Antimicrobial Stewardship in a Pediatric Hospital
Lessons Learned

Marian G. Michaels, MD, MPH
Professor of Pediatrics and Surgery
Division of Pediatric Infectious Diseases
Children’s Hospital of Pittsburgh of UPMC
Disclaimers

• I have no relevant conflict of interests
• I may discuss off label use of drugs or devices
Learning Objectives

- At the end of the talk attendees should be able to:
  - Recognize the necessity for antimicrobial stewardship programs
  - Describe the essential components of ASP
  - Understand value of ASP for inpatient settings
A story

• 2 year old child with leukemia is admitted to PICU with high fever, decreased BP, and respiratory distress requiring resuscitation and ventilatory support
• Vancomycin, meropenem, clindamycin, liposomal amphotericin and high dose acyclovir
• All cultures are negative
• But because “he seems better” they continue antimicrobials
• Kidney dysfunction develops
• Day 10: trach culture has MDR bacteria
What happened?

• This is a sick child
• But doing everything isn’t necessarily the right thing …. 
• …and can cause harm
• Hopefully an antimicrobial stewardship program (ASP) would help this child avoid untoward side effects…
• ….and help the hospital have less resistant microbes
Origins of Antimicrobial Stewardship: 
Explosion of Antimicrobial Resistance


![Graph showing resistance rates of various antimicrobial-resistant pathogens](image-url)
Here Come the Superbugs!
Antimicrobial Resistance hits the News: USA Today (3/6/13)

CDC sounds alarm on deadly, untreatable superbugs

DEADLY BACTERIA THAT DEFY DRUGS OF LAST RESORT

A new family of antibiotic-resistant bacteria, known as CRE, is raising concerns across the medical community because of its ability to cause infections that defy even the strongest antibiotics. The antibiotic resistance is spread by mobile pieces of DNA that can move between different species of bacteria, creating new, drug-defying bugs.

How a resistance gene moves between bacteria

When antibiotic-resistant bacteria are present in the body and antibiotics are introduced...

Where the organisms can infect the body

- Skin/soft tissue
- Lungs
- Bloodstream
- Urinary tract
FACT SHEET: Obama Administration Releases National Action Plan to Combat Antibiotic-Resistant Bacteria

Judicious use of antibiotics in healthcare and agricultural settings is essential to slow the emergence of resistance and extend the useful lifetime of effective antibiotics. The CDC estimates that up to half of all human antibiotic use is unnecessary or inappropriate. The Action Plan includes activities to foster improvements in the appropriate use of antibiotics (i.e., antibiotic stewardship) by improving prescribing practices across all healthcare settings, preventing the spread of drug-resistant threats in healthcare facilities and communities, and continuing to eliminate the use of medically-important antibiotics for growth promotion in animals.

By 2020, significant outcomes in this area will include:

- Establishment of antimicrobial stewardship programs in all acute care hospitals and improved antimicrobial stewardship across all healthcare settings.
- Reduction of inappropriate antibiotic use by 50% in outpatient settings and by 20% in inpatient settings.
- Establishment of State Antibiotic Resistance (AR) Prevention (Protect) Programs in all 50 states to monitor regionally important multi-drug resistant organisms and provide feedback and technical assistance to health care facilities.
- Elimination of the use of medically-important antibiotics for growth promotion in food-producing animals.
Four Core Actions to Fight Resistance

1. Prevent infections & spread of resistance
2. Track rates of resistance over time
3. Improve Antibiotic Prescribing / Antimicrobial Stewardship
4. Develop New Drugs & Diagnostic Tests

(http://www.cdc.gov/drugresistance/pdf/4-2013-508.pdf)
What Can ASP DO?

