Update on Antibiotic Stewardship

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Bio
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Conflict of Interest
- I have no disclosures.
Update on Antimicrobial Stewardship

Objectives: Pharmacists
• Describe the prevalence of antimicrobial resistance.
• Discuss the consequences of inappropriate antimicrobial prescribing.
• Describe the principles and objectives of an antimicrobial stewardship program.
• Discuss key strategies for developing an institutional program to enhance antimicrobial stewardship.
• Explain the pharmacist’s role in antimicrobial stewardship programs.

Objectives: Pharmacy Technicians
• Discuss the consequences of inappropriate antimicrobial prescribing.
• List the objectives of an antimicrobial stewardship program.
• Identify antimicrobial stewardship activities in an institutional setting.

“The development of new antibiotics without having mechanisms to ensure their appropriate use is much like supplying your alcoholic patients with a finer brandy.”

-Dennis Maki, 1998
Introduction

- The management of healthcare-associated infections (HAI) has become an urgent healthcare priority.
- HAI account for an estimated 2 million infections, 90,000 deaths, and $4.5 billion in excess healthcare costs annually.
- An increasing percentage of these infections are attributed to antimicrobial-resistant pathogens.

Introduction

- Resistant gram-positive organisms continue to be important causes of HAI.
  - Methicillin-sensitive *S. aureus* (MRSA)
  - Vancomycin-resistant *Enterococcus* (VRE)
- The emergence of resistant gram-negative pathogens is perhaps of even greater concern.
  - Extended-spectrum β-lactamases (ESBL) producing pathogens
  - Multidrug-resistant *Acinetobacter* organisms
  - *Klebsiella pneumoniae* carbapenemases (KPC)

Increasing Frequency of Resistance

- MRSA = methicillin-resistant *Staphylococcus aureus*
- VRE = Vancomycin-resistant *Enterococcus*
- FQRP = Fluoroquinolone-resistant *Pseudomonas aeruginosa*
The “Superbugs” Aren’t Waiting!

- The pipeline of new antibiotics is drying up.
- Industry is losing interest in the antibiotic market because these drugs are simply not as profitable.
- From discovery to FDA approval can be 10 years or more.
- No new class of antibiotics targeting resistant Gram-negative organisms.


Declining New Antibacterial Drug Approvals, U.S.


History of Medicine

- 2000 BC: Here, eat this root.
- 1000 AD: That root is bad. Here, say this prayer.
- 1850 AD: That prayer is superstition. Here, drink this potion.
- 1940 AD: That potion is snake oil. Here, take this antibiotic.
- 2000 AD: That antibiotic doesn’t work anymore. Here, eat this root.
Factors Increasing Antimicrobial Resistance

- Increased severity of illness
- Severe immunosuppression
- Presence of invasive devices (for longer duration)
- Inadequate infection control practices
- Increased use of empiric, prophylactic antibiotics
- Higher antibiotic use per area, per unit of time

Patterson JE. Chest 2001;119:426S-430S

Inappropriate antibiotic use is associated with:
- Increased morbidity and mortality
- Increased length of stay (LOS)
- Increased antimicrobial resistance
- Increased adverse events
- Increased cost

Inappropriate antibiotic use has been linked to which negative outcomes?

a. Antimicrobial resistance  
b. Increased mortality  
c. Increased cost  
d. All of the above
Information You Must Collect First…

- What are your institution’s problem pathogens?
  - Speak to your hospital microbiologist and epidemiologist
- What do I do with the information?
  - Work proactively with the ID physicians and hospital
    administrative support to implement a plan that is best
    suitable for your institution
- What has been shown to work?
  - Antimicrobial stewardship programs

Antimicrobial Stewardship

- Infectious Diseases Society of America (IDSA) Guidelines for Developing an
  Institutional Program (ASP) to Enhance Antimicrobial Stewardship
  - Based on a collaborative review and supported by
    - American Society of Health-System Pharmacists
    - Society of Infectious Diseases Pharmacists
    - American Academy of Pediatrics

