Antimicrobial Stewardship:
The Role of the ID Pharmacist

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Disclosures

• None
Objectives

1. Describe the infectious diseases (ID) pharmacist's role within an institution as well as accompanying priorities and values.

2. Outline antimicrobial stewardship strategies, such as antimicrobial restriction and post-prescription review.

3. Discuss challenges of the ID pharmacist from a systems perspective and potential strategies to overcome them.
ID Pharmacist Manifesto

• Antibiotic stewardship is a public good
  – Protect resources
  – Value current patients and future patients
  – Akin to herd immunity
• Evidence-based medicine beyond the guidelines
• Challenge “provider preference” and then some
• Find the happy place between medicine as an “algorithm” and medicine as an “art-form”
• Embrace uncertainty
Antimicrobial Market Failure

- Low hanging fruit have been plucked
- Antimicrobial discovery and FDA approval process have become more complex & expensive
- Limited use + shorter durations = decreased revenue
  - New drug for hypertension vs. new drug for invasive aspergillosis?
  - Antimicrobial resistance further decreases lifespan
- Opportunity cost
  - Cost of drug development estimated to be ~$1.2 billion
  - Drug companies may lose money on antimicrobials
- Prices are based on public perception and fear
  - Public willing to pay more for cancer than infection?
• The Gain Act (2012)
  – Created an Antibacterial Drug Development Task Force to develop and revise guidance for antibacterial drug development
  – Released a list of pathogens with the potential to pose a public health threat
    • Acinetobacter, Aspergillus, Burkholderia cepacia, Campylobacter spp., Candida, C. diff., Pseudomonas, Non-TB Mycobacteria, Enterococcus
  – Drafted guidance for companies for developing antibiotics that address unmet needs
Recent antimicrobial approvals

- Dalbavancin (Dalvance) 2014
- Oritavancin (Orbactiv) 2014
- Peramivir (Rapivab) 2014
- Tedizolid (Sivextro) 2014
- Ceftolozane-tazobactam (Zerbaxa 2014
- Ceftazidime-avibactam (Avycaz) 2016
- Isavuconazonium sulfate (Cresemba) 2015
- Bezlotoxumab 2016
- Delafloxacin 2017
- Meropenem/vaborbactam (Vabormere) 2017
The Pipeline

- Fosfomycin IV
- Plazomicin (aminoglycoside)
- Omadacycline (tetracycline)
- Imipenem-relebactam
- Lefamulin (pleuromutilin)

GAIN Act gives Zavante a shot at new antibiotic development
Be careful what you wish for

- Delafloxacin (Baxdela)
  - MRSA
  - MSSA
  - *S. lugdunensis*
  - *Strep spp.*
  - *Enterococcus faecalis*
  - Enterobacteriaceae
  - *Pseudomonas aeruginosa*
  - Very broad spectrum and oral
- Available for prescribing!
Everything is investigational

• Ceftazidime-tazobactam
  – Approved for cIAI, cUTI
  – Studied against carbapenems
  – Prescribed for carbapenem-resistant Enterobacteracieae

• Ceftolozane-tazobactam
  – Approved for cIAI, cUTI
  – Studied against carbapenems
  – Prescribed for carbapenem-resistant *Pseudomonas* isolates

• Supporting data is in vitro
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<td>Active management of high dollar agents or those on shortage</td>
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<td>Working actively with fellows</td>
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CDC: Core Elements of Hospital Antibiotic Stewardship Programs

• Broad interventions
  - Antibiotic time-outs
    • Does this patient have an infection that will respond to antibiotics?
    • If so, is the patient on the right antibiotic(s), dose, and route of administration?
    • Can a more targeted antibiotic be used to treat the infection (de-escalate)?
    • How long should the patient receive the antibiotic(s)?
  - Prior authorization
    • Take the mystery out – read the Antibiotic control program (ACP)
    • Hospital in UK implemented restrictions – decreased CTX by 95%, and cipro by 73%; C diff rate decreased from 2.4 to 0.6 cases/1000 pt-beds) and MRSA by 25% and ESBL by 17%.
  - Prospective audit and feedback (AKA “post-prescription review” or PPR)
• Other: IV to PO, dose optimization, removing duplicates, screening for Ab-related ADR or drug interaction

Dancer S, Int J of Antimicrob Agents 2013
Elements of an antimicrobial stewardship program

- Prospective audit with intervention and feedback
- Formulary restriction and pre-authorization
- Education
- Guidelines and clinical pathways
- Antimicrobial cycling (insufficient data to recommend)
- Streaming or de-escalation of therapy
- Dose optimization
- Parenteral to IV conversion
**Stewardship Activities**

**Pre-approvals**
- AKA Antibiotic Debate Club
- Restrict use of certain antibiotics until approved by ID
- Antibiogram-driven
- Enforce empiric guidelines
- Managing prescriber preferences
- Teaching opportunities
- Can fix doses from day-one

**Post-prescription Review**
- Reviewing patients downstream; looking for opportunities to de-escalate or discontinue
- Many times culture driven
- Can leave stewardship notes
- Stopping antibiotics tied to decrease in C diff rates
What Is the More Effective Antibiotic Stewardship Intervention: Pre-prescription Authorization or Post-prescription Review With Feedback?

Pranita D. Tamma,¹ Edina Avdic,² John F. Keenan,³ Yuan Zhao,⁴ Gobind Anand,⁵ James Cooper,⁶ Rebecca DeSantis,⁷

¹Division of Infectious Diseases, Department of Pediatrics, Johns Hopkins University School of Medicine, and ²Department of Pharmacy. of Family Medicine, Lynchburg General and Virginia Baptist Hospital, Lynchburg; ³Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health; ⁴Department of Medicine, University of California, San Diego; ⁵Division of Hematology, Department of Medicine, National Institutes of Health; ⁶Division of Infectious Diseases, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore; ⁷Cardiology, and ⁸Infectious Diseases, Department of Medicine, Johns Hopkins University School of Medicine, Ba...
Tension #1

- When two disciplines read the exact same study in polar opposite ways.
Tension #2

- Antibiotic last rights
- “Patient is on max dose pressors & we want to escalate empirically”
Tension #3

• Choosing between:
  – A more narrow spectrum agent that is costly vs. a more broad agent that is less costly
  – A more narrow spectrum agent that carries a higher risk of $C\ diff$ vs a more broad agent that has a lower risk of $C\ diff$
Tension #4

• Temporal discounting: using levofloxacin today versus levofloxacin susceptibility next month

• Flip-side: Using a broader agent on second course empirically

Antibiotic exposure and resistance development in *Pseudomonas aeruginosa* and *Enterobacter* species in intensive care units*

David S. Y. Ong, MD, PharmD; Irene P. Jongerden, RN, PhD; Anton G. Burting, MD, PhD; Maurine A. Leverstein-van Hall, MD, PhD; Ben Speelberg, MD, PhD; Jozef Kesecioglu, MD, PhD; Marc J. M. Bonten, MD, PhD

Ong D, Crit Care Med 2011
Challenges

• Making stewardship matter to others
• Outpatient stewardship
• Changing patient population
• How to risk adjust metrics
• Sharing micro data when patients transfer
• The dreaded calls: *M. abscessus*, XDR TB, middle-of-the-night malaria (bad bugs no drugs part deux)
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