Practically Implementing Antimicrobial Stewardship in an Evolving Landscape

Yi Guo, PharmD
Belinda Ostrowsky, MD
Priya Nori, MD
On behalf of the Montefiore ASP
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Objectives

- Review the data to support antimicrobial stewardship programs (ASP)
- Review evolving landscape in ASP
- Describe practical ASP of activities (“inside & outside the box”)
What is Antimicrobial Stewardship (ASP)?

✔ A healthcare institutional program to improve appropriateness of antimicrobial prescribing to:
  • Optimize clinical outcomes
  • Reduce adverse events
  • Reduce healthcare costs while maintaining quality of care

✔ Who are we?
  • Multidisciplinary team of ID trained physicians and pharmacists
    – Liaisons throughout the Healthcare System

http://www.cdc.gov/getsmart/healthcare
Why Stewardship?

• Up to 50% of all human antibiotic use is unnecessary or “inappropriate”
• Drug-resistant bacteria cause 23K deaths and 2M illnesses per year in the US
• FY 2016 federal budget for combating antibiotic resistance = $1.2 billion
• Goal by 2020:
  – All acute care hospitals will have ASP
  – ASP will cover all healthcare settings
  – 30% reduction of “Inappropriate” Abx use

Source: President’s National Action Plan, 3/2015
“Meaningful Use” of Antibiotics

- “Appropriate” means…
  - Antibiotic Indicated?
  - Right Drug?
  - Right Dose and Interval?
  - Right Route?
  - Right Duration?
Combating Antibiotic Resistance
PCAST 9/2014

1) Slow the Emergence & Spread of Resistant Bacteria with help from ANTIMICROBIAL STEWARDSHIP
2) Strengthen National Surveillance Efforts
3) Advance Rapid Diagnostics
4) Research for New Antibiotics
5) Improve International Collaboration
It is unclear how each will be interpreted.
CDC’s ASP Core Measures – How Do We Measure Up?

- Leadership commitment
- Accountability
- Drug Expertise
- Action
- Tracking & Reporting
- Education

**Core Activities**
- Multidisciplinary team
- Formulary restrictions
- Audit/Feedback

**Supplemental Activities**
- Streamlining/de-escalation
- Dose optimization
- IV to PO conversion
- Clinical pathways

**Education**
- Prescribing tools/algorithms
- Conferences with prescribers at all levels
Stewardship Interventions

- Dose optimization
- IV to PO conversion
- Streamlining & de-escalation
- Adjusting durations in accordance with guidelines
- Clinical pathways and treatment algorithms
- Maximizing functionality of electronic medical record (EMR)
Guidelines, Not One Size Fits All

“Tailor” to your own reality (needs, size and resources)
## ASP Strategies Varies By Campus

<table>
<thead>
<tr>
<th>Campus</th>
<th>Resources</th>
<th>Restrictions*</th>
<th>Audit**</th>
<th>Highlights</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moses (2008-)</td>
<td>✔✔✔</td>
<td>✔✔</td>
<td>✔✔</td>
<td>-ER (CAP, Sepsis) - Zosyn Time Out</td>
</tr>
<tr>
<td>Einstein (2008-)</td>
<td>✔✔✔</td>
<td>✔✔</td>
<td>✔✔</td>
<td>-ER ID Consults - Surgical prophylaxis bundles</td>
</tr>
<tr>
<td>Wakefield (2013-)</td>
<td>✔✔</td>
<td>✔ Modified at 72 hrs</td>
<td>✔✔✔</td>
<td>-Hospitalist De-escalation</td>
</tr>
<tr>
<td>Children’s (2013-)</td>
<td>✔✔</td>
<td>✔ shared ID PharmD</td>
<td>✔ Peds List</td>
<td>-Antiviral/antifungal appropriateness, -Dosing</td>
</tr>
<tr>
<td>Ambulatory (2016)</td>
<td>✔</td>
<td>N/A</td>
<td>✔</td>
<td>-Pilot for adult respiratory</td>
</tr>
</tbody>
</table>
Case #1:

58 y.o. female smoker from with habitual alcohol intake presents to the ER in August with fever to 102F, myalgias, and diarrhea for 4 days. She is found to have a large left sided consolidation on X-ray. Urine Legionella antigen is positive as is culture of bronchial fluid.
Which interventions can facilitate appropriate antibiotic management of patients with community acquired pneumonia (CAP)?