ASP

- Primary goal
  - To optimize clinical outcomes while minimizing
    unintended consequences of antimicrobial use, including
    - Emergence of resistance
    - Selection of pathogenic organisms, such as C. difficile
    - Toxicity
- A multidisciplinary, prospective, and interventional
  approach
- Types of stewardship programs
  - Concurrent review with feedback, or
  - Preauthorization requirements and formulary restriction
Access the Experts

Antimicrobial Stewardship: Key Elements

- Education
- Guidelines and clinical pathways (national and localized)
- Antimicrobial order forms, computerized physician order entry (CPOE) templates
- Streamlining or de-escalation of empirical antimicrobial therapy
  - Based on culture and sensitivity results
  - Elimination of redundant combination therapy

Antimicrobial Stewardship: Key Elements

- Dose optimization
  - Based on individual patient characteristics
  - Causative organism
  - Site of infection
  - PK/PD characteristic of the drug
- Parenteral to oral conversion
  - Agents with enhanced oral bioavailability
    - i.e. Quinolones, linezolid, metronidazole, fluconazole
    - Facilitates early hospital discharge

References:

Clin Infect Dis 2007;44:159-77
The Pharmacist’s Role

- Promote multi-disciplinary collaboration
- Work with ID physicians and P&T to develop and implement localized antibiotic guidelines
- Recommend appropriate antimicrobial therapy and dose optimization
- Provide therapeutic drug monitoring
- De-escalation of antimicrobial therapy


Antimicrobial Utilization Strategies to Reduce Resistance

- “Fool them” strategy
  - Best exemplified by antimicrobial cycling or “crop rotation”
    - Based on the concept that alternating antibiotics periodically will help decrease selective pressure favoring the growth of resistant bacteria
  - No compelling data to support antimicrobial cycling as an effective strategy for preventing or reducing resistance


Antimicrobial Utilization Strategies to Reduce Resistance

- “Blast them” strategy
  - Using more than 1 antimicrobial agent to prevent the emergence of resistance.
  - Derived from early observation that multiple antibiotics were effective at preventing the emergence of resistance in *M. tuberculosis*.
  - However, application of this strategy to most routine bacteria may be problematic. Evidence suggests that more antibiotics will likely lead to more resistance.
  - No convincing data has validated this strategy for HAI.

Antimicrobial Utilization Strategies to Reduce Resistance

• “Stop irritating them” strategy
  – Reduce the use of antibiotics to the bare minimum necessary to safely treat patients with serious infections → reduce selective pressure → reduce the prevalence of resistance
  – Seems to be the most reasonable strategy to minimize resistance

What is the goal of ASP?

a. Optimize clinical outcomes while minimizing unintended consequences of antibiotic use
b. Make pharmacists fight off Superbugs
c. All of the above
d. None of the above

The Target Points

• Before initiating therapy
  – Treat only those patients who are truly infected
• During therapy
  – Avoiding the use of combination agents when a single antibiotic is sufficient
• At the completion of therapy
  – Treat only for as long as is required to cure the infection
Optimizing Pharmacokinetic (PK) and Pharmacodynamic (PD) Principles

• Time-dependent agents
  – Time above the minimum inhibitory concentration (MIC) is the key predictor of outcome.
  – β-lactam antibiotics, vancomycin

• Concentration-dependent agents
  – Maximum serum concentration (Cmax)/MIC ratio is the key predictor of outcome.
  – Aminoglycosides, fluoroquinolones

Maintaining the appropriateness of existing antibiotics

• Duration of therapy
  – A shorter course of treatment can be as clinically effective as a longer course, i.e. 8 days vs. 15 days for VAP

• Alternative dosage regimens
  – I.e. high-dose (2 g) infusion of meropenem over 3 hours to overcome pathogens with high MIC
  – High peak concentrations
  – Continuous infusion

Longer infusion of meropenem: *P. aeruginosa*
Shorter Courses of Antibiotic Treatment

- Prolonged administration of antibiotics in ICU patients has been shown to be an important risk factor for emergence of colonization and infection with antibiotic-resistant bacteria.
- Several studies now show that 7-8 days of antibiotic treatment is acceptable for most patients with ventilator-associated pneumonia (VAP).

