

Antimicrobial Stewardship for Hospital Acquired Infection Prevention: Focus on *C. difficile* infection

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Objectives

- Describe the elements of a successful antimicrobial stewardship program (ASP)
- Evaluate the modifiable risk factors for hospital acquired *Clostridium difficile* Infection
- Analyze the available data on curbing *C. difficile* infection rates with an active ASP

Global Threat

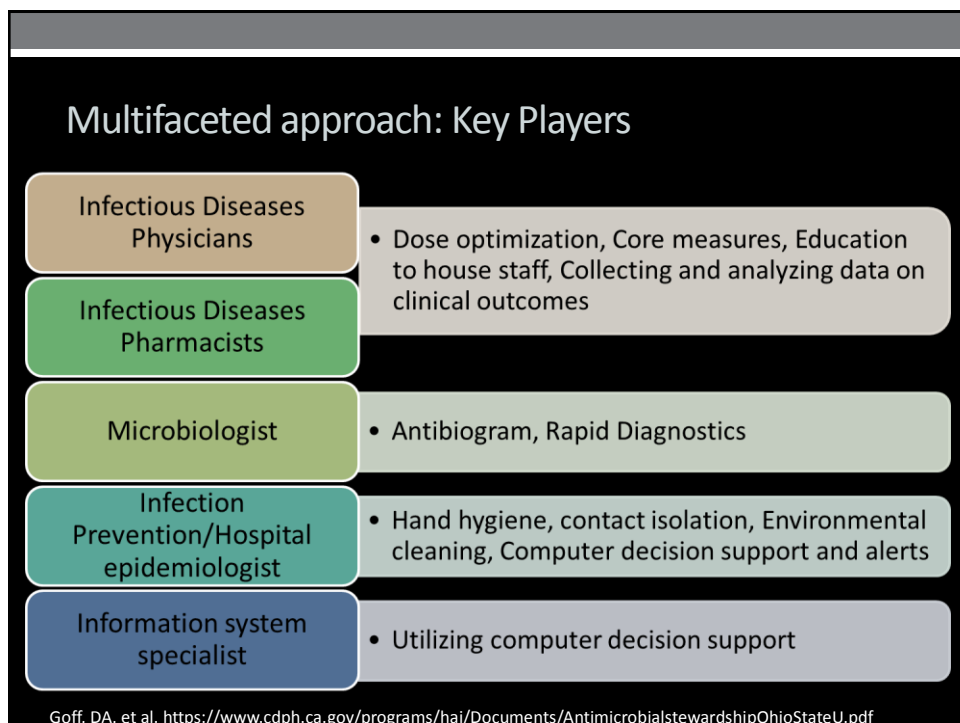