a) Placement of PO azithromycin in ER Pyxis MedStation™
b) Automated stop duration of 14 days for CAP regimens
c) Upfront restriction of IV piperacillin/tazobactam
d) Developing CAP order sets in EMR
e) All but b)
Multidisciplinary task force to improve compliance with CMS CAP measures (QI, ASP, ED)

Quasi-experimental, before-and-after study, QI methodology ("plan, do, check, act") w/ a bundled intervention:

1. Treatment algorithm for ED providers
2. "CAP Kit" with first line antibiotics and dosing
3. Preloaded ER Pyxis with regimens, access audited

Results

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Pilot ED</td>
<td>54.9%</td>
<td>93.4%</td>
<td>P = .001</td>
</tr>
<tr>
<td>2nd ED</td>
<td>64.6%</td>
<td>91.3%</td>
<td>P = .004</td>
</tr>
</tbody>
</table>

- In an interrupted time-series logistic regression analysis, intervention was statistically associated with improved prescribing.
- Antibiotic administration within 6 hours not statistically different before and after.

Interventions for CAP

**Pre-authorization**
- Upfront restriction of IV azithromycin and fluoroquinolones
- 72h authorization of IV vancomycin

**Formulary Restriction**
- Levofloxacin as Respiratory Fluoroquinolone of choice
- Ceftaroline non-formulary, restricted to ID consultation

**Audit & Feedback**
- Antibiotic orders by medicine house staff and hospitalist services
- Ambulatory antibiotic prescriptions for acute respiratory tract infections

**Education**
- First line CAP regimens
- Allergy regimens
- Newer literature on durations
Case #2

A 75-year-old female with COPD and active tobacco use presents with 3 days of productive cough and fevers. The patient has a remote history of rash due to penicillin given for an STD at age 18. She was hospitalized 6 weeks ago for community acquired pneumonia (CAP) and treated with levofloxacin. On exam, she is febrile and tachycardic. She is also frail, weighing only 45kg. CXR shows a right sided consolidation. WBC count is 13. Serum creatinine is 1.6mg/dL.

The patient is started on broad spectrum antibiotics and feels much improved 48 hours later.
Identify opportunities for pharmacy-driven interventions presented in the scenario

a) Debunking allergy history
b) Optimizing dose for host factors
c) Duration adjustment per newer guidelines
d) Bug-drug match by respiratory culture
e) De-escalation from broad spectrum regimen
f) All of the above
Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society

- 1 in 10 ventilated patients get VAP,
  - 13% mortality rate
  - Increases ventilator days and LOS ≥ 3 days
- 7 day course of therapy for hospital-acquired or ventilator-associated pneumonia (HAP, VAP) is sufficient
- Shorter course does not reduce benefits or therapy and may reduce antibiotic-associated adverse events
Penicillin Allergies

- Only 2-15% of patients with reported penicillin allergy have a positive skin test
- 80% loss of IgE occurs after 10 years
- These patients receive suboptimal, more broad, and more toxic agents
  - Associated with increased resistance, cost, hospital LOS, and mortality
  - In matched cohort study – higher rates of C. diff, MRSA, and increased hospital LOS

Macy E et al. Allergy Clin Immunol 2013
Unger NR et al. Pharmacotherapy 2013
Using Antibiogram Data for Teaching Campus 1 & 2

<table>
<thead>
<tr>
<th>Inpatient Isolates (% susc.)</th>
<th>Cipro (or Levo)</th>
<th>Cefepime</th>
<th>Gentamicin</th>
<th>Aztreonam</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Escherichia coli</strong>&lt;br&gt;Campus 1&lt;br&gt;Campus 2</td>
<td>52&lt;br&gt;55</td>
<td>90&lt;br&gt;93</td>
<td>80&lt;br&gt;83</td>
<td>69&lt;br&gt;73</td>
</tr>
<tr>
<td><strong>Klebsiella pneumoniae</strong>&lt;br&gt;Campus 1&lt;br&gt;Campus 2</td>
<td>63&lt;br&gt;67</td>
<td>61&lt;br&gt;65</td>
<td>75&lt;br&gt;75</td>
<td>56&lt;br&gt;59</td>
</tr>
<tr>
<td><strong>Pseudomonas aeruginosa</strong>&lt;br&gt;Campus 1&lt;br&gt;Campus 2</td>
<td>75&lt;br&gt;76</td>
<td>93&lt;br&gt;95</td>
<td>92&lt;br&gt;91</td>
<td>69&lt;br&gt;75</td>
</tr>
</tbody>
</table>
70 year old male with DM, active tobacco and EtOH use presents with 48 hours of cough with dark sputum, fevers up to 101F and rigors. On exam, he appears ill and has rhonchi at the R. base. CXR confirms an infiltrate. He reports a remote penicillin allergy when he was treated for syphilis in the army. **Which of the following is true about penicillin allergies?**