Cumulative survival estimates according to duration of antimicrobial treatment

Surgical Care Improvement Project (SCIP)

- Guidelines are intended to provide practitioners with standardized approach to rational, safe, and effective use of antimicrobial agents for the prevention of surgical-site infections
- Pharmacist’s role
  - Decide what antimicrobials will be included for each surgery type
  - Work with anesthesiology and surgery
SCIP Process Measures

- Pre-operative dose-timing
  - 60 mins before surgical incision
- Selection and dosing
  - Recommendations for selection of antibiotics for specific surgical procedures
- Duration of prophylactic antibiotic therapy
  - Single dose or less than 24 hours

AJHP 2013;70:195-208

Computer Surveillance and Decision Support

- CPOE and clinical decision support enhances antimicrobial decisions through the incorporation of:
  - Patient-specific microbiology data
  - Renal and hepatic function
  - Drug interactions
  - Antibiotic expenditures
- Computer-based surveillance facilitates tracking of:
  - Antimicrobial resistance patterns
  - Identification of HAI infections and adverse drug events

Clin Infect Dis 2007;44:159-77.

Which strategies can be used to limit emergence of resistance?

- Develop localized antibiotic use guidelines
- Antibiotic de-escalation
- Provide education to key prescribers
- All of the above
Monitoring of Process and Outcome Measures

- Process measure
  - Did the intervention result in the desired change in antimicrobial use?
- Outcome measures
  - Did the process implemented reduce or prevent resistance or other unintended consequences of antimicrobial use?


Outcome Measures

- Antimicrobial use data can be standardized using
  - Defined daily dose (DDD)
    - Calculated as the total number of grams of an antibiotic used divided by the number of grams in an average adult dose
    - The World Health Organization (WHO) publishes DDD values for nearly all antibiotics
    - By using DDD, hospitals may compare their antibiotic use with that of similar hospitals

http://www.whocc.no/ddd/definition_and_general_considerations/

SUCCESSFUL ANTIMICROBIAL STEWARDSHIP PROGRAMS
Successful Stewardship Programs

- Prospective audit with intervention and feedback
  - Study conducted in a large teaching hospital
  - House staff were randomized to receive either no intervention or one-on-one education by a clinical specialist
  - Intervention prompted by an order for either levofloxacin or ceftazidime
  - Educational intervention emphasized microbiological data, local resistance patterns, and clinical literature


- Study results
  - 37% decrease in days of unnecessary antibiotics for the intervention services compared to controls (p <0.001)
  - Reduction of new antibiotic initiation
  - Length of stay, ICU transfers, readmission rates, and in-hospital death rates similar in both groups


Successful Stewardship Programs

- Intervention
  - Prospective evaluation of the impact of a multidisciplinary antibiotic management program to minimize the inappropriate use of third-generation cephalosporins

- Results
  - 22% decrease in the use of parenteral broad-spectrum antibiotics (p <0.0001)
  - Decrease in nosocomial infections caused by C. difficile (p= 0.002) and resistant Enterobacteriaceae (p= 0.02)

Successful Stewardship Programs

- ASP conducted at a large teaching institution for 7 years
- ASP goal
  - Reduce 10-20% of antibiotic costs (savings of $600,000 to $1,200,000 over a 3-year period)
- Results
  - 45% decrease in antibiotic utilization costs
  - Reduction of about $3 million in the first 3 years, primarily due to a decrease in antifungal therapy use

Stewardship Decreases Resistance

Rate of Resistant Enterobacteriacae Infections

- Antimicrobial Use and Cost
- MBSA rates stayed the same

Clinical Outcomes

- Appropriate Cure Failure
  - RR 2.8 (2.1-3.8)
  - RR 1.7 (1.3-2.1)
  - RR 0.2 (0.1-0.4)


Stewardship Decreases Resistance Rate of VRE Antimicrobial Use and Cost


MRSA rates stayed the same

A Time of Challenge and Opportunity

- The high prevalence of antimicrobial resistance is associated with increased morbidity and mortality.
- However, this challenge creates tremendous opportunities for infectious diseases specialists and infection control experts.
- Successful strategies include proactive interventions, such as antibiotic stewardship programs, and optimal infection control measures.

