An Overview of Antimicrobial Stewardship:

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Disclosure

• NONE
Objectives

• be familiar with concerns of antibiotic overuse and resistance
• understand the goals of antimicrobial stewardship (AMS)
• know the “tools” of AMS
• Review opportunities for stewardship
  – Inpatient
  – Outpatient
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.
Vital Signs: Improving Antibiotic Use Among Hospitalized Patients

Scott Fridkin, MD1, James Baggs, PhD1, Ryan Fagan, MD1, Shelley Magill, MD, PhD1, Lori A. Pollack, MD1, Paul Malpiedi, MPH1, Rachel Slayton, PhD1, Karim Khader, PhD2 Michael A. Rubin, MD, PhD2, Makoto Jones, MD1, Matthew H. Samore, MD2, Ghinwa Dumyati, MD3, Elizabeth Dodds-Ashley, PharmD3, James Meek, MPH4, Kimberly Yousey-Hindes, MPH4, John Jernigan, MD1, Nadine Shehab, PharmD1, Rosa Herrera1, L. Clifford McDonald, MD1, Amy Schneider, MPH1, Arjun Srinivasan, MD1 (Author affiliations at end of text)

Background: Antibiotics are essential to effectively treat many hospitalized patients. However, when antibiotics are prescribed incorrectly, they offer little benefit to patients and potentially expose them to risks for complications, including Clostridium difficile infection (CDI) and antibiotic-resistant infections. Information is needed on the frequency of incorrect prescribing in hospitals and how improved prescribing will benefit patients.

Methods: A national administrative database (MarketScan Hospital Drug Database) and CDC's Emerging Infections Program (EIP) data were analyzed to assess the potential for improvement of inpatient antibiotic prescribing. Variability in days of therapy for selected antibiotics reported to the National Healthcare Safety Network (NHSN) antimicrobial use option was computed. The impact of reducing inpatient antibiotic exposure on incidence of CDI was modeled using data from two U.S. hospitals.

Results: In 2010, 55.7% of patients discharged from 323 hospitals received antibiotics during their hospitalization. EIP reviewed patients’ records from 183 hospitals to describe inpatient antibiotic use; antibiotic prescribing potentially could be improved in 37.2% of the most common prescription scenarios reviewed. There were threefold differences in usage rates among 26 medical/surgical wards reporting to NHSN. Models estimate that the total direct and indirect effects from a 30% reduction in use of broad-spectrum antibiotics will result in a 26% reduction in CDI.

Conclusions: Antibiotic prescribing for inpatients is common, and there is ample opportunity to improve use and patient safety by reducing incorrect antibiotic prescribing.

Implications for Public Health: Hospital administrators and health-care providers can reduce potential harm and risk for antibiotic resistance by implementing formal programs to improve antibiotic prescribing in hospitals.
We forget about: Collateral Damage-esp antibiotic resistance
Background in Antimicrobial Resistance
The Hinshelwood College for Bacteria

RIGHT! TODAY WE'RE GOING TO TEACH YOU HOW TO RESIST ANTIBIOTICS!
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?
Infect Control Hosp Epidemiol 2011;32(7):714-718

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-Marín, 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 overprescribe 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 statistically significant difference in prescribing.
CAN ANTIMICROBIAL MANAGEMENT LIMIT THE EMERGENCE OF RESISTANCE?

- Vancomycin restriction may decrease VRE
- Macrolide susceptibilities of GAS recovered after nationwide reduction of usage in Finland¹
- Decreased pneumococcal penicillin resistance in Iceland²
- Prior approval program resulted in recovery of susceptibilities to β-lactam and quinolone antibiotics³

¹Seppälä et al. N Engl J Med 1997;337:441-6
²Stephenson et al. JAMA 1996;275:175

MAYBE
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

Prevent Infections

Diagnose & Treat Effectively

Use Antimicrobials Wisely

Prevent Transmission
CMS – Medicare Proposal

• All participating Medicare hospitals will need an AMS program that:
  – Tracks antimicrobial utilization
  – Requires an indication for use
  – Eventually…… QA measures and hospital comparisons will occur

• CDC has recommended that all acute care hospitals implement Antibiotic Stewardship programs.
What is the Current State of Hospital Antibiotic Stewardship?

