Antimicrobial Stewardship in Acute and Long Term Healthcare Facilities: Design, Implementation and Challenges

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February 24, 2010

Antimicrobial Stewardship: Design, Implementation and Efficacy

- Background
- Conceptual framework for use of antibiotics
- Strategies to improve antibiotic use
- Can antimicrobial stewardship limit resistance?
- The Future

MAGNITUDE OF ANTIMICROBIAL USE

- Antibiotics are the second most commonly used class of drugs in the United States
- More than 8.5 billion dollars are spent on anti-infecives annually
  - 200-300 million antimicrobials prescribed annually
    - 45% for outpatient use
- 30-50% of all hospitalized patients receive antibiotics
Anti-Infective Use in US Hospitals


### Table 5. Top 10 Therapeutic Classes by Expenditures for Nonfederal Hospitals

<table>
<thead>
<tr>
<th>Therapeutic Class</th>
<th>Total 2005 Expenditure ($ Thousands)</th>
<th>Percentage of Total 2005 Nonfederal Hospital Expenditures</th>
<th>Percent Increase over 2004</th>
<th>2006 Expenditures (Through Sep 2006) ($ Thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic antibiotics</td>
<td>3,107,632</td>
<td>12.0</td>
<td>7.1</td>
<td>3,298,876</td>
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<tr>
<td>Antimicrobial agents</td>
<td>2,901,424</td>
<td>10.8</td>
<td>7.9</td>
<td>2,906,742</td>
</tr>
<tr>
<td>Blood products</td>
<td>1,642,378</td>
<td>6.4</td>
<td>7.4</td>
<td>2,136,230</td>
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<tr>
<td>Diagnostics</td>
<td>1,380,280</td>
<td>5.4</td>
<td>5.6</td>
<td>1,396,353</td>
</tr>
<tr>
<td>Hospital solutions</td>
<td>1,172,584</td>
<td>4.5</td>
<td>3.5</td>
<td>865,330</td>
</tr>
<tr>
<td>Psychotherapeutics</td>
<td>1,128,017</td>
<td>4.4</td>
<td>1.5</td>
<td>841,730</td>
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<tr>
<td>Anesthetics</td>
<td>1,125,912</td>
<td>4.4</td>
<td>5.8</td>
<td>713,932</td>
</tr>
<tr>
<td>Biologics</td>
<td>1,064,736</td>
<td>4.3</td>
<td>2.4</td>
<td>821,579</td>
</tr>
<tr>
<td>Gastrointestinal agents</td>
<td>967,589</td>
<td>3.7</td>
<td>1.1</td>
<td>784,039</td>
</tr>
</tbody>
</table>

Causal Association Between Antimicrobial Use and Resistance In Healthcare: Lines of Evidence

- Changes on antimicrobial use are paralleled by changes in prevalence of resistance
- Resistance more prevalent in healthcare associated infections compared with community-acquired infections
- Patients with infections caused by resistant strains more likely to have received prior antimicrobials
- Areas in hospitals with highest rates of antimicrobial use have highest rates of resistance
- Increased duration of antimicrobial exposure increases risk of colonization with resistant organisms

Unnecessary Use of Antimicrobials in Hospitalized Patients

- Prospective observational study in ICU
- 576 (30%) of 1941 antimicrobial days of therapy deemed unnecessary

#### Most Common Reasons for Unnecessary Days of Therapy

- Duration of Therapy Longer than Necessary: 192
- Noninfectious or Nonbacterial Syndrome: 187
- Treatment of Colonization or Contamination: 94

Hecker MT et al. Arch Intern Med. 2003;163:872-878
New Antibacterial Drugs Approved By FDA

Antimicrobial Stewardship Goals

► Ensure the proper use of antimicrobials
  • To optimize clinical outcomes
  • Decrease the risk of adverse effects
  • Reduce or stabilize resistance
► Promote cost effectiveness

From the Prescriber’s Perspective, How Should Antibiotic Stewardship Be Prioritized Relative to Clinical Outcomes In Individual Patients?
What Are the Consequences of Failing to Prescribe an Antibiotic When The Patient Needs It?

