Meet the Antimicrobial Stewardship Pharmacists

Thursday, April 21st, 2016
Ohio Society of Health-System Pharmacists Annual Meeting
Objectives

By the end of this session, the listener should be able to:

• **PHARMACISTS:**
  • Identify the impetus for OSHP to focus on the Pharmacy Practice Model Initiative’s recommendation related to antimicrobial stewardship
  • Explain one method of implementing or expanding an antimicrobial stewardship program within my institution

• **PHARMACY TECHNICIANS:**
  • Identify the impetus for OSHP to focus on the Pharmacy Practice Model Initiative’s recommendation related to antimicrobial stewardship
  • Explain the purpose of an antimicrobial stewardship program
Why is OSHP Focusing on Antimicrobial Stewardship?

• Pharmacy Practice Model Initiative (PPMI) Summit – 2010
• Development of Hospital Self-Assessment Survey
• OSHP develops Ohio PPMI (OPPMI) Steering Group & Professional Affairs Division reaches out to hospitals throughout Ohio
• National dashboard sparks idea for state-level dashboard metrics
• Antimicrobial stewardship initially and continually top priority and feasibility for expansion of pharmacy practice in Ohio
<table>
<thead>
<tr>
<th>Do pharmacists take a leadership role in an antimicrobial stewardship program in your hospital?</th>
<th>Ohio</th>
<th>National</th>
<th>Ohio opportunity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>64.89%</td>
<td>76.92%</td>
<td>YES</td>
</tr>
</tbody>
</table>

Hospital Self-Assessment Question
Taking Leadership in Antimicrobial Stewardship
Your Antimicrobial Stewardship Pharmacists

• Rachael Craft, Pharm.D.
  • PGY1 Pharmacy Resident, Southwest General

• Riane Ghamrawi, Pharm.D., BCPS
  • Clinical Pharmacy Specialist, Adult Antimicrobial Stewardship, University Hospitals
    Case Medical Center, Department of Pharmacy Services

• Zach Jenkins, Pharm.D., BCPS
  • Clinical Pharmacy Specialist – Infectious Disease, Premier Health Partners; Assistant
    Professor of Pharmacy Practice, Cedarville University

• Rebecca Margevicius, Pharm.D., BCPS
  • Clinical Pharmacy Specialist, Southwest General

• LeAnne Moore, Pharm.D., BCPS
  • Clinical Pharmacy Specialist – Antimicrobial Stewardship, University Hospitals
    Rainbow Babies and Children's Hospital
Bacteria that resist 'last antibiotic' found in UK

Health

E. Coli Bacteria Can Transfer Antibiotic Resistance To Other Bacteria

Health

Apocalypse Pig: The Last Antibiotic Begins to Fail

WORLD

THE LANCET Infectious Diseases

Dissemination of the mcr-1 colistin resistance gene

DOI: http://dx.doi.org/10.1016/S0140-6736(16)31139-1

W. Article Info
CRE Distribution - 2001


CRE Distribution - 2006


CRE Distribution – February, 2015


Pseudomonas spp. Resistance

CDC: Antibiotic Resistance threats in the United States, 2013
Acinetobacter spp. Resistance

CDC: Antibiotic Resistance threats in the United States, 2013
Resistance Close to Home

TK 23 yo female  s/p double lung transplant secondary to CF

- **POD #5**: febrile, hypotensive, requiring fluids and NE → AKI
- **SCr**: 2.78 mg/dL (baseline 0.9 mg/dL; on CVVH)
- **BCx**: + GNB, sputum Cx: + GNB

<table>
<thead>
<tr>
<th><strong>BCx: <em>Klebsiella Pneumoniae</em></strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antibiotic</strong></td>
<td><strong>Interpretation</strong></td>
</tr>
<tr>
<td>Amikacin</td>
<td>S (MIC ≤ 16)</td>
</tr>
<tr>
<td>Ampicillin/sulbactam</td>
<td>R</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>R</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>R</td>
</tr>
<tr>
<td>Cefepime</td>
<td>R</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>R</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>R</td>
</tr>
<tr>
<td>Colistin</td>
<td>S (MIC = 2)</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>R</td>
</tr>
<tr>
<td>Meropenem</td>
<td>R (MIC ≤ 32)</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>R</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>R</td>
</tr>
</tbody>
</table>
Antimicrobial Resistance

• ESKAPE Pathogens
  • *Enterococcus faecium*
  • *Staphyloccoccus aureus*
  • *Klebsiella pneumoniae*
  • *Acinetobacter baumannii*
  • *Pseudomonas aeuroginosa*

• Antibiotic-resistant bacteria causes ~ 2 million illnesses annually in the US

The Issue at Hand

Antimicrobial Development

Number of approved antibiotics during the last 30 years.