- **a.** Up to 10% of patients report penicillin allergies
- **b.** Skin testing shows that most are not IgE mediated
- **c.** Loss of IgE titers occurs with each decade of life
- **d.** Most patients can be successfully challenged with Beta-lactam antibiotics
- **e.** All of the above
At 20 months: **92% of doses and 86% of durations** were correctly chosen by house staff

>90% of house staff were analyzed only once

Positive impact on house staff prescribing sustained almost two years after introduction of intervention

**Results**

<table>
<thead>
<tr>
<th>Time frame</th>
<th>Antibiotics Indicated</th>
<th>Appropriate Regimen by Syndrome</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-intervention (-1 month)</td>
<td>87% (n = 187)</td>
<td>60% (n = 187)</td>
<td>--</td>
</tr>
<tr>
<td>Post-intervention (1 month)</td>
<td>85% (n = 163)</td>
<td>70% (n = 163)</td>
<td>0.0496</td>
</tr>
<tr>
<td>Post- intervention (20 months)</td>
<td>80% (n = 75)</td>
<td>80% (n = 75)</td>
<td>P &lt; 0.01</td>
</tr>
</tbody>
</table>

Bhar S, Nori P, Ostrowsky B. Improving Antibiotic Use Starts with Our Trainees. IDWeek 2015 oral presentation
## Antibiotic Prescribing by Syndrome

### Pre-intervention vs. 20 month Post-intervention by Syndrome

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>-1 month (n)</th>
<th>20 months (n)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>UTI</td>
<td>57% (42)</td>
<td>86% (28)</td>
<td>0.011</td>
</tr>
<tr>
<td>Respiratory</td>
<td>59% (80)</td>
<td>75% (20)</td>
<td>0.001</td>
</tr>
<tr>
<td>SSTI/OM</td>
<td>73% (22)</td>
<td>67% (12)</td>
<td>0.001</td>
</tr>
<tr>
<td>GI</td>
<td>50% (28)</td>
<td>75% (4)</td>
<td>0.34</td>
</tr>
<tr>
<td>Other</td>
<td>73% (15)</td>
<td>82% (11)</td>
<td>0.61</td>
</tr>
</tbody>
</table>

### Infectious Syndrome

- UTI
- Respiratory
- SSTI/OM
- GI
- Other

-1 month
1 month
20 months
Antibiotic Regimens - EPIC Order Sets

Non-severe

Severe sepsis/shock

Severe PCN Allergy Options

Montefiore
Inspired Medicine

THE UNIVERSITY HOSPITAL FOR
EINSTEIN
Albert Einstein College of Medicine
Maximizing Use of EMR

Stewardship Dashboard

AS Tab
Educational Tools Evolved Over Time
#Stewardship_Problems

1. Why are we suddenly using so much X (tigecycline, pip/tazo, etc.) for CAP?
2. Should we bring ceftaroline onto formulary for complicated MRSA?
3. Yes, but use should be restricted to ID consultation
4. Okay, now it’s on formulary, let’s monitor use
5. Now on to the next problem

- Med. Use Evaluation
- Formulary Restriction
- Education on Appropriate Prescribing
- Pre-authorization
- Audit & Feedback
## So Many MUEs, So Much to Do…

