Role of the Microbiologist in Antimicrobial Stewardship

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Role of the Microbiologist in Antimicrobial Stewardship: ID Pharmacist Perspective

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Disclosures

I am a consultant, speakers bureau member or have received research funding from: Achaogen, Bayer, Cepheid, Medicine Co., Merck, Pfizer, Shionogi

Advisory Member: Clinical Laboratory Standards Institute (CLSI)
Improving the Probability of Positive Outcomes

IMPROVING THE ODDS

HOST

BUG

DRUG

The Primary Goal of Antimicrobial Stewardship:
“Optimize clinical outcomes while minimizing unintended consequences of antimicrobial use”

Antimicrobial Stewardship Team: Hospital Setting
Multidisciplinary Team Approach to Optimizing Clinical Outcomes

ASP Directors
• ID PharmD
• ID Physician

Hospital Epidemiologist
Infectious Diseases Division
Director, Outcomes Research
Chairman, P&T Committee
Partners in Optimizing Antimicrobial Use Such as Pulmonologists and Surgeons

Infection Control
Medical Information Systems
ASP Directors
Clinical Pharmacy Specialists
Decentralized Pharmacy Specialist
Microbiology Laboratory

Institutional Based Antimicrobial Stewardship Programs

The Role of Microbiology Department

• Do you (and/or your department) actively participate in the program?

• What’s done to aid in the AMS efforts?

• Is this proactive or reactive, are you and/or your department advocating for AMS activities?
Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America

TF Barlam, SE Cosgrove, LM Abbo, C MacDougall, AN Schuettel, EJ Septimus, A Srinivasan, TH Dellit, YT Falck-Ytter, NO Fishman, CW Hamilton, TC Jenkins, PA Lipsett, PN Malani, LS May, GJ Moran, MM Neuhauser, JG Newland, CA Ohl, MH Samore, SK Seo, KK Trivedi

Evidence-based guidelines for implementation and measurement of antibiotic stewardship interventions in inpatient populations including long-term care were prepared by a multidisciplinary expert panel of the IDSA and the SHEA.

These recommendations address the best approaches for ABX stewardship programs to influence the optimal use of antibiotics.
Changing the Paradigm of How We Steward: Syndrome-Based Stewardship

“Disease State Management”

• Don’t focus on components of care (i.e., medicines or a test) and lose sight on the process of care → Quality
  » Process measure: DDD or days of therapy
  » Outcome measure: length of stay, overall cost of care

• Can broaden impact of interventions to appropriate diagnostics, imaging, time to therapy, etc.

• Easier to provide education and gather meaningful evidence for a specific infectious indication

• Focused message facilitates provider learning
  – Intervention seen as educational compared with broader stewardship methods
  – Learning = sustainable change

DDD, defined daily dose

How Does Your Institution Measure the Value of an Antimicrobial Stewardship Program

• Reduction in antimicrobial resistance?
• Reduction in amount of antimicrobials used?
• Reduction in the cost of antimicrobials?
• Improvement in quality and efficiency of care? (i.e., reduction in length of stay, readmissions)
• Reductions in cost of care?
• Enhancement of revenue (consideration of reimbursement in context of cost of care)?
• Reduction or Escalation in laboratory testing?
Pharmacy Assessment: Cost v. Value

Cost is of little value if the results are inaccurate
  - Low sensitivity
  - Low specificity
  - Repeat testing

Value is measured by impact of the test result on the patient and the facility
  - Increased sensitivity
  - Increased specificity
  - Increased productivity
  - Improved patient care

The most expensive DRUG is one that does not work
Implementing Antibiotic Stewardship

Microbiology and Laboratory Diagnostics

• Advocate for:

  » Stratified antibiograms (i.e., location, age)
  » Selective or Cascade reporting of AST results
  » Rapid viral testing for respiratory pathogens
  » Rapid diagnostic testing on Blood specimens
  » Nonculture-based fungal markers in hematology malignancy patients at risk for invasive fungal disease
Preparation of the Antibiogram

• Tools for building a better antibiogram
  – Utility: It provides the % of samples of given organism that were sensitive to the selected ABXs
  – CLSI (M39) provides guidance for creating accurate antibiogram
    » # of isolates of give organism (≥ 30 organisms)
    » Include only the 1st isolate from each patient
    » Update annually
    » Use of technologies (i.e., EMR systems)
    » Delineate differing populations (i.e., ICUs, wards, peds v. adults, inpatient v. outpatient
  – Limitations:
    » Does not incorporate patient-specific factors (i.e., h/o resistant bug, drug exposures, allergies)
    » May not reflect most current epidemiologic changes (i.e., 1 yr old data, outbreaks)
  – Combination antibiograms
Combination Antibiogram: Empirical Coverage of Nosocomial Pneumonia Pathogens

