Antimicrobial Stewardship: Guidelines for its Implementation
Loliet Gonzalez Martinez, Pharm.D.
Palmetto General Hospital
PGY-1 Pharmacy Resident

Disclosure
The author of this presentation has nothing to disclose concerning possible financial or personal relationships with commercial entities that may have direct or indirect interest in the subject matter of this presentation.

Objectives
- Identify the core members constituting a multidisciplinary antimicrobial stewardship team
- List the goals and outcomes of an antimicrobial stewardship
- List the core strategies for the foundation of an antimicrobial stewardship program
- Explain the elements of an antimicrobial stewardship program
Background

- 20-50% of prescribed antibiotics in hospitals are unnecessary or inappropriate
- Antimicrobial misuse has contributed to the growing resistance in both inpatient and outpatient settings

The Centers for Disease Control and Prevention (CDC) estimates “more than two million people are infected with antibiotic-resistant organisms, resulting in approximately 23,000 deaths annually”

Antimicrobial misuse increases the risk of Clostridium difficile

Executive order
National Action Plan

- Goals
  - Slow emergence of resistant bacteria
  - Strengthen National One-Health Surveillance
  - Advance development and use of rapid diagnostic test
  - Accelerate research of new antibiotics, other therapeutics and vaccines
  - Improve international collaboration

- National Strategy
  - Prevention, detection and control of resistant pathogens

Antimicrobial Stewardship Efforts Advance in US Health Systems

“The order directed the secretary of Health and Human Services to propose regulations by the end of 2016 requiring US inpatient facilities to “implement robust antibiotic stewardship programs that adhere to best practices.” The President’s Council of Advisors on Science and Technology recommended that antimicrobial stewardship programs should be mandated as a Condition of Participation (CoP) for the Centers for Medicare & Medicaid Services (CMS) for inpatient and long-term care facilities by the end of 2017.”

Antibiotic Resistance Solutions Initiative

Fiscal year 2016 (FY16) budget: $264M

- A Comprehensive Approach
- Facilitate action to combat antibiotic resistance in every state, accelerate outbreak detection and prevention innovation, and improve antibiotic use
WHERE DO INFECTIONS HAPPEN?

Estimated minimum number of illnesses and deaths due to Carbapenem-Resistant ESBL (CRE), a unique bacterial infection that, although not significantly resistant to the drugs used to treat it, is directly related to antibiotic use and resistance:

At least 250,000 illnesses,
14,000 deaths

WHERE DO INFECTIONS HAPPEN?

Estimated minimum number of illnesses and deaths caused by antibiotic resistance:

At least 2,049,442 illnesses,
23,000 deaths

WHERE DO INFECTIONS HAPPEN?

CAUSES OF ANTIBIOTIC RESISTANCE

- Over-prescribing of antibiotics
- Patients not taking antibiotics as prescribed
- Unnecessary antibiotics used in agriculture
- Poor infection control in hospitals and clinics
- Poor hygiene and sanitation practices
- Lack of rapid laboratory tests
THE GLOBAL THREAT
The full impact is unknown. There is no system in place to track antibiotic resistance globally.

A GROWING CRISIS WORLDWIDE
- In the EUROPEAN UNION, antibiotic-resistant MRSA causes the death of 25,000 per year and 3.5m extra hospital stays.
- In INDIA, over 34,000 babies died in 2002 due to pneumonia, of which 70% were infected with resistant bacteria usually passed on from their mothers.
- In THAILAND, antibiotic resistance causes 34,000 deaths and 300,000 lives shortened.
- In the UNITED STATES, antibiotic resistance causes 23,000 deaths and 2 million hospital stays.

The action
The national strategy identifies five core actions:
- Save the Development of Resistant Bacteria and Prevent the Spread of Antimicrobial-Resistant Infections
- Strengthen and/or Expand Surveillance Efforts to Enable Resistance
- Advance Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria
- Accelerate Data and Applied Research and Development for New Antimicrobials, other Therapeutics, and Vaccines
- Improve Interagency Collaboration and Capacities for Antimicrobial Resistance Prevention, Surveillance, Control, and Antimicrobial Resistance and Development

The results
The PCMG All-Solution Initiative fully implements the National Strategy for Combating Antimicrobial-Resistant Bacteria:
- Comprehensive Testing
- Rapid Detection
- Faster Outbreak Response
- Insights for Research Innovation
- Better Patient Care
- Improved Prescribing
- Site-Specific Susceptibility Testing
- Nationwide Implementation of CDC Core Elements of Hospital Antimicrobial Stewardship
- Global Partnerships for Prevention and Detection

