Antimicrobial Stewardship: An Important Piece of the Puzzle To Improving Patient Outcomes and Reducing Healthcare-Associated Infections

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Division of Geographic Medicine and Infectious Disease
Objectives

At the end of this presentation attendees will be able to:

- Define antimicrobial stewardship and describe its importance in healthcare systems
- Describe specific examples of the two most commonly used methods of antimicrobial stewardship
- Describe how implementation of institutional guidelines may improve antimicrobial use and patient outcomes
Risking Threat of Infections
Unfazed by Antibiotics

A minor-league pitcher in his younger days, Richard Armbruster kept playing baseball recreationally into his 70s, until his right hip started bothering him. Last February he went to a St. Louis hospital for what was to be a routine hip replacement.

By late March, Mr. Armbruster, then 78, was dead. After a series of postsurgical complications, the final blow was a bloodstream infection that sent him into shock and resisted treatment with antibiotics.

"Never in my wildest dreams did I think my dad would walk in for a hip replacement and be dead two months later," said Amy Fix, one of his daughters.
Mr C.

- Mr C is a 35 year old healthy man who comes to GMA complaining of 7 days of a runny nose, frontal sinus congestion, sore throat, and myalgias.
- His vital signs are stable and he is afebrile. His exam is notable for mild tonsillar erythema and some generalized sinus tenderness.
- He states that he is really busy working for a big financial services company and has 2 young kids at home (who both have colds). His symptoms have been going on for a week and he wants a prescription so he get better fast.
Antimicrobial Therapy

Appropriate initial antibiotic while improving patient outcomes and healthcare

Unnecessary antibiotics and adverse patient outcomes and increased cost

A Balancing Act
Antimicrobial Prescribing

Empiric

- Initial administration of a broad-spectrum antibiotic regimen that attempts to improve outcomes and minimize resistance.

Defined or Targeted

- Modification of antimicrobial therapy once the cause of infection is identified. Therapy may also be discontinued if the diagnosis of infection becomes unlikely.¹

- Focus on de-escalation of antibiotic therapy with the goal of minimizing resistance and toxicity, and improving cost-effectiveness.²,³

Bad Bugs: No ESKAPE

- Enterococcus
- S. aureus
- Klebsiella spp.
- Acinetobacter
- P. aeruginosa
- Enterobacter spp.

Mortality Associated With Initial Inadequate Therapy in Critically III Patients With VAP or Septicemia, Severe Sepsis, or Community-Acquired Bloodstream Infection in Critically III Patients

Luna (1997) – VAP\(^1\)
- Initial Adequate Therapy
- Initial Inadequate Therapy
- 15.6% 37% 60.8%
- 38% 91%

Rello (1997) – VAP\(^2\)
- 28.4% 39% 61.9%

Kollef (1998) – VAP\(^3\)
- Ibrahim (2000) – Septicemia, severe sepsis, or bloodstream infection\(^4\)
- Harbarth (2003) – Severe sepsis\(^5\)
- Vallés (2003) – Bloodstream infection\(^6\)

\(^1\) Crude (overall) mortality.
\(^2\) Infection-related mortality.

Efforts to Improve Antimicrobial Prescribing and Control Resistance

- Develop New Drugs and Vaccines
- Improved Diagnostics
- Reduce Resistance Reservoirs
- Antimicrobial Stewardship
- Infection Control
- Research & Public Policy
- Education
Efforts to Control Resistance

- Develop New Drugs and Vaccines
- Improved Diagnostics
- Antimicrobial Stewardship
- Infection Control
- Research & Public Policy
- Education
- Reduce Resistance Reservoirs
What is Antimicrobial Stewardship

- Antimicrobial stewardship involves the *optimal selection, dose and duration* of an antibiotic resulting in the cure or prevention of infection with minimal unintended consequences to the patient including emergence of resistance, adverse drug events, and cost.

