The Nuts and Bolts of Antibiograms in Long-Term Care Facilities

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Disclosures

• Applied BioCode - Research Grant
• Beckman Coulter - Speaker
• bioMérieux - Speaker
• M39 Working group member
Objectives

• Review core concepts of antibiotic susceptibility and cumulative antibiotic susceptibility data/antibiograms
• Identify best practices for developing and maintaining annual antibiograms in long-term care
• Define how cumulative susceptibility data/antibiograms can be used in surveillance programs.
Antimicrobial Susceptibility Test

• Only performed on bacteria in which susceptibility to standardized treatment is not predictable.
  – Predictable
    • $\beta$-Streptococcus
  – Not-predictable
    • E. coli
• Antibiotics reported
  – Cascading antibiotics
  – Additional antibiotics fro MDROs
  – What methods
  – Breakpoints used
Antibiotic Susceptibility Testing

- Disk Diffusion
- Dilution
- Dilution and Diffusion

**Qualitative**
- Kirby Bauer
- Tube Dilution
- Agar Dilution

**Quantitative**
- E test
Terminology

• Sensitive
  • Based on the pharmaco-dynamics of an antimicrobial agent administered according to the normally recommended dosage and the organism causing an infection, the agent *will most likely inhibit the organism in vivo.*

• Intermediate (indeterminate)/Susceptible Dose Dependent
  • *might inhibit the organism in vivo.* /Use higher dose

• Resistant
  • *will most likely not inhibit the organism in vivo.*

• Non-Susceptible
  • *Not enough data to know if it is likely to inhibit the organism in vivo.*

• Epidemiological Cutoff Values
  • Determines the MIC of Wildtype and non-WT.
Where does the data come from?

- Microbiology AST instruments
- Microbiology LIS
- Electronic Health Records (EHR)
- Clinical decision support system (CDSS)
3 Types of Cumulative AST Data Reports

1. Traditional Antibiogram
2. Enhanced Antibiogram
3. Non-Traditional Antibiograms
   - Combined Antibiograms
   - Antimicrobial Resistance Surveillance Programs

Local Level – A single facility

Regional, National or Global
What Is An Antibiogram?

- Presentation of cumulative antimicrobial susceptibility testing (AST) data from a single institution on an annual basis.

“Routine” Cumulative antibiogram
Generally... all isolates from a facility

Appendix E1. Cumulative Antimicrobial Susceptibility Report Example – Antimicrobial Agents Listed Alphabetically (Hypothetical Data)
The **Why?** - Purpose of the Antibiogram

- To help clinicians choose initial empiric therapy

- Many more applications
  - Dr. Kim Claeys presentation on February 6th discussed using the antibiogram for Antimicrobial Stewardship applications
Importance & Reliance on Antibiograms Grow!

Direct from specimen diagnostics

Direct from + blood diagnostics

MALDI-TOF MS

Traditional Methods: Same day ID & AST

Day 0

Collection and plating of specimen in the lab

Day 1

Isolation of your organism on solid media
  • MALDI-TOF MS ID
  • Set up of AST panels

Day 2

Standard AST panel results available
  • Setup of additional antimicrobials

Day 3

Additional AST results

Empiric Treatment

Narrowed Treatment

Targeted Treatment

Courtesy of Trish Simner
Who is Responsible for Creating the Antibiogram?

• Traditionally the microbiology laboratory
  – Driven by access to the data from AST instruments or the LIS

• Shifting towards stronger collaborations with Antimicrobial Stewardship Programs
  – Automated EHR based antibiograms

• Should be a collaborative effort
  – Clinical microbiologists, pharmacists, physicians, IT specialists
Where Do You Start?

