From Concept to Accomplishments: 7 Years of Antimicrobial Stewardship at CHP

Michael D. Green, MD, MPH
Professor of Pediatrics, Surgery and Clinical & Translational Research
University of Pittsburgh School of Medicine
Division of Infectious Diseases
Children’s Hospital of Pittsburgh, Pittsburgh, PA
Disclaimers

- I have no relevant conflict of interests to disclose
- I will NOT discuss off label use of drugs or devices
Learning Objectives

At the end of this talk attendees should be able to:

– Recognize the historical basis & necessity for antimicrobial stewardship

– Describe the essential components of antimicrobial stewardship programs nationally & at CHP

– Understand that antimicrobial stewardship can & has worked at CHP
Outline

- Overview of Trends in Antimicrobial Resistance
- Historical review of the emergence of ASP
  - National Goals
  - Recommended structure
- Antimicrobial Stewardship & CHP
  - “Unique model” built on OUR expertise
  - Overview of accomplishments
- Expanding Goals of Antimicrobial Stewardship at CHP
Origins of Antimicrobial Stewardship: Explosion of Antimicrobial Resistance

Selected antimicrobial-resistant pathogens associated with nosocomial infections in ICU patients, comparison of resistance rates from 2003 with 1998 through 2002, NNIS system. (Figure from NNIS, 2004).
Origins of Antimicrobial Stewardships: Here Come the Superbugs!

[Graph showing the percentage of strains resistant to MRSE, MRSA, NPSP, VRE, and VISA from 1975 to 2000]
THE RESISTANCE MOVEMENT
Carbapenem-resistant Enterobacteriaceae have been on the move since at least 1996.


2. 2003: KPC-positive bacteria are found spreading rapidly through hospitals across New York City. By 2007, 21% of Klebsiella in the city carry the resistance gene.

3. 2005: KPC-positive bacteria make their way from New York to several other countries, including Israel. From Israel, the bacteria travel to Italy, Colombia, the United Kingdom and Sweden.

4. 2008: Doctors in Sweden find a new carbapenem-resistance gene, NDM. Traced back to India, NDM-positive bacteria have moved quickly.
Trends in Antimicrobial Resistance

Graph showing the increase in resistant bacteria and the decrease in antibiotics from 1985 to 2016.

- Resistant bacteria on the rise
- Antibiotics on the fall

Source: TRENDS in Microbiology
Antimicrobial Resistance in the News: USA Today (3/6/13)

CDC sounds alarm on deadly, untreatable superbugs

DEADLY BACTERIA THAT DEFINE 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 ...
NATIONAL SUMMARY DATA

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

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

*bacteria and fungus included in this report

Estimated minimum number of illnesses and death due to *Clostridium difficile* (*C. difficile*), 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?

Antibiotic-resistant infections can happen anywhere. Data show that most happen in the general community; however, most deaths related to antibiotic resistance happen in healthcare settings, such as hospitals and nursing homes.
Global Impact of Antimicrobial Resistance

Deaths attributable to antimicrobial resistance every year by 2050

- Asia: 4,730,000
- Europe: 390,000
- North America: 317,000
- Latin America: 392,000
- Africa: 4,150,000
- Oceania: 22,000

Source: Review on Antimicrobial Resistance 2014
Global Response to Antimicrobial Resistance

Global action plan to combat antimicrobial resistance

World Health Organization

EUROPE’S FIGHT AGAINST ANTIMICROBIAL RESISTANCE

WHAT IS ANTIMICROBIAL RESISTANCE (AMR)?

Antimicrobials?

Substances used to treat a wide variety of infectious diseases in humans and animals. They:
- Kill microorganisms
- Stop microorganisms from growing and multiplying
Example: antibiotics

Antimicrobial resistance?
The ability of microorganisms to withstand antimicrobial treatments. Example: AMR (antimicrobial resistance)

Why is resistance growing?
- Overuse of antibiotics
- Misuse of antibiotics
- Spread through various routes

Effect of growing resistance?
- Treatment may become ineffective
- Serious risk to public health

CDC’s Work to Prevent Antibiotic Resistance

- Systems to track resistant infections and changes in resistance trends
- Improving prescribing strategies,
  - Get Smart program
  - At least 50% of antibiotics prescribed are not needed
- Limiting the spread of infections
  - Vaccinations
  - Effective treatment guidelines
- The CDC encourages efforts to minimize the inappropriate use of antibiotics in animals.
FACT SHEET: Obama Administration Releases National Action Plan to Combat Antibiotic-Resistant Bacteria

Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections

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

- Preventing infections & the spread of Resistance
- Tracking of rates of resistance over time
- Improving Antibiotic Prescribing/Stewardship
- Developing New Drugs & Diagnostic Tests
Four Core Actions to Fight Resistance

3 IMPROVING ANTIBIOTIC PRESCRIBING/STEWARDSHIP

Perhaps the single most important action needed to greatly slow down the development and spread of antibiotic-resistant infections is to change the way antibiotics are used. Up to half of antibiotic use in humans and much of antibiotic use in animals is unnecessary and inappropriate and makes everyone less safe. Stopping even some of the inappropriate and unnecessary use of antibiotics in people and animals would help greatly in slowing down the spread of resistant bacteria. This commitment to always use antibiotics appropriately and safely—only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case—is known as antibiotic stewardship.
What Can Antimicrobial Stewardship DO?