  Ultimate goal is improved patient care and healthcare outcomes

Dellit TH, et al. CID 2007;44:159-77,
ASHP Statement on the Pharmacist’s Role in Antimicrobial Stewardship and Infection Prevention and Control

Promoting optimal antimicrobial use
Reducing the transmission of infections
What Every Health Care Executive Should Know: The Cost of Antimicrobial Resistance

- Antimicrobial Resistance: Patients and hospitals in Peril
- The Clinical Consequences of Antimicrobial Resistance
- Transmission Control to Prevent the Spread of MDROs in Health Care Facilities
- Antimicrobial Stewardship
Critical Aspects of Antimicrobial Stewardship Programs

- Must gain support and collaboration
- Hospital administration
  - Medical/surgical staff
  - Local providers
- Must coordinate activities
  - Infection control
  - Pharmacy and Therapeutics
- ID and PharmD should be compensated, have authority, and clear expectations from hospital administration
- Should be under the umbrella of quality and patient safety

Dellit TH, et al. CID 2007;44:159-77, 
Building The Team

Antimicrobial Control

Infectious Diseases Specialists
Infection Control
Microbiology
Pulmonary/Intensivist
Nursing
OR Personnel
Surgical Infection Control Experts/Surgeons
Clinical Pharmacists
Administration
Antimicrobial Stewardship Strategies

- Prospective audit with intervention and feedback
- Formulary restriction and preauthorization

Supplemental Strategies
- Education, guidelines, clinical pathways
- Dose optimization via PK-PD
- De-escalation/Streamlining
- Antimicrobial order forms/order sets if CPOE
- IV-PO switch
- Computerized decision support
- Others

Dellit TH, et al. CID 2007;44:159-77
Antimicrobial Stewardship at Tufts Medical Center: ?? years and Going Strong

- Improve patient outcomes
- Slow antimicrobial resistance
- Ensure appropriate empirical antimicrobial therapy
  - Antimicrobial choice, dosage, route, and duration
- Educate providers on the importance of prudent antimicrobial prescribing
- Reduce medication errors related to antimicrobials
- Reduce cost
  - Duration of treatment
  - IV to PO
  - Antimicrobial de-escalation and stopping unneeded treatment
- 2 part time ID physicians, 1 full time ID PharmD
Table 1. Characteristics of Survey Participants

<table>
<thead>
<tr>
<th>Practice Area</th>
<th>Number</th>
<th>Percent</th>
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<tbody>
<tr>
<td>Pharmacy Director</td>
<td>21</td>
<td>60.0%</td>
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<tr>
<td>Clinical Pharmacist/Coordinator/Other</td>
<td>11</td>
<td>31.4%</td>
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<tr>
<td>ID Pharmacist</td>
<td>3</td>
<td>8.6%</td>
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<table>
<thead>
<tr>
<th>Antimicrobial % of Total Pharmacy Drug Budget</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10%</td>
<td>7</td>
<td>20.0%</td>
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<tr>
<td>10-15%</td>
<td>13</td>
<td>37.1%</td>
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<tr>
<td>16-25%</td>
<td>9</td>
<td>25.7%</td>
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<td>&gt;26%</td>
<td>1</td>
<td>2.9%</td>
</tr>
<tr>
<td>Unknown</td>
<td>5</td>
<td>14.3%</td>
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<table>
<thead>
<tr>
<th>Healthcare System Type</th>
<th>Number</th>
<th>Percent</th>
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<tbody>
<tr>
<td>Not a teaching hospital</td>
<td>17</td>
<td>48.6%</td>
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<tr>
<td>University (affiliated) hospital</td>
<td>7</td>
<td>20.0%</td>
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<tr>
<td>Rural/critical access</td>
<td>6</td>
<td>17.1%</td>
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<tr>
<td>Non-university teaching hospital</td>
<td>5</td>
<td>14.3%</td>
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<tr>
<td>Acute/rehab</td>
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<td>5.7%</td>
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<table>
<thead>
<tr>
<th>Antimicrobial Management Pharmacist</th>
<th>Number</th>
<th>Percent</th>
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<tbody>
<tr>
<td>Yes</td>
<td>6</td>
<td>17.1%</td>
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<tr>
<td>No</td>
<td>29</td>
<td>82.9%</td>
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<table>
<thead>
<tr>
<th>Existence of ASP</th>
<th>Number</th>
<th>Percent</th>
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<tr>
<td>Yes</td>
<td>15</td>
<td>42.9%</td>
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<tr>
<td>No</td>
<td>20</td>
<td>57.1%</td>
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<table>
<thead>
<tr>
<th>Antibiogram</th>
<th>Number</th>
<th>Percent</th>
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<td>94.3%</td>
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<tr>
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<td>5.7%</td>
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<table>
<thead>
<tr>
<th>Number of Licensed Beds</th>
<th>Number</th>
<th>Percent</th>
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<td>101-300</td>
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<td>301-500</td>
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<td>20.0%</td>
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<tr>
<td>&gt;500</td>
<td>1</td>
<td>2.9%</td>
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</table>

