Antimicrobial Stewardship Update

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Assistant Director Internal Medicine Residency Program
Florida Hospital Orlando
• No conflicts of Interest to report.
Antimicrobial Stewardship Goal

“*To improve patient safety through the optimization of antibiotic use*’
Antimicrobial Stewardship Goal

“To improve *patient safety* through the optimization of antibiotic use’
Outline

– 1) Why is Antimicrobial Stewardship Important?

– 2) Evidence supporting the implementation of Antimicrobial Stewardship

– 3) Antimicrobial Stewardship at Florida Hospital
1) Why is Antimicrobial Stewardship Important?
Patient at onset of Penicillin Therapy. Extensive cellulitis and edema may be noted...patient moribund.
Mortality rates associated with erysipelas before and after the introduction of antimicrobial agents.

“... I remember when the first cases of lethal blood infections were treated with antibiotics in Boston in 1937... Here were moribund patients, improving within a matter of hours...

...we became convinced, overnight, that nothing lay beyond reach for the future. Medicine was off and running...”
Increase in Antibiotic Resistance

- MRSA
- VRE
- FQRP

Percent Resistance:

- 0%
- 10%
- 20%
- 30%
- 40%
- 50%
- 60%

Years:
- 1981
- 1985
- 1989
- 1993
- 1997
- 2001
Emergence of New Delhi Metallo-beta-lactamase 1 (NDM 1)

Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study

Emergence of New Delhi Metallo-beta-lactamase 1 (NDM 1)

Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study


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<tr>
<th>Antibiotic</th>
<th>MIC (µg/mL)</th>
<th>Resistance</th>
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<tr>
<td>Imipenem</td>
<td>32; 128</td>
<td>Resistant</td>
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<td>Meropenem</td>
<td>32; 32</td>
<td>Resistant</td>
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<tr>
<td>Piperacillin-tazobactam</td>
<td>&gt;64; &gt;64</td>
<td>Resistant</td>
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<td>Cefotaxime</td>
<td>&gt;256; &gt;256</td>
<td>Resistant</td>
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<td>Cefazidime</td>
<td>&gt;256; &gt;256</td>
<td>Resistant</td>
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<td>Cefpirome</td>
<td>&gt;64; &gt;64</td>
<td>Resistant</td>
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<td>Ciprofloxacin</td>
<td>&gt;8; &gt;8</td>
<td>Resistant</td>
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<td>Gentamicin</td>
<td>&gt;32; &gt;32</td>
<td>Resistant</td>
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<td>Tobramycin</td>
<td>&gt;32; &gt;32</td>
<td>Resistant</td>
</tr>
<tr>
<td>Amikacin</td>
<td>&gt;64; &gt;64</td>
<td>Resistant</td>
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Lancet Infect Dis 2010;10: 597-602
Dr. Fred Tenover
Director Antimicrobial Resistance
Center for Disease Control (CDC)
“…The last decade has seen the inexorable proliferation of a host of resistant bacteria, or bad bugs…What do you do when you are faced with a serous infection, and you get a lab report back and every single drug is listed as resistant?... This is a major blooming health crisis.”
How did we get to this point?

TIME

Today

New Antibiotics

Resistance

TIME
Propranolol
Propanolol

Penicillin
Propanolol

Penicillin
Evolution of *Staphylococcus Aureus* Resistance

Adapted from Nature Reviews Drug Discovery 6, 1 (January 2007)
Evolution of *Staphylococcus Aureus* Resistance

Adapted from Nature Reviews Drug Discovery 6, 1 (January 2007)
Evolution of *Staphylococcus Aureus* Resistance

- **Penicillin**
- **Vancomycin/Methicillin**
- **MRSA**
- **PRSA**

1942 - 1950s
1947 - 1961

Adapted from Nature Reviews Drug Discovery 6, 1 (January 2007)
Evolution of *Staphylococcus Aureus* Resistance

- **Penicillin**: 1942
- **Vancomycin/Methicillin**: 1950s
- **Cephalosporins**: 1970s
- **MRSA**: 1961
- **PRSA**: 1947
- **CRSA**: 1982

Adapted from Nature Reviews Drug Discovery 6, 1 (January 2007)
Evolution of *Staphylococcus Aureus* Resistance

Adapted from *Nature Reviews Drug Discovery* 6, 1 (January 2007)
Evolution of *Staphylococcus Aureus* Resistance

Adapted from Nature Reviews Drug Discovery 6, 1 (January 2007)
Total Number of New Antibacterial Agents

- 1983-1987: 10
- 1988-1992: 8
- 1993-1997: 4
- 1998-2002: 2
- 2003-2007: 1
- 2008-2012: 0

ANTIBIOTIC DEVELOPMENT IS DWINDLING

Source: The Epidemic of Antibiotic-Resistant Infections, CID 2008:46 (15 January)
Are we using existing antibiotics appropriately?

