ANTIMICROBIAL STEWARDSHIP PROGRAM: NOWHERE TO HIDE

“The widespread use of antimicrobial agents is among the most important public health issues.”

INTRODUCTION

• Disclosures: none
• Outline:
  1. Historical aspects of AMS
  2. Current challenges
  3. A few examples
AN ABRIDGED HISTORY OF ANTIMICROBIAL THERAPY

- 2000 B.C.: “Eat this root, you will feel better, or not...”
- 1000 A.D.: “This root is evil, say this prayer instead.”
- 1860 A.D.: “Prayer is superstition, drink this potion.”
AN ABRIDGED HISTORY OF ANTIMICROBIAL THERAPY

- 1940 A.D.: “This potion is snake oil, take penicillin, it’s a new wonder drug.”
- 1980 A.D.: “Penicillin is useless, take this antibiotic, it’s bigger and better.”
AN ABRIDGED HISTORY OF ANTIMICROBIAL THERAPY

- 20?? A.D.: “Our antibiotics don’t work anymore, why don’t you try this root.”
- Can we avoid this?
THE FUTURE IS NOW

- Enterococcus resistant to Daptomycin, Linezolid
- Carbapenem resistant GNR (Pseudomonas, Klebsiella, ...)
- XDR TB
WHAT CAN WE DO?

- IDSA 10x20 initiative: 10 new antibiotics by 2020, targeting “ESKAPE” pathogens (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species)

- But...easier said than done
WHAT CAN WE DO?

- In the meantime, the only solution is to use our existing antibiotics as wisely as possible.
- In other words, what we need is......
WHAT CAN WE DO?

- A WONDER CURE!
DEFINITIONS

- 1970s: Antibiotic Control/Management
- But...physician don’t like to be controlled/managed
- Focusing on financial aspects (ABX expenditure used to represent up to 50% of a hospital drug budget)
DEFINITIONS

- Antibiotics have characteristics not shared by other medications:
  - they are “auto-obsolete”
  - use in one patient can affect outcomes in another patient
- Preferred terminology: antimicrobial stewardship
SCOPE OF PROBLEM

- 50-60% of hospitalized patients receive at least one dose of antimicrobial therapy
- Associated with direct and indirect costs
- Up to 50% of prescriptions are probably unnecessary
FACTORS AFFECTING ANTIMICROBIAL MISUSE

- Good intentions
- Patient pressure
- Fear of litigation
- Inappropriate prophylaxis
- Inappropriate dosing ("more is better")
FACTORS AFFECTING ANTIMICROBIAL MISUSE

- Time pressure
- Inappropriate diagnostic evaluation
- “Spiraling empiricism” or: "We are going to broaden the spectrum"
- Previous experience (positive or negative)
ANTIMICROBIAL STEWARDSHIP STRATEGIES

- Educational programs:
  - lectures/conferences
  - guidelines
  - utilization review and feedback

- Impact difficult to assess
- Needs continuous reinforcement
ANTIMICROBIAL STEWARDSHIP STRATEGIES

- Formulary restrictions:
  - limiting availability of antimicrobial agents
  - usually targeting new or expensive drugs
- Requires ongoing reevaluation
ANTIMICROBIAL STEWARDSHIP STRATEGIES

- Prior-approval programs:
  - phone approval
  - antibiotic order forms
  - automatic stop orders

- Good data to support, but time-consuming and difficult to enforce
ANTIMICROBIAL STEWARDSHIP STRATEGIES

- Prospective audit and feedback:
  - “real time” chart review
  - emphasis on step-down therapy (IV to oral) and streamlining (broad to narrow-spectrum)
- Good data for some infections (UTI, pneumonia)
ANTIMICROBIAL STEWARDSHIP STRATEGIES

- Computer-assisted programs: makes recommendations for antibiotic choice, dose, duration
- Limited data
ANTIMICROBIAL STEWARDSHIP OUTCOMES

▪ Clinical outcomes:
  - improving cure rates
  - less adverse reaction
  - decreased rates of nosocomial infections
▪ Limited-quality evidence
ANTIMICROBIAL STEWARDSHIP OUTCOMES

- Impact on antimicrobial resistance: no simple answer, but probably positive effect
- Affected by antimicrobial agents prescription in the community and other facilities (NH/ LTAC)
ANTIMICROBIAL STEWARDSHIP CONSIDERATIONS