<table>
<thead>
<tr>
<th></th>
<th>C/T</th>
<th>FEP</th>
<th>CRO</th>
<th>CAZ</th>
<th>CIP</th>
<th>ETP</th>
<th>ATM</th>
<th>IPM</th>
<th>TZP</th>
<th>MEM</th>
<th>TOB</th>
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<tbody>
<tr>
<td>Enterobacteriaceae &amp; PSA MonoTx</td>
<td>%</td>
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<td>Enterobacteriaceae &amp; PSA + CIP</td>
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<tr>
<td>Enterobacteriaceae &amp; PSA + TOB</td>
<td>%</td>
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<td>85</td>
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</table>

Monotherapy with ceftolozane/tazobactam provides similar or greater activity than other β-lactams plus ciprofloxacin or tobramycin.

ceftolozane/tazobactam (C/T), cefepime (FEP), ceftriaxone (CRO), ceftazidime (CAZ), ciprofloxacin (CIP), aztreonam (ATM), ertapenem (ETP), imipenem (IPM), piperacillin/tazobactam (TZP), meropenem (MEM), tobramycin (TOB)

Sutherland CA, Nicolau DP. *Journal of Thoracic Disease*, 2017 Jan;9(1):214-221
Appropriate Antimicrobial Therapy

- Matches antibiotic susceptibilities of the organism to the antibiotic used

  "S" = Success

Improved Outcomes = Reductions in:

- Hospital and infection-related mortality
- Infection-related morbidity
- Length of hospital stay
- Days of antimicrobial therapy
- Cost of hospitalization


Assessment of *In Vitro* Potency Breakpoints

Breakpoints defined using highest registered doses

- **S** = Susceptible
- **I** = Intermediate
- **R** = Resistant

**MIC** (µg/mL)

Low — MIC (µg/mL) — High
Institutional Based Antimicrobial Stewardship Programs

The Role of Microbiology Department

- Beyond “S” providing the MIC?
- Routinely available from your AST or Ellipsometry?
Assessing Antimicrobial Potency: Beyond the “S”

MIC Distribution for *P. aeruginosa* from 40 U.S. Hospitals (n= 1044)

Optimizing β-lactam Therapy: Maximizing Percent T>MIC

Dosing strategies to improve T> MIC

• *Increased duration of infusion*
  – Continuous infusion
    » Administer loading dose, then use pump to give total daily dose IV over 24 hr period
  – Prolonged infusion
    » Same dose and dosing interval, however, change duration of infusion (0.5 hr → 3hr)

– Infusion Strategies PLUS Higher Doses
Susceptibility Reporting

When “S” Does NOT = SUCCESS

• Due in part to DISCORDANCE between:
  – *In vitro* susceptibility
  – *In vivo* exposures

Improving Concordance:
- Revise the BREAKPOINTS
Institutional Based Antimicrobial Stewardship Programs

The Role of Microbiology Department

• Are your current breakpoints consistent with CLSI?

• How do your clinicians know if breakpoint changes undertaken?

• How do your clinicians know if other changes undertaken in laboratory?
<table>
<thead>
<tr>
<th>Organism</th>
<th>MIC (µg/ml)</th>
<th>Zone (mm)</th>
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<tr>
<td></td>
<td>Susc</td>
<td>Int</td>
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<tr>
<td>Acinetobacter spp.</td>
<td>≤2</td>
<td>-</td>
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<tr>
<td>Pseudomonas aeruginosa</td>
<td>≤2</td>
<td>-</td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
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</tbody>
</table>

**Insufficient clinical and PK/PD data to set “breakpoint”**

**ECV (µg/ml)**

Enterobacteriaceae

**NOT a clinical breakpoint!!**
Failure of Previous Cefepime Breakpoints to Predict Clinical Outcomes in Gram-Negatives

Why S-DD?

• **Intermediate** too often means resistant because most caregivers don’t appreciate the entire definition or when each part of the definition is in play.

• The approach of using one breakpoint for one dose wasn’t working – what do you do when a lower dose is used?

