MDRO’s, Stewardship and Beyond

Linda R. Greene RN, MPS, CIC
linda_greene@urmc.rochester.edu
Evolving Threat of Antimicrobial Resistance
Why are MDROs important?

• Limited treatment options
• Associated with:
  increased cost
  increased length of stay
  increased morbidity and mortality
• Worse outcomes for patients with MDROs and *c. difficile*
Mortality associated with MDROs

Patients with an MDRO have an increased risk of death compared to patients with a susceptible strain

• Any MRSA infection – 2 x Risk
• VRE bloodstream infection – 2-2.5 x Risk
• MDR acinetobacter bloodstream infection - 5 x Risk
• ESBL bloodstream infection - 2 x Risk
## Impact of MDRO

### Table 5. Mean Cost and Length of Stay for Patients with Antimicrobial-Resistant Infection (ARI), Compared with Matched Control Subjects

<table>
<thead>
<tr>
<th>Propensity score</th>
<th>Patients with ARI</th>
<th>Patients without ARI</th>
<th>Mean difference</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Propensity score 2</strong></td>
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<td></td>
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<tr>
<td>No. of patients</td>
<td>169</td>
<td>169</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>Total cost, US$</td>
<td>53,863 ± 60,720</td>
<td>24,794 ± 23,231</td>
<td>29,069</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total length of stay, days</td>
<td>23.8 ± 20.3</td>
<td>12.8 ± 10.2</td>
<td>11.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Propensity score 3</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>138</td>
<td>138</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>Total cost, US$</td>
<td>52,211 ± 59,456</td>
<td>31,003 ± 26,325</td>
<td>21,208</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total length of stay, days</td>
<td>22.5 ± 20.1</td>
<td>15.9 ± 11.3</td>
<td>6.7</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

**NOTE.** Data are mean ± standard deviation, unless otherwise indicated.

*a* Comorbidities, surgery, and intensive care unit stay.

*b* Comorbidities, surgery, intensive care unit stay, and health care–acquired infection.
Is it Necessary? Does it matter?

• The incidence, mortality, and medical care costs of CDIs have reached historic highs
  – 3,000 CDI attributable deaths/yr in 1999–2000
  – 14,000 CDI attributable deaths/yr in 2006–2007
  – $5,042–$7,179 excess costs per case of HO-CDI
  – Nationally excess $897 million to $1.3 billion

CDC Vital Signs - March 2012
Impact of C. difficile infection (CDI)

- Hospital-acquired, hospital-onset: 165,000 cases, $1.3 billion in excess costs, and 9,000 deaths annually

- Hospital-acquired, post-discharge (up to 4 weeks): 50,000 cases, $0.3 billion in excess costs, and 3,000 deaths annually

- Nursing home-onset: 263,000 cases, $2.2 billion in excess costs, and 16,500 deaths annually

CRE are epidemiologically important for several reasons:

• CRE have been associated with high mortality rates (up to 40 to 50% in some studies).

• In addition to β-lactam/carbapenem resistance, CRE often carry genes that confer high levels of resistance to many other antimicrobials, often leaving very limited therapeutic options. “Pan-resistant” KPC-producing strains have been reported.

• CRE have spread throughout many parts of the United States and have the potential to spread more widely.
What is the Scope of the Problem?

Multidrug-Resistant Organisms (MDROs):

Greece


1.1 Background: the problem of antimicrobial resistance in Hong Kong

1. The emergence of resistance has threatened the successful treatment of patient with infections [1-5].
2. Antimicrobial resistance increases drug costs, length of stay and adversely affects patient’s outcome [6].
3. Resistance to all classes of antibiotics has developed to various extents among the common and important nosocomial pathogens (Tables 1.1-1.3).
Why is resistance increasing in the healthcare environment?