<table>
<thead>
<tr>
<th>Number of Annual Admissions</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2,500</td>
<td>5</td>
<td>14.3%</td>
</tr>
<tr>
<td>2,501-5,000</td>
<td>6</td>
<td>17.1%</td>
</tr>
<tr>
<td>5,001-10,000</td>
<td>11</td>
<td>31.4%</td>
</tr>
<tr>
<td>&gt;10,000</td>
<td>6</td>
<td>17.1%</td>
</tr>
<tr>
<td>Unknown</td>
<td>7</td>
<td>20.0%</td>
</tr>
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<table>
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<tr>
<th>ID Consult Service</th>
<th>Number</th>
<th>Percent</th>
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<tr>
<td>Yes</td>
<td>28</td>
<td>80.0%</td>
</tr>
<tr>
<td>No</td>
<td>7</td>
<td>20.0%</td>
</tr>
</tbody>
</table>

Stewardship Strategies: Prospective Audit & Feedback

- Design:
  - Prospective evaluation of antimicrobial management program implemented
  - Originally started in 1991 to minimize inappropriate use of 3rd-generation cephalosporins, broadened to audit use of other antimicrobials
  - Time period: 7 years
  - ¼-time ID physician, full-time ID PharmD
- Assessed incidence of *C. difficile*, resistant Enterobacteriaceae, VRE, and MRSA in NNIS system hospitals of comparable size

NNIS = National Nosocomial Infections Surveillance system

Stewardship Strategies: Review & Feedback Example

MRSA & VRE rates before and after implementation of Antimicrobial Management Program vs. rates in NNIS system hospitals


Also: Reduction in CDAD (p=0.002)
Antimicrobial Stewardship Care Bundle

- Prospective audit system
  - Stewardship program
- Outcomes
  - Reason for treatment, cultures, empirical, and de-escalation
  - LOS, mortality, and % interventions accepted

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Control Phase</th>
<th>Intervention Phase</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Documented indication for antibiotic therapy</td>
<td>76/80 (95)</td>
<td>80/80 (100)</td>
<td>0.12</td>
</tr>
<tr>
<td>Appropriate cultures collected</td>
<td>70/80 (87)</td>
<td>76/80 (95)</td>
<td>0.09</td>
</tr>
<tr>
<td>Appropriate empirical therapy</td>
<td>55/80 (69)</td>
<td>65/80 (81)</td>
<td>0.06</td>
</tr>
<tr>
<td>Appropriate deescalation²</td>
<td>41/57 (72)</td>
<td>52/58 (90)</td>
<td>0.01</td>
</tr>
<tr>
<td>All indicators concurrently</td>
<td>13/80 (16)</td>
<td>43/80 (54)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**IV to Oral interchange**

Antimicrobial Stewardship in LTACs

- Eight public LTACs in Montreal
- Two prescriber groups (N=36)
- Educational intervention (twice, Q4 months)
  - Antimicrobial guide
  - Prescribing profiles (appropriate or inappropriate)
  - Targeted infections: UTI, LRTI, SSSI, and sepsis
- Inappropriate prescribing decreased 20% vs. 5%
- Prescribers less likely to prescribe inappropriate therapy