• **S-DD is more specific and it communicates what we know – a higher dose is indicated**

• **S-DD has been used for antifungal susceptibility testing for years**
Microbiology Plate Rounds

• ID pharmacist attending daily Micro Plate Rounds
  » Prospective monitoring of critical cultures
  » Microbiology lab workflow & data management
    • Promote rationale ABX use
    • Reduce unnecessary cultures → poor quality / inappropriately collected

  – 85 interventions from 19 daily sessions
    » Liaison between lab & clinicians (42%)
    » Management of MDR organisms (22%)
    » Clarification of culture & AST results (18%)

  – Enhance Patient Safety; Reduce Lab & Pharmacy $$

MacVane SH, Hurst JM, Steed LL. Open Forum Infect Dis 2016 Sep 21;3(4):ofw201. eCollection Sep 21
Anti-Fungal Stewardship (AFS) Strategies for Invasive Candidiasis

- AFS strategies:
  - Identifying high-risk patients: risk factors and prediction rules
  - Potential use of β-glucan
  - Correct approach (pre-emptive vs empiric)
  - Early diagnosis & treatment
  - Timeous administration ("hang-time")
  - Source control
  - Get it right first time
  - De-escalation & step-down therapy
  - Duration

Personal Communication: Dr. A Brink
De-Escalation of Candida Directed Therapies

Impact of In-house susceptibility testing

• 302 Candidemia episodes → Initial 210 (70%) echinocandin
• Implemented fluconazole disk diffusion testing in lab
  » Simple
  » Inexpensive
  » Accurate
• 137 (73%) patient with fluconazole-S isolates changed to fluconazole and safely completed treatment
• De-escalation of echinocandin therapy
  » Reduces potential development of resistance
  » Limits patient exposure to toxic agents
  » Improve quality of care (IV → PO)
  » Reduced overall cost

Kubiak DW, et al. DMID 2016; March 84(3):223-226
Implementing Antibiotic Stewardship

Microbiology and Laboratory Diagnostics

• Advocate for:
  » **Stratified** antibiograms (i.e., location, age)
  » **Selective** or **Cascade** reporting of AST results
  » **Rapid viral testing** for respiratory pathogens
  » **Rapid diagnostic testing** on **Blood** specimens
  » **Nonculture-based fungal markers** in **hematology malignancy** patients at risk for invasive fungal disease
Susceptibility Reporting

• Cascade Reporting
  – Withhold susceptibility reporting of broad spectrum ABX for PAN-S organisms
    » *Enterobacteriaceae*: hold TZP, cefepime, carbapenem → report cefazolin, ceftriaxone
    • SPACE bugs?
    » *Staphylococci*: MSSA hold vancomycin → CFZ/NAF
    » *PSA*: Cefepime & TZP “S” & carbapenem-NS (on meropenem)

– What about PAN-S organisms with R to broad spectrum ABX
  » Newly recognized *E. coli* and *K. pneumoniae* → TZP-R / PAN-S β-lactams

• Sutherland CA, Nicolau DP. *Clinical Therapeutics* 2015;37(7):1564-1571.
• Mediavilla JR et al. (Abstract No. 1181). IDWeek 2015, San Diego, CA, October 2015
Detection of Piperacillin-Tazobactam-Resistant/Pan-β-Lactam-Susceptible *E. coli* with Current Automated Susceptibility Test Systems

<table>
<thead>
<tr>
<th></th>
<th>BMD</th>
<th>(TZP MIC)</th>
<th>MicroScan®</th>
<th>Phoenix™</th>
<th>Vitek2®</th>
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<td>R</td>
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<td>EC C6 -25</td>
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<td>EC C10 -11</td>
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<td>EC C12 -1</td>
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<td>EC C18 -6</td>
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<tr>
<td>EC C30 -5</td>
<td>R</td>
<td>(256)</td>
<td>I</td>
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<td>R</td>
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</tbody>
</table>

Susceptibility Reporting

• Reflex Testing
  – Organism testing non-susceptibility to the primary panel undergoes additional MIC testing:
    » **Enterobacteriaceae**: carbapenem-NS → ?
    » **PSA**: carbapenem-NS → ?