The Race Against Antibiotic Resistance

Adapted from, Rice LB. Mayo Clin Proc 2012. 87(2): 198-206
Resistance IS NOT NEW

“There may be a danger, though, in underdosage. It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them...”

Sir Alexander Fleming
Nobel Lecture, December 11, 1945
The Future of Resistance

Consequences of Inappropriate Use of Antimicrobials

- *Clostridium difficile* infections (CDI)
- MDR Pathogens (ESBL, CRE)
- Adverse Drug Events/Toxicity
- Excess Mortality and Cost

Solution?

- IDSA recommendations for establishing antimicrobial stewardship programs
  - Active resistance monitoring, appropriate antimicrobial use, and collaboration with infection control efforts
  - Optimization of antimicrobial selection, dosing, route, and duration of therapy
    - Balance efficacy, limit unintended consequences

**ULTIMATE GOAL:** IMPROVE PATIENT CARE, HEALTH CARE OUTCOMES

Defining Stewardship

“Antimicrobial stewardship refers to coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration.”

5Ds

DIAGNOSIS
DRUG
DOSE
DURATION
DE-ESCALATION

IDSA Stewardship Policy
A Critical Balance

Importance of appropriate empiric therapy

Mortality increase when initial therapy is inappropriate

Identify source of infection to narrow empiric treatment

De-escalation of empiric therapy with cultures and sensitivities

Increase in resistance with broad spectrum antimicrobial use

Cost increase with broad spectrum antimicrobials
Stewardship Purpose

Limit inappropriate and excessive antibiotic use
Improve and optimize therapy and clinical outcomes
Ensure cost effectiveness
Stewardship Purpose

ONE SIZE STEWARDSHIP PROGRAM DOES NOT FIT ALL!

Resources, Demographic, Experience, Flexibility...
Antimicrobial Stewardship at the System-Level

Example Stewardship Program Reporting Structure

**System-Level Interventions**

<table>
<thead>
<tr>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formulary management</td>
</tr>
<tr>
<td>Formulary restrictions and pre-authorizations</td>
</tr>
<tr>
<td>Guidelines and clinical pathways</td>
</tr>
<tr>
<td>Antibiogram development</td>
</tr>
<tr>
<td>Antibiotic “time outs”</td>
</tr>
<tr>
<td>Automatic adjustment policies</td>
</tr>
<tr>
<td>Antimicrobial cycling</td>
</tr>
</tbody>
</table>
Antimicrobial Stewardship at the System-Level

Example: University Hospitals Health System
• 13 hospitals + 2 Joint Ventures + Home Care
• Includes:
  • Case Medical Center
  • Seidman Cancer Center
  • Rainbow Babies & Children’s Hospital
  • Macdonald Women’s Hospital
  • 7 community hospitals
  • 2 Critical Access hospitals

Adapted from Shawn Osborne, Pharm.D., MBA
University Hospitals

MEC / CMO

Formulary Subcommittee

Medication Safety Subcommittee

Anti Infective Subcommittee

Ad Hoc Subcommittees

Babies / Children Committee

Cancer Care Subcommittee

SMST

EMC MST

RBC MST

GMC MST

AMC MST

BMC/RMC MST

POR MST

CON MST

GEN MST

Adapted from Shawn Osborne, Pharm.D., MBA
System-Level Program Considerations

- **Staffing**
  - Clinical pharmacy staff
  - Pharmacy staff
  - ID trained staff

- **Structure**
  - Compensation and workload
  - Reporting
  - Metrics
  - Centralized vs. local

- **Site(s)**
  - Academic vs. community hospital
  - # Beds
# Guidelines and Clinical Pathways

## Benefits
- May improve antimicrobial use
- May limit practice variations

## Includes
- Empiric and targeted antimicrobial regimen selections
- Diagnostic testing modalities
- Admission and advancement criteria

## Reflects
- Current evidence (including guidelines and primary literature)
- Local formulary
- Local microbiology and resistance patterns

Clostridium difficile Infection Treatment Algorithm
Premier Health Infectious Disease Subcommittee

Age >70 years
OR
Continuation of concomitant antibiotics
OR
Recurrent C. difficile infection
OR
Moderate-severe symptoms*

yes

no

Hypotension, Shock / Critical Illness
OR
Dehydration
OR
Toxic megacolon

Metronidazole 500 mg by mouth
two times daily x 10-14 days

yes

no

Consider surgical and infectious disease consult

Vancomycin 500 mg by mouth four times daily
PLUS
Methronidazole 500 mg intravenously three times daily

If acute abdomen consider adding vancomycin 500mg enema every 6 hours

*Moderate-severe symptoms: ≥6 bowel movements/day, significant abdominal pain, WBC count >15 x 10⁹/L, renal insufficiency, or albumin <3 g/dL