Computer Surveillance and Decision Support in Antimicrobial Stewardship

- Sentri7
- SafetySurveillor
- TheraDoc
- Computerized physician order entry
- Benchmarking and local antimicrobials point prevalence surveys (state may consider doing this)

Decision Support for Antimicrobial Stewardship
Antimicrobial Management Team Question of the Week

Doron, Shira
To: Tufts MC Antimicrobial Management Team
Cc:

Q: Three days ago, I admitted a 72 year old patient from a long-term acute care facility to the MICU with ventilator associated pneumonia (VAP). The patient had recently been treated with a cephalosporin for a complicated UTI and I was concerned about infection due to an Extended Spectrum Beta-lactamase (ESBL) producing organism, so I prescribed meropenem, as well as cipro and vancomycin. The sputum culture on admission to the MICU did indeed grow an ESBL Klebsiella pneumoniae. The isolate was susceptible to ertapenem (MIC<0.5), meropenem (MIC<1), and amikacin (MIC<2). Since the antibiotics prescribed using the VAP order form are about to expire I want to renew the patient’s antibiotics to finish an 8 day course. Should I continue meropenem? Is there a difference in the clinical efficacy between ertapenem and meropenem for the treatment of pneumonia?

A: Ertapenem has excellent penetration into the lung tissue and the epithelial lining fluid and is a good choice for treatment of pneumonia caused by Gram positive or Gram negative pathogens. In this case, there would be no reason to continue treatment with meropenem. At Tufts, one of the most common causes of late-onset VAP is Pseudomonas aeruginosa, against which ertapenem does not provide sufficient *in vitro* activity, making it a poor choice for empiric therapy (before you know the culture results). However, in this case, since you know the organism is Klebsiella, ertapenem would be the most appropriate. We always recommend de-escalating antibiotics, since the spectrum of ertapenem is narrower than meropenem, we would recommend switching to ertapenem for the remainder of the treatment course. In addition, once the organism is identified there is no need for double coverage with cipro, and the vancomycin can be safely discontinued as well.

The recommendations in this e-mail are based on published guidelines and the clinical expertise of our staff and may not apply to every patient. Please use clinical judgment when applying these concepts. The Antimicrobial Management Team serves adult patients at Tufts Medical Center. Some of the concepts presented here may not be appropriate for pediatric patients. Please do not hit "reply all" when responding to this message. To view previous AMT questions of the week, please see http://intranet.nemc.org/nmPharm2/Guidelines_Forms-ID.htm.

The Antimicrobial Management Team
Shira Doron, MD  Kenneth Lawrence, PharmD  Lisa Davidson, MD
# Antimicrobial Order Forms

## DATE: TIME: (24-hour clock)

<table>
<thead>
<tr>
<th>Patient Allergies</th>
<th>Weight (kg)</th>
<th>Status</th>
<th>Coordination</th>
<th>Order Date (MM/ DD)</th>
</tr>
</thead>
</table>

### MEDICATION ORDERS ONLY

**INCLUSION OF MEDICATIONS**

- Patients in the hospital for more than 3 days and who do NOT have HSIs for multi-drug resistant organisms (see Table 1 at right) should receive the following medications in the AMT approval required:
  - Gentamicin 1 g IV Q8h
  - Meropenem 2 g IV Q6h
  - Vancomycin 10 mg/kg IV Q6h

- Patients in the hospital for 5 days or longer who have HSIs for multi-drug resistant organisms (see Table 1 at right) should receive the following medications (no AMT approval required for 72 hours):
  - Piperacillin/tazobactam 4.5 g IV Q6h x 72 hours OR
  - Piperacillin/tazobactam 4.5 g IV Q6h x 72 hours OR
  - Ceftazidime 1 g IV Q8h x 72 hours OR