Findings from the Advisory Board’s Survey of Antibiotic Stewardship Programs

Antibiotic resistance has emerged as a major imperative for the United States, linked to an estimated two million infections annually. In response to such concerns—as well as pressure from federal agencies—many hospitals are stepping up their efforts to better manage antibiotic use. Yet hospitals often lack the resources to implement every stewardship strategy recommended by experts. This survey explores trends in hospital-based antibiotic stewardship programs (ASPs) and identifies what stewardship challenges still remain.

Hospitals are Investing in ASPs…

Percent of responding hospitals that have an ASP in place ($n = 415$)

- **81%**

A Relatively Recent Development

- Nearly 70% of programs have existed for five years or less, including 35% that launched within the last two years

Less Common at Smaller Hospitals

- Among hospitals with more than 300 beds, 89% report having an ASP, compared with 73% of smaller hospitals
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(S5):S397–S428

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?
Goals of Antimicrobial Stewardship

• Promote quality healthcare
• Improve patient outcomes
• Improve institutional outcomes
• Limit emergence of resistance
• Decrease healthcare costs
“The development of new antibiotics without having mechanisms to insure their appropriate use is much like supplying your alcoholic patients with a finer brandy.”

- Dennis Maki, 1998

- From “Managing the Minefield” Satellite Symposium Annual Meeting of the Infectious Diseases Society of America
Core Hospital Services

- Antimicrobial stewardship
- Microbiologic surveillance
- Infection control

Antimicrobial Stewardship Team
AMS team
What has been done in the UW Antimicrobial Stewardship Program?

- Antimicrobial Stewardship Team
- Antibiotic Order Form
- Electronic based antimicrobial monitoring
- Targeted educational programs
- Computer assisted support
### Antibiotic Order Form

<table>
<thead>
<tr>
<th>Prompt</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. [DAPTOMycin] Indication</td>
<td>Prophylaxis-Surgical</td>
</tr>
<tr>
<td></td>
<td>Infection-Documented</td>
</tr>
<tr>
<td>2. [DAPTOMycin] Site (select ALL that apply)</td>
<td>Abdominal/Pelvic</td>
</tr>
<tr>
<td></td>
<td>Non-infectious</td>
</tr>
<tr>
<td>3. [DAPTOMycin] Cultures Ordered</td>
<td>Yes</td>
</tr>
<tr>
<td>4. [DAPTOMycin] Type of Therapy</td>
<td>New Therapy</td>
</tr>
<tr>
<td>5. [DAPTOMycin] Coverage (select ALL that apply)</td>
<td>Anaerobes</td>
</tr>
<tr>
<td></td>
<td>Mycobacteria</td>
</tr>
<tr>
<td></td>
<td>Staph-Methicillin Resistant</td>
</tr>
<tr>
<td></td>
<td>Streptococcal-Penicillin Resistant</td>
</tr>
<tr>
<td>6. [DAPTOMycin] Authorizing ID</td>
<td></td>
</tr>
<tr>
<td>attending/medical (From 23-07 a single dose may be ordered without ID approval)</td>
<td></td>
</tr>
</tbody>
</table>
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 PtDays
DOT/1000 PtDays
EDUCATIONAL PROGRAMS

- One-on-one instruction most successful
- Results extinguish rapidly
- Cannot stand alone, but should be the cornerstone of any Antimicrobial Management Program
Quinolone Use is a good target for Educational Effort

• Overuse has led to increased resistance in gram negative bacteria
• Less efficacy for Urinary (and abdominal ) infections
• Besides Clindamycin, likely the #2 culprit in increased risk of C DIFF
• Single doses of aminoglycosides are unlikely to cause renal failure!
New FDA advisory action?

