INSTITUTIONAL PROGRAMS FOR IMPROVING ANTI-INFECTIVE THERAPY

Antimicrobial Stewardship: HealthCare Provider to Hospital and Patients
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Disclosure

• Merck Independent investigator grant regarding antimicrobial de-escalation
OBJECTIVES—Upon completion of this lecture the audience should:

- be familiar with concerns of antibiotic overuse and resistance
- understand the goals of antimicrobial stewardship (AMS)
- know the “tools” of AMS
- Review some inpatient and outpatient opportunities for stewardship

WHY DO WE NEED AN ANTIMICROBIAL STEWARDSHIP PROGRAM?
Background in Antimicrobial Use

MAGNITUDE OF ANTIMICROBIAL USE

• Antibiotics are the second most commonly used class of drugs in the United States
• More than 8 billion dollars are spent on anti-infectives annually
• 60% of all UW hospitalized patients were receiving AB in recent prevalence study
50% of antimicrobial use is either unnecessary or inappropriate
We forget about: Collateral Damage-esp antibiotic resistance

Background in Antimicrobial Resistance
Antimicrobial Resistance among Nosocomial Infections with Gram-positive Pathogens, by ICU Status

In Vitro Resistance Rates for *Pseudomonas aeruginosa* 1993 - 2002
General Opinion:

- Antimicrobial use in hospitals is one of many variables attributed to antimicrobial resistance and likely the most important one.

Are Clinician Perceptions of Antibiotic prescribing and resistance realistic?
Faculty and Resident Physicians’ Attitudes, Perceptions, and Knowledge about Antimicrobial Use and Resistance

Lilian Abbo, MD;1,2 Ronda Sinkowitz-Cochran, MPH;3 Laura Smith, PharmD;2 Ella Ariza-Heredia, MD;1 Orlando Gómez-Marin, PhD;1,4 Arjun Srinivasan, MD;3 Thomas M. Hooton, MD1

Of antibiotics is professionally unethical.

While 62% of respondents agreed that other doctors over-prescribe antibiotics, only 13% agreed that they themselves over-prescribe antibiotics, with residents more likely to agree (P < .01). Most respondents agreed that they would like more education about antibiotics and feedback about their antibiotic selections.

There was practically significant differences among
12 Steps to Prevent Antimicrobial Resistance: Hospitalized Adults

1. Vaccinate
2. Get the catheters out
3. Target the pathogen
4. Practice antimicrobial control
5. Use local data
6. Access the experts
7. Treat infection, not contamination
8. Treat infection, not colonization
9. Know when to say “no” to vanco
10. Stop treatment when cured
11. Isolate the pathogen
12. Contain your contagion

Campaign to Prevent Antimicrobial Resistance in Healthcare Settings

We are facing a shortage of NEW antibiotics
Combating Antimicrobial Resistance: Policy Recommendations to Save Lives

Infectious Diseases Society of America (IDSA)*

Clinical Infectious Diseases 2011;52(5):S393-S428

![Graph showing number of new antibacterial agents from 1983-1987 to 1998-2012.]

**Figure 1.** Number of New Molecular Entity (NME) Systemic Antibiotics Approved by the US FDA Per Five-year Period, Through 3/11.

Who are you going to Call?

![Image of the movie Ghostbusters.]

**Caption:** Ghostbusters.
New Innovations

French's Introduces Antibacterial Mustard

ROCHESTER, NY—In response to increasing American demand for tangier, more hygienic meals, condiment giant
French’s has introduced a new antibacterial mustard.

"Each year, 25 million cases of bacterial food poisoning originate in U.S. home kitchens, resulting in nausea, diarrhea, fever, and even death," read a press release French’s issued Monday. "Now, lunch doesn’t have to endanger your health! All-new French’s Antibacterial Mustard is the perfect way to add flavor to, and subtract harmful disease-causing bacteria from, your family’s favorite meals."

According to French’s representative Dalia Nelson, the new hypoallergenic mustard complements the company’s expanding line—which includes French’s Honey Dijon Mustard and French’s Sweet & Tangy Honey Mustard—and kills over 99.99% of harmful germs.

The mustard is orange in color, more translucent than the traditional varieties, and somewhat medicinal in flavor. In product trials performed by French’s, mothers preferred antibacterial mustard five to one when informed of its sterilizing properties.