### PHYSICIAN'S ORDERS

**EXCLUSION OF MEDICATION ORDERS**

<table>
<thead>
<tr>
<th>TABLE 1: Risk Factors for Multi-Drug Resistant Organisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Hospitalized for more than 3 days in the preceding 30 days</td>
</tr>
<tr>
<td>- Residence in a nursing home or extended care facility</td>
</tr>
<tr>
<td>- Recipient of home infusion therapy</td>
</tr>
<tr>
<td>- Chronic dialysis within the preceding 30 days</td>
</tr>
<tr>
<td>- Recipient of home wound care</td>
</tr>
<tr>
<td>- Family member with multi-drug resistant pathogen</td>
</tr>
<tr>
<td>- Antimicrobial therapy in the preceding 30 days</td>
</tr>
<tr>
<td>- Immune suppression disease or therapy</td>
</tr>
</tbody>
</table>

### DRUG 1: Piperacillin/Tazobactam 4.5 g IV Q6h x 72 hours OR

- If patient has received a treatment course with a penicillin or cephalosporin in the past 14 days:
  - Meropenem 2 g IV Q6h x 72 hours OR
  - Vancomycin 10 mg/kg IV Q6h x 72 hours OR

- If patient has a history of methicillin resistance:
  - Methicillin 2 g IV Q6h x 72 hours OR
  - Vancomycin 10 mg/kg IV Q6h x 72 hours OR

### DRUG 2: If the patient is INTUBATED

- Tobramycin 4 mg/kg IV loading dose, then
  - Tobramycin 4 mg/kg IV x 72 hours OR

**PLUG**

- If the patient is NOT intubated:
  - Ciprofloxacin 500 mg PO TID x 72 hours OR

- If the patient is NOT intubated or has already received vancomycin:
  - Vancomycin 10 mg/kg IV Q6h x 72 hours OR

### DRUG 3: If the patient is INTUBATED

- Levofloxacin 500 mg IV QID x 72 hours OR

**PLUG**

- If the patient is NOT intubated or has already received vancomycin:
  - Vancomycin 10 mg/kg IV Q6h x 72 hours OR

### Footnotes:

- ACI: Adj. dose for renal dysfunction. See Table/HMECC. Dosage Adjustment for Renal Failure patient or the Antibiotic Guidelines.
- See Antibiotic Guidelines for tobramycin dosing.
- Evidence suggests that broad-spectrum antibiotics are appropriate and may be clinically superior in patients with lesser TISS-28 scores.
- Vancomycin dosing for pneumococcal infection:
  - S. aureus: 15 mg/kg IV Q6h
  - MRSA: 10 mg/kg IV Q6h
  - Enterococcus: 15 mg/kg IV Q6h
  - S. pneumoniae: 15 mg/kg IV Q6h

## Appendix

- Oral Vancomycin: 750 mg every 8 hours
Benefits of a HAP Protocol at Tufts Medical Center

Impact of a HAP Protocol at Tufts Medical Center

Ms. T is a 70-year-old admitted for community acquired pneumonia and started on moxifloxacin.

- Cultures were not obtained on admission.
- She is afebrile by hospital day 3 with normal vital signs and is tolerating room air and a regular diet, so you decide to discharge her.
What Is the Appropriate Duration of Therapy for cIAI?

- Antimicrobial therapy of established infection should be limited to 4–7 days, unless it is difficult to achieve adequate source control.
- Bowel injuries due to penetrating, blunt, or iatrogenic trauma repaired within 12 h and any other intraoperative contamination of the operative field by enteric contents should be treated with antibiotics for ≤24 hours.

Lack of evidence of infections includes, being afebrile, have normal WBC, and tolerating an oral diet.
92% thought ASP was very or somewhat important
58% were sometimes confused about ASP procedures
96% reported a good or very good experience
84% reported a positive educational experience
66% reported a change in the drug prescribed due to AMT less than 40% of the time
23% said AMT prevented a medication error
43% stated that AMT reminded them to adjust for kidney function and 17% reminded them of patent’s allergies
Diagnostic and Pathogen Identification Techniques

- Biomarkers
  - Procalcitonin
  - CRP
- PNA FISH
- PCR
- E-test of patient samples

Bouza E, et al CID 2007;44:382-7
Measuring the Effectiveness of an Antimicrobial Stewardship Program