ANTIBIOTIC STEWARDSHIP
IN YOUR FACILITY WILL

DECREASE
- ANTIBIOTIC RESISTANCE
- C. DIFFICILE INFECTIONS
- COSTS

INCREASE
- GOOD PATIENT OUTCOMES

Children’s Hospital of Pittsburgh of UPMC
ASP Strategies: Inpatient Focus

• **Core strategies**
  – Formulary restriction and preauthorization
  – Prospective audit with intervention and feedback

• **Supplemental Strategies**
  – Education
  – Clinical Guidelines
  – IV to PO conversion
  – Dose optimization
  – Antimicrobial Order Forms

Newland & Hersh/PIDJ/2010
ASP Core Strategies: PROS

• Preauthorization:
  – ↓starting unnecessary/inappropriate Abx
  – Direct control of chosen Abx use/ cost
  – Prompts review of available data at time of initiation of Abx

• Prospective audit and feedback:
  – Review when more clinical data available
  – Greater flexibility in timing of recommendation
  – Prescriber autonomy maintained
  – Can address de-escalation, duration & switch to oral Abx

Barlam et al CID 2016 IDSA Guidelines
ASP Core strategies: Cons

• Preauthorization:
  – Only impacts “chosen Abx”
  – Real-time resource intensive
  – May delay therapy
  – Loss of prescriber autonomy

• Prospective audit and feedback:
  – Compliance voluntary
  – Typically labor-intensive
  – Requires technology support

Barlam et al CID 2016 IDSA Guidelines
Antimicrobial Stewardship Program: CHP
CHP: Then

• > 30 yrs preauthorization approval for “restricted antibiotics” by ID group
  – Not approved for children - Ex: quinolones
  – Very broad spectrum drugs - Ex: carbapenems
  – Expensive new drugs- Ex: linezolid
  – Direct towards “drugs of choice”

• Downside:
  – No tracking of antibiotic use once approved
  – Development of antimicrobial resistance
  – No formal antimicrobial stewardship program
Antimicrobial Susceptibility Tracking
<table>
<thead>
<tr>
<th>Models of ASP:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>“Traditional Model”</strong></td>
</tr>
<tr>
<td>Includes Involvement of:</td>
</tr>
<tr>
<td>• ID Physician Leader</td>
</tr>
<tr>
<td>• Dedicated ASP Pharmacist with ID Training</td>
</tr>
<tr>
<td>• Pharmacy Director</td>
</tr>
<tr>
<td>• P&amp;T Committee</td>
</tr>
<tr>
<td>• Infection Prevention</td>
</tr>
<tr>
<td>• Informatics</td>
</tr>
<tr>
<td>• Hospital Administration</td>
</tr>
<tr>
<td><strong>CHP Model Includes Involvement of:</strong></td>
</tr>
<tr>
<td>• ID Physician Leader &amp; Full ID Division</td>
</tr>
<tr>
<td>• Team of 7 Service-based Pharmacists</td>
</tr>
<tr>
<td>• Pharmacy Director</td>
</tr>
<tr>
<td>• P&amp;T Committee</td>
</tr>
<tr>
<td>• Infection Prevention</td>
</tr>
<tr>
<td>• Informatics</td>
</tr>
<tr>
<td>• Hospital Administration</td>
</tr>
</tbody>
</table>
PHIS Antimicrobial Analysis: 2007

Case-Mix Adjusted % Drug Days, CHP and all PHIS Hospitals

Levin J, 2007, Unpublished Data

- Vanco: 13.9%
- Linezolid: 1.3%
- Pip-Tazo: 7.5%
- Meropenem: 2.4%

PHIS Median
A Quality Assessment of a Collaborative Model of a Pediatric Antimicrobial Stewardship Program

Phuong-Tan Nguyen-Ha, PharmD, Denise Howrie, PharmD, Kelli Crowley, PharmD, Carol G. Vetterly, PharmD, William McGhee, PharmD, Donald Berry, RPh, Elizabeth Ferguson, PharmD, Emily Polischuk, Pharm D, Maria Mori Brooks, PhD, Jeffrey Goff, RPh, MS, Terri Stillwell, MD, MPH, Toni Darville, MD, Ann E. Thompson, MD, James E. Levin, MD, PhD, Marian G. Michaels, MD, MPH, Michael Green, MD, MPH