• M39-A4: Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline—Fourth Edition

• M39-A5 currently being worked on. 2019-2020
  – A newly created section on LTC
Preparation of Cumulative Antibiogram Recommendations

• **WHEN?**-Analyze/present data at least annually
• Include only verified **final results**
• Include only species with ≥ 30 isolates
• Include **diagnostic** (not surveillance) isolates
• Include the **1st isolate/patient**; no duplicate isolates
• Only include **routinely tested** antimicrobial agents
• Report only **%S** and do not include **I%**
The Cumulative Antibiogram Report

- Analyzes data from **routine antimicrobial susceptibility tests** performed in the clinical laboratory
- Separate report prepared for each **healthcare facility**
- Primarily used to guide **empiric therapy**
- Sometimes used to monitor resistance
  - Changes in %S from year to year
- **Highly impacted** by
  - Patient population served
  - Culturing practices
    - If cultures only performed when patients fail therapy
  - Laboratory antimicrobial susceptibility testing and reporting policies
  - Temporal outbreaks
# Organism Specific Recommendations

<table>
<thead>
<tr>
<th>Bug/Drug</th>
<th>Presentation of Data</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Streptococcus pneumoniae</em> and penicillin</td>
<td>List the %S using oral, meningitis and non-meningitis breakpoints</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em> and cefotaxime, ceftriaxone, cefepime</td>
<td>List the %S using meningitis and non-meningitis breakpoints</td>
</tr>
<tr>
<td>Viridans group streptococci and penicillin</td>
<td>List both the %S and %I</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>List %S for all isolates and the methicillin-resistant <em>S. aureus</em> (MRSA) subset</td>
</tr>
<tr>
<td><em>E. coli, K. pneumoniae</em> and <em>P. mirabilis</em> and cefazolin</td>
<td>List % S using urine and non-urine breakpoints</td>
</tr>
</tbody>
</table>
Stratification of Antibiograms

• Nursing site or site of care
  – ICU, burn unit, ED, outpatient clinic
• Specimen type of infection site
  – Urine, blood
• Clinical service or patient population
  – Surgical, pediatric, transplant, cancer
Answers to Commonly Asked Questions
How do I Apply Intrinsic Resistance?

The most up-to-date Intrinsic Resistance tables are located in the current M100 document.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Ampicillin</th>
<th>Amoxicillin-clavulanate</th>
<th>Ampicillin-sulbactam</th>
<th>Piperacillin</th>
<th>Ticarcillin</th>
<th>Cephalosporin I: Cefazolin, Cephalothin</th>
<th>Cephamycins: Cefoxitin, Cefotan</th>
<th>Cephalosporin II: Cefuroxime</th>
<th>Imipenem</th>
<th>Tetracyclines</th>
<th>Tigecycline</th>
<th>Nitrofurantoin</th>
<th>Polymyxin B</th>
<th>Colistin</th>
<th>Aminoglycosides</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citrobacter freundii</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Citrobacter koseri</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
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</tr>
<tr>
<td>Enterobacter cloacae complex*</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
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<tr>
<td>Escherichia coli</td>
<td></td>
<td>R</td>
<td>R</td>
<td>R</td>
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<td>R</td>
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<tr>
<td>Escherichia hermannii</td>
<td>R</td>
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<td>R</td>
<td>R</td>
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<tr>
<td>Hafnia alvei</td>
<td>R</td>
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<td>R</td>
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<tr>
<td>Klebsiella (formerly Enterobacter) aerogenes</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
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<tr>
<td>Klebsiella pneumoniae</td>
<td>R</td>
<td>R</td>
<td>R</td>
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<td>R</td>
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<td>R</td>
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<tr>
<td>Morganella morganii</td>
<td>R</td>
<td>R</td>
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<td>R</td>
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<td>R</td>
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<tr>
<td>Proteus mirabilis</td>
<td>R</td>
<td>R</td>
<td>R</td>
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<td>R</td>
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<tr>
<td>Proteus penneri</td>
<td>R</td>
<td>R</td>
<td>R</td>
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<td>R</td>
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<td>R</td>
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<tr>
<td>Proteus vulgaris</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
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<td>R</td>
<td>R</td>
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<tr>
<td>Providencia rettgeri</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
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<td>R</td>
<td>R</td>
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</tr>
<tr>
<td>Providencia stuartii</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
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<td>R</td>
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</tbody>
</table>
What Do You Do With Susceptible Dose Dependent (SDD) Results?