- Antimicrobial usage
  - Days of therapy
  - Appropriateness of treatment
- Antimicrobial cost
- Bacterial susceptibilities
- Patient outcomes
- Antimicrobial adverse events
- Acceptance of recommendations
- Prescribers surveys
## Microbiology of Abscess Material, Deep Tissue or Blood*

<table>
<thead>
<tr>
<th>Isolate</th>
<th>Abscess (n=77)</th>
<th>SSTI with Complications (n=73)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. aureus</em></td>
<td>52 (68)</td>
<td>45 (62)</td>
</tr>
<tr>
<td>MRSA</td>
<td>34 (44)</td>
<td>30 (41)</td>
</tr>
<tr>
<td>Streptococci</td>
<td>29 (38)</td>
<td>31 (42)</td>
</tr>
<tr>
<td><em>S. aureus</em> or Streptococcus</td>
<td>75 (97)</td>
<td>70 (96)</td>
</tr>
<tr>
<td><em>S. aureus</em> or Streptococcus only</td>
<td>59 (77)</td>
<td>52 (71)</td>
</tr>
<tr>
<td>Aerobic Gram negative bacteria</td>
<td>10 (13)</td>
<td>10 (14)</td>
</tr>
<tr>
<td>Anaerobes</td>
<td>13 (17)</td>
<td>16 (22)</td>
</tr>
</tbody>
</table>

* Data are No (%) of patients
# Antimicrobial Therapy

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Cellulitis (n=66)</th>
<th>Abscess (n=103)</th>
<th>SSTI with Complications (n=153)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient Antibiotics (at least 1 dose administered)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Vancomycin</td>
<td>52 (79)</td>
<td>75 (73)</td>
<td>112 (73)</td>
</tr>
<tr>
<td>B-lactam/β-lactamase inhibitors</td>
<td>35 (53)</td>
<td>67 (65)</td>
<td>101 (66)</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>13 (20)</td>
<td>21 (20)</td>
<td>26 (17)</td>
</tr>
<tr>
<td>Broad spectrum Gram negative Rx</td>
<td>40 (61)</td>
<td>69 (67)</td>
<td>123 (80)</td>
</tr>
<tr>
<td>3 or more antibiotics</td>
<td>34 (52)</td>
<td>41 (40)</td>
<td>74 (48)</td>
</tr>
<tr>
<td>Discharge Antibiotics</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Bactrim</td>
<td>32 (48)</td>
<td>49 (48)</td>
<td>38 (25)</td>
</tr>
<tr>
<td>Amox/Clav</td>
<td>12 (18)</td>
<td>23 (22)</td>
<td>40 (26)</td>
</tr>
<tr>
<td>Median Duration Inpatient</td>
<td>4 (3-5)</td>
<td>4 (3-5)</td>
<td>5 (3-7)</td>
</tr>
<tr>
<td>Median Duration Outpatient</td>
<td>7 (7-10)</td>
<td>10 (7-10)</td>
<td>9 (7-10)</td>
</tr>
</tbody>
</table>

* Data are No (%) of patients
Modification of Risk Factors for CDI

- Antimicrobial use
  - Fluoroquinolones
  - Clindamycin
  - 3rd generation cephalosporins
- Prolonged antimicrobial therapy
- Proton pump inhibitors
Environmental Issues and CDI

- *C difficile* spores contaminate patients and equipment
  - These are reservoirs for disease
  - Little contamination outside of rooms
- Develop protocols for daily and terminal cleaning for patient rooms
  - 1:10 dilute sodium hypochlorite
  - Adequate training and education of personnel
Sites of Action of Antimicrobial Agents in Clinical Use

- **Cell wall synthesis**
  - Cycloserine
  - Vancomycin, Teichoplanin
  - Bacitracin
  - Penicillins
  - Cephalosporins
  - Monobactams
  - Carbapenems

