Stewardship and antimicrobial drug shortages

The Problem
Drug shortages across multiple therapeutic categories continue to challenge the healthcare system nationally and locally at BIDMC. For anti-infectives, this presents a particular challenge for a variety of reasons. Formulary antibiotics are ingrained in institutional practice as common empiric or targeted selections. Microbiologic reporting is selective for these agents, and first-dose packages using these drugs are available in Critical Care areas to improve the time to antibiotic administration. Alternate agents is selective for these agents, and first-dose packages using these drugs are available in institutional practice as common empiric or targeted selections. Microbiologic reporting is selective for these agents, and first-dose packages using these drugs are available in Critical Care areas to improve the time to antibiotic administration. Alternate agents are sometimes less active microbiologically, more costly, or also in shortage. In the last six months, critical shortages of the following agents required attention:

- Meropenem, the BIDMC formulary carbapenem with activity against multidrug-resistant Gram-negative pathogens including Pseudomonas
- Piperacillin-tazobactam, the BIDMC formulary anti-pseudomonal beta-lactam/beta-lactamase inhibitor combination with enhanced activity against Gram-positive bacteria (e.g., Enterococcus) and anaerobes
- Cefepime, the BIDMC formulary fourth-generation cephalosporin with enhanced antipseudomonal activity and activity against some multidrug-resistant Gram-negative pathogens

Aim/Goal
- Evaluate and quickly respond to supply interruptions to prevent lapses in therapy for multiple patients, particularly those with the highest need
- Utilize evidence-based clinical guidelines, electronic systems, and stakeholder providers to develop and implement multifaceted response plans such as identification and, as necessary, prioritization of at-risk patients

The Team (Antimicrobial Stewardship Team = AST)
- Christopher McCoy, PharmD  Pharmacy
- Howard S. Gold, MD  Health Care Quality/Infectious Diseases
- Monica Mahoney, PharmD (AQ-ID)  Pharmacy
- Graham Snyder, MD  Health Care Quality/Infectious Diseases
- Ethan A. Smith, PharmD  Pharmacy

The Interventions
- A systematic review of the supply/demand for drugs in shortage was performed, including: analysis of local utilization, identification of patient care implications, computerized provider entry inventory, assessment of the availability of substitute agents and review of targeted and evidence-based practice implications
- A multifaceted shortage management response package was developed based on the particulars of each shortage including directions for therapeutic substitution and recommendations for additional microbiologic testing

The Results/Progress to Date
- Antibiotic utilization is not easily adjusted at the institutional level and required a multifaceted intervention including AST interventions, cPOE clinical decision support adjustments and staff communications. Formulary adjustments also were required. Imipenem was added back to the formulary, ertapenem use was expanded and alternate class antibiotics were often recommended based on case reviews.

Figure 1: Average daily use (grams) of meropenem and alternate carbapenems during the acute shortage.
Average daily use of meropenem was reduced 36% via the multifaceted intervention. Ertapenem was recommended only if Pseudomonas was not present and susceptibility could be confirmed upon request to the Micro Lab. Overall carbapenem utilization did not rise significantly. Imipenem was recommended when there was a specific need for coverage of pathogens such as Nocardia or mixed cultures with Enterococcus.

Figure 2: Average daily use (grams) of piperacillin tazobactam (TZP) and cefepime. The goal TZP utilization in order to maintain supply is ~100-150g per day. Given the high baseline utilization of this agent, efforts had to be intensified through AST interventions, alternate drug combinations to cover anaerobes and avoid carryover from the carbapenem shortage. Other challenges included the availability of first doses in the ICUs to maintain a short time to first dose.

Lessons Learned
Antimicrobial shortages require intensive labor to redirect therapy because treatment should be pathogen directed and simple substitution is not usually an option. We thank our BIDMC colleagues for their outstanding cooperation in this effort. Transitions to outpatient care must include appreciation of shortages on a national scale. More targeted therapy was often achieved due to the shortage.

Next Steps/What Should Happen Next
Resource allocation in the form of manpower for Stewardship, Pharmacy purchasing, and Information Services is critical. The effects of these shortages on patient care outcomes are unknown without further investigation.

For more information, contact:
Christopher McCoy PharmD cmccoy@bidmc.harvard.edu