ANTIBIOTIC STEWARDSHIP IN YOUR FACILITY WILL

DECREASE
- ANTIBIOTIC RESISTANCE
- C. DIFFICILE INFECTIONS
- COSTS

INCREASE
- GOOD PATIENT OUTCOMES
What Can Antimicrobial Stewardship DO?

PROMOTE ANTIBIOTIC BEST PRACTICES—
A FIRST STEP IN ANTIBIOTIC STEWARDSHIP

- Ensure all orders have dose, duration, and indications
- Get cultures before starting antibiotics
- Take an “Antibiotic Timeout” reassessing antibiotics after 48–72 hours
What Can Antimicrobial Stewardship DO?

ANTIBIOTIC STEWARDSHIP PROGRAMS ARE A “WIN-WIN” FOR ALL INVOLVED

A UNIVERSITY OF MARYLAND STUDY SHOWED ONE ANTIBIOTIC STEWARDSHIP PROGRAM SAVED A TOTAL OF $17 MILLION OVER EIGHT YEARS

ANTIBIOTIC STEWARDSHIP HELPS IMPROVE PATIENT CARE AND SHORTEN HOSPITAL STAYS, THUS BENEFITING PATIENTS AS WELL AS HOSPITALS
Antimicrobial Stewardship Strategies
(Trainland & Hersh/PIDJ/2010)

Core strategies
- Prospective audit with intervention and feedback
- Formulary restriction and preauthorization

Supplemental Strategies
- Education
- Clinical Guidelines
- IV to PO conversion
- Dose optimization
- Antimicrobial Order Forms
Core members of multidisciplinary antimicrobial stewardship team include:
- ID physician, clinical pharmacist with ID training, clinical microbiologist, an information system specialist, an infection control professional, and hospital epidemiologist

Collaboration between ASP AND hospital Infection Control and Pharmacy & Therapeutics committees essential

The support & collaboration of hospital administration, medical staff leadership, and local providers in development and maintenance of ASP is essential

ID physician and head of pharmacy, as appropriate, should negotiate with hospital administration to obtain adequate authority, compensation, and expected outcomes for the program

Hospital administrative support for the necessary infrastructure to measure antimicrobial use and to track use on an ongoing basis is essential
Antimicrobial Stewardship At CHP: Then

As of 2007, CHP had a long standing requirement for drug approval for “restricted antibiotics” CHP:

- Some “direction” towards “drugs of choice”
- No tracking of antibiotic use once approved
- High prevalence of antimicrobial resistance in ESKAPE pathogens
- No formal antimicrobial stewardship program
PHIS Antimicrobial Analysis
2007

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>CHP</th>
<th>PHIS Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vanco</td>
<td>13.9%</td>
<td>10.4%</td>
</tr>
<tr>
<td>Linezolid</td>
<td>7.5%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Pip-Tazo</td>
<td>1.3%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Meropenem</td>
<td>2.4%</td>
<td>2.3%</td>
</tr>
</tbody>
</table>

Levin J, 2007, Unpublished Data
Ambisome APR-DRG v20 Case-Mix Adjusted % Drug Days, 40 Children's Hospitals

Median 1.0%

CHP 2.6%

Levin J, 2007, Unpublished Data
ASP AT CHP
Models of ASP:

“Traditional Model” Includes Involvement of:
- ID Physician Leader
- Dedicated ASP Pharmacist with ID Training
- Pharmacy Director
- P&T Committee
- Infection Prevention
- Informatics
- Hospital Administration

CHP Model Includes Involvement of:
- ID Physician Leader & Full ID Division
- Team of 7 Service-based Pharmacists
- Pharmacy Director
- P&T Committee
- Infection Prevention
- Informatics
- Hospital Administration
What Makes CHP’s ASP Unique?

- Use of Service-based pharmacists
  - Integrated into daily rounding activities for KEY patient populations
  - Already trusted participants in clinical decision making

- Participation of FULL ID Division
  - All Drug Approvals & Weekend/Holiday Day 3 Auditing
  - Global commitment to antimicrobial stewardship

- Leveraged use of EMR & CHP Data warehouse
  - Identify those requiring Day 3 auditing
  - Review patient records & communicate recommendations
  - Continuously track Antimicrobial use to measure impact of program
CHP ASP: Development of Guidelines

- Multistep process for development of guidelines for use of “targeted” antimicrobials

- Guideline development includes
  - 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

- Once approved, guidelines serve as 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 rationale:** Treatment of proven infection.

**Histories**
- Device placement per documentation: Central Arterial or Venous Catheters.
- Risks in past 7 days: Lymphopenia <1500, Renal insufficiency.
- Hx of antimicrobial resistance: MRSA infection, VRE infection, Multi-Drug Resistant GNR.
- History of recurrent infections present.
- Notable antimicrobial allergies: None.