- Endemic strain vs epidemic strain
- Antibiotic rotation/cycling vs. antibiotic heterogeneity
- Study design: quasi-experimental such as interrupted time series
ANTIMICROBIAL STEWARDSHIP DESIGN AND IMPLEMENTATION

IDSA/SHEA guideline from 2007
Core members:
- ID physicians
- Clinical pharmacist with ID training
- Ideally, involvement from microbiology and information system specialist
ANTIMICROBIAL STEWARDSHIP DESIGN AND IMPLEMENTATION

- Collaboration with Infection Control and Pharmacy P and T committee
- Support from hospital administration, medical staff leadership and local providers
- Supervision by Patient safety/quality insurance
ANTIMICROBIAL STEWARDSHIP DESIGN AND IMPLEMENTATION

- Adequate resources available (including compensation)
- Measure outcomes
- Two core strategies recommended:
  - Prospective audit and feedback
  - Formulary restrictions and preauthorization
ANTIMICROBIAL STEWARDSHIP DESIGN AND IMPLEMENTATION

- Other elements:
  - Education
  - Guidelines
  - Order forms
  - Streamlining/ step-down therapy
  - Dose optimization
ANTIMICROBIAL STEWARDSHIP DESIGN AND IMPLEMENTATION

- Step-by-step approach:
  - Define philosophy of program
  - Gather baseline data (antimicrobial usage and cost, antibiogram)
  - Define structure
  - Develop a budget
ANTIMICROBIAL STEWARDSHIP DESIGN AND IMPLEMENTATION

- Step-by-step approach:
  - Involve administration and physician leadership
  - Develop guidelines (ABX choices and dosage)
  - Start program and monitor outcomes
President Obama’s Executive Order 13767: Combating Resistant Bacteria (Sept 2014)

5 Major goals that include:

#1- Slow emergence of resistant bacteria

Goal 1 activities include:

- Optimal vaccine use
- **Implement healthcare policies and antimicrobial stewardship programs**

- By 2020 reduce **inappropriate** antibiotic use by 20% in inpatient settings & 50% in outpatient settings
NATIONAL ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

- Objective 1: Implement public health programs and reporting policies
  - **Strengthen AMS programs**
    - Within 3 yrs, all hospitals will comply with CMS CoP
  - Strengthen educational programs
    - By 5 years, CDC will evaluate impact of quality measures

FACT SHEET:
THE FUTURE OF AMS

CDC’s 7 Core Elements of Hospital Antibiotic Stewardship Programs

1. Leadership Commitment
   - Dedicate necessary human, financial, and IT resources.

2. Accountability
   - Appoint a single leader responsible for program outcomes. (Physician Champion)

3. Drug expertise
   - Appoint a single pharmacist leader to support improved antibiotic prescribing. (Pharmacist Champion)
THE FUTURE OF AMS

4. Actionable Goals
   ▪ Implementing at least one recommended action, such as requiring reassessment within 48 hours to check drug choice, dose, and duration.

5. Tracking
   ▪ Monitor prescribing and antibiotic resistance patterns

6. Reporting
   ▪ Regularly report to staff prescribing and resistance patterns, and steps to improve

7. Education
   ▪ Educating clinicians about resistance & optimal prescribing.
Section 1.C. Systems to Prevent Transmission of MDROs and Promote Antimicrobial Stewardship

1. C.9 The hospital has **written policies and procedures** whose purpose is to improve antibiotic use (antibiotic stewardship).

1. C.10 The hospital has **designated a leader** (e.g., physician, pharmacist, etc.) responsible for program outcomes of antibiotic stewardship activities at the hospital.
1. C.11 The hospital’s antibiotic stewardship policy and procedures requires practitioners to document in the medical record or during order entry an indication for all antibiotics, in addition to other required elements such as dose and duration.
1.C.12 The hospital has a formal procedure for all practitioners to **review the appropriateness** of any antibiotics prescribed after 48 hours from the initial orders (e.g., antibiotic time out)

1.C.13 The hospital **monitors antibiotic use** (consumption) at the unit and/or hospital level.
PROBLEMS

- Medico legal aspects: so far, no lawsuits but it’s probably a matter of time
- Communication and documentation of interventions
- Credibility of program
Concerns about medicolegal aspects of stewardship are frequently raised. These include such matters as the creation of discoverable recommendations (e.g., in progress notes) which may or may not be accepted by the primary team in cases with poor outcomes. A Best Practice Advisory, even if not included in a progress note, might also be of concern. Another concern may be related to forced discontinuation of a therapy. Concerns about use of decision support systems have also been raised. Despite such often raised concerns, I am unaware of actual legal actions related to stewardship activities. I would appreciate learning of such cases.