PEDIATRICS Volume 137, number 5, May 2016
CHP ASP: Development of Guidelines

- **Multistep process: targeted antimicrobials**
  - Review of literature
  - Small group meeting with representatives from key stakeholder groups
  - Development of “draft” guideline followed by review by full stakeholder groups, P & T Committee and Clinical Resource Management Committee

- **Approved guidelines = basis for Day 3 Audits**

- **Guidelines include:**
  - Post-op prophylaxis & antifungal use for Liver & Intestinal Tx
  - Use of ciprofloxacin & vancomycin for IBD patients
  - Use of meropenem (all CHP patient populations)
  - Empiric antimicrobial regimens for surgical infants in NICU
  - Empiric antimicrobial regimens in the CICU
Communicating Recommendations

Initial antimicrobial rational: Treatment of proven infection.

Histories:
Device placement per documentation: Central Arterial or Vencous Catheters.
Risks in past 7 days: Lymphopenia <1500, Renal insufficiency.
Mix of antimicrobial resistance: MRSA infection, VRE infection, Multi-Drug Resistant GNR.
History of recurrent infections: present.
Notable antimicrobial allergies: etrapenem.

Review/ Management
Relevant antimicrobials: Meropenem.
Significant cultures:
- Positives: Specimen Source (Respiratory, OTHER moderate WBC.), 11/19/14.
- Isolate: Pseudomonas, Klebsiella, S. aureus.
- Positives: Specimen Source (Urine), 11/19/14.
- Isolate: Pseudomonas, Chiostriobacteriae, Serratia, MRSA, enterococcus, VRE.
- Positives: Specimen Source (Urine), 11/24/14.
- Isolate: Pseudomonas, S. aureus (MR), enterococcus.

Proven or likely organism being treated: Gram Negatives: Pseudomonas, Serratia, Stenotrophomonas, Klebsiella.
Proven or likely site of infection: Urine.

Relevant Information: patient has extensive history of urinary tract infections requiring meropenem due to multiple drug-resistant organisms.

Impression and Plan
Proven Infection: Continue Meropenem (Per culture & sensibilities for 10 days, OTHER up to 14 days total duration as clinical condition dictates). Communication of ASP recommendation: Minimize to review and communicate: 10 min.

Note: These recommendations are not a medical consult. They are based primarily on a review of the electronic record of the patient's medications and microbiology results as part of the antibiotic stewardship program at Children's Hospital of Pittsburgh of UPMC.
The PDSA cycle is shorthand for testing a change by developing a plan to test the change (Plan), carrying out the test (Do), observing and learning from the consequences (Study), and determining what modifications should be made to the test (Act)
Quarterly reports generated automatically from Data warehouse
Antimicrobial Stewardship At CHP: Where are we now?

- ASP officially in use since January 2009
- Still require ID Pre-approval for selected Abx
- Guidelines for use of “targeted” antimicrobials developed with stakeholders
- Day 3 Auditing for caspofungin, meropenem & vancomycin
- Results reviewed as part of PDSA process on quarterly basis
- The role of ASP established in culture of CHP
Vancomycin Drug Use

Pre-intervention
Slope = 0 per 1000 pt-days per year

Post-intervention
Slope = -19.1 per 1000 pt-days per year

Test that Post-intervention Slope = 0, p-value = 0.00

Intervention Initiated 2010 Quarter 2
Meropenem Drug Use

Intervention Initiated 2010 Quarter 4

Pre-intervention
Level = 20.0 per 1000 pt-days

Post-intervention
Level = 13.8 per 1000 pt-days

Test of Equality of Levels
p-value = 0.021
Guidelines: Another story:

