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

![Graph showing resistance among Gram-negative organisms over time.](image)

* K. pneumoniae
* A. baumannii* (not tested in 2006)


Impact of Antibiotic Resistance

![Graph showing impact of antibiotic resistance.](image)

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)

Description of CTX-M (1990)

First clinical ESBL (1985)

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.
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
  – 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

• 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.

- Isolate #1: MIC 1 mg/L
- Isolate #2: MIC 2 mg/L

- ~30% T>MIC
- ~50% T>MIC

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*  
MDR *P. aeruginosa*

- NHSN 2007-2008
- NHSN 2009-2010
- Your hospital 2007-2008
- Your hospital 2009-2010

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

DANGER THIN ICE
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

[Graph showing Antimicrobial Expenditures ($) over Time (yrs.) with an arrow indicating ASP]
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!