Stan Deresinski, Redwood City, CA
PROBLEMS

I know of no instance where individual antibiotic stewardship guidelines have been cited, but good plaintiff’s attorneys do know IDSA guidelines and guidelines promulgated by many specialty societies. They certainly use them as established standards of care when not followed for an individual patient. When such guidelines are in conflict, e.g. Ortho and IM guidelines for post-op anticoagulation or Ortho and IDSA/AHA guidelines concerning the need for antibiotic prophylaxis following joint replacement, they pick the ones suited to their post bad outcome argument.
PROBLEMS

It is never good when doctors in different specialties point fingers at each other in the courtroom (nor is it wise in the medical record). Institutional policies might be reasonably construed as even more “binding” than national society guidelines. Nonadherence to Ab stewardship policies is probably best handled out of the medical record for many reasons, but if an individual physician, wishes to violate them for an individual patient, he or she would be prudent to justify the rationale in the record. If institutional policies are different from national guidelines, the policymakers had better be prepared someday to justify those differences.
PROBLEMS
I have testified in a number of malpractice cases where alleged deviation from institutional infection control policies and a variety of other patient safety related policies are cited to justify claims of “beneath the standard of care.” Certainly, this may vary from one state to another, but it is hard for me to imagine that antibiotic stewardship policies would be sacrosanct or treated any differently by plaintiff’s attorneys than other institutional policies.

In omnia paratus!

John R. Black, MD
Adj. Professor of Clinical Medicine, IU School of Medicine
Indianapolis, IN
PROBLEMS

- Careful wording of recommendations
- Documentation of rationale for recommendation as well as reasons for refusal
- Credibility and success of program depends upon buy-in from medical staff
How can we classify interventions:
1. Wrong
2. Best option
3. Room for improvement
EXAMPLES

• Cefazolin for MRSA infection
• Vanco for MRSA osteomyelitis
• Carbapenem for UTI
• Vancomycin and Zosyn for cellulitis in diabetic patient
• Zosyn for acute cholecystitis
• Daptomycin for MRSA pneumonia
• Vanco for HAP with sputum negative for MRSA, in addition to Zosyn
• Unasyn for perforated diverticulitis
OUR PROGRAM

- Several antimicrobial formulary restrictions already in place
- Dose optimization strategies by pharmacy
- Add prospective audit and feedback with Infectious Disease physician rounding
PURPOSE

- Optimize use of antimicrobials
- Minimizing unintended consequences of antimicrobial use:
  - Toxicity
  - Emergence of resistance
- Reduce healthcare costs without adversely impacting quality of care.
THE TEAM

- Infectious Disease Physician
- Clinical Pharmacist
- Infection Control
- Clinical Microbiologist
THE AMS PROGRAM SO FAR

- Promote appropriate selection through concurrent monitoring (3x/week chart review of all patients on antibiotics)
- Monitor resistance patterns through updated antibiogram
- Develop best practice empiric antimicrobial therapy guidelines adapted to our antibiogram
THE AMS PROGRAM SO FAR

- Focus on broad-spectrum, high-risk or high-cost agents
- Promote antibiotic streamlining and de-escalation
- Perform education on a variety of levels to healthcare professionals (Grand Round/ key physician committee presentation)
- Guidelines for Use of Procalcitonin
## The AMS Program So Far

<table>
<thead>
<tr>
<th></th>
<th>Acute Care Antimicrobial Expenditures</th>
<th>% Antimicrobial Expenditures/Pharmaceutical Expenditures</th>
<th>Antimicrobial Expenditures/Patient Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>$464,010.56</td>
<td>9.1%</td>
<td>$10.64</td>
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<tr>
<td>2012</td>
<td>$529,713.48</td>
<td>11%</td>
<td>$13.26</td>
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<tr>
<td>*2011</td>
<td>$526,551.37</td>
<td>11.71%</td>
<td>$13.97</td>
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<tr>
<td>2010</td>
<td>$685,667.72</td>
<td>15.5%</td>
<td>$17.16</td>
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<tr>
<td>2009</td>
<td>$554,370</td>
<td>*14%</td>
<td>$13.67</td>
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<td>2008</td>
<td>$523,643</td>
<td>12%</td>
<td>$15.88</td>
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*Note: The * symbol indicates a notable change in antimicrobial expenditures.*
THE AMS PROGRAM SO FAR