A television commercial for the mustard plays up its prominent role in luncheon sanitation.

Goals of Antimicrobial Stewardship

• Promote quality healthcare
• Improve patient outcomes
  – Improve cure rates
  – Decreased failure rates
  – Fewer adverse drug events
  – Decrease antimicrobial errors
• Limit emergence of resistance
• Improve institutional outcomes
• Decrease healthcare costs

Delitt et al. Clin Infect Dis 2007;44:159-177
Core Hospital Services

**Antimicrobial stewardship**

**Microbiologic surveillance**

**Infection control**


Antimicrobial Stewardship Team
Classification of AMS Programs

- Education and Guideline Implementation Strategies
- Formulary and Restriction Strategies
- Review and Feedback Strategies
- Computer Assisted Strategies
Classification of AMS Programs

- Education and Guideline Implementation Strategies
- Formulary and Restriction Strategies
- Review and Feedback Strategies
  - Use Antimicrobial Order Form
- Antibiotic Cycling Strategies
- Computer Assisted Strategies

Antibiotic Utilization Report
SERVICE - HOSPITALIST
7/1/2010 - 9/1/2012

Pneumonia

ceftriaxone (IV)
Service - Hospitalist
7/1/2010 - 9/1/2012

DDD/1000 Pts/ays
DOT/1000 Pts/ays
Restriction-PRIOR APPROVAL PROGRAMS

• State the vision for these activities as improving rather than controlling or restricting use
  – Potentially most onerous to physicians
• Most effective single intervention!
  – McGowan and Finland. J Infect Dis 1974;130:165-8
  – Recco et al. JAMA 1979;241:2283-6

Classification of AMS Programs

• Education and Guideline Implementation Strategies
• Formulary and Restriction Strategies
• Review and Feedback Strategies
  – Therapeutic substitution, etc
  – De-escalation
THERAPEUTIC SUBSTITUTION & DEESCALATION PROGRAMS

- Alternative to “policing” programs
- Three approaches:
  - Therapeutic equivalent within a class
  - Change to a different class that allows IV to oral conversion
  - Refine choice based upon culture results

What has been done in the UW Antimicrobial Stewardship Program?

- Antimicrobial Stewardship Team
- Antibiotic Order Form
- Premier- Electronic based antimicrobial monitoring
- Targeted educational programs
- Clinical research in high use anti-infective areas
### Antibiotic Order Form

#### 1. (DAPT/Enoxaparin) Indication
- Prophylaxis Surgical
- Prophylaxis Medical
- Nonprophylaxis

#### 2. (DAPT/Enoxaparin) Site (Select ALL that apply)
- Abdominal-Pelvic
- Bloodstream
- Gun
- Cellulitis
- Head/ENT
- IV Line
- Lower Ext.
- Menopausal
- Musculoskeletal
- Neutropenic Fever
- Surgical Wound
- URI/UTI
- Noninfectious

#### 3. (DAPT/Enoxaparin) Duration Ordered
- Yes
- No

#### 4. (DAPT/Enoxaparin) Type of Therapy
- New Therapy
- Modification of Therapy

#### 5. (DAPT/Enoxaparin) Coverage (Select ALL that apply)
- Staphylococci
- Pseudomonas aeruginosa
- Staphylococcus Lactococcus
- Gram Negative Resistant
- Streptococcus Penicillin Sensitive
- Escherichia Coli
- Noninfectious

### Classification of AMS Programs

- **Education and Guideline Implementation Strategies**
- **Formulary and Restriction Strategies**
- **Review and Feedback Strategies**
- **Computer assisted support**
Antimicrobial Stewardship
BEST PRACTICE ALERTS IN EPIC
Changes in Health Link to Improve Anti-infective Prescribing

Alert

1. Antimicrobial Stewardship Recommendations
   Recommendations have been left for this patient by the Antimicrobial Stewardship team.
   Action Steps:
   1. Please review the team’s recommendations by going to the Antimicrobial Navigator
   2. Make necessary treatment changes or explain why the changes are not necessary.

   If you have clinical questions you may contact the Antimicrobial Stewardship Pharmacist, Pager 4321.
   Optional: You may click on this link to send questions or feedback to CCKM.

