Key Concepts in Antifungal Stewardship

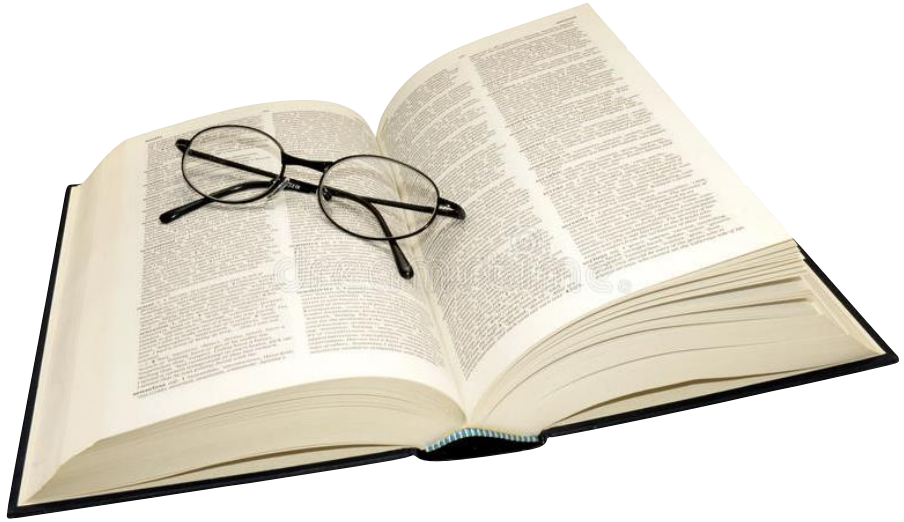
Paschalis Vergidis, MD MSc, FECMM
Associate Professor of Medicine, Mayo Clinic College of Medicine & Science
@pascalisID

Learning Objectives

- Describe the Core Elements of Antimicrobial Stewardship
- What are the 5 D's of Antifungal Stewardship?
- How does Antifungal Stewardship differ from Antibiotic Stewardship?
- Applying the concepts of Antifungal Stewardship in the hematologic patient

Stewardship

- “The careful and responsible management of something entrusted to one’s care.” Webster’s Dictionary
- Implementation of coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents



The Journal of Infectious Diseases

SUPPLEMENT ARTICLE

Core Recommendations for Antifungal Stewardship: A Statement of the Mycoses Study Group Education and Research Consortium

Melissa D. Johnson,[1,a] Russell E. Lewis,[2,a] Elizabeth S. Dodds Ashley,[1,a] Luis Ostrosky-Zeichner,[3] Theoklis Zaoutis,[4] George R. Thompson III,[5] David R. Andes,[6] Thomas J. Walsh,[7] Peter G. Pappas,[8] Oliver A. Cornely,[9,10,11,12] John R. Perfect,[1] and Dimitrios P. Kontoyiannis[13]; for the Mycoses Study Group Education and Research Consortium

Core Elements of Hospital Antibiotic Stewardship Programs

Hospital Leadership Commitment
Dedicate necessary human, financial, and information technology resources.

Accountability
Appoint a leader or co-leaders, such as a physician and pharmacist, responsible for program management and outcomes.

Pharmacy Expertise (previously "Drug Expertise"):
Appoint a pharmacist, ideally as the co-leader of the stewardship program, to help lead implementation efforts to improve antibiotic use.

Action
Implement interventions, such as prospective audit and feedback or preauthorization, to improve antibiotic use.

Tracking
Monitor antibiotic prescribing, impact of interventions, and other important outcomes, like *C. difficile* infections and resistance patterns.

Reporting
Regularly report information on antibiotic use and resistance to prescribers, pharmacists, nurses, and hospital leadership.

Education
Educate prescribers, pharmacists, nurses, and patients about adverse reactions from antibiotics, antibiotic resistance, and optimal prescribing.