Days of Therapy (DOT)/1,000 Patient Days &
Total Costs (2014) with
Cost savings/loss (2010 vs. 2014)

- Vancocin: $34,739 (↑ $1,209)
- Linezolid/Daptomycin/Tigecycline: $16,087 (↑ $4,930)
- 3rd/4th Generation Cephalosporins: $414,23 (↓ $1,364)
- Piperacillin/Trambeclam: $5,756 (↓ $1,893)
- Quinolones: $20,645 (↓ $2,039)
- Carbapenems: $3,503 (↓ $134)
- Fluconazole: $25,999 (↓ $843)
- Other antifungals: $42

Bar graph showing the comparison of costs and days of therapy for various classes of antibiotics.
## THE AMS PROGRAM SO FAR

<table>
<thead>
<tr>
<th>Gram Positive Organisms</th>
<th>Ampicillin</th>
<th>Vancomycin</th>
<th>Nafcillin (oxacillin)</th>
<th>Clindamycin</th>
<th>Doxycycline</th>
<th>TMP/SMZ (Bactrim)</th>
<th>Penicillin G</th>
<th>Ceftriaxone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Enterococcus Species</strong></td>
<td>2010 80%</td>
<td>2010 87%</td>
<td>2014 85%</td>
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<tr>
<td><strong>Staphylococcus aureus</strong></td>
<td>2010 100%</td>
<td>2010 61%</td>
<td>2014 68%</td>
<td>2010 73%</td>
<td>2010 98%</td>
<td>2010 98%</td>
<td>2010 99%</td>
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<tr>
<td><strong>Staph aureus - MRSA</strong></td>
<td>2010 100%</td>
<td>2014 100%</td>
<td>---</td>
<td>2010 57%</td>
<td>2010 100%</td>
<td>2010 99%</td>
<td>2010 99%</td>
<td>2014 96%</td>
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<tr>
<td><strong>Staph aureus - MSSA</strong></td>
<td>2010 100%</td>
<td>2010 100%</td>
<td>2014 100%</td>
<td>2010 82%</td>
<td>2010 97%</td>
<td>2010 99%</td>
<td>2010 98%</td>
<td>2014 98%</td>
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<tr>
<td><strong>Strep Pneumo (meningitis sensitive)</strong></td>
<td>2010 72%</td>
<td>2014 91%</td>
<td>2014 91%</td>
<td>2010 90%</td>
<td>2014 100%</td>
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<tr>
<td>Gram Negative Organisms</td>
<td>Cefazolin</td>
<td>Ceftriaxone</td>
<td>Ampicillin+Sulbactam (Unasyn)</td>
<td>FQ - Cipro/Levofloxacin</td>
<td>Piperacillin+Tazobactam</td>
<td>Cefepime</td>
<td>Carbapenem-Imipenem/Meropenem</td>
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<tr>
<td>Escherichia coli</td>
<td>2010 89%</td>
<td>2010 97%</td>
<td>2010 73%</td>
<td>2010 89%</td>
<td>2010 96%</td>
<td>2010 97%</td>
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<td>2014 89%</td>
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<td>Klebsiella pneumonia</td>
<td>2010 93%</td>
<td>2010 96%</td>
<td>2010 88%</td>
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<td>Proteus sp</td>
<td>2010 96%</td>
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<td>Enterobacter sp.</td>
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<td>Pseudomonas Aeruginosa</td>
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<td>2014 92%</td>
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Total antibacterial drug use (days of therapy per 1000 patient-days), ranked from lowest use to highest, during calendar year 2009 in 70 academic medical center hospitals.

Ron E. Polk et al. Clin Infect Dis. 2011;cid.cir672
The ratio of hospital-wide observed (O) antibacterial drug use and expected (E) use for 70 academic medical center (AMC) hospitals.

Ron E. Polk et al. Clin Infect Dis. 2011;cid.cir672

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NEW GOALS
The ratio of observed (O) to expected (E) antibacterial use (solid bar, DOT per 1000 patient-days; open bar, LOT per 1000 patient-days) by clinical service line (CSL) for 3 hospitals from Figure 1.

Ron E. Polk et al. Clin Infect Dis. 2011;cid.cir672

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STRAIN OF 2000

You are the next class of drug-resistant bacteria. As humans continue to abuse and overuse antibiotics, your ranks will swell. So, go out there and mutate! And remember: that which does not kill us makes us stronger!!