ANTICIPATED % REDUCTION RATE
- 2016
- 2017
- 2018
- 2019
- 2020
- 2021
- 2022
Antimicrobial Stewardship

- Defined as coordinated interventions performed to improve and measure appropriate use of antimicrobials
- Promotes
  - Optimal antimicrobial drug regimen
  - Dose
  - Duration of therapy
  - Route of administration

Process Goal and Measurement

- Goal
  - Change use of a specific antimicrobial or class of antimicrobials
- Measurement
  - Successful implementation of the intervention

Outcome Goal and Measurement

- Goal
  - Reduce and prevent resistance or other unintended consequence of antimicrobial use
- Measurement
  - Antimicrobial resistance
  - Adverse drug events
  - Cost
  - Unintended consequences
  - Clostridium difficile
  - Use of non-targeted antimicrobials
Core Members

Infectious Disease Physician
- Provides legitimacy among physicians practicing at the hospital
- Ensures therapeutic guidelines and antimicrobial restriction policies are based on best evidence and practice for the patients

Clinical Pharmacists
- Act as “effector arms” for antimicrobial stewardship programs
- Staff pharmacists
  - Notify physician for an authorization when restricted antimicrobials are ordered
  - Identify orders for review by infectious disease specialist
Clinical Pharmacists

- Infectious disease clinical pharmacists
  - Develop guidelines for antimicrobial use
  - Educate physicians and other healthcare providers
  - Review hospital antimicrobial orders and provide feedback to providers
  - Administration of restrictive strategies
  - Pharmacokinetic consultations
  - Research on program outcomes

- Restricted antimicrobials required approval by paging a dedicated beeper
- Clinical pharmacists staffed beeper on weekdays. Infectious disease physician fellows staffed the beeper in nights and weekends

Table 5. Factors making AMT and ID fellow recommendations for antimicrobial treatment inappropriate.

<table>
<thead>
<tr>
<th>Factor</th>
<th>AMT % (n = 10)</th>
<th>ID fellows % (n = 30)</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>6 (1)</td>
<td>26 (87)</td>
<td>0.2 (0.1-0.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Spectrum too broad</td>
<td>4 (40)</td>
<td>7 (23)</td>
<td>0.2 (0.1-0.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Antibiotics too narrow</td>
<td>1 (10)</td>
<td>1 (3.3)</td>
<td>0.2 (0.0-1.4)</td>
<td>.11</td>
</tr>
<tr>
<td>Infection inappropriate (other than too broad or narrow)</td>
<td>1 (10)</td>
<td>14 (47.0)</td>
<td>0.1 (0.0-4.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Antimicrobial agent not indicated</td>
<td>6 (60)</td>
<td>9 (30)</td>
<td>0.7 (0.2-2.0)</td>
<td>.5</td>
</tr>
<tr>
<td>Route inappropriate</td>
<td>0 (0)</td>
<td>2 (6.7)</td>
<td>—</td>
<td>.17</td>
</tr>
<tr>
<td>Dose inappropriate</td>
<td>0 (0)</td>
<td>2 (6.7)</td>
<td>—</td>
<td>.17</td>
</tr>
</tbody>
</table>

Note: Some recommendations were inappropriate for ≥ 1 reason. AMT: Antimicrobial Manager; ID: Infectious Disease Fellowship.
Additional Members

- Clinical Microbiologists
  - Provide data on antimicrobial resistance rates
- Infection control staff/hospital epidemiologists
  - Studies effect of antimicrobial stewardship measures
- Hospital administrators
  - Provide hospital funding, and institutional policies
- Information system specialists
  - Computer support necessary for surveillance

Core Strategies

- Retrospective review (hours to days) of antimicrobial orders
  - Optimize antimicrobial therapy
  - Assess inappropriate order
  - Adherence to hospital guidelines
  - Provide streamline strategy
  - Contact prescriber
  - Create a chart note
Formulary Restriction and Preauthorization

- Most effective method of controlling antimicrobial use
- Restrict dispensing
- May include:
  - Telephone authorization from an infectious diseases physician
  - Automatic infectious diseases consultation
  - Infectious diseases physician on call has the final authority to dispense

Supplemental Elements

Education

- Defines what is considered appropriate antimicrobial use by the institution
  - Conference Presentations
  - Student and house staff teaching sessions
  - Provision of written guidelines
Involved different periods
- Active strategies
- Education phase
Education following an active strategy decreased antimicrobial consumption