Are we using existing antibiotics appropriately?

50% of all antibiotic use is inappropriate

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America
Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

Timothy H. Dellit,1 Robert C. Owens,2 John E. McGowan, Jr.,3 Dale N. Gerding,4 Robert A. Weinstein,5
John P. Burke,6 W. Charles Huskins,7 David L. Paterson,8 Neil O. Fishman,9 Christopher F. Carpenter,10 P. J. Brennan,9
Marianne Billeter,11 and Thomas M. Hooton12

1Harborview Medical Center and the University of Washington, Seattle; 2Maine Medical Center, Portland; 3Emory University, Atlanta, Georgia;
4Hines Veterans Affairs Hospital and Loyola University Stritch School of Medicine, Hines, and 5Stroger (Cook County) Hospital and Rush
University Medical Center, Chicago, Illinois; 6University of Utah, Salt Lake City; 7Mayo Clinic College of Medicine, Rochester, Minnesota;
8University of Pittsburgh Medical Center, Pittsburgh, and 9University of Pennsylvania, Philadelphia, Pennsylvania; 10William Beaumont Hospital,
Royal Oak, Michigan; 11Ochsner Health System, New Orleans, Louisiana; and 12University of Miami, Miami, Florida
Antimicrobial Stewardship Program

• “The primary goal of antimicrobial stewardship is to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including toxicity, the selection of pathogenic organisms (such as \textit{Clostridium difficile}), and the emergence of resistance”

Dellit et al. CID 2007:44 (15 January)
IDSA Guidelines for Antimicrobial Stewardship

• Defined the ideal structure of AS Programs.
• Recommended specific practices to achieve the goals of AS Programs.

Dellit et al. CID 2007:44 (15 January)
• CMS
• California
II. Evidence supporting the implementation of an Antimicrobial Stewardship Program
Impact of Antimicrobial Stewardship

- Clostridium Difficile Infections
- Bacterial Resistance
- HealthCare associated Outcomes
Impact of Antimicrobial Stewardship

- Clostridium Difficile Infections
- Bacterial Resistance
- HealthCare associated Outcomes
- Effect of antimicrobials on the Microbial Ecology of Humans
1) Antimicrobial Stewardship Decreases the incidence of Clostridium Difficile Infections (CDI)
Incidence and mortality of CDI are increasing in the US


Estimated burden of healthcare-associated CDI

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

- Clearly association between antibiotics and CDI

Targeted antibiotic consumption and nosocomial C. difficile disease

Tertiary care hospital; Quebec, 2003-2006

Tertiary care hospital; Quebec, 2003-2006

Targeted antibiotic consumption and nosocomial C. difficile disease

Targeted antibiotic consumption and nosocomial C. difficile disease

CDI studies
Antimicrobial Stewardship and Bacterial Resistance
Distribution of klebsiella producing carbapenemase in the US
Mortality is increased with carbapenem resistant Klebsiella pneumoniae (CRKP)

OR 3.71 (1.97-7.01) OR 4.5 (2.16-9.35)

*p<0.001*

Pseudomonas aeruginosa susceptibilities before and after implementation of antibiotic restrictions

P<0.01 for all increases

Pseudomonas aeruginosa susceptibilities before and after implementation of antibiotic restrictions

$P \leq 0.01$ for all increases
Impact of Improving Antibiotic Use on Rates of Resistant *Enterobacteriaceae*

Antimicrobial Stewardship Improves patient safety and decreases health care expenditures
Better Clinical outcomes with antimicrobial management program (AMP) vs usual practice (UP)

Hospital and Societal Costs of Antimicrobial-Resistant Infections in a Chicago Teaching Hospital: Implications for Antibiotic Stewardship

- 1400 patients – Antimicrobial resistance : 13.5%
  - US$ 10,688,004
  - Decrease in resistance to 10%
    - Savings of US$ 2.7 million

Impact of Antibiotics in The Microbial Ecology of Humans
The Human Microbiome
Human Genome Project (1990-2003)
The Human Microbiome Project

Diversity and Association between the Microbiome and Human Diseases

Microbiome A
Healthy

Microbiome B
- Inflammatory Bowel Disease
- Cancer

Microbiome C
Obesity
Diabetes
Effect of Antibiotics on the Composition of the Human Microbiome

Ciprofloxacin

Effect of Antibiotics on the Composition of the Human Microbiome

Ciprofloxacin

Effect of Antibiotics on the Composition of the Human Microbiome

Ciprofloxacin

10 months

Impact of Antimicrobial Stewardship

- Clostridium Difficile Infections
- Bacterial Resistance
- HealthCare associated Outcomes
- Effect of antimicrobials on the Microbial Ecology of Humans
III. Antimicrobial Stewardship at FH
Vision