  – On request

  – Automatically
Implementing Antibiotic Stewardship

Microbiology and Laboratory Diagnostics

• Advocate for:
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  » **Nonculture-based fungal markers** in **hematology malignancy** patients at risk for invasive fungal disease
Influenza Respiratory Tract Infections: Opportunities for Stewardship

- **Hospitalized Patients With Influenza RTI**
  - Inappropriate antibiotic duration (IAD) = ABX >24h after + influenza test [RT-PCR Xpert Flu, Cepheid, Sunnyvale, CA] in pts <72h of RTI symptoms and no other bacterial infection
  - 322 patients → Resp. cultures were ordered for 50 (15.5%); 71 (22%) had a positive chest x-ray
  - On admission ABX prescribed to 211 (65.5%) → inappropriately continued in 73 patients (34.5%)
  - IAD patients had longer LOS (median, 6 days; range 4-9) compared with those whose ABX were discontinued appropriately (5 days; range 3-8) and those who were not treated (4 days; range 3-6; P<.001).
  - No difference in mortality or 30-day readmission rates
  - Total hospital costs were greater IAD ($10,645) compared with the appropriate ABX duration ($7,479) and No ABX ($5,961)
  - Hospital experienced loss in net hospital revenue of $2,076 per IAD patient compared with a appropriate duration of ABX

Implementing Antibiotic Stewardship

Microbiology and Laboratory Diagnostics

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  » Nonculture-based fungal markers in hematology malignancy patients at risk for invasive fungal disease
# Microbiology Laboratory Evolution & the Need for Multidisciplinary AMS TEAM?

<table>
<thead>
<tr>
<th>Study</th>
<th>RDT/pathogen(s)</th>
<th>Study Design</th>
<th>Outcomes</th>
</tr>
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<tbody>
<tr>
<td>Forrest, 2006</td>
<td>PNA-FISH Candida spp.</td>
<td>Pre/post-intervention: RDT + AST</td>
<td>ID of <em>C. albicans</em> 3 days earlier (9.5h vs 44h), ↓ antifungal costs by $1,978/patient</td>
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<tr>
<td>Forrest, 2008</td>
<td>PNA-FISH Enterococcus spp.</td>
<td>Pre/post-intervention: RDT + AST</td>
<td>↓ mortality (45% vs 35%), ↓ time to appropriate abx (1.3 vs 3.1 days)</td>
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<tr>
<td>Ly, 2008</td>
<td>PNA-FISH S. aureus vs GPCs</td>
<td>Pre/post intervention: RDT and pre/post AST</td>
<td>↓ mortality (17% vs 8%), ↓ inappropriate abx use by 2.5 days*, trend towards ↓ LOS and cost</td>
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<tr>
<td>Carver, 2008</td>
<td>RT-PCR mecA (MRSA)</td>
<td>Pre/post intervention: RDT and pre/post AST</td>
<td>↓ time to optimal abx (64.7h vs 39.9h), ↓ duration of <em>S. aureus</em> BSI</td>
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<tr>
<td>Wong, 2010</td>
<td>rPCR S. aureus</td>
<td>Pre/post intervention: RDT + AST</td>
<td>↓ LOS (21.5d vs 15.3d)</td>
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<tr>
<td>Perez, 2013</td>
<td>MALDI-TOF GNRs</td>
<td>Pre/post intervention: RDT + AST</td>
<td>↓ LOS (11.9d vs 9.3d), Trend towards ↓ mortality (10.7 vs 5.6%)</td>
</tr>
<tr>
<td>Huang, 2013</td>
<td>MALDI-TOF All Pathogens</td>
<td>Pre/post intervention: RDT + AST</td>
<td>↓ 30d mortality (20.3 vs 12.7%), ↓ LOS (21 vs 16.7d)</td>
</tr>
</tbody>
</table>
Antimicrobial Stewardship: Does the Name Fit Task

• Focus on “BEST PRACTICE” processes → optimal delivery of care

• Best Practice in…… Carbapenemase-Producing Enterobacteriaceae (CPE)
  – Initial assessment – Infection v. Colonization
  – Diagnostic approaches → rapid, sensitive
  → Genotypic & Phenotypic profiling
  – Initiation of Appropriate ABX therapy
  – Infection Control
CPEs Rapidly Spreading Across the US

Carbapenemase-producing Enterobacteriaceae (CPE) in U.S Reported to the CDC EIP & NHSN (Updated 2015)

http://www.cdc.gov/hai/organisms/cre/TrackingCRE.html
Accessed 02Jan2016
Handling and Interpretation
Issues with Culture Tests

Culture-based tests → the Modified Hodge Test (MHT) or disk diffusion are commonly used for carbapenemase confirmation.