- Increasingly complex healthcare delivery
- Overuse of antibiotics
- Increasing prevalence of MDRO’s - colonization pressure
- Increasing risk of environmental contamination
- Lack of resources or institutional will to enforce compliance
Bad Bugs, No Drugs: No ESKAPE! An Update from the Infectious Diseases Society of America

Helen W. Boucher, George H. Talbot, John S. Bradley, John E. Edwards, Jr., David Gilbert, Louis B. Rice, Michael Scheld, Brad Spellberg, and John Bartlett
“Bad Bugs”

- Drugs for bad bugs: confronting the challenges of antibacterial discovery. (2007)
- The epidemic of antibiotic-resistant infections: a call to action for the medical community from the Infectious Diseases Society of America. (2008)
- Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. (2009)
- Bad bugs, no drugs: no ESCAPE revisited. (2009)
- Challenges in anti-infective development in the era of bad bugs, no drugs: a regulatory perspective using the example of bloodstream infection as an indication. (2010)
What Every Health Care Executive Should Know:

The Cost of Antibiotic Resistance

CHAPTER 1 - Antibiotic Resistance: Patients and Hospitals in Peril
Why is the issue of antibiotic resistance important to you and your organization?
Stephen Weber, M.D., M.S.
Barbara M. Soulia, R.N., M.P.A., C.I.C.

CHAPTER 2 - The Clinical Consequences of Antibiotic Resistance
How many patients at your institution died last year as a result of infection with multidrug-resistant organisms?
Thomas R. Talbot, M.D., M.P.H.

CHAPTER 3 - The Financial Impact of Antibiotic Resistance
How much did it cost your hospital last year to prevent and manage infections caused by multidrug-resistant organisms?
Keith Eage, M.D., M.S.

CHAPTER 4 - Transmission Control to Prevent the Spread of MDRs in Health Care Facilities
How frequently do clinicians at your organization clean their hands before and after seeing a patient?
Christopher J. Cimikoski, M.D., M.S.
Stephen Weber, M.D., M.S.
Barbara M. Soulia, R.N., M.P.A., C.I.C.

CHAPTER 5 - Antibiotic Stewardship
Is antibiotic misuse promoting the spread of MDRs and unnecessarily increasing costs at your institution?
Paul Cooke, M.D.

CHAPTER 6 - Challenges on the Path to Higher Performance
Is your organization ready to implement the changes needed to control MDRs?
David M. Boman, Ph.D.
Deborah Najarian, R.N., PhD.

CHAPTER 7 - Call to Action
Why now? Why now?
Stephen Weber, M.D., M.S.
Barbara M. Soulia, R.N., M.P.A., C.I.C.

APPENDIX - Additional Readings

http://www.jcrinc.com/MDRO-Toolkit/
How do we control MDROs?

1. Hand Hygiene – WHO
Barriers

• Compliance often sub optimal
• Measurement and monitoring systems inadequate
• Technology can be a barrier
• Complexity of Healthcare
Successful Strategies

- Education
- Reinforcement
- Team work
- Culture
Limiting the Approach to Isolation

Horizontal vs. Vertical Approach

Standard precautions vs. isolation

All patients vs. targeted MDRO’s only

Patient satisfaction vs. protection
Stewardship

The ABC’S of AS:
Awareness, Assessment and Activities
Behavior
Collaboration
Antimicrobial Stewardship (AS) is a coordinated program that:

- Promotes the appropriate use of antimicrobials (including antibiotics)
- Improves patient outcomes
- Reduces microbial resistance
- Decreases the spread of infections caused by multidrug-resistant organisms
What does the word “Stewardship” mean?

• An ethically-driven responsibility for protecting and developing one's limited resources.
• A steward must provide the necessary leadership to establish the rules by which all stakeholders behave in ways that reflect the interests of both public and private sectors.
• Stewards must ensure corrective action when behavior by stakeholders becomes a potentially harmful to the population served.
• Stewardship's main goal is to help the population being served achieve positive outcomes while carefully managing the limited resources available.
Stewardship Goals

• Prevent or slow emergence of ABX resistance
• Optimize selection, dose, duration of Treatment
• Reduce adverse drug events
• Reduce secondary infection (e.g., CDI, MDROs)
• Reduce morbidity and mortality
• Reduce length of stay
• Reduce health care expenditure
The Big Picture

- Pharmacy
- IP
- Prevention
- ID
- Medical Staff
- Micro
Why AS?