• SDD: an interpretive category defined by a breakpoint that susceptibility of an isolate is dependent on the dosing regimen that is used in the patient
  – Cefepime and *Enterobacteriaceae*
  – Fluconazole and *C. albicans, C. glabrata, C. parapsilosis, & C. tropicalis*
  – New in 2019:
    • Daptomycin and *Enterococcus* spp
    • Ceftaroline and *Staphylococcus aureus*
  – Report both % S & %SDD either in the Table or as a footnote

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>% S Cefepime</th>
<th>%SDD Cefepime</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>574</td>
<td>92&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>132</td>
<td>84&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2</td>
</tr>
</tbody>
</table>

<sup>a</sup>: “In addition, to the 92% S results, 3% were SDD (MIC 4 to 8 µg/mL) and 5% were R (MIC >16 µg/mL) to cefepime”
Why Do We Need a Minimum of N=30?

- Less statistical validity of data
  - Small numbers can skew the data

How Reliable is a Report of 80% Susceptible for *E. coli* and Ciprofloxacin?

<table>
<thead>
<tr>
<th>Sample size</th>
<th>% S (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>44 to 97</td>
</tr>
<tr>
<td>100</td>
<td>71 to 87</td>
</tr>
<tr>
<td>1000</td>
<td>77 to 82</td>
</tr>
</tbody>
</table>
What Do I Do If We Don’t Reach \( N \geq 30 \)?

- So what can you do?
  - Analyze multiple years – add footnote
  - Report the results from \( N < 30 \) with a footnote
    - “Calculated from fewer than the standard recommendation of 30 isolates”
  - Group several species within a genus together
  - Aggregate data from multiple smaller facilities with a similar patient population in the same geographic area

Discuss more LTCF specific later
Enhanced Antibioagram
What Are Enhanced Antibiograms?

- Segregating cumulative antibiogram data by one or more of the following:
  - **Location** – e.g., Inpatient vs Outpatient or ICU vs Oncology vs Non-ICU/Non-Oncology Wards
  - **Specimen type** – e.g. urine or blood specific
  - **Clinical condition** – e.g. cystic fibrosis, burn patients
  - **Patient Age** – e.g., pediatrics vs adults
  - **Resistance Phenotype** – e.g., MRSA, MSSA, carbapenem-resistant *Enterobacteriaceae*
  - **Organism** – e.g. anaerobe antibiogram
  - **ASP Antibiograms** – e.g. novel agents or last resort agents (colistin)

- **Resistance Profiles**
  - % Susceptible for combinations of drugs
  - % Susceptible for groups of organisms (e.g., all GNR from blood)
## Combination of Antimicrobial Agents

<table>
<thead>
<tr>
<th>Organism</th>
<th>No. Strains</th>
<th>CIP</th>
<th>CTZ</th>
<th>IMP</th>
<th>TOB</th>
<th>CTZ and/or CIP</th>
<th>IMP and/or CIP</th>
<th>CTZ and/or TOB</th>
<th>IMP and/or TOB</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>814</td>
<td>69</td>
<td>80</td>
<td>79</td>
<td>86</td>
<td>86</td>
<td>84</td>
<td>91</td>
<td>91</td>
</tr>
</tbody>
</table>
Organisms resistance characteristics