• Labeling currently has warnings about the risks for tendonitis, tendon rupture, central nervous system effects, QT prolongation and Torsades de Pointes, phototoxicity, and hypersensitivity.

• But panel members called for stronger wording, with some suggesting the risks be called out with a black box warning…and not using for sinusitis, AECB!
ANTIMICROBIAL FORMULARY

RESTRICTION

• Most direct method to influence antimicrobial utilization - Efficacy well documented
• Minimum number of agents required for effective therapy
• Eliminate duplicate agents within each class
• Restrict certain agents (indication, toxicity, cost)
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
Reviewing: Third party tracking or new EPIC module

<table>
<thead>
<tr>
<th>Zosyn New Starts</th>
<th>Patient name</th>
<th>GYNUROL-F6/6</th>
<th>piperacillin/tazobactam</th>
<th>07/13/2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linezolid use without MRSA or VRE</td>
<td>0131389</td>
<td>TLC-South-B6S3</td>
<td>linezolid</td>
<td>07/13/2005</td>
</tr>
<tr>
<td>Five days of amp/sulbactam, cefepime, imipenim, meropenim, pip/tazo, or ticar/clav</td>
<td>1861323</td>
<td>PULM-D6/5</td>
<td>ampicillin/sulbactam</td>
<td>07/13/2005</td>
</tr>
<tr>
<td>Five days of amp/sulbactam, cefepime, imipenim, meropenim, pip/tazo, or ticar/clav</td>
<td>1912415</td>
<td>GYNUROL-F6/6</td>
<td>ampicillin/sulbactam</td>
<td>07/13/2005</td>
</tr>
<tr>
<td>Fungal Double Coverage: voriconazole &amp; caspofungin</td>
<td>1807522</td>
<td>CSH-D4/4</td>
<td>voriconazole</td>
<td>07/13/2005</td>
</tr>
<tr>
<td>Fungal Double Coverage: voriconazole &amp; caspofungin</td>
<td>1807522</td>
<td>CSH-D4/4</td>
<td>caspofungin</td>
<td>07/13/2005</td>
</tr>
<tr>
<td>Gm- Double Coverage: cefepime &amp; moxifloxacin</td>
<td>1684314</td>
<td>HEMBMT-B6/6</td>
<td>cefepime</td>
<td>07/13/2005</td>
</tr>
<tr>
<td>Gm- Double Coverage: cefepime &amp; moxifloxacin</td>
<td>1684314</td>
<td>HEMBMT-B6/6</td>
<td>moxifloxacin</td>
<td>07/13/2005</td>
</tr>
<tr>
<td>Gm- Double Coverage: cefepime &amp; moxifloxacin</td>
<td>1845769</td>
<td>HEMBMT-B6/6</td>
<td>cefepime</td>
<td>07/13/2005</td>
</tr>
<tr>
<td>Gm- Double Coverage: cefepime &amp; moxifloxacin</td>
<td>1845769</td>
<td>HEMBMT-B6/6</td>
<td>moxifloxacin</td>
<td>07/13/2005</td>
</tr>
<tr>
<td>IV to PO protocol drugs</td>
<td>0623691</td>
<td>PULM-D6/5</td>
<td>ciprofloxacin</td>
<td>07/13/2005</td>
</tr>
</tbody>
</table>
Classification of AMS Programs

• Education and Guideline Implementation Strategies
• Formulary and Restriction Strategies
• Review and Feedback Strategies
• Computer assisted support
Clinical ID resource tab EPIC
Antimicrobial Stewardship
BEST PRACTICE ALERTS IN EPIC

Changes in Health Link to Improve Anti-infective Prescribing
Alert

• Click on “Jump to Antimicrobial Stewardship” to review recommendations, manage orders and address alert
What about antimicrobial costs?
Antimicrobial stewardship has decreased antibiotic drug spent per patient and antibiotic % of total drug expense.

Represents a $643,000 cost-avoidance versus FY06 antibiotic cost/admission.
The Core Elements of Antibiotic Stewardship for Nursing Homes
adverse drug events and drug interactions, and colonization and/or infection with antibiotic-resistant organisms.