   • Click on “Jump to Antimicrobial Stewardship” to review recommendations, manage orders and address alert
Sample AMS Note

Antimicrobial Stewardship Recommendations

Patient: Ams A Ziteg; 55 year old MRN: 123456
Location: OHSU RN: 01234
Primary Service: PULMONARY MEDICINE - Attending: Buchanan, Joel MD
Admit Date: 8/23/2010 - Hospital Day: 100

Recommendation:
Your patient has completed 72 hours of broad spectrum empiric antimicrobial therapy. Microbiology results show mixed respiratory bacteria and no resistant microorganisms. If the patient is improving please consider narrowing antimicrobial therapy to ampicillin/subactam. If de-escalation cannot be accomplished, please explain.

Sincerely,

Submitted by: Deborah B Dunham, RPH - 12/17/2010 - 4:53
Additional References

1. Click on Discharge navigator
2. Click on Discharge Instructions navigator
3. Enter antibiotic-specific smart phrase: .opatdrug name
What about OUTPATIENT Stewardship?

• Prudent use of antibiotics for respiratory infections
• Handling patient expectations
• Optimal therapy for various conditions with minimizing adverse effects

Community based program for Preventing Antibiotic Resistance and Promoting Appropriate Antibiotic Use

Strategies for Optimal Care and Satisfied Patients

www.warnwisconsin.org
Get Smart In Action: Old Challenges, New Challenges, Innovative Solutions

Cindy Friedman, MD
Medical Director
http://www.cdc.gov/getsmart/

Acute Maxillary Sinusitis: uncomplicated

<table>
<thead>
<tr>
<th>1st choice</th>
<th>2nd choice</th>
<th>3rd choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>amoxicillin, doxycycline or macrolide if penicillin-allergic</td>
<td>amoxicillin-clavulanate, cefuroxime or similar cephalosporin</td>
<td>fluoroquinolone if penicillin-allergic</td>
</tr>
</tbody>
</table>

Acute Otitis Media: uncomplicated, age > 6 months

<table>
<thead>
<tr>
<th>1st choice</th>
<th>2nd choice</th>
<th>3rd choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>amoxicillin-clavulanate, cefuroxime or similar cephalosporin, macrolide if penicillin-allergic</td>
<td>high-dose amoxicillin (95-135 mg/kg/day)</td>
<td>cefazolin, ceftriaxone</td>
</tr>
</tbody>
</table>

Group A Streptococcal Pharyngitis (lab confirmed)

<table>
<thead>
<tr>
<th>1st choice</th>
<th>2nd choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>penicillin VK or amoxicillin (oral)</td>
<td>penicillin VK or amoxicillin (oral)</td>
</tr>
</tbody>
</table>

Adult Community-Acquired Pneumonia (outpatient)

<table>
<thead>
<tr>
<th>1st choice</th>
<th>2nd choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>macrolide or doxycycline</td>
<td>extended-spectrum macrolide plus high dose amoxicillin-clavulanate, clindamycin or similar cephalosporin</td>
</tr>
</tbody>
</table>

Skin and Soft Tissue Infections: uncomplicated and not bite wound

<table>
<thead>
<tr>
<th>1st choice</th>
<th>2nd choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>cephalosporin</td>
<td>nitrofurantoin</td>
</tr>
</tbody>
</table>

Cystitis: women, uncomplicated, not pregnant

<table>
<thead>
<tr>
<th>1st choice</th>
<th>2nd choice</th>
<th>3rd choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>trimethoprim-sulfamethoxazole</td>
<td>nitrofurantoin or cephalosporin</td>
<td>nitrofurantoin or cephalosporin</td>
</tr>
</tbody>
</table>

Use 24 h of antibiotic for: 1-7 days of age, 3 months to 3 years of age, pregnant, diabetes, moderate to severe, hospitalizations, and persistent or recurrent infections.
Potential Reduction in Antibiotic Prescribing Among Wisconsin Clinicians

“In your own practice, how much could you reduce antibiotic prescribing with no adverse impact on quality of care?”