Benefits
- Accessible to most labs
- Low reagent cost

Potential sources for ambiguous or erroneous results
- Hands on, multi-step testing procedure
- Isolates can show variable patterns of growth requiring operator interpretation
- 25% false positive rate observed using MHT (with some ESBLs containing CTX-M* or AmpC*)
- CarbaNP cannot differentiate between various carbapenemases
- Results must be manually entered & communicated to clinical & Inf. control staff

1 J. Clin. Microbiol. April 2010 vol. 48 no. 4 1323-1332
* CTX-M-β-lactamases: ‘active on CefoTaXime, AmpC: Ampicillin class C beta lactamase
Handling and Interpretation
Issues with CarbaNP

CarbaNP Test, based on hydrolysis, can also be used for detecting the presence or absence of carbapenemases.

Benefits

- Accessible to most labs
- Low reagent cost
- Fast results

Potential sources for ambiguous or erroneous results

- Hands on, multi-step testing procedure
- Visually reading of color based results can be subjective
- Reproducibility of results is an issue due to variable levels of carbapenemase activity, especially OXA-48 like carbapenemases.
- CarbaNP cannot differentiate between various carbapenemases
- Results must be manually entered and communicated to clinical and infection control staff

1J. Clin. Microbiol. April 2010 vol. 48 no. 4 1323-1332
•CTX-M-β-lactamases: ‘active on CefoTaXime, AmpC: Ampicillin class C beta lactamase
Handling and Interpretation Issues with mCIM

mCIM Test [Modified Carbapenem Inactivation Method] based on hydrolysis, can also be used for detecting the presence or absence of carbapenemases

Benefits
• Accessible to most labs
• Low reagent cost

Potential sources for ambiguous or erroneous results
• Hands on, multi-step testing procedure
• 24h, requires overnight incubation
• Lower subjective interpretation [zone v. color]
• Good sensitivity for Ambler class A, B, D in Enterobacteriaceae
• Poor sensitivity for carbapenemases in Acinetobacter
• mCIM cannot differentiate between various carbapenemases
• Results must be manually entered and communicated to clinical and infection control staff
# Molecular Testing for Carbapenemase

<table>
<thead>
<tr>
<th>Test Name/ MFG</th>
<th>Approved Specimens</th>
<th>Key Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>FilmArray® BCID Panel Biofire Dx</td>
<td>Blood Culture</td>
<td>Detects the most prevalent CP in US – KPC Comprehensive 27 target panel for most common causes of blood stream infections</td>
<td>Does not detect NDM, VIM, OXA-48, IMP Not cost effective for carbapenemase detection and routine use Limited in sample throughput</td>
</tr>
<tr>
<td>Verigene® System Nanosphere, Inc.</td>
<td>Blood Culture</td>
<td>Comprehensive panel detects most common carbapenemases and CTX-M ESBL</td>
<td>Limited in sample throughput Not cost effective for routine use</td>
</tr>
<tr>
<td>Xpert CarbaR Cepheid, Inc.</td>
<td>Resistant culture isolates from blood, urine, sputum, rectal/peri-rectal swabs Direct detection from rectal/perirectal swabs</td>
<td>Rapid – 48 min. to result Comprehensive – 91 gene targets for carbapenemase producing organisms, reported as 5 gene families - KPC, NDM, VIM, IMP, OXA-48</td>
<td>Higher cost than culture / phenotypic methods. Specific for carbapenemases Does not detect ESBLs</td>
</tr>
</tbody>
</table>

[http://jac.oxfordjournals.org/content/early/2014/03/26/jac.dku083.full.pdf](http://jac.oxfordjournals.org/content/early/2014/03/26/jac.dku083.full.pdf)
Treatment of $\text{Bla}_{\text{kpc-2}}$-Positive $\text{Klebsiella pneumoniae}$ Blood Stream Infection With Continuous Infusion Meropenem

58 yo hospitalized for aortic dissection complicated by intra-abdominal catastrophe and acute kidney injury → developed bacteremia

- MDR KPC (MICs: AMK 16, TAZ ≥ 64, P/T ≥ 128, Tige ≥ 8, PMX B 32, Mer 8)
- Cl cr ~45 ml/min
- Meropenem 2 g q8 by continuous infusion

- Meropenem serum concentrations 22 mg/L (range 20-29)
- Microbiologic and clinical cure