MAYO CLINIC

www.cdc.gov/antibiotic-use/core-elements/hospital.html

#1 Hospital Leadership Commitment

- Dedicate necessary human, financial and information technology resources
- Hospital Accreditation Organizations
- Antifungal Stewardship integrated into existing Antimicrobial Stewardship Programs

#2 Accountability

- Appoint a leader and co-leaders
- Core Members should have in-depth knowledge and clinical experience
  - Utilizing resources within a health network
  - Contracting or resource-sharing with other hospitals

#3 Pharmacy Expertise (“Drug Expertise”)

- Appoint a pharmacist ideally as a co-leader to lead implementation efforts

#4 Action

- Prospective audit and feedback
- Prior authorization
- Patient care recommendations are more likely to be accepted when colleagues are viewed as team members
- “Handshake stewardship”

#5 Tracking

- Tracking antifungal drug use
- Standard metric: Days of Therapy (DOT) vs Defined daily doses (DDD)
- Benchmarking antifungal use

#6 Reporting

- Performance measures (mortality, clinical response, adherence to guidelines)
- Direct data feedback to prescribers
- Reporting back to hospital leadership

The 5 D's of Antifungal Stewardship

- **DIAGNOSIS:** Does the diagnosis require antifungal therapy?
  - Septic shock, febrile neutropenia, lung nodule, *Aspergillus* in sputum culture
- **DRUG:** Is the antifungal appropriate?
  - Empiric treatment, Azole-/echinocandin-resistant *Candida*, azole-resistant *Aspergillus* spp

The 5 D's of Antifungal Stewardship

- **DOSE:** What is the recommended dose and route of administration?
  - Obesity, renal failure, CNS infection. Administration via gastric/enteral feeding tubes
- **DURATION:** What is the recommended duration?
  - Deep-seated candidiasis (ocular candidiasis), Secondary prophylaxis in immunosuppressed patients
- **DE-ESCALATION:** Can treatment be de-escalated to a narrow-spectrum antifungal?
  - Echinocandin to azole, Induction to consolidation

Challenges in Antifungal Stewardship

- IFIs afflict mostly critically ill or immunocompromised patients with complex underlying disease states
- IFIs are associated with significant morbidity, mortality, and costs
- The sensitivity of current fungal diagnostic tools is limited

Antifungal Stewardship Interventions

- Engagement of high-prescribing specialists
- Access to timely diagnostics and antifungal susceptibility testing
- Screening for drug-drug interactions and therapeutic drug monitoring

Multifaceted Approach

- University Hospital in Spain
- Year 1: pocket-size treatment guidelines were distributed to prescribers, an order entry tool for antifungals was incorporated into the electronic medical record, and interactive training courses were developed.
- Year 2: All antifungal prescriptions were prospectively audited by infectious disease specialists. Feedback was provided to prescribers.

Valerio M et al. Clin Microbiol Infect. 2015;21(5):492 e1-9

Multifaceted Approach

- Incidence of and mortality secondary to candidemia was reduced
- Number of defined daily doses of antifungals decreased
- The program led to significant cost savings
- Sustainability of the intervention was demonstrated up to 36 months after implementation.

Valerio M et al. Clin Microbiol Infect. 2015;21(5):492 e1-9

ROLES AND RESPONSIBILITIES OF THE ANTIFUNGAL STEWARDSHIP TEAM

- Hematologist
- Infectious Disease specialist
- Clinical Microbiologist
- Pharmacist

MAYO CLINIC

Vergidis P et al. Curr Fungal Infect Rep 2023; 17(2): 108-118

HEMATOLOGIST

- Impact of chemotherapy on host immune responses
- Advising on anticipated duration of neutropenia and lymphopenia
- Risk stratification based on HSCT type
- Degree of immunosuppression conferred by prophylaxis or treatment for GVHD
- Implications of antifungal use in patients participating in hematology trials
- Overall cancer prognosis