<table>
<thead>
<tr>
<th>Problem/Antimicrobial</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adult</strong></td>
<td></td>
</tr>
<tr>
<td>Quinolones</td>
<td>Restriction changes</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>De-escalating to other alternatives</td>
</tr>
<tr>
<td>Ganciclovir/Foscarnet</td>
<td>Presenting institution specific data to oncology department</td>
</tr>
<tr>
<td>Ceftaroline</td>
<td>Monitor appropriateness</td>
</tr>
<tr>
<td>Ceftolozane/tazobactam, Ceftazidime/avibactam</td>
<td>Monitor appropriateness</td>
</tr>
<tr>
<td><strong>Pediatric</strong></td>
<td></td>
</tr>
<tr>
<td>Palivizumab</td>
<td>Restriction/tracking/batching</td>
</tr>
<tr>
<td>Meropenem</td>
<td>Restricting to NICU</td>
</tr>
<tr>
<td>Antifungals</td>
<td>Ongoing monitoring</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td></td>
</tr>
<tr>
<td>CAP Treatment guidelines</td>
<td>Reducing inappropriate antibiotic use</td>
</tr>
<tr>
<td>Surgical prophylaxis guidelines</td>
<td>Reducing inappropriate antibiotic use</td>
</tr>
<tr>
<td>High risk or last resort antimicrobials</td>
<td>Ongoing monitoring</td>
</tr>
</tbody>
</table>
1. ID pharmacy manager at each campus
2. Systems director, medical directors, ASP fellow
3. New ID/ASP - CCM service
4. Data analyst
5. On-site clinical microbiology lab

Hyun et al JAMA 2013
Partner with Microbiology

• **Early:**
  – Creation and dissemination of Antibiograms
  – Creation of testing and reporting cascades

• **Intermediate:**
  – New viral and influenza testing platforms
  – Sensitive *Clostridium difficile* testing

• **Complex:**
  – Introduction rapid diagnostics (e.g., MALDI-TOF)
## Preliminary Outcomes for Severe Sepsis/Shock (conventional vs MALDI-TOF)

<table>
<thead>
<tr>
<th></th>
<th>March-April 2013 (n=96)</th>
<th>March-April 2014 (n=69)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gram-negative + <em>S. aureus</em></strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to Org ID (hours)</td>
<td>51.8</td>
<td>31.8</td>
</tr>
<tr>
<td>Time to Streamlined Susceptible Regimen (hours)</td>
<td>74.2</td>
<td>58.1</td>
</tr>
<tr>
<td>Time to ID consultation (hours)</td>
<td>35.1</td>
<td>16.3</td>
</tr>
<tr>
<td>Time to microbiological clearance (hours)</td>
<td>69.2</td>
<td>55.9</td>
</tr>
<tr>
<td>Unadjusted mortality (%)</td>
<td>23.9</td>
<td>18.8</td>
</tr>
<tr>
<td>Length of Stay (days)</td>
<td>10.6</td>
<td>10.1</td>
</tr>
</tbody>
</table>

Relationship holds when subgrouped by Gram-negative or *S. aureus*
Park et al. IDweek abstract, 2015
Let the Debate Begin… Use the Data

- Attended Hematology/Oncology QI meeting
- ASP and ID went as team with data

Our own institutional data ..... That was helpful but ...next time, show me the data that supports my beliefs!
Making a Persuasive ASP Case Using Pilot days of therapy (DOT) data

Antimicrobial Utilization by Agent and Hospital

- Cefepime
  - Montefiore: 3.01
  - NY State: 3.47

- Meropenem/Imipenem
  - Montefiore: 2.29
  - NY State: 1.68

- Piperacillin/Tazobactam
  - Montefiore: 8.09
  - NY State: 6.16

Antimicrobial Agent by Hospital
Antimicrobial Utilization by Nursing Units

Antimicrobial Utilization (%)

<table>
<thead>
<tr>
<th>Nursing Unit</th>
<th>Utilization (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10N</td>
<td>1.23</td>
</tr>
<tr>
<td>10S</td>
<td>1.12</td>
</tr>
<tr>
<td>11N</td>
<td>1.60</td>
</tr>
<tr>
<td>11S</td>
<td>0.79</td>
</tr>
<tr>
<td>1A</td>
<td>0.48</td>
</tr>
<tr>
<td>2N</td>
<td>0.14</td>
</tr>
<tr>
<td>4ECI</td>
<td>0.23</td>
</tr>
<tr>
<td>4WIC</td>
<td>0.19</td>
</tr>
<tr>
<td>5N</td>
<td>0.04</td>
</tr>
<tr>
<td>5S</td>
<td>0.04</td>
</tr>
<tr>
<td>6S</td>
<td>0.32</td>
</tr>
<tr>
<td>7N</td>
<td>0.77</td>
</tr>
<tr>
<td>7S</td>
<td>0.66</td>
</tr>
<tr>
<td>8N</td>
<td>0.81</td>
</tr>
<tr>
<td>8S</td>
<td>0.51</td>
</tr>
</tbody>
</table>

PIPERACILLIN/TAZOBACTAM

Campus B Hospital Nursing Units
This is Not a New Finding…

2009
-Audit ED pip/tazo use (Hip fracture, ETOH intoxication)

2010
-Resident project: investigating pip/tazo prescribing pattern

2011
-ERASE: pip/tazo is the #1 antibiotic associated with C. difficile colitis
-MUE-assess use
-Pilot auditing

2012-2013
-ID fellow & pharmacy driven pip/tazo de-escalation intervention

Pip/tazo: Piperacillin/tazobactam
Action Plan

Piperacillin/tazobactam De-escalation

Review Patient List
Identify patients on pip/tazo therapy for >72 hours without ID consult.

EMR Chart Review
Review indication, dosing, duration, culture results and clinical progress.

Contact Primary Team
Have a meaningful discussion with house staff about the patient and make appropriate recommendations.
## Results (May-July 2013, n=60)

<table>
<thead>
<tr>
<th>Type of Intervention</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shorter Duration</td>
<td>38%</td>
</tr>
<tr>
<td>Narrow Therapy</td>
<td>22%</td>
</tr>
<tr>
<td>Discontinuation</td>
<td>17%</td>
</tr>
<tr>
<td>ID consult</td>
<td>7%</td>
</tr>
<tr>
<td>Switch to Oral Regimen</td>
<td>7%</td>
</tr>
<tr>
<td>Continue Therapy</td>
<td>7%</td>
</tr>
<tr>
<td>Others</td>
<td>1%</td>
</tr>
</tbody>
</table>
## Collaboratives—Working Together in NYS on CDI*

<table>
<thead>
<tr>
<th>Dates</th>
<th>Facilities (n)</th>
<th>Collaborators</th>
<th>Interventions</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008-2009(^1)</td>
<td>35</td>
<td>NYS DOH + GNYHA/ UHF</td>
<td>-IPC &amp; Cleaning Bundles -Education</td>
<td>↓ Mean HO-CDI</td>
</tr>
<tr>
<td>2010-2012,(^2,3)</td>
<td>10</td>
<td>GNYHA/ UHF + AHRQ/ CDC + Montefiore</td>
<td>-CDI directed ASP -Education</td>
<td>↓ CDI Targeted antibiotics AHRQ CDI Toolkit</td>
</tr>
<tr>
<td>2015- on</td>
<td>80</td>
<td>GNYHA/ UHF + NYSCHSP + Montefiore</td>
<td>-ASP Course -ASP survey -CDI Point Prevalence -CDI ASP Posters</td>
<td>Facilities (n) 80 61 53 16</td>
</tr>
</tbody>
</table>

GYNHA/ UHF=Greater NY Hospital Association/ United Hospital Fund, NYSCHSP= NYS Council Health Systems Pharmacists, HO-CDI= Hospital onset CDI


* Addition NYSDOH collaborative LTCF and CDI
Additional Montefiore ASP Activities

- Antibiotic empiric regimen card
- Sepsis protocol
- Noon conferences & other education sessions

- Antibiotic time out (IT declined)
- Default duration of 7 days (approved by P&T)
- Antibiotic prescribing screens

- SENTRI-7/Antibiotic surveillance report

- MALDI-TOF + Stewardship intervention for positive blood cultures
Stewardship Program “Timeout”

1. Examine your routine activities
2. Take credit for strategies already in place
3. Address new federal regulations with well documented policies
4. Perform a needs assessment and ask “what am I not yet doing?”
Take Home Lessons

• CDC Core ASP Strategies are resources
• ASP needs to be tailored to your facility.
• ASP development & implementation takes time
• ASP is a team sport
• ASP activities:
  – Likely already exist
  – Can start simple, grow/ expand with the program
  – Must do because regulated (should do because it is important for your patients)
• Learn from other ASPs (we can be your resources)
Acknowledgments

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MMC Infection Prevention & Control Team

MMC Microbiology

MMC Leadership, Performance Improvement & Safety

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