Up to 70% of nursing home residents received one or more courses of systemic antibiotics in a year.
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
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
propriate in many cases. The letter read as follows:

We want to give you some important information about antibiotics.

Antibiotics, like penicillin, fight infections due to bacteria that can cause some serious illnesses. But these medicines can cause side effects like skin rashes, diarrhea, or yeast infections. If your symptoms are from a virus and not from bacteria, you won’t get better with an antibiotic, and you could still get these bad side effects.

Antibiotics also make bacteria more resistant to them. This can make future infections harder to treat. This means that antibiotics might not work when you really need them. Because of this, it is important that you only use an antibiotic when it is necessary to treat your illness.

How can you help? Carefully follow your doctor’s instructions. He or she will tell you if you should or should not take antibiotics.

When you have a cough, sore throat, or other illness, your doctor will help you select the best possible treatments. If an antibiotic would do more harm than good, your doctor will explain this to you, and may offer other treatments that are better for you.

Your health is very important to us. As your doctors, we promise to treat your illness in the best way possible. We are also dedicated to avoid prescribing antibiotics when they are likely to do more harm than good.

If you have any questions, please feel free to ask your doctor, nurse, or pharmacist.
Narrow-spectrum medications listed individually:

Which one of the following antibiotics would you choose to treat this patient?

☐ cephalexin

☐ dicloxacillin

☐ erythromycin

☐ penicillin V

Broader-spectrum antibiotics:

☐ amoxicillin-clavulanate  ☐ azithromycin  ☐ cefadroxil  ☐ cefuroxime  ☐ cefadroxil  ☐ cefuroxime  ☐ clindamycin  ☐ moxifloxacin

Fig. 1. a-b. Example of menu partition intervention
Behavioral feedback interventions with 10-20% reduction

*JAMA.* 2016;315(6):562-570
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>
Most episodes of acute otitis media (AOM) are self-limited, although antibiotics can provide some benefit.

Amoxicillin remains the drug of choice for initial AOM treatment.

Uncomplicated AOM may be treated for 5-7 days in children at low risk for treatment failure:
- ≥ 24 months old
- not in day care
- no antibiotic use past 3 months
Group A Strep is an Uncommon Cause of Exudative Pharyngitis with Fever

The Common Cold

- Purulent rhinitis frequently accompanies the common cold.
- Antibiotic treatment is not recommended and does not prevent bacterial complications.
- Patients often expect antibiotics for purulent rhinitis
Duration of Symptoms in 139 Rhinovirus Colds

Gwaltney, JAMA 1967;202:158
Antibiotic Treatment Does Not Benefit Purulent Rhinitis

Outcome at 5-6 days
Cephalexin (n=55) vs. placebo (n=51)

*Otitis media or more severe illness

Todd et al. Ped Infect Dis 1984; 3:226
Asymptomatic bacteruria

- Overtreatment!
- 10% of women over 60, 20% over 75
- In CDC 2014 report, accounted for 30% of excess antibiotic use in the hospital
Association Between Outpatient Antibiotic Prescribing Practices and Community-Associated Clostridium difficile Infection

Raymund Dantes,¹ Yi Mu,¹ Lauri A. Hicks,¹ Jessica Cohen,¹,² Wendy Bamberg,³ Zintars G. Beldavs,⁴ Ghinwa Dumyati,⁵ Monica M. Farley,⁶,⁷ Stacy Holzbauer,⁸ James Meek,⁹ Erin Phipps,¹⁰ Lucy Wilson,¹¹,¹² Lisa G. Winston,¹³,¹⁴ L. Clifford McDonald,¹ and Fernanda C. Lessa¹

Conclusions. Community-associated CDI prevention should include reducing unnecessary outpatient antibiotic use. A modest reduction of 10% in outpatient antibiotic prescribing can have a disproportionate impact on reducing CA-CDI rates.
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**
- **Improve outpatient prescribing of AB**
If all else fails
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, 15 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 Darla 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 sanitization.
Questions??