INFECTIOUS DISEASE SPECIALIST / CLINICAL MICROBIOLOGIST

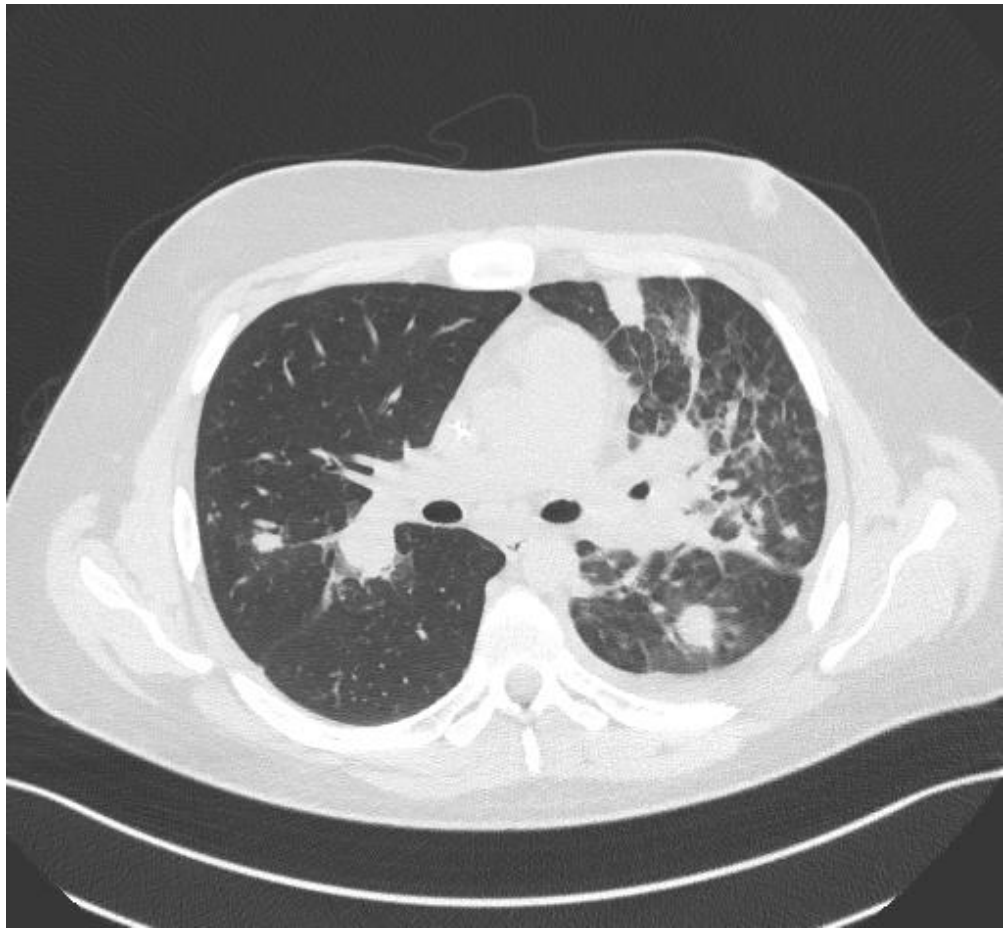
- Significance of isolated pathogen (colonization versus infection)
- Use of fungal biomarkers
- Appropriateness of primary/secondary prophylaxis
- Appropriateness of antifungal treatment (regimen, duration)
- Assessing response to treatment, need for therapy modification
- Use of novel antifungals

CLINICAL PHARMACIST

- Drug-drug interactions
- Route of administration and appropriate dosing
- Pharmacokinetic issues in specific populations
- Incorporating pharmacogenomics
- Adjusting dose based on TDM
- Evaluating side effects
- Proposing alternative regimens
- Developing metrics

Case

- 20 yo M with Philadelphia-negative, CD20+ B-Cell ALL undergoing cycle 1 of the Alliance clinical trial
  - Days 1, 8, 15, 22: **Vincristine** and Daunorubicin
  - Days 1-7, 15-21: Dexamethasone
  - Day 4: Pegasparaginase
  - Days 8, 29: IT methotrexate
- Randomized to **Inotuzumab**



Summary

- Antifungal stewardship has received less attention compared to antibiotic stewardship
- Antifungal stewardship interventions may be implemented within an existing antimicrobial stewardship program
- Recommendations are more likely to be accepted when the stewardship physician/pharmacist are viewed as team members rather than external auditors