Additional Considerations
- Discontinue concomitant antimicrobials whenever possible
- Consider consult to infectious disease if:
  - Concomitant antimicrobials need to be continued
  - Recurrent C diff
  - Inability to tolerate oral C diff treatment
- Do NOT send stool for follow-up testing to confirm resolution of disease (test-of-cure)
- Vancomycin taper should be considered for 3rd or subsequent episode of C diff
  - Vancomycin 125 mg by mouth four times daily x 10-14 days, then
  - Vancomycin 125 mg by mouth twice daily x 7 days, then
  - Vancomycin 175 mg by mouth daily x 7 days, then
  - Vancomycin 125 mg by mouth every other day x 2-8 weeks
- Failure of vancomycin taper may warrant consideration of fecal microbiota transplant. Consider consultation by GI and/or ID

The above guideline should be utilized in conjunction with evaluation of the patient's clinical status and the clinician's professional judgement.

**“Front End” Pathway Implementation**

- **Order for Antimicrobial Placed**
- **Reviewed by pharmacist or other responsible party before dispensing**
- **Provider notified if discrepancy exists between order and clinical pathway**
- **Order approved or changed**

**Pros:**
- Deviations from pathway may not “hit” the patient
- Proactive interventions may not be as necessary after providers gain experience

**Cons:**
- Potential for delays in care depending on provider response time
- Higher resource utilization up front
“Back End” Pathway Implementation

Order for Antimicrobial Placed → Order verified and dispensed → Targeted review by responsible party at a later date or time (e.g., ASP pharmacist) → Provider notified if discrepancy exists between order and clinical pathway → Order continued or changed

Pros:
- Less resource utilization up front
- Less potential for delays in care

Cons:
- Deviations from pathway will “hit” the patient
- More frequent interventions over a longer period of time may be necessary, as there are usually few (if any) hard stops in place
Other Considerations

• Enforcing and expanding on existing Antimicrobial Stewardship initiatives

• Applying national ASP recommendations

• Improving system-wide, institution-wide, and patient-specific antimicrobial usage

• Communicating recommendations to system hospitals
System-Wide Effort

Anti-Infective or Antimicrobial Stewardship Meetings:

• Multi-disciplinary meetings
  • ID, pharmacy, microbiology, nursing, quality staff, and trainees
  • Information technology

• Attendees from each hospital site
  • Pharmacists, ID Physicians

• Meetings and communication amongst ASP hospital representatives regularly
System-Wide Effort

• Flexibility of program is **key**
  • e.g., Antimicrobial restriction processes
    • ID support at main campus vs. community hospitals
  • e.g., ASP initiatives
IT Support Across the System

- Different EMRs across health-system hospitals?
- Central vs. local laboratories
- Similar capabilities/testing/guidelines?

Availability of additional ASP IT resources and support?
Stewardship In Pediatric Hospitals
Antibiotic Prescribing in Children

AAP Advises Physicians to Use Antibiotics Judiciously

• Report published in 2013 in collaboration with the CDC
• Goal: reduce unnecessary antibiotic prescriptions
  • Provide recommendations for stringent diagnostic criteria to distinguish between viral and bacterial infections
• Focus
  • Ear infections
  • Sinus infections
  • Strep throat

Prevalence & Characteristics of ASP in Children’s Hospitals in the United States

• Electronic survey of 42 children’s hospitals

• Thirty-Eight hospitals responded to the survey
  • 16 (38%) had a formal ASP
  • 15 (36%) were in the process of implementing a program
  • Hospitals without ASP were performing stewardship activities

Show Me the Data

• Antibiotics are prescribed during more than 50% of hospitalizations for children, often unnecessarily

• Study Objective
  • Compare antibiotic prescribing rates in a group of pediatric hospitals with formalized ASPs (ASP+) to a group of concurrent control hospitals without formalized stewardship programs (ASP-)

• Hypothesis
  • ASPs are effective in reducing antibiotic use

ASP in Freestanding Children’s Hospitals

Black Line = ASP + (9)
Gray Line = ASP – (22)

Select antimicrobials = vancomycin, linezolid, carbapenems

Stewardship at
The Team

• ID trained physician

• ID trained Pharm.D.
Components of Stewardship

• Prospective Audit and Feedback
  • Daily review of all patients receiving broad spectrum Gram-positive acting agents and carbapenems
  • For patients receiving therapy >72 hours primary team is contacted to streamline therapy and/or ID consult required

• Formulary Restriction
  • Carbapenems, Linezolid, Daptomycin, Ceftaroline
Prospective Audit & Feedback

• Daily review of patients on parenteral antibiotics
  • Recommendations
    • De-escalate
    • Discontinue
    • Dose change
    • ID consult
    • Length of therapy
Procedure

Each morning, ASP/ID pharmacist generate patient list & review all patients on IV antibiotics for appropriateness.