Antimicrobial Stewardship Program

Research
Clinical Practices
Education

## Antimicrobial Stewardship Practices

<table>
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<tr>
<th>Core Strategies</th>
<th>Other</th>
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<tbody>
<tr>
<td>• Prospective audit with intervention and feedback.</td>
<td>• Education.</td>
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<td>• Formulary restriction and preauthorization.</td>
<td>• Antimicrobial Guidelines.</td>
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<td></td>
<td>• Clinical pathways and decision support systems</td>
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</table>

Dellit et al. CID 2007:44 (15 January)
Real Time Chart Audit and Feedback (AI)

**INTERVENTIONS**

- Streamlining (AI)
- Optimal Dosing (AI)
- IV to PO switch (AI)

Dellit et al. CID 2007:44 (15 January)
Cost-Effectiveness of rounding pharmacist in an internal medicine Teaching Service

Study:

- From August to October 2011
- Pharmacist rounded with IM team and performed daily review of antimicrobials

Kristina Jose. ACP Regional Meeting Florida Chapter. Fall 2011. Oral Presentation
P. Bagla. IDSA National Meeting Scientific October 2012. Poster. Accepted
Cost-Effectiveness of rounding pharmacist in an internal medicine Teaching Service

Study:
- From August to October 2011
- Pharmacist rounded with IM team and performed daily review of antimicrobials

• Results:
  • 85 recommendations performed
  • US$ 8,000.00 savings during the study period (drug cost)

Kristina Jose. ACP Regional Meeting Florida Chapter. Fall 2011. Oral Presentation
P. Bagla. IDSA National Meeting Scientific October 2012. Poster. Accepted
Antimicrobial Stewardship in a Decentralized Pharmacy Practice Model at a Large Community-Teaching Hospital

Kristie Zappas, Pharm.D., Sarah Brooks, Pharm.D., Rania El-Lababidi, Pharm.D., BCPS (AQ-ID), AAHPV

Background
- The Pyrexia Hospital (a large teaching hospital) in New York City experienced a significant increase in bloodstream infections (BSIs) due to antimicrobial resistance.
- The American Society of Health-System Pharmacists (ASHP) recommended implementing antimicrobial stewardship programs to address this issue.

Objective
To evaluate the outcomes of implementing an antimicrobial stewardship program with a decentralized pharmacy practice model at a large community-teaching hospital.

Methods
- This study was conducted at Pyrexia Hospital, a large community-teaching hospital in New York City.
- The study included all antimicrobial interventions from February 1, 2012, to December 31, 2012.
- Antimicrobial stewardship program was implemented by pharmacists working in the hospital's central pharmacy.
- The program included the following interventions:
  - Review of antimicrobial prescriptions
  - Education and training
  - Formulary management

Results
- The program led to a significant reduction in the number of BSIs.
- The number of antimicrobial interventions was increased.

Conclusion and Future Directions
- The results of this study are preliminary and suggest that the decentralized pharmacy practice model is effective in improving antimicrobial stewardship.
- Future research should focus on the long-term impact of the program.

Disclosure
- The authors report no conflicts of interest related to the study.

References
## Monitoring of Process and Outcomes Measures

### Florida Hospital Antimicrobial Stewardship Program Scorecard - System

**Goals:** To establish mechanisms to effectively assess & continuously improve antimicrobial therapy across the hospital. Implementation & utilization of computer-based surveillance tools to track interventions, resistance patterns, drug use and adverse drug events. Antimicrobial formulary improve awareness & knowledge of antimicrobial stewardship through educational processes across the organizations.

<table>
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<tr>
<th>Objective</th>
<th>Measure</th>
<th>Goal</th>
<th>January</th>
<th>February</th>
<th>March</th>
<th>April</th>
<th>May</th>
<th>June</th>
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<th>November</th>
<th>December</th>
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<td>Implement a program for antimicrobial stewardship recommendations</td>
<td>Number of recommendations</td>
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<td>Optimize antimicrobial therapy</td>
<td>(LINEZOLID) IV : PO percentage</td>
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<td>Frequency of inappropriate antimicrobial use - drug/bug mismatches</td>
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<td>Decrease antibiotic costs (utilization)</td>
<td>Antimicrobial costs /APDs</td>
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<td>DDD/1000 patient days</td>
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<td>Reduce incidence of unintended consequences related to antibiotic therapy</td>
<td>VRE infections</td>
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<td>C. Diff infections</td>
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<td>KPC/ESBL infections</td>
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<td>Other infectious indices tracked</td>
<td>MRSA infections</td>
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<td>MDR E. coli</td>
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Dellit et al. CID 2007:44 (15 January)
Antimicrobial Stewardship
Multidisciplinary Approach

Microbiology

Information Systems
Thank you,

victor.herrera.md@flhosp.org
Association of Vancomycin use with resistance

Kim NJ et al. JID 1999;179:163