- **Topoisomerase IV**
  - DNA gyrase

- **DNA-directed RNA polymerase**
  - Rifampin

- **Folic acid metabolism**
  - Trimethoprim
  - Sulfonamides

- **Periplasmic space**
  - β-Lactamases
  - Aminoglycoside-modifying enzymes

- **Cell membrane**
  - PABA
  - Polymyxins

- **Protein synthesis**
  - 50S inhibitors
    - Erythromycin (Macrolides)
    - Chloramphenicol
    - Clindamycin
  - 30S inhibitors
    - Tetracycline
    - Spectinomycin
    - Streptomycin
    - Gentamicin, Tobramycin (aminoglycosides)
    - Amikacin
  - Protein synthesis (tRNA)
    - Mupirocin

Neu HC. Science 1992; 257:1064-73
Bowel Colonization Sub-Study

**Methods:** OASIS-2

- OASIS-2 was a prospective, open-label, multicenter, multinational trial of ertapenem (1 g once a day) versus ceftriaxone (2 g once a day or 1 g every 12 hours) plus metronidazole (30 mg/kg/day, in 2–4 divided doses) in patients with intra-abdominal infection.

- The objective of the bowel colonization sub-study of OASIS-2 was to compare the frequency with which ertapenem and ceftriaxone plus metronidazole selected for resistant Enterobacteriaceae, ESBL-producing Enterobacteriaceae, and imipenem-resistant *P. aeruginosa* (n=450).

- Rectal swabs were collected at baseline, discontinuation of therapy, and follow-up (2–4 weeks post-therapy).

- Samples were shipped to Merck Research Laboratories for testing.

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Navarro N et al. Presented at 3<sup>rd</sup> ACCP, October 2003.

Friedland I et al. 3<sup>rd</sup> ACCP, Santa Margherita, Portofino, Italy, October 2003.
OASIS-1 Sub-analysis in Patients with IAI (n=341): Low Risk for Resistance Selection among *P. aeruginosa* in the Bowel

<table>
<thead>
<tr>
<th><em>P. aeruginosa</em> resistant to imipenem</th>
<th>Baseline</th>
<th>DCOT</th>
<th>DCOT and/or TOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ertapenem</td>
<td>0/169 (0%)</td>
<td>0/152* (0%)</td>
<td>0/153* (0%)</td>
</tr>
<tr>
<td>Piperacillin/tazobactam</td>
<td>2/172 (1.2%)</td>
<td>1/153 (0.7%)</td>
<td>1/153 (0.7%)</td>
</tr>
</tbody>
</table>

Ertapenem did not select for imipenem-resistant *P. aeruginosa* in the bowel.

DCOT=Discontinuation of therapy; TOC=Test of cure, 2 weeks post therapy.

*One patient had an imipenem-intermediate *P. aeruginosa* at discontinuation of therapy.*

OASIS-2 Sub-analysis in Patients with IAI (n=389): Low Risk for Resistance Selection among Gram-Negative Bacilli in the Bowel

Enterobacteriaceae resistant to study drug

- ertapenem (1 g once daily); n=196
- ceftriaxone (2 g, once a day or 1 g twice daily) plus metronidazole (30 mg/kg/day in 2–4 divided doses after loading dose of 15 mg/kg); n=193

*p<0.001
Friedland I et al. 3rd ACCP, Santa Margherita, Portofino, Italy, October, 2003.
The Public is Aware of Antimicrobial Resistance

Online Reference Guide to Preventing Infections

Introduction

What are Health Care Acquired Infections?

One Family's True Story

What is MRSA?

Surgical Site Infections

Hand Hygiene

C difficile

Pediatric Infection Prevention

For the Patient:

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CAMPAIGN.org

Look for this throughout the site for even more in-depth infection prevention information.

Ventilator-Associated Pneumonia

Urinary Tract Infections

Catheter-Related Bloodstream Infections

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Bad Bugs Need Drugs

10x'20

Ten new ANTIBIOTICS by 2020
Antibiotic resistance in GNRs is a serious and complex issue.
Antimicrobial stewardship and infection prevention are critical keys to mitigating the dissemination of MDROs.
Effective antimicrobial therapy for treatment of some MDROs is lacking.
Governments and private industry must work together to develop compounds for treatment of MDROs.