ASP/ID pharmacist meets with ASP medical director to discuss recommendations.

ASP team meets with primary teams after daily rounds to provide recommendations.
## Daily Review of Parenteral Antibiotics

<table>
<thead>
<tr>
<th>Date</th>
<th>Patient</th>
<th>Team</th>
<th>Antibiotic</th>
<th>Indication</th>
<th>Cultures</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/1</td>
<td>Duck, Daffy</td>
<td>PICU</td>
<td>Pip/taz</td>
<td>PNA</td>
<td>Sputum: Haemophilus BL (-)</td>
<td>de-escalate to ceftriaxone</td>
</tr>
<tr>
<td>2/1</td>
<td>Mouse, Mickey</td>
<td>Surgery</td>
<td>Cefoxitin</td>
<td>Appendicitis</td>
<td>none</td>
<td>-</td>
</tr>
<tr>
<td>2/1</td>
<td>Mermaid, Ariel</td>
<td>Yellow</td>
<td>Ceftriaxone</td>
<td>UTI</td>
<td>Urine: <em>Klebsiella</em></td>
<td>Plan 3 days</td>
</tr>
<tr>
<td>2/1</td>
<td>Carpet, Aladdin</td>
<td>NICU</td>
<td>Ampicillin Gentamicin</td>
<td>r/o sepsis</td>
<td>Blood: NG</td>
<td>-</td>
</tr>
<tr>
<td>2/1</td>
<td>King, Nala</td>
<td>Red</td>
<td>Pip/taz</td>
<td>FN</td>
<td>Blood: NG</td>
<td>Change interval to q6h</td>
</tr>
</tbody>
</table>
Other Stewardship Activities

• Antimicrobial dosing recommendations

• Vancomycin dosing protocol

• Antimicrobial stewardship pager
  • Approval of restricted antimicrobials
  • Antimicrobial therapy recommendations
The Future

• Fully automated microbiology laboratory stewardship opportunity
  • Culture results finalized 24 hours earlier
    • De-escalate from broad spectrum
    • Broaden therapy if necessary

• Antimicrobial stewardship website
Stewardship in a Non-Teaching Community Hospital

Rebecca S. Margevicius, PharmD, BCPS
Rachael M. Craft, PharmD
Southwest General

- Non-profit community hospital
- No medical residents
- 350 bed >> average census 250 patients
- 6.1 FTE Clinical Pharmacists
- 2 PGY-1 Residents, 1 PGY-2 Resident (TOC)
- Business plan for Stewardship Pharm.D. effective January 2015
- Decentralized Staffing Model
- Cerner EHR >> **No Formal Clinical Surveillance Methods**
Pharmacist Driven Stewardship Efforts

- Decentralized pharmacists
  - ED C/S Review
  - IV to PO
  - Aminoglycoside dosing and monitoring >> pharmacist orders labs (CBC, BMP)
  - Vancomycin dosing and monitoring >> pharmacist orders labs (CBC, BMP)
  - Renal adjustments

- ID pharmacist
  - Restricted antimicrobials
  - Housewide antimicrobials
    - Duration of therapy
    - Restricted (ID Consult?)
    - ≥ 2 Antimicrobial agents
    - Vanco/Piperacillin/tazobactam List
    - Renal
  - Drug-bug mismatch (finalized cultures)
  - Culture/sensitivity review (finalized cultures)
The Team

- Pharmacist
- Micro
- ID Physician
- IT
- Infection Control
Accomplishments

• In 1 year (January 2015-December 2015) of implementing a stewardship pharmacist, true acquisition cost was reduced by 29.5% ($192,752.43)

• Intervention acceptance rate= 79.5%

• Broad Spectrum Reduction 2014 → 2015 DOT per 1000 patient days
  • Reduction of MRSA agents
    • Linezolid 6.0 → 4.5
    • Daptomycin 1.9 → 0.3
    • Ceftaroline 5.5 → .07
  • Reduction of Meropenem 19.2 → 17.3
  • Reduction of Aztreonam 3.0 → 1.4
Current Projects

- Antimicrobial Stewardship Guide
- Sepsis Coordinator/Code Sepsis
- Sputum >> “Negative for MRSA/Negative for Pseudomonas”
- Automatic Stop Order/Time Out
  - 5 days for inpatient (all antibiotics)
  - 3 days for geriatric/behavioral health
- Fecal Microbiota Transplant
  - Follow up Interviews
  - Success or failure
- Penicillin Allergy
  - Patient Interviews
  - Allergy Testing
  - Education

Barriers

• ASP members have multiple roles in a community hospital
• Continuous surveillance lacking
• No formal mechanism of data collection
• No clinical decision support technology
• Who to call?
OPEN DISCUSSION