- Preventable morbidity, possibly mortality occurs
- Physician bears sole responsibility-personal impact high

Ibrahim EH et. al. Chest 2000;118:146-155

What Are the Consequences of Prescribing an Antibiotic When The Patient Does Not Need It?

- Small, incremental contribution to ecology of resistance
- Small, incremental contribution to cost of care
- Responsibility shared equally by all prescribing physicians-personal impact small
- Small chance of toxicity
Should This Antimicrobial Agent Be Prescribed To This Patient At This Time?

- Probability of preventing morbidity and mortality if prescribed
- Contribution to resistance
- Toxicity
- Cost

Or

- Increased morbidity and mortality if NOT prescribed

The Default Condition for Most Prescribers In The Setting of Diagnostic/Therapeutic Uncertainty:

- Probability of preventing morbidity and mortality if prescribed
- Resistance
- Toxicity
- Cost

“The Tragedy of the Commons”

Hardin G. Science 1968;162:1243-8
Antimicrobial Stewardship Interventions

- Education
- Formulary restriction
- Prior approval
- Prospective Audit with Feedback (Streamlining)
- Cycling/rotation
- Computer-assisted programs
- Comprehensive programs

CONCEPTUAL FRAMEWORK

Antimicrobial Stewardship Interventions

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- Comprehensive programs
Knowledge of Infectious Diseases

Knowledge of Patient

Knowledge of Antibiotics

Physician’s Attitude

Decision to Use Antibiotics

Patient’s Attitude and Desires

Availability of Antibiotics

Choice of Antibiotics

Refine Choice of Antibiotics

Culture Results

**FORMULARY RESTRICTION/PRIOR APPROVAL PROGRAMS**

- Multiple approaches
  - Phone approval
  - Antibiotic order forms
  - Automatic stop orders
  - Direct interaction
  - Simple chart entry
- Most onerous to physicians
- Most effective single intervention to decrease use of specific antimicrobials
  - McGowan and Finland. J Infect Dis 1974;130:165-8
  - Recco et al. JAMA 1979;241:2283-6

**Antimicrobial restriction: unintended consequences?**

- Pre-approval policy for cephalosporins in response to increased incidence of cephalosporin-resistant Klebsiella
  - 80% reduction in cephalosporin use
  - 44% hospital-wide reduction in incidence of cephalosporin-resistant Klebsiella
  - Imipenem use increased 141%
  - 69% increase of carbapenem-resistant Pseudomonas

References: JAMA: 1998;280:1233-77
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Choice of Antibiotics

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Prospective Audit & Feedback Example

Prospective Audit & Feedback Example

Parenteral antibiotic use, cost per 1000 patient-days, and Medicare Case Mix Index (MCCMI)

Percent

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ANTIMICROBIAL CYCLING

► Withdrawal of an antibiotic or antibiotic class from general use (either within a patient care ward or institution) for a designated period of time, and then substituting it with antibiotics from a different class possessing comparable spectrum of activity but different mechanisms of antimicrobial resistance. The process is repeated at scheduled intervals

RATIONALE FOR ANTIMICROBIAL CYCLING

► “It’s hard to hit a moving target”
► Resistance will decline or emerge at a slower rate by limiting bacterial exposure to specific agents
► Frequent switching will decrease resistance to any single agent
Knowledge of Infectious Diseases
Knowledge of Patient

Physician's Attitude

Decision to Use Antibiotics

Patient's Attitude and Desires

Availability of Antibiotics

Refine Choice of Antibiotics

Culture

CYCLING/ROTATION

AminoGlycoside Cycling


Bergstrom C. T. et.al. PNAS 2004;101:13285-13290

Mean resistance levels as a function of cycle period

Gerding C. T. et.al. PNAS 2004;101:13285-13290

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Computerized Antibiotic Assistant: LDS Hospital

Clinical Outcomes

- Significant reductions in:
  - Orders for drugs with reported allergies (35 vs. 146)
  - Excess drug dosages (87 vs. 405)
  - Antibiotic-susceptibility mismatches (12 vs. 206)
  - Mean number of days of excessive dosages (2.7 vs. 5.9)
  - Adverse events (4 vs. 28)