<table>
<thead>
<tr>
<th>Organism</th>
<th>No. Strains</th>
<th>CLI</th>
<th>DOX</th>
<th>ERY</th>
<th>GEN</th>
<th>OXA</th>
<th>PEN</th>
<th>RIF</th>
<th>SXT</th>
<th>VAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>All <em>S. aureus</em></td>
<td>1317</td>
<td>80</td>
<td>98</td>
<td>50</td>
<td>93</td>
<td>68</td>
<td>13</td>
<td>98</td>
<td>96</td>
<td>100</td>
</tr>
<tr>
<td>Oxacillin-resistant <em>S. aureus</em> (MRSA)</td>
<td>449</td>
<td>44</td>
<td>96</td>
<td>4</td>
<td>79</td>
<td>0</td>
<td>0</td>
<td>95</td>
<td>94</td>
<td>100</td>
</tr>
<tr>
<td>Oxacillin-susceptible <em>S. aureus</em> (MSSA)</td>
<td>904</td>
<td>97</td>
<td>99</td>
<td>72</td>
<td>99</td>
<td>100</td>
<td>18</td>
<td>99</td>
<td>97</td>
<td>100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Organism</th>
<th>No. Strains</th>
<th>AMK</th>
<th>AMP</th>
<th>CFZ</th>
<th>CRO</th>
<th>CIP</th>
<th>GEN</th>
<th>IMP</th>
<th>PTZ</th>
<th>TET</th>
<th>SXT</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>K. pneumoniae</em> (all)</td>
<td>1163</td>
<td>63</td>
<td>-</td>
<td>44</td>
<td>48</td>
<td>46</td>
<td>74</td>
<td>64</td>
<td>53</td>
<td>84</td>
<td>46</td>
</tr>
<tr>
<td><em>K. pneumoniae</em> (ESBL-producing)</td>
<td>233</td>
<td>30</td>
<td>-</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>48</td>
<td>100</td>
<td>0</td>
<td>84</td>
<td>3</td>
</tr>
<tr>
<td><em>K. pneumoniae</em> (KPC-producing)</td>
<td>361</td>
<td>5</td>
<td>-</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>28</td>
<td>0</td>
<td>0</td>
<td>82</td>
<td>0</td>
</tr>
<tr>
<td><em>K. pneumoniae</em> (non-ESBL or KPC-producing)</td>
<td>569</td>
<td>100</td>
<td>-</td>
<td>84</td>
<td>99</td>
<td>94</td>
<td>96</td>
<td>100</td>
<td>88</td>
<td>87</td>
<td>95</td>
</tr>
</tbody>
</table>
Non-Traditional Antibiograms
What About Non-Traditional Antibiograms?

• Accumulate AST data outside of a single institution
  – Combined Regional Antibiograms
  – Antimicrobial Resistance Surveillance Programs (ARSP)
    • Creating an ARSP report – New in M39-A5

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Routine Antibiogram</th>
<th>Non-Traditional Antibiogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Period</td>
<td>Annually</td>
<td>Defined by study</td>
</tr>
<tr>
<td># of Institutions</td>
<td>One</td>
<td>Multiple</td>
</tr>
<tr>
<td>Presentation</td>
<td>Table</td>
<td>Report with I, M&amp;M, R and D</td>
</tr>
</tbody>
</table>
When To Consider Utilizing Non-Traditional Antibiogram Data?

• The use of a local cumulative antibiogram is preferred to guide initial empiric therapy

• Non-Traditional antibiogram data:
  – Used when local AST data are not available, are limited in size or scope
  – Used as a benchmark to compare local data to regional and national findings
Combined REGIONAL Antibiotics

- Compilation of data from facility-level antibiograms
- Susceptibility was defined by local labs in all circumstances
- Created a report with an Introduction, Methodology Notes, Antibiogram Table & Breakdown by Individual Organisms
- Methodology Notes Included:
  - Differences in breakpoints (eg cephalosporin & carbapenem breakpoints)
  - Differences in agents within a class (eg ciprofloxacin vs levofloxacin)

http://publichealth.lacounty.gov/acd/AntibiogramData.htm
Applications of Cumulative AST Data
## Many Applications of Cumulative AST data