<table>
<thead>
<tr>
<th>Potential Reduction in Antibiotic Use</th>
<th>Number (%) of Clinicians</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10%</td>
<td>48 (25%)</td>
</tr>
<tr>
<td>10% to 19%</td>
<td>71 (37%)</td>
</tr>
<tr>
<td>20% to 29%</td>
<td>47 (25%)</td>
</tr>
<tr>
<td>30% or more</td>
<td>25 (13%)</td>
</tr>
</tbody>
</table>

Primary Care Clinician Survey; Wisconsin 1999

Community and Clinician Education Can Effectively Reduce Antibiotic Use

A controlled intervention trial was conducted in several northern Wisconsin communities during 1997-98.

INTERVENTION:

✓ Distribution of materials and presentations to clinic staff, parents, day care providers, community groups.
✓ Small group presentations for clinicians.

OUTCOME:

✓ 22% reduction in new antibiotic prescriptions following intervention; no change in control region.
Bronchitis/Cough Illness

- Most cough illness is caused by viruses.
  - Sputum production is nonspecific and does not imply bacterial infection.
- Do not use antibiotics for cough < 3 weeks in a well-appearing patient without clinical evidence of pneumonia.
- Use the term “chest cold” rather than “bronchitis”.
  - Most patients expect antibiotics for “bronchitis”.

Antibiotics Have Little Impact on Acute Bronchitis

Results of Six Placebo-Controlled Trials in Adults

<table>
<thead>
<tr>
<th>Drug</th>
<th>Year</th>
<th>No.</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetracycline</td>
<td>1970</td>
<td>829</td>
<td>No benefit</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>1976</td>
<td>212</td>
<td>No benefit</td>
</tr>
<tr>
<td>TMP-SMX</td>
<td>1984</td>
<td>67</td>
<td>Cough days decreased 6% during first week</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>1984</td>
<td>74</td>
<td>No benefit</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>1986</td>
<td>52</td>
<td>No benefit</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>1987</td>
<td>63</td>
<td>Lower symptom scores, days 6-10</td>
</tr>
</tbody>
</table>
Acute Pharyngitis

- Antibiotics are recommended **only** for pharyngitis caused by Group A *Streptococcus pyogenes*.
- Diagnosis of group A streptococcal pharyngitis should be made using a laboratory test in conjunction with clinical and epidemiological findings.

Group A Strep is an Uncommon Cause of Exudative Pharyngitis with Fever

- **Group A Strep**
  - 12%

- Other
  - 88%

Goals of Antimicrobial Stewardship

- Promote quality healthcare
- Improve patient outcomes
- Limit emergence of resistance
- Improve institutional outcomes
- Decrease healthcare costs
- Improve outpatient prescribing of AB

Questions??
# Anti-Infective Drugs before and after De-escalation BPA by Response

<table>
<thead>
<tr>
<th>BPA Response</th>
<th>Accept</th>
<th>Accept w/ Mod</th>
<th>Reject</th>
<th>Oneway ANOVA</th>
<th>Means Comparison w/ Student's t</th>
</tr>
</thead>
<tbody>
<tr>
<td>N Rows</td>
<td>108</td>
<td>21</td>
<td>27</td>
<td></td>
<td></td>
</tr>
<tr>
<td># Drugs BPA Response Date -1</td>
<td>2.44</td>
<td>2.24</td>
<td>2.19</td>
<td>p = 0.2805</td>
<td></td>
</tr>
<tr>
<td># Drugs BPA Response Date +1</td>
<td>1.32</td>
<td>1.29</td>
<td>1.85</td>
<td>p = 0.0063*</td>
<td>A&gt;R; M&gt;R; A=M</td>
</tr>
<tr>
<td>Difference (Date -1) - (Date +1)</td>
<td>1.12</td>
<td>0.95</td>
<td>0.33</td>
<td>p = 0.0009*</td>
<td>A&gt;R; M&gt;R; A=M</td>
</tr>
</tbody>
</table>