How to Manage CRE in the Daily Practice *(Historical Perspective)*

- Role of colistin, meropenem, tigecycline
  - Colistin 9MU load, 4.5MU q12-8

  PLUS

  - Meropenem 2g q8 Prolonged Inf (3hr)
  - Importance of phenotypic profile, MIC ≤ 16mg/L

  PLUS

  - Tigecycline 200mg load, 100mg q12
Novel $\beta$-lactam / $\beta$-lactamase Inhibitors for CRE

- **$\beta$-lactam plus Novel Inhibitor**
  - Ceftazidime - Avibactam [KPC, OXA]
  - Ceftaroline - Avibactam
  - Aztreonam - Avibactam [MBL activity]
  - Imipenem - Relebactam
  - Cefepime - AAI101

- **Meropenem – Vaborbactam [KPC]**

- Cefepime – Zidebactam [KPC, OXA, MBL]
Application of “Precision Medicine” Through the Molecular Characterization of Extensively Drug-Resistant *K. pneumoniae* in a Multivisceral Transplant Patient

<table>
<thead>
<tr>
<th>Drug</th>
<th>AMK</th>
<th>ATM</th>
<th>CAZ</th>
<th>AVI</th>
<th>CIP</th>
<th>CRO</th>
<th>CST</th>
<th>C/T</th>
<th>ETP</th>
<th>FEP</th>
<th>MEM</th>
<th>TGC</th>
<th>TZP</th>
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</thead>
<tbody>
<tr>
<td>MIC (µg/mL)</td>
<td>&gt;512</td>
<td>64</td>
<td>&gt;64</td>
<td>&gt;128/4</td>
<td>&gt;16</td>
<td>&gt;64</td>
<td>&gt;16</td>
<td>&gt;64/4</td>
<td>&gt;16</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>1</td>
<td>&gt;256/4</td>
</tr>
</tbody>
</table>

**Molecular characteristics**: NDM+, OXA 48+, CTX-M+

Potential Synergistic Combinations against New Delhi Metallo-β-Lactamase-Producing *K. pneumoniae*??

Rosa R, et al. Clinical Infectious Diseases 2017;00(00):1–2
In Vitro Susceptibility and Synergy

XDR *K. pneumoniae* [NDM, Oxa-48, CTX-M]
CAZ/AVI >128; ATM >64, MER >64; CST > 16, Tig 1

Ceftazidime-Avibactam + Aztreonam

Evolving *In Vivo* Understanding of Carbapenemases

KPC

Class A (serine based): SME, IMI, NMC, GES

Other Metallo-β-lactamases: SPM, GIM, and SIM

- Versatile hydrolytic capacities
  - Phenotypic profiles
- Variable fitness
- Variable virulence
  - Clonal backbone
Carbapenemase-Producing Enterobacteriaceae (CRE)

Managing the DOUBLE EDGED SWORD

• Infection
  • ↑ infection related mortality
  • Need for prompt recognition & initiation of ABX
  • Phenotypic & Genotypic profiling

• Colonization
  • Risk to the patient
  • Risk to others
Antimicrobial Stewardship: Does the Name Fit Task

- Focus on “BEST PRACTICE” processes → optimal delivery of care

- Best Practice in... Management of Patient with Diarrhea
  - Initial assessment – Likelihood of Infection
  - Diagnostic approaches → rapid, sensitive
  - Need for ABX therapy
  - Infection Control
C. difficile: An Old Bug Providing Contemporary Clinical and Laboratory Challenges

Contemporary Testing Schemes

– Alternatives to EIA for toxins A/B alone

– Difficile Dancing?
  » 2-test / 1 card EIA for GDH and Toxins A/B with discrepant results resolved by a molecular technique
  » GDH screen with GDH positives tested by a molecular assay
  » Direct to molecular assay

Suggested reading: Point-Counterpoint: What is the optimal approach for detection of Clostridium difficile?
**C. difficile**: An Old Bug Providing Contemporary Clinical and Laboratory Challenges

**Who to Test:**

- **✓** Persons with $\geq 3$ unformed BM within 24 hours with risk factors for CDI (Clinically Significant Diarrhea)
- **✓** ↑ WBC, ↑ creatinine, ↓ albumin, antibiotics, IBD, surgery and older age
- **✓** Patients who completed therapy who still have CSD

