Implementation of an Antimicrobial Stewardship Program: Justification, Cost, and Challenges

Elizabeth D. Hermsen, Pharm.D., M.B.A., BCPS-ID
Director, Global Antimicrobial Stewardship
Merck
elizabeth.hermsen@merck.com

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Objectives

• List the resources necessary to initiate an antimicrobial stewardship program (ASP).
• Identify potential financial and institutional barriers to implementation of an ASP.
• Justify the benefits of an ASP to administrative and clinical leadership.
Outline

- Background
- Antimicrobial stewardship
  - Introduction
  - Guidelines/strategy summary
  - Implementation
  - Subsequent justification
  - Best practices/Barriers
- Summary

Resistance Among Gram-Positive Organisms

- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- Vancomycin-Resistant Enterococci (VRE)

Accessed April 2013.
Resistance Among Gram-Negative Organisms

Impact of Antibiotic Resistance

* A. baumannii not tested in 2006.

New Antibacterial Agents

United States, 1983-2012

Key Points

• Antimicrobial-resistant organisms are prevalent and are increasingly encountered.

• Antibiotic resistance is bad for our patients and our healthcare system.

• Novel antimicrobial agents are sparse.
Pattern of Antibiotic Resistance

Discovery

Exuberant Use

Development of Resistance through Mutation and Natural Selection

Rapid Dissemination via Clonal Expansion and Horizontal Transmission

Timeline of Resistance

First clinical use

1940

Penicillin (1942)
Ampicillin (1962)
Cefotaxime (1979)
Imipenem (1985)

2000

First resistance

Osteomyelitis due to penicillinase-producing S aureus (1949)
Description of TEM penicillinase (1966)
First clinical ESBL (SHV-2) (1985)
Description of CTX-M (1990)
Carbapenemase from Enterobacteriaceae (1993)

Controlling Erythromycin Resistance in Group A Streptococci, Finland

Key Points

• Antimicrobial use is the key driver of antimicrobial resistance.

• More prudent use of antimicrobial agents can slow or reverse the development of resistance.

Seppala NEJM. 1997;337:441
Post-study data courtesy of Ron Rolk, Pharm.D.
Antimicrobial Stewardship

• A rational, systematic approach to the use of antimicrobial agents in order to achieve optimal outcomes. Focus = patient and public health.

  Correct agent  Cure/prevent infection
  Right dose   Minimize toxicity
Appropriate duration Prevent emergence of resistance

Guidelines Summary

• Acute care setting
• Multidisciplinary involvement
  – A multidisciplinary ASP team should include an infectious diseases (ID) physician and pharmacist and other key stakeholders as determined by the institution
  – Policy statement – physician-directed or supervised multidisciplinary ASP team with ≥ 1 member trained in antimicrobial stewardship
• Core strategies:
  – Prospective audit with intervention and feedback
  – Formulary restriction and authorization
• Supplemental strategies:
  – Education
  – Guidelines/clinical pathways
  – Order forms
  – De-escalation
  – Dose optimization
  – IV-to-oral conversion

Prospective Audit with Intervention & Feedback

- Prescribing/dispensing occurs as usual
- Targets established for potential intervention
  - Examples:
    - Drug-bug mismatch
    - Redundant therapy
    - Poly-antibacterial therapy
- Retrospective review & intervention if needed
  - Start/stop/change therapy
  - De-escalation
  - Dosing optimization
Prospective Audit & Feedback

• Advantages
  – Maintain prescriber autonomy
  – Educational opportunity
  – Review patient information before interaction
  – May decrease inappropriate antimicrobial use

• Disadvantages
  – Compliance voluntary
  – Identification of patients may require computer support
  – Reluctance to change therapy if the patient is doing well
  – Permits some inappropriate antimicrobial use (with retrospective audit)
  – May be difficult to identify decision-making team

Formulary Restriction & Preauthorization

• Restricted antimicrobial formulary developed with criteria to define appropriate use
  – Example: micafungin
    • Invasive aspergillosis in a patient failing/intolerant of therapy with voriconazole.
    • Empiric treatment of moderate-severe invasive candidiasis or those with recent azole exposure.
    • Candidal infections refractory to azoles.
    • Invasive candidiasis due to non-albicans species.