**Review/Management**
- Relevant antimicrobials: Meropenem.
- Significant cultures:
  - Positives: Specimen Source (Urine), 11/19/14. Isolate: Pseudomonas, Stenotrophomonas, Serratia, MRSA, enterococcus, VRE.
- Proven or Likely organism: 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 & sensitivities for 10 days, OTHER up to 14 days total duration as clinical condition dictates).
- Communication of ASP recommendation: Minutes 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.
Tracking Results to Enhance Quality

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).
Using CHP Data Warehouse to Track Results over Time

Quarterly reports generated automatically from Data warehouse.
Analyzing Results: The role of the Statistician

- Interrupted time series: State of the art for analysis
- Essentially compares slope of results over time Before & After intervention
- Illustrates the necessity of statistical support to accurately assess key outcomes

Maria Mori Brooks, PhD at GSPH to our Rescue

(Thank you Thank you Thank you Thank you)
Antimicrobial Stewardship At CHP: Where are we now?

- ASP officially in place for 7 years (January 2009)
- ID Pre-approval for selected antimicrobials continues
- Day 3 Auditing for caspofungin, meropenem & vancomycin
- Guidelines for use of “targeted” antimicrobials developed with stakeholders
- Results reviewed as part of PDSA process on quarterly basis
- Role of ASP established in culture of CHP
- Ongoing question: What should we do next?
Caspofungin Drug Starts

**Intervention Initiated 2009 Quarter 1**

- **Pre-intervention**
  - Slope = 19.1 per 1000 pts per year
- **Post-intervention**
  - Slope = -0.6 per 1000 pts per year

**Test of Equality of Slopes**
- p-value = 0.001

**Drug Cases per 1000 Cases**

Caspofungin Drug Use

Intervention Initiated 2009 Quarter 1

Pre-intervention Slope = 22.1 per 1000 pt-days per year

Post-intervention Slope = 0.5 per 1000 pt-days per year

Test of Equality of Slopes
p-value = 0.014

Meropenem Drug Starts

Intervention Initiated 2010 Quarter 4

Pre-intervention
Level= 14.3 per 1000 pts

Post-intervention
Level= 11.3 per 1000 pts

Test of Equality of Levels
p-value =0.067

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

Vancomycin Drug Starts

**Pre-intervention**
Slope = 0 per 1000 pts per year

**Post-intervention**
Slope = -11.1 per 1000 pts per year

*Test that Post-intervention Slope=0, p-value =0.001*

*Intervention Initiated 2010 Quarter 2*

Vancomycin Drug Use

**Intervention Initiated 2010 Quarter 2**

**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 = 0.001

Before initiation of the ASP, there was a significant upward quarter-to-quarter trend in vancomycin starts ($p=0.049$). Immediately following initiation of the ASP, there was a significant increase in vancomycin starts ($p<0.001$). After initiation of the ASP, there was a significant change in the quarter-to-quarter trend in vancomycin starts ($p<0.001$).
Vancomycin Use in ICUs

Results of an Antimicrobial Stewardship Program (ASP) on Vancomycin Prescribing Practices in Pediatric Intensive Care Units

Drug use (# drug days/# service days, %) – Overall

Vancomycin Use by Year and Quarter

The estimated vancomycin use at the beginning of the 1st quarter of 2006 was 31%.

Before the initiation of the ASP there was no significant quarter-to-quarter trend in vancomycin use (p=.93).

Immediately following initiation of the ASP, there was no significant change in vancomycin use (p=.93).

After initiation of the ASP, there was a significant change in the quarter-to-quarter trend in vancomycin use (p=.008).

Crowley et al, (Manuscript In preparation)
Monitoring Acceptance of ASP Recommendations

- Recommendation “accepted” when followed within 24 hours of completion of eNote.
- Compliance: % ASP recommendations accepted/# eNotes written in 3 month “audit” period for each drug
- Overall acceptance rate of 90%, 93% & 100% for recommendations relating to vancomycin, caspofungin & meropenem, respectively.

Decline in ASP notes over time suggests that clinicians are making decisions in advance of audit note.

Maintaining Stewardship Overtime Requires Ongoing Attention

Vancomycin Starts
(Time=Analysis for publication)

Vancomycin Starts
(Time=3rd Quarter 2015)

Is this increase real?
If so, why is it happening?
ASP actively watching to answer these questions
Maintaining Stewardship: Should other drugs be restricted or audited?

Not Calculated: COST of ASP effort to audit a drug used as much as piperacillin/ tazobactam?
ASP at CHP: What’s Next?

Potential Initiatives:

- Work with DRG to identify targets for guidelines and stewardship in treatment of hospitalized children with community acquired infection
- Work with CCP & GAP to identify targets for guidelines and stewardship in ambulatory treatment of community acquired infection in children

Continue to review data & seek opportunities for cost-effective stewardship in all settings
Recognizing the CHP ASP

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Questions?
Thank you to all CHP Clinicians and Stakeholders for your support and contributions to CHP Stewardship Efforts!