Questions?

NJPHA OVERVIEW
NJPhA Mission

To advance the profession of pharmacy enabling our members to provide optimal care to those they serve.

NJPhA Membership

Becoming an Active Member
• Founded in 1870 as a not-for-profit corporation to represent pharmacists in the State of New Jersey who practice in all areas of pharmacy.
• Get involved in ways that meet your specific goals:
  – Write for our peer reviewed journal
  – Submit a poster to our annual convention
  – Join one of our Academies (Consultant, Compounding, Disaster Management)
• Learn skills outside of the office that hasten your development:
  – Network and Make Connections
  – Be Recognized
  – Advance Your Expertise
  – Champion the Profession

NJPhA Legislative Representation
• Organizational leadership and support has led to the development of many legislative reforms on a state and federal level. Some include:
  – 1985: NJPhA proposed limited quantity of children’s aspirin
  – 1989: First public anti-smoking campaign
  – 1970: First mandatory patient profile
  – 1975: Concern for senior citizens health prompted development of PAPAD law in NJ
  – 1994: Pharmacists may be reimbursed as Diabetes Educators by NJ Reg. Insurance Plans
  – 1999: Insurance audits must be performed at a mutually agreeable time
  – 2000: Mandatory Mail Order is not permitted for NJ State Regulated Plans.
  – 2005: Modernization of the Practice of Pharmacy
  – 2009: Pharmacists immunize patients in New Jersey; 2013: bill was amended to lower the age for flu vaccine administration
  – 2013: Collaborative Practice between Physicians and Pharmacists
  – 2014: Separation between consultant and provider extended
**NJPhA Federal Advocacy**

**Strength in Numbers!**
- NJPhA is an active member of APhA – American Pharmacists Association, NASPA – National Alliance of State Pharmacy Associations, NCPA - National Community Pharmacists Association and others. Our state leadership works in concert with these groups to promote grassroots federal advocacy on key issues.
- NJPhA is supporting APhA’s initiative to advocate for national healthcare provider status for pharmacists. This will allow pharmacists, not just pharmacy technicians, to bill and receive reimbursement for patient care related services.

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**NJPhA Regulation Representation**

**Influence Laws and Regulation to Impact Change**
- NJ Board of Pharmacy
- NJ Board of Medical Examiners
- NJ Drug Utilization Review Board
- NJ Health Information Technology Committee
- National Organizations
  - NABP
  - APhA
  - CMS

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**In Summary...**

**We are committed to...**
- Presenting a unified voice for NJ pharmacists and pharmacy technicians.
- Providing a forum for exchange of innovative ideas to establish progressive health systems.
- Promoting the optimization of drug therapy for the patients our members serve.
- Anticipating future information and professional development needs.
- Strengthening relationships between practitioners, student pharmacist, pharmacy technicians, and other health professionals.
Becoming an Active Member
Sign up at today’s event – see the registration desk for details

• The online evaluation code will be sent from the office tomorrow morning:
  • This code will be active for one week from the date of the lecture.
    – Deadline: November 12, 2014
  • NOTE: your credits will be posted to CPE monitor within 45 days of program date

• It is critical that you have signed in to this live presentation (either in person or via the Join Me webinar) and that you have provided your correct NABP number; both your name and NABP number must be legible
• You are accountable to check your CE Monitor account for the credit for all CE programs including this one
• Everyone’s credits are uploaded to the CE Monitor when all individuals have completed the post-lecture evaluation
• When a failure occurs during the upload to CE Monitor, the failure will not identify the individual with the issue; therefore, there is no way for the office to contact the individual with the error
• The credit for this program will appear at a maximum of 60 days after the program; please do not contact the office prior to this for “missing” credit