• Authorization prior to dispensing
• Selective susceptibility reporting
Formulary Restriction & Preauthorization

- **Advantages**
  - Direct control over antimicrobial use
  - Effective control of antimicrobial use during outbreaks
  - Decreased inappropriate use of antimicrobials

- **Disadvantages**
  - Personnel needs
  - Antagonistic relationship (loss of autonomy)
  - Therapy may be delayed
  - Manipulation of the system
  - ID physicians often exempt
  - “Squeezing the balloon”

Education

- **Essential foundation of every ASP**

- **Large group/general vs. one-on-one/patient-specific**

- **Attempt to change behavior through acquisition of new knowledge or reminder of existing knowledge**
Core Principles for Education

- Extent, causes, and spread
- Mechanism of action, toxicity, and costs (collateral damage)
- Infection, isolation and identification of bacteria, susceptibility to antibiotics
- Indication for antimicrobials
- Antibiotic prophylaxis
- Recording and documentation of antimicrobial choice, duration, and timing
- Empiric therapy, communication with microbiology laboratory, following guidelines in clinical practice
- Discussion technique

Education

- **Advantages**
  - Increase awareness of guidelines, susceptibility patterns
  - May influence prescribing behavior
  - Promotes acceptance of ASP

- **Disadvantages**
  - Passive
  - Time consuming
  - Attendance often mandatory
  - Dilution
Guidelines/Clinical Pathways

• Create protocols to guide antimicrobial use for a given infection
  – Specific to institutional formulary, patient populations, and resistance patterns

• Evidence-based

Guidelines/Clinical Pathways

• Advantages
  – Decrease inappropriate antimicrobial use
  – Form of education

• Disadvantages
  – Adherence is usually voluntary
  – “Cookbook medicine”
  – Maintenance
  – Awareness
Antimicrobial Order Forms

• Paper vs. integrated into electronic health record
  – Optional vs. mandatory
• Potential Uses:
  – Support guidelines/pathways
  – Communicate/enforce ASP recommendations
  – Enhance documentation & thought process

Example: Surgical Prophylaxis

• Features of Form
  – Antibiotic recommendations with alternatives for allergies
  – Dosing automatically adjusted by pharmacists for weight and renal function
  – Automatic antibiotic discontinuation at 24 hours
  – Flexibility for "off-protocol" prescribing

  – Pre-/post-intervention study (n=406; n=396, respectively)
    – Significantly increased appropriate antibiotic choice (62% vs. 85%, p<0.001), dose (62% vs. 90%, p<0.001), and duration (78% vs. 89%, p<0.001) and decreased cost ($46 vs. $40, p=0.02)

Order Forms

• Advantages
  – Increase compliance with guidelines/pathways
  – Form of education
  – Enhance documentation
  – Decrease inappropriate use

• Disadvantages
  – Availability
  – “Cookbook medicine”
  – Maintenance
  – Potential for therapy to be inadvertently stopped

De-Escalation

• Narrow spectrum of activity as appropriate in response to culture/susceptibility results and clinical response
De-escalation Case

• EB, a 61 y.o. female, was admitted to the hospital on 12/26 with abdominal pain, brown vomit, fever, and chills.
  – Started on piperacillin/tazobactam and metronidazole
• Underwent appendectomy and abscess drainage on 12/30
  – Culture → Bacteroides spp.
• Increased O₂ requirements over the next two days. Chest X-ray – LLL consolidation
  – Added ciprofloxacin and vancomycin
  – Sputum culture – K. pneumoniae and C. albicans
  – Added fluconazole

De-escalation Case

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De-escalation

• Advantages
  – Balance need for initial use of broad-spectrum therapy to “get it right up front” with need to target the organism
  – May influence future prescribing behavior
  – Decrease inappropriate use

• Disadvantages
  – Reluctance to change therapy if patient is doing well
  – May narrow therapy inappropriately

Dose Optimization

• Use pharmacokinetic (PK)/pharmacodynamic (PD) principles to choose dose that will most likely eradicate the organism, minimize toxicity, and prevent resistance
• Affected by minimum inhibitory concentration (MIC)
• Examples:
  – Once-daily dosing of aminoglycosides
  – Extended infusion β-lactams
Impact of MIC value on PD Targets

Beta-lactam via standard 30-minute infusion

Breakpoint for susceptibility = 4 mg/L. Both isolates are susceptible, but isolate #2 has a higher MIC & therefore less T>MIC when administered the same dose.

~30% T>MIC

~50% T>MIC

Isolate #2

MIC 2 mg/L

Isolate #1

MIC 1 mg/L

Concentration (mg/L)

Time (hrs)

1 2 3 4 5 6

Impact of MIC value on PD Targets

Piperacillin/tazobactam Target Attainment vs. P. aeruginosa

3.375g q8h over 4h achieves over 90% probability of target attainment up to an MIC of 16 mg/L versus an MIC of 1 mg/L for standard dose of 3.375g q6h over 30min

Dose Optimization

• Advantages
  – Increase likelihood of achieving PD target
  – May decrease resistance
  – May decrease drug costs
  – May allow use of drug for organisms with increased MICs

• Disadvantages
  – Logistics
  – Lack of MIC data
  – May increase pharmacy/nursing time
  – Potential for error

How to Start
Steps Toward Building an ASP

Identify Key Stakeholders

Build Buy-In

How do you gain support?