• 5 year old girl worsening abdominal pain, fever and vomiting x 3 days
• Comes to Emergency Department
  – Paucity of bowel sounds
  – Rebound tenderness
  – Diagnosed with ruptured appendicitis
• Laparascopic surgery performed
• Ertapenem given
• PIC line placed, home on IV abtiotics for two or more weeks
Appendicitis Guidelines CHP

• Surgical NPs and MDs noted problem with prolonged antibiotic use
• Prolonged use of PIC lines
  – Complications:
  – thrombus, line infection, *C diff*
• Could we do better?
• Met with ID and PharmD
  – Literature review
  – Development of guidelines
  – Buy in from all surgeons
Summary of Guidelines

• Perforated appendicitis
  – At 24 hours: stable and meet d/c criteria
    • Change to oral antibiotics (5 days total Abx)

• Complicated appendicitis
  – When afebrile can be switched to oral Abx for total of 7 days

• Follow up phone call: set questionnaire by pediatric surgical RN
  • Screen positive come back to clinic
Difference in Length of Stay (LOS) “On” vs “Off” Pathway Post-Operatively

LOS - Uncomplicated Appendicitis

Consensus for Management Obtained

"Off Pathway" Post-Operatively Median LOS: 33 hrs

"On Pathway" Post-Operatively Median LOS: 26 hrs

LOS Before Pathway Median LOS: 36 hrs
Difference in LOS
"On" vs "Off" Pathway Post-Operatively

LOS - Complicated Appendicitis

Consensus for Management Obtained

LOS Before Pathway
Median LOS: 155 hrs

"Off Pathway" Post-Operatively
Median LOS: 110 hrs

"On Pathway" Post-Operatively
Median LOS: 107 hrs

- Actual LOS
- Median LOS (prior to Pathway)
- Actual LOS for Patients "On Post-Op Pathway"
- Median LOS for Patients "On Post-Op Pathway"
- Actual LOS for Patients "Off Post-Op Pathway"
- Median LOS for Patients "Off Post-Op Pathway"
Readmission Rate: Appendicitis Patients
Administration of Appropriate Pre-Operative Antibiotics

(Type & Timing within 60 minutes of Surgical Incision)

& Prevalence of Surgical Site Infections

Percent of Acute Appendicitis Patients that received appropriate* antibiotic within 60 minutes of surgical incision

Percentage of Patients with an SSI

Decreased Surgical Site Infections

Appropriate pre-op Abx
Summary

• One size doesn’t fit all
  – See what works at your institution

• CHP using combination
  – Pre-authorization
  – 3 day monitoring
  – Individual guidelines with specific group
Recognizing the CHP ASP

- **Clinical Pharmacy Team**
  - Don Berry
  - Kelli Crowley
  - Elizabeth Ferguson
  - Denise Howrie
  - Bill Mcghee
  - Tan Nguyen
  - Carol Vetterly
  - Emily Polischuck
  - Jen Shenk

- **Infectious Diseases**
  - Brian Campfield
  - Toni Darville
  - Michael Green
  - Jim Levin
  - Ling Lin
  - Judy Martin
  - Marian Michaels
  - Andy Nowalk
  - Terri Stillwell
  - John Williams
  - ID Fellows

- **Pharmacy**
  - Jeff Goff

- **Medical Director’s Office**
  - Ann Thompson

- **GSPH Biostatistics**
  - Maria Mori Brooks
  - Jong-Hyeon Jeong
  - Marcia Kurs-Lasky
Questions?

- Antibiotic resistance is not coming. It is here right now.
- The discovery of penicillin was so important. It was awarded a Nobel Prize.
- Antibiotics are losing their power.
- Winter is coming. NPS.org.au
- Antibiotic resistance knows no geographical bounds.
- Antibiotics won’t make your cold or flu better faster.
- Don’t ask for antibiotics when you don’t need them.