- Multiply Drug Resistant Organisms (MDROs) cause a significant proportion of serious healthcare-associated infections and pose a serious risk to patient safety.
- Regulatory, accrediting agencies and legislative bodies continue to make MDROs a priority.
- Integrated, multidisciplinary ASPs are crucial to promoting the prudent use of antimicrobials.
The idea that penicillin and the subsequent “miracle drugs” were the end of any threat from infection led to increased use, overuse, and abuse – flooding the environment with antibiotics and POTENTIATING RESISTANCE.
Since the 1960’s there have been increasingly frequent reports of antibiotic resistant bacteria in hospitalized patients (and consequently in long-term care).
Health and Human Services (HHS) Action Plan

C difficile goals:

1. Improve Antimicrobial Stewardship

2. Improve environmental contamination
Reducing Central Line-Associated Bloodstream Infections

AIM FOR ZERO
Eliminating HAIss

A = Antimicrobial Stewardship
I = Insertion Bundle Practices
M = Maintenance Bundle Practices including timely removal
2 Approaches to AS

1. Limiting Prescriptions

1. Proactive interventions
Techniques

- Formulary restrictions
- Order sets and treatment plans
- Clinical Guidelines
- Education
- Pharmacodynamic dose optimization
- Pharmacy driven IV to oral
- Computer assisted support
Assessment

Which best describes your organization?

1. We do not have an AS program
2. We have a program but IP is not involved
3. We are just starting a program
4. We have a well functioning program
## Assessment

<table>
<thead>
<tr>
<th>STAFF RESOURCE</th>
<th>Check if Available:</th>
</tr>
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<tbody>
<tr>
<td>Infectious disease–trained physician</td>
<td>□</td>
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<tr>
<td>Clinical pharmacist</td>
<td>□</td>
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<tr>
<td>Clinical microbiologist</td>
<td>□</td>
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<tr>
<td>Infection control representative</td>
<td>□</td>
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<tr>
<td>Hospital epidemiologist</td>
<td>□</td>
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<tr>
<td>Information technology</td>
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</table>

### STRATEGIES IN PLACE

<table>
<thead>
<tr>
<th>Prospective audit with intervention and feedback</th>
<th>□</th>
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</thead>
<tbody>
<tr>
<td>Education</td>
<td>□</td>
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<tr>
<td>Guidelines and clinical pathways</td>
<td>□</td>
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<tr>
<td>Antimicrobial cycling</td>
<td>□</td>
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<tr>
<td>Antimicrobial order forms</td>
<td>□</td>
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<tr>
<td>Formulary restriction and preauthorization</td>
<td>□</td>
</tr>
<tr>
<td>Combination therapy</td>
<td>□</td>
</tr>
<tr>
<td>Streamlining or de-escalation of therapy</td>
<td>□</td>
</tr>
<tr>
<td>Dose optimization</td>
<td>□</td>
</tr>
<tr>
<td>Parenteral to oral conversion</td>
<td>□</td>
</tr>
<tr>
<td>Health care information technology</td>
<td>□</td>
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</tbody>
</table>

## Assessment

<table>
<thead>
<tr>
<th>IP Assessment</th>
<th>Y</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>I am an active member of our AS team and activities</td>
<td></td>
<td></td>
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<tr>
<td>I understand the role of IP in AS</td>
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<tr>
<td>I am knowledgeable as it pertains to prophylactic SSI guidelines</td>
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<tr>
<td>When investigating HAIs, I do pay attention to antimicrobial therapy</td>
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<tr>
<td>I am comfortable asking a question of a provider if I am confused about rationale for antibiotic treatment or prophylaxis.</td>
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<tr>
<td>I believe IP should be a key stakeholder in AS efforts</td>
<td></td>
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<tr>
<td>I believe that I can improve my efforts to be involved in AS programs or efforts</td>
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</table>
Which Best Describes You?

1. I believe that I am integral to the AS program.

2. I believe that anything to do with antibiotics is best left to physicians or providers.

3. I believe that my primary responsibility is prevention of HAIs.

4. Both 1 and 3
Differences in NYS among IPs and their Relationship to ASP Programs

- Work with Surgical Prophylaxis Team
- No involvement
- Ad hoc member of P and T
- Full involvement in ASP program routine meetings with ASP Pharm and ID
- Informal Input - feedback to ID or provider as needed
- Susceptibility reporting
What are the Components of a High Functioning ASP Team?