Institutional Outcomes

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>PREINTERVENTION PERIOD</th>
<th>INTERVENTION PERIOD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>REGIMEN FOLLOWED</td>
<td>REGIMEN OVERRIDDEN</td>
</tr>
<tr>
<td>LOS - ICU (days)</td>
<td>4.9</td>
<td>2.7</td>
</tr>
<tr>
<td>Total LOS (days)</td>
<td>12.9</td>
<td>10.0</td>
</tr>
<tr>
<td>Cost of antiinfective ($)</td>
<td>340</td>
<td>102</td>
</tr>
<tr>
<td>Total cost ($)</td>
<td>35,283</td>
<td>26,315</td>
</tr>
</tbody>
</table>

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Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

CID 2007; 44:159
### Core members: (A-II)
- Infectious diseases physician
- Clinical pharmacist with ID Training
- Optimally to also include: infection control professionals, hospital epidemiologists, clinical microbiologists, and information specialists when available (A-III)

### Close collaboration with the Pharmacy and Therapeutics Committee (A-III)

### Development with the support administration and the collaboration with quality assurance and patient safety teams or their equivalents (A-III)

### Intervention and feedback critical to success

### IDSA/SHEA Guidelines: Specific Language

**CAN ANTIMICROBIAL STEWARDSHIP LIMIT THE EMERGENCE OF RESISTANCE?**

**Best Evidence**

- Decreased CDI
- Decreased resistant GNB
- Decreased VRE

### POOR STUDY DESIGN ISSUES

- Selection biases
- Insufficient power
- Varying duration of intervention
- Failure to deal with confounders
  - Cause of resistance is multifactorial
  - Community vs. nosocomial pathogens
  - Multiple concurrent control measures
  - Colonization pressure
- Generalizability
  - Bug/drug combinations
  - Setting
Distribution of Antimicrobial Use Between Nursing Homes, September 2001 to February 2002, (N=73 facilities in 4 States)


42% of residents received antibiotics during the six month study.

Successful Intervention in a Chicago Nursing Home


- Developed diagnostic and treatment algorithms in collaboration with clinicians
- Education sessions which included case reviews and feedback

The Future of Antimicrobial Stewardship?

- Improved Medical Informatics
  - Better computerized decision support
  - Standardized measurement of use with comparative feedback
    - Individual prescriber
    - Unit
    - Service
    - Hospital
Should This Antimicrobial Agent Be Prescribed To This Patient At This Time?

Probability of preventing Morbidity and mortality If prescribed Or Increased morbidity and Mortality of NOT prescribed

Contribution to Resistance
Toxicity
Cost

YES
NO

Ease of Prioritizing Antibiotic Stewardship Relative to Clinical Outcome In Individual Patients

High

More Difficult       Most Difficult

Least Difficult     Less Difficult

Low

Severity of Illness (Margin for Therapeutic Error)

Diagnostic/Clinical Complexity

Low

The Future?

- Randomized controlled trials that inform antibiotic use
    - Randomized patients with suspected pneumonia, but with low CPIS (<6)
      - Intervention group-discontinue abx at day 3 if CPIS remains low
      - Control group-per clinician preference
    - Significant decrease in duration of therapy (3 vs 9.8 days)
    - Lower rates of bacterial superinfection and recovery of resistant organisms in intervention group
  - Comparison of 8 vs 15 days of antibiotic therapy for ventilator associated pneumonia in adults. Chastre et al. JAMA 2003;290:2588-98
    - No difference in mortality
    - More antimicrobial free days in 8 day group
    - Decreased antimicrobial resistance among those with recurrence of pulmonary infection
The Future?

- Better Epidemiologic studies of inpatient antimicrobial use
  - Who, what, when, and where?
  - Will help target efforts
- Behavioral interventions
- Antimicrobial use optimization collaboratives
  - Multiple facilities sharing stewardship strategies and comparative rates of antimicrobial use
- Better Diagnostics