<table>
<thead>
<tr>
<th>Stake Holder</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physicians</td>
<td>Empiric therapy decisions</td>
</tr>
<tr>
<td>Clinical Microbiology Laboratories</td>
<td>Benchmarking, quality control, role of rapid diagnostics</td>
</tr>
<tr>
<td>Antimicrobial Stewardship Programs</td>
<td>Antimicrobial therapy recommendations and formulary decisions</td>
</tr>
<tr>
<td>Infection Prevention and Control</td>
<td>Benchmarking to evaluate infection control practices</td>
</tr>
<tr>
<td>Pharmaceutical Industry</td>
<td>Informs new drug development</td>
</tr>
<tr>
<td>Regulatory</td>
<td>Informs regulatory practices</td>
</tr>
<tr>
<td>Public Health</td>
<td>Monitoring changes in resistance levels and public health interventions</td>
</tr>
</tbody>
</table>

Courtesy of Trish Simner
Increasing Awareness of 
Antibiograms
Increasing Awareness of Antibiogram Data

Methods for Antibiogram Data Dissemination

<table>
<thead>
<tr>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pocket guides/booklets</td>
</tr>
<tr>
<td>Laminated posters</td>
</tr>
<tr>
<td>Hospital newsletter article</td>
</tr>
<tr>
<td>Posting within hospital intranet/EMR</td>
</tr>
<tr>
<td>Email to all prescribers</td>
</tr>
<tr>
<td>Smartphone or tablet applications</td>
</tr>
<tr>
<td>Presentations</td>
</tr>
</tbody>
</table>
Increasing Awareness of Antibiogram Data

Appendix G – provides stepwise instructions on presenting the local cumulative antibiogram data to healthcare professionals

- Explain purpose of the local cumulative antibiogram with a brief description of how the report is prepared
- Describe any software limitations
- Describe the rationale used for separating data into subgroups for the report
- Present graphs and charts for trends that are monitored each year
Recommendations in the New M39-A5 for LTC
Optimizing Culturing Practices in LTCF

- **Suspected Urinary Tract Infection** – To avoid over-culturing, consider developing a policy with the LTCF reference lab to determine if culture can be performed ONLY on urine specimens with significant pyuria (auto-reflex to culture).
- **Suspected Pneumonia** – Obtain an expectorated sputum sample, if possible, for Gram stain and culture.
- **Suspected Skin and Soft Tissue Infection** – If the skin infection is associated with an abscess or area of purulence, send a sample of the pus to the lab for culture.
Responsibility for Cumulative Antibiogram Development

• The willingness of the referral lab to either develop the antibiogram or provide susceptibility reports for antibiogram development should be determined.
  – Guidelines that will be followed for antibiogram development (e.g., CLSI M39)
  – Information (e.g., bacteria, antibiotics, etc.) that should be included in the antibiogram
  – Method for collection of cumulative susceptibility data
  – Method for data analysis, presentation and formatting (e.g., time period of antibiogram, data segregation techniques, the utility of infection-specific reports, etc)

• Multiple Referral Labs
  – Variations in laboratory practice must be considered (breakpoints)
  – Data formatted the same way
  – Appropriate and correct data from each laboratory
Data Analysis Techniques

• First Isolate per Patient
  – First isolate per reporting period

• Handling of small numbers (≤30)
  – Consider combining data from multiple years
  – Consider combining species, if applicable
  – Consider using data from other sources
  – Evaluate current culturing practices to assure that all patients with suspected infection are being cultured appropriately.
  – Consider constructing a cumulative antibiogram from patients in the general community in age category 65 and older.
More information and resources on the development of a LTCF Antibiogram

• https://www.ahrq.gov/nhguide/toolkits/help-clinicians-choose-the-right-antibiotic/index.html
Summary

• M39-A4 provides guidelines for creating a cumulative antibiogram
• There are 3 types of cumulative antibiograms
• Cumulative antibiograms can be stratified by different patient, hospital, or organism characteristics
• New Guidelines specific for LTCF will be in the new edition of M39-A5 coming out in 2020