
<td>82</td>
<td>66</td>
<td>60</td>
<td>54</td>
<td>49</td>
<td>53</td>
<td>56</td>
<td>53</td>
</tr>
<tr>
<td>Heidelberg</td>
<td>14</td>
<td>19</td>
<td>33</td>
<td>16</td>
<td>24</td>
<td>33</td>
<td>9</td>
<td>11</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>I 4,[5],12:i:-</td>
<td>0</td>
<td>0</td>
<td>34</td>
<td>42</td>
<td>86</td>
<td>35</td>
<td>16</td>
<td>28</td>
<td>34</td>
<td>52</td>
</tr>
<tr>
<td>Other</td>
<td>310</td>
<td>400</td>
<td>341</td>
<td>341</td>
<td>384</td>
<td>323</td>
<td>295</td>
<td>334</td>
<td>340</td>
<td>357</td>
</tr>
<tr>
<td>All serotypes</td>
<td>692</td>
<td>832</td>
<td>927</td>
<td>634</td>
<td>735</td>
<td>592</td>
<td>470</td>
<td>552</td>
<td>541</td>
<td>591</td>
</tr>
</tbody>
</table>
Findings

Number and percent of all non-typhoidal *Salmonella* isolates from Wisconsin and U.S. that are resistant to individual antibiotics, from all years (2003-2012) combined

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Wisconsin (N=6566)</th>
<th>U.S. (N=21589)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>194</td>
<td>3.0%</td>
<td>336</td>
</tr>
<tr>
<td>Kanamycin</td>
<td>360</td>
<td>5.5%</td>
<td>529</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>2046</td>
<td>31.2%</td>
<td>2234</td>
</tr>
<tr>
<td>Amoxicillin-clavulanic acid</td>
<td>780</td>
<td>11.9%</td>
<td>713</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>414</td>
<td>6.3%</td>
<td>690</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>1071</td>
<td>16.3%</td>
<td>2236</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>12</td>
<td>0.2%</td>
<td>46</td>
</tr>
<tr>
<td>Nalidixic Acid</td>
<td>172</td>
<td>2.6%</td>
<td>456</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>524</td>
<td>8.0%</td>
<td>669</td>
</tr>
<tr>
<td>Sulfisoxazole</td>
<td>1521</td>
<td>23.2%</td>
<td>2369</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>159</td>
<td>2.4%</td>
<td>341</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>763</td>
<td>11.6%</td>
<td>1361</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>1348</td>
<td>20.5%</td>
<td>2727</td>
</tr>
</tbody>
</table>
Findings

Trends in resistance to individual antibiotics

Ampicillin resistance

% resistant (WI)

% resistance (U.S.)

Findings

Trends in resistance to combinations of antibiotics

At Least ACSSuT Resistance

ACSSuT Resistance (WI)

"ACSSuT Resistance (U.S.)"
Comparison of ACSSuT resistance rates by county over time

All Salmonella Serotypes
ACSSuT Resistance Rates: 2005

All Salmonella Serotypes
ACSSuT Resistance Rates: 2012
Observations

Resistance rates to nearly all tested antibiotics in WI and U.S. have decreased over the studied time period.

WI isolates are generally more resistant than national averages.
CRE Surveillance

Hospital Based

Laboratory Based
CRE
Hospital-Based Surveillance in Wisconsin

- Reporting became mandatory during Dec 2011
- Hospital inpatient-based
- Requires use of the National Healthcare Safety Network (NHSN) for reporting
- Purposes
  - Identify areas of high CRE prevalence
  - Identify “high risk” facilities
  - Assess healthcare-associated transmission
CRE Surveillance in Wisconsin

N = 137 hospitals

Hospitals required to report cases of CRE among inpatients

- 71 acute care
- 58 critical access
- 2 children’s
- 6 long-term acute care
CRE
Surveillance in Wisconsin

2014 NHSN definition

Any *E. coli* or *Klebsiella* spp. non-susceptible to imipenem, meropenem, or doripenem, by standard susceptibility testing methods or by a positive result for any method FDA-approved for carbapenemase detection from specific specimen sources. Includes clinical isolates from hospital inpatients.
### Wisconsin 2014 Hospital-based CRE Data