FQ-resistant *E. coli*

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MDR *P. aeruginosa*

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National Hot Topic

- CDC NHSN AUR Module
- CDC: 7 Core Elements of Hospital Antimicrobial Stewardship Programs
- CMS Proposed Rule(s)

https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf

Steps Toward Building an ASP

1. Identify Key Stakeholders
2. Build Buy-In
3. Identify Core/Supplemental Strategies
4. Delineate Goals & Outcome Measures
Outcome Measures

- **Patient outcomes**
  - Clinical cure
  - LOS/ICU LOS
  - Readmission
  - Patient mortality

- **Collateral damage**
  - Selection of pathogenic organisms (e.g., CDI)
  - Resistance
  - Toxicity

- **Drug consumption/costs**
  - Defined daily doses, days of therapy, length of therapy
  - Predefined costs, prices, or charges

- **Process measures**
  - Appropriateness of therapy
  - Adherence to guidelines
  - Time to appropriate therapy


Steps Toward Building an ASP

1. Identify Key Stakeholders
2. Build Buy-In
3. Identify Core/Supplemental Strategies
4. Delineate Goals & Outcome Measures
5. Draft Formal Proposal
Formal Proposal

- Background
  - Impact of resistance
  - ASP literature
  - Legislative/policy proposals/changes
- Proposed Program
  - Goals
  - Required core personnel & compensation
  - Core/supplemental strategies
- Benefits & Outcome Measures
  - Focus on more appropriate patient care… then reduced costs
  - Period of review
- Future plans & Areas of Growth
- Financial Justification

Initial Cost Justification

- Personnel
- Cost savings vs. Cost avoidance
- Length of stay
ASP is approved! Now what?

Recruitment...
Implementation Plan: Key Considerations

- Low hanging fruit
- Data availability
- Core strategy
  - "Hours of operation"
  - Coverage in the absence of ASP personnel
- Mechanism of communication
- Prescriptive authority
- Intervention documentation/tracking
- Trending/benchmarking
- Reporting structure and frequency
- Integration across multiple institutions

Building Buy-In

- Identify key opinion leaders
  - Individual meetings
- Marketing
  - Branding
  - Elevator pitch
  - Newsletters/"Launch"
- Communication/Education
Committee Infrastructure

- Antimicrobial Subcommittee
- Pharmacy & Therapeutics Committee
- Medical Executive Committee
- Clinical Microbiology Operations Committee
- Infection Prevention Committee
- Quality/Patient Safety Committee

Subsequent Cost Justification
Subsequent Cost Justification (cont.)

- Specific projects

  - Blood culture contamination in ED
    - 7.4% in Oct 06 to 2.1% in May 08
    - ~4800 blood cultures/year
    - Previous study → contaminated culture costs $104.75
    - Saved ~$26,500
Subsequent Cost Justification (cont.)

- Antimicrobial surgical prophylaxis order form
  - Pre-/post-intervention study
  - Average cost of antimicrobial surgical prophylaxis decreased by $6/patient ($p=0.02$)
  - 70% compliance with form
  - Save ~$30,000/year


Subsequent Cost Justification (cont.)

- *Clostridium difficile* infection (CDI) management
  - 2001 to 2007 → CDI rate increased from 0.99 to 1.46 cases/1000 patient days
  - Management algorithm and cleaning procedures implemented July 2007
    - ASP, Infection Control, Microbiology, Environmental Services, ID, Gastroenterology, Hem/Onc, Solid Organ Transplantation, and Pediatrics
Subsequent Cost Justification (cont.)

- **Clostridium difficile** infection (CDI) management
  - From Jul 2007-Aug 2008, decreased CDI rate by 1.21 cases/1000 patient days → 194 cases/year
  - $2,454 attributable costs/CDI episode* → saved ~$475,000

Tips for Success

- Round with ID team, study antibiogram trends, and meet with key stakeholders to survey for ID problems
- Network!
- Marketing
- Information resource (website)
- Build relationships across disciplines
- Standard operating procedures, policies
- Ensure appropriate data and timing
- Establish mechanism for evaluation
- Study what you do
- Partner with Finance Dept.
- Budget for growth
- Baby steps

Potential Barriers

- Enhancing patient care vs. saving money
- Human and financial resources
- Information systems
- Communication
- Inflation/new products
- Evaluation
- ID staff resistance
- Internal medical staff resistance
  - Enforcement
- Competing initiatives
Summary

- Antimicrobial resistance is increasing → negatively affects patients & healthcare systems

- More prudent use of antimicrobial agents can slow or reverse the development of resistance → antimicrobial stewardship
  – Focus is patient outcomes and public health

- Many potential best practices and barriers → learn by sharing experiences!