• Established compelling need and goals for ASP
• Senior leadership support
• Effective local physician champion
• Adequate resources i.e. Pharmacy, Infection Preventionist (IP), Microbiology, Information Technology (IT)
• Primary objectives: optimize clinical outcomes and reduce adverse events, not reduce costs
• Good teamwork
• Agreed upon process and outcome measures
"To get to the next level in interprofessional patient care, pharmacists need to recognize the social and interpersonal aspects of medical decision making."
Conan MacDougall

"Antimicrobial stewardship is a new skill that IPs are learning"
Moody ICT today August 2013

"Get rid of the hierarchy"
Septimus ICT Today August 2013

A culture of “noninterference” in the antimicrobial prescribing practice of peers prevents intervention into prescribing of colleagues Charani, Clin Infect Dis. 2013 July 15; 57(2): 188–196
The Ideal Program

One Size Does Not fit all

What are the strengths And weaknesses of your program?
**Collaboration**

**Overarching Driver: Leadership and Culture**

<table>
<thead>
<tr>
<th>Secondary Driver</th>
<th>Key Change Concepts</th>
<th>Specific Change Ideas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Promote a culture of optimal antibiotic use within the facility</td>
<td>Engage administrative and clinical leadership to champion stewardship effort</td>
<td>1. Identify clinical providers as champions to be thought leaders about antibiotic stewardship.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Work with administrators to ensure that they understand the rationale and goals for stewardship programs and interventions so that they can provide support (financial and non-financial).</td>
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<tr>
<td></td>
<td></td>
<td>3. Engage a physician champion and core team to enhance the focus of antimicrobial stewardship into the current process of care.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4. Bring disciplines together to improve communication and collaboration about improving antibiotic use, including, as appropriate:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Infection preventionists;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hospitalists;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Intensivists;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emergency department physicians;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Microbiologists;</td>
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<tr>
<td></td>
<td></td>
<td>• Pharmacists;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Nurses; and</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Infectious disease experts.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5. Consider having the multidisciplinary group perform a gap analysis of antimicrobial use at the facility to identify priority areas for improvement.</td>
</tr>
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</table>

Key Collaborators

• Information Technology

• Electronic Health Record (EHR) and/or Automated Surveillance packages provide information, structure and support.
Advantages to Automated Technology

• Information on emerging trends in HAIs and MDROs
• Facilitate the management of antimicrobial utilization by allowing the AS Team to intervene on more patients receiving inadequate antimicrobial therapy and to achieve substantial time and cost savings for the hospital.
• Generate unit or area specific antibiograms for clinicians use when making decisions about empiric therapy
## Focused ASP Interventions

Evaluation and Research on Antimicrobial Stewardship’s Effect on *Clostridium difficile* (ERASE *C. difficile*) Project: 
*Toolkit for Reduction of Clostridium difficile Through Antimicrobial Stewardship*