Guideline Implementation
- Incorporates local microbiology and resistance
- Recommendation
  - Diagnosis and testing
  - Admission criteria
  - Nursing care
  - Conversion to oral medication
  - Discharge planning
Clinical practice guidelines
- Intraabdominal infection
- Complicated skin
- Postoperative wound and skin structure infection
- Lower respiratory tract
- Urinary tract infection
- Sepsis of undetermined cause
- IV catheter related infection

Implemented in an intensive care unit setting

Table 1. Comparison of types of infections and clinical outcome: Phase 1 vs. Phase 2

<table>
<thead>
<tr>
<th></th>
<th>Phase 1</th>
<th>Phase 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total infections</td>
<td>15 (9)</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Outcome of infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement/improvement</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Persist</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Clinical failure</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Death</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Total infections</td>
<td>24 (15)</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Outcome of infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement/improvement</td>
<td>19</td>
<td>5</td>
</tr>
<tr>
<td>Persist</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Clinical failure</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Death</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>18 (18)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Outcome of infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement/improvement</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Persist</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Clinical failure</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Intraabdominal infection</td>
<td>8 (8)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Outcome of infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement/improvement</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Persist</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Clinical failure</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Death</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>IV catheter related infection</td>
<td>9 (9)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Outcome of infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement/improvement</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Persist</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Clinical failure</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Death</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Sepsis of undetermined cause</td>
<td>16 (16)</td>
<td>9 (9)</td>
</tr>
<tr>
<td>Outcome of infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement/improvement</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Persist</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Clinical failure</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Death</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>

Antimicrobial Cycling
- Scheduled removal of antimicrobial within a time frame
- Prevents development of antimicrobial resistance
- Reintroduction of original antimicrobial is likely to reintroduce resistance
- Insufficient data to recommend routine use
Antimicrobial Order Forms

- Decreases antimicrobial consumption
- Provides automatic stop orders
- Requires physician justification

- Provided antibiotic order sheet on each patient’s chart
- Required clinical indication for antibiotic order
- Number of antibiotic treatment courses and percentage of patients receiving antibiotics decreased by 30% and 17% respectively over a 25-month period

Streamlining and De-escalation of Therapy

- Decreases antimicrobial exposure and cost savings
- Performed after availability of cultures and sensitivities
- Includes discontinuation of empirical therapy
Pharmacists reviewed patients charts
- 192/1182 patients with redundant combinations
- 71% found to be inappropriate
- Physician overprescribing errors accounted for 56%

Figure 1. Flow diagram of inpatient antibiotic recipients during 23 surveillance days. The distribution of cases of potentially redundant regimens, their appropriateness, sources of confirmed redundancies, and intervention acceptance rate are shown.

Dose Optimization
- Based on
  - Individual patient characteristics
  - Causative organism
  - Site of infection
  - Pharmacokinetic characteristics of the drug
IV-to-PO Therapy Conversion

- Enhanced oral bioavailability among certain antimicrobials
- Results in reduced
  - Length of stay
  - Healthcare costs
  - Complications due to intravenous access

Pharmacoeconomics

A Pharmacist-Initiated Program of Intravenous to Oral Antibiotic Conversion

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminoglycoside</td>
<td>17.5%</td>
</tr>
<tr>
<td>Cephalosporin</td>
<td>20.0%</td>
</tr>
<tr>
<td>Other</td>
<td>27.5%</td>
</tr>
<tr>
<td>Cefuroxime axetil</td>
<td>19.0%</td>
</tr>
</tbody>
</table>

Figure 3: Oral antibiotic conversions

Computer Surveillance

- Facilitates stewardship
  - Targets antimicrobial interventions
  - Tracks antimicrobial resistance patterns
  - Identifies nosocomial infections and adverse drug events
- Sentri7
  - Interfaces hospital’s databases to identify at-risk patients
  - Provides customizable alerts based on the rules created
Computer Surveillance

CDC Core Elements Checklist

Clinical Pearls

✓ According to CDC, half of antibiotics prescribed in outpatient settings are unnecessary
✓ Outpatient pharmacists
  • Appropriate antimicrobial utilization
  • Dose verification
  • Length of treatment
  • Patient education
Conclusions

- A multidisciplinary team approach is required for the proper implementation of an antimicrobial stewardship
- Combination of proactive strategies and elements to supplement it enhances adherence

T/F Questions

- T/F According to the CDC, 20-50% of antibiotics prescribed in the United States’ acute care hospitals are either unnecessary or inappropriate
- T/F Antimicrobial restriction poses additional problems to pharmacists, with little to no benefit in reducing overall antimicrobial use
- T/F There are two core strategies that provide the foundation for an antimicrobial stewardship program, these includes formulary restriction/preauthorization and antimicrobial cycling

Questions
References