- **o** Do not perform tests on everyone with diarrhea
  - Tube-feeding, Laxatives, other medicines
- **o** Do not perform tests on asymptomatic patients
- **o** Do not get coerced by “Test of Cure” requests
  - Cured patients can carry toxigenic *C. difficile*
Laboratory Information System Interventions

Using the EMR to guide best practice:

- **Pop-up Question** when placing the order:
  - Is the patient on Tube-feeding, Laxatives, other medicines that may result in loose stool

- **Reflex order** for isolation precautions is generated upon prescriber order

- **Automatic stop order** for *C. difficile* test if patient hasn’t produced a qualified stool within 24hrs

- **Triggers Infection Control** to review isolation status

SB Nicolau, Personal Communication
Molecular Detection of Carriers of CDI at Time of Hospital Admission

- Screened rectal swabs from new admissions for \textit{tcd}B gene by PCR
- Carriers placed on contact precautions during hospitalization
- CDI rates were compared for pre and post intervention
- During intervention CDI rate was 3.0/10000 patients days (down from 6.9)
- Concluded that detecting and isolating CD carriers was associated with a significant decrease in HA-CDI

Antimicrobial Stewardship: Does the Name Fit Task

- Focus on “BEST PRACTICE” processes → optimal delivery of care

- Best Practice in…… Management of UTIs
  - Initial assessment - Colonization v. Infection
  - Need for culture → rapid diagnostics
  - Need for ABX therapy
  - Etiology of disease → Urology consult
Urinary Cultures in the Emergency Department

• Reflex-Culture Cancelation Protocol
  – Cultures initiated in the Emergency Dept
  – Patients > 5 yrs old
  – Cancel urine culture if urinalysis within NL limits

  – 1546 patients → 314 (20%) had positive urine cultures
  – Restriction of culture testing to samples with + urinalysis
    [+ Leukocyte esterase, + Nitrates, WBC >10 H-P field, and/or bacteria]
  – Reflex culture cancellation protocol based on these criteria would have:
    » Eliminated 604 of 1546 cultures (39%)
    » 11 of 314 positive cultures (3.5%) would have been missed

  – Implementation → Decreased use of laboratory resources

Appropriate Antimicrobial Therapy
An Increasing Challenge

- Impact of ESBLs on Clinical and Economic Outcomes in Patients with Urinary Tract Infection
  - 55 ESBL (cases) & matched controls (non-ESBL UTI)
    - Failure of initial antibiotic regimen (62% vs. 6%; P<0.001) & time to appropriate therapy (51 vs. 2.5 hours; P<0.001) were greater in ESBLs
    - Median cost of care was greater (additional $3,658; P=0.02) and median length of stay (LOS) was prolonged for ESBLs (6 vs. 4 days; P=0.02)
    - Antimicrobials comprised less than 1% of cost of care
  - Cost of care & LOS with ESBLs were 1.5 times those caused by non-ESBL UTIs; this resulted in net hospital loss of $3,200 per ESBL UTI

MacVane SH, Tuttle LO, Nicolau DP. *Journal of Hospital Medicine* 2014:9(4);232-238
Strategies to Optimize Clinical & Microbiologic Outcomes

• **Best Practice ..... Antimicrobial Stewardship**

  – Appropriate Use of Cultures
  – Appropriate Initial Therapy
    » Right DRUG(s)
      • Rapid diagnostics → ID; pheno / geno profile
    » Optimize Exposures (PD profile)
  – De-escalation → Narrow Spectrum
  – Reduce Duration of Therapy (Biomarkers)
  – Economic considerations:
    » Cost of ABX & Lab tests v. Cost of Care
Antimicrobial Stewardship Team: Hospital Setting

Multidisciplinary Team Approach to Optimizing Clinical Outcomes

ASP Directors:
- ID PharmD
- ID Physician

ASP = Antimicrobial Stewardship Program, ID = infectious disease, P&T = Pharmacy and Therapeutics.

AMS Habits to Meet Joint Commission Standards for Hospitals

- Established as organizational priority
- Hospital [Microbiology] educates staff → ABX ordering, resistance and AMS practices
- Hospital educates patients & families
- Hospital has AMS multidisciplinary team [Microbiology]
- Hospital AMS includes 7 core elements from CDC
- Hospital [Microbiology] uses organizational multidisciplinary protocols
- Hospital [Microbiology] collects, analyses and reports data on its AMS program
- Hospital [Microbiology] takes action on improvement opportunities identified in its Hospital AMS program