### Summary of Tools and Resources

<table>
<thead>
<tr>
<th>Section</th>
<th>Question Addressed</th>
<th>Resources and Tools</th>
</tr>
</thead>
</table>
| 1. Is our organization ready for an ASP to reduce *C. difficile*? | 1.1. Do we have the appropriate ASP foundation on which to build? | Ø 1a RESOURCE: SHEA/IDSA/FDa Policy Statement: Policy Statement on Antimicrobial Stewardship by the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and the Pediatric Infectious Diseases Society (PIDS)  
Ø 1b RESOURCE: GNYHA/UHF Antimicrobial Stewardship Toolkit  
Ø 1c RESOURCE: Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship  
Ø 1d RESOURCE: Examples of State and Local Stewardship Programs  
Ø 1e TOOL: Assessment of Current ASP Elements  
Ø 1f TOOL: Common Evidence-Based Infection Prevention Measures |
| 1.2. What do we need to do before we begin to use our ASP to target *C. difficile*? | Ø 1g TOOL: Assessing Leadership Support  
Ø 1h TOOL: Stakeholder Analysis  
Ø 1i TOOL: Survey of Staff Attitudes Toward ASP and Current Practices  
Ø 1j RESOURCE: Antimicrobial Stewardship: Implementation Tools & Resources  
Ø 1k TOOL: Developing Business Case  
Ø 1l TOOL: Assessing Resource Needs  
Ø 1m TOOL: Potential Barriers to Implementing an ASP |
| 2. How do we determine which interventions for reducing *C. difficile* to implement? | 2.1. What is the institutional risk assessment approach and how can it help us? | Ø 2a RESOURCE: Institutional Risk Assessment Approach to Selecting Stewardship Interventions  
Ø 2b RESOURCE: A Comparison of Antibiotic Data Sources  
Ø 2c RESOURCE: Possible Methods for Evaluating Antibiotic Use |
| 2.2. How do we conduct a time-limited internal case-control study for *C. difficile*? What are some of the challenges? | Ø 2d RESOURCE: Does Choice of Control Group Affect the Association of Antibiotics With *Clostridium difficile*-Associated Diarrhea?  
Ø 2e RESOURCE: Sample Tracking and Summary Forms for Case-Control Study (can be used to organize your case-control comparisons and summarize results and potential antibiotic targets) |
| 2.3. What methods can we use to review the use of potential target antibiotics for intervention activities? | Ø 2f RESOURCE: A Comparison of Potential Antimicrobial Stewardship Interventions  
Ø 2g RESOURCE: A Review of Antimicrobial Stewardship Interventions With Suggested Process/Monitoring, Antibiotic Use, and Additional Measures of Impact  
Ø 2h RESOURCE: Specific Intervention Examples From ERASE *C. difficile* Project |
| 2.4. What factors do we need to consider in choosing interventions? |
Enhancing the role of the IP

Back to the beginning:

Stewardship's main goal is to help the population being served achieve positive outcomes while carefully managing the limited resources available.
Case Scenario

A line tip was cultured after removal of a central line. The patient’s blood cultures are negative.

The line culture notes less than 200 CFU’s of Coag. negative staph.

The residents notes “Will Start vancomycin for suspected line sepsis with MRSA”
You would

1. Do nothing- the senior resident or attending will pick this up.

2. Communicate to ID doctor or pharmacist.

3. Initiate a conversation with the resident.
<table>
<thead>
<tr>
<th>Get Smart Principles</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accurately identify patients who need antibiotic therapy</td>
<td>Obtain 2 blood cultures for evaluation of late-onset sepsis before starting antibiotics</td>
</tr>
<tr>
<td>Use local and regional antibiograms</td>
<td>Avoid use of meropenem for empiric treatment of suspected late-onset sepsis if rates of multidrug-resistant gram-negative bacilli are low</td>
</tr>
<tr>
<td>Avoid therapy with overlapping activity</td>
<td>Avoid simultaneous use of metronidazole and meropenem to treat necrotizing enterocolitis</td>
</tr>
<tr>
<td>Give the right dose and interval of drug</td>
<td>Target vancomycin trough to 15-20 mg/L to treat pneumonia caused by MRSA</td>
</tr>
<tr>
<td>Review culture results and adjust antibiotics</td>
<td>Review microbiology results at transitions of care (eg, sign out, weekend cross-coverage) and narrow antibiotic coverage promptly</td>
</tr>
<tr>
<td>Monitor for toxicity and adjust therapy accordingly</td>
<td>Adjust antibiotic dose for patients with deteriorating renal function</td>
</tr>
<tr>
<td>Stop therapy promptly if indicated by culture results</td>
<td>Discontinue antibiotics after 48 hours if blood cultures are negative and ongoing infection is not suspected</td>
</tr>
</tbody>
</table>
How can I Increase my Value?

Basic Level

• Understanding of the program and your role
• Hand Hygiene, Isolation, MDRO’S
• Observing issues during HAI review

Level 2

• Collaboratives (i.e. C difficile)
• Report at meetings
• Work on standard guidelines and order sets
• Start the conversation
• Use your leadership skills
The Objective

Improve **teamwork** and communication....ultimately, creating a **culture of safety**..... It starts with conversation.