<table>
<thead>
<tr>
<th>Measure</th>
<th>n = 26 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of males</td>
<td>13/26 (50%)</td>
</tr>
<tr>
<td>Median age (range), years</td>
<td>65 (32–94)</td>
</tr>
<tr>
<td>Carbapenemase (KPC) positive</td>
<td>10/26 (38%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Specimen source</th>
<th>n = 38 specimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine</td>
<td>23 (60%)</td>
</tr>
<tr>
<td>Blood, other sterile sites</td>
<td>7 (18%)</td>
</tr>
<tr>
<td>Other (sputum, wound, SST)</td>
<td>5 (13%)</td>
</tr>
<tr>
<td><em>Klebsiella</em> spp.</td>
<td>30 (79%)</td>
</tr>
<tr>
<td>Hospital onset (specimen collected on or after day 4 of admission)</td>
<td>15 (39%)</td>
</tr>
</tbody>
</table>
Findings:
The southeastern public health region has a relatively high prevalence of CRE.
- One “high risk” facility has been identified.
- At least three probable incidents of healthcare-associated transmission have been identified.
Laboratory-Based Surveillance

"You might call them scientists, but for me they are "paparazzi"!

http://www.christoon.com
Isolate Criteria for CRE Surveillance

- Enterobacteriaceae nonsusceptible to carbapenems
  - Imipenem, Meropenem, doripenem, or ertapenem
  - Excluding *Proteus* spp., *Providencia* spp., and *Morganella morganii*
# TYPES OF CARBAPENEMASES

<table>
<thead>
<tr>
<th>Enzyme Type</th>
<th>Ambler Class</th>
<th>Activity Spectrum</th>
<th>Organism(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>KPC (1-10) (plasmid)</td>
<td>A</td>
<td>All β-lactams</td>
<td>Enterobacteriaceae <em>Ps. aeruginosa</em></td>
</tr>
<tr>
<td>SME</td>
<td>A</td>
<td>Carbapenems and aztreonam, but not 3rd/4th Gen cephalosporins</td>
<td><em>S. marcescens</em>, not plasmid Associated.</td>
</tr>
<tr>
<td>NMC–A, IMI</td>
<td>A</td>
<td>Same as for SME</td>
<td><em>Enterobacter</em> spp.</td>
</tr>
<tr>
<td>GES</td>
<td>A</td>
<td>Imipenem and 3rd/4th cephalosporins</td>
<td><em>Ps. Aeruginosa</em> and Enterobacteriaceae</td>
</tr>
<tr>
<td>IMI, VIM, NDM-1</td>
<td>B (metallo-β-lactamases)</td>
<td>All β-lactams; can test susceptible to aztreonam (NDM-1 variable AZT resistance)</td>
<td><em>Pseudomonas</em> spp. <em>Acinetobacter</em> spp. Enterobacteriaceae</td>
</tr>
<tr>
<td>OXA (Oxacillin hydrolyzing)</td>
<td>D</td>
<td>Weakly active against carbapenems</td>
<td><em>A. baumanii, P. Aeruginosa</em>, and rare Enterobacteriaceae</td>
</tr>
</tbody>
</table>

*Note: MNC = Not metallo carbapenemase, IMI = IMI hydrolyzing β-lactamase, GES = Guiana extended spectrum (plasmid)*

January 2010 to July 2014 CRE Surveillance

• Of 316 isolates tested for KPC, 84 positive (27%)
  • Most cases sporadic, but clusters were detected by PFGE and epidemiological linkage

• Of 196 isolates tested for NDM-1, 6 were positive (3%)
  • 5 cases were part of tightly linked epidemiological cluster
  • Index case had medical treatment on Indian subcontinent
January 2010 to July 2014 CRE Surveillance

Positive for KPC

- Klebsiella 59 (70%)
- Enterobacter, 11 (13%)
- E. coli 8 (10%)
- Citrobacter 6 (7%)
CRE Laboratory Surveillance

Number of Isolates Tested

Number of Isolates Positive for KPC

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Isolates Tested</th>
<th>Number of Isolates Positive for KPC</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>2011</td>
<td>34</td>
<td>0</td>
</tr>
<tr>
<td>2012</td>
<td>78</td>
<td>0</td>
</tr>
<tr>
<td>2013</td>
<td>102</td>
<td>0</td>
</tr>
<tr>
<td>2014</td>
<td>151</td>
<td>0</td>
</tr>
</tbody>
</table>
Conclusion

- Increasing antimicrobial resistance requires enhanced surveillance
- Antimicrobial resistance surveillance requires a strong clinical laboratory network
- Surveillance must include many partners: state and local public health, healthcare facilities, infection preventionists, and clinicians
- Surveillance requires funding
Acknowledgements

Gwen Borlaug, WDPH
Sam Keepman, MPH Student
The Laboratories of the WCLN
The Bacteriology Unit, WSLH
  Kristin Gundlach      Sara Wagner
  Alicia Jaedike       Juliann Whirry
  Tim Monson           Mike Rauch
  Ann Valley
The Data Crunchers
  Barb Rosenthal
  Mary Wedig
Thank You