# of Broad Spectrum Anti-Infective Drugs before and after De-escalation BPA by Response

<table>
<thead>
<tr>
<th>BPA Response</th>
<th>Accept</th>
<th>Accept w/ Mod</th>
<th>Reject</th>
<th>Oneway ANOVA</th>
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</thead>
<tbody>
<tr>
<td>N Rows</td>
<td>108</td>
<td>21</td>
<td>27</td>
<td></td>
<td></td>
</tr>
<tr>
<td># Broad Spectrum Anti-Infectives, BPA Response Date -1</td>
<td>2.111</td>
<td>2.048</td>
<td>2.000</td>
<td>p = 0.8127</td>
<td></td>
</tr>
<tr>
<td># Broad Spectrum Anti-Infectives, BPA Response Date +1</td>
<td>0.806</td>
<td>1.048</td>
<td>1.593</td>
<td>p &lt; 0.0001*</td>
<td>A&lt;R; A=M; R&gt;M</td>
</tr>
<tr>
<td>Difference (Date -1) - (Date +1)</td>
<td>1.306</td>
<td>1.000</td>
<td>0.407</td>
<td>p &lt; 0.0001*</td>
<td>A&gt;R; A=M; R&lt;M</td>
</tr>
</tbody>
</table>

* indicates statistical significance.
Antimicrobial stewardship has decreased antibiotic drug spent per patient and antibiotic % of total drug expense

**Antimicrobial Stewardship**

- Drug Cost per Admission
- Percent of Total IP Drug Cost

<table>
<thead>
<tr>
<th></th>
<th>FY06</th>
<th>FY07</th>
<th>FY08</th>
<th>FY09</th>
<th>FY10</th>
<th>FY11 (ann)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amount</td>
<td>$173</td>
<td>$175</td>
<td>$162</td>
<td>$155</td>
<td>$167</td>
<td>$149</td>
</tr>
<tr>
<td>%</td>
<td>23.0%</td>
<td>22.0%</td>
<td>21.1%</td>
<td>19.5%</td>
<td>21.4%</td>
<td>18.1%</td>
</tr>
</tbody>
</table>

Represents a $643,000 cost-avoidance versus FY06 antibiotic cost/ admission

**Comparison of Prior Authorization and Prospective Audit with Feedback for Antimicrobial Stewardship**

Jethesh M. Mehta, PharmD, MSCE; Kevin Haynes, PharmD, MSCE; E. Paul Wilieto, PhD; Jeffrey S. Gerber, MD, PhD, MSCE; Daniel R. Timko, PharmD, BCPS; Steven C. Morgan, PharmD, BCPS, QA; ID; Shawn Biskley, PharmD, BCPS
Neil O. Fishman, MD; Ebbing Lautenbach, MD, MPH, MSCE; Theoklitis Zouridas, MD, MSCE
for the Centers for Disease Control and Prevention Epicenter Program

**OBJECTIVE.** Although prior authorization and prospective audit with feedback are both effective antimicrobial stewardship program (ASP) strategies, the relative impact of these approaches remains unclear. We compared these core ASP strategies at an academic medical center.

**DESIGN.** Prospective study.

**METHODS.** We compared antimicrobial use during the 24 months before and after implementation of an ASP strategy change. The ASP used prior authorization alone during the preintervention period, June 2007 through May 2009, In June 2009, antimicrobials were restricted and prospective audit was implemented for cephalosporins, piperacillin/tazobactam, and vancomycin, marking the start of the postintervention period, July 2009 through June 2011. All adult inpatients who received more than or equal to 1 dose of an antimicrobial were included. The primary end point was antimicrobial consumption in days of therapy per 1,000 patient-days (DOT/1,000-PD). Secondary end points included length of stay (LOS).

**RESULTS.** In total, 55,356 patients were included (29,600 preintervention and 25,756 postintervention). During the preintervention period, both total antimicrobial (DOT/1,000-PD) and broad-spectrum anti-gram-negative antimicrobial use (DOT/1,000-PD) declined. After the introduction of prospective audit with feedback, however, both total antimicrobial use (+4.65 DOT/1,000-PD in $P < .001$) and broad-spectrum anti-gram-negative antimicrobial use (+4.80 DOT/1,000-PD in $P < .001$) increased significantly. Use of cephalosporins and piperacillin/tazobactam both significantly increased after the intervention ($P = .02$). Hospital LOS and LOS after first antimicrobial dose also significantly increased after the intervention ($P < .001$ and .001, respectively).

**CONCLUSIONS.** Significant increases in antimicrobial consumption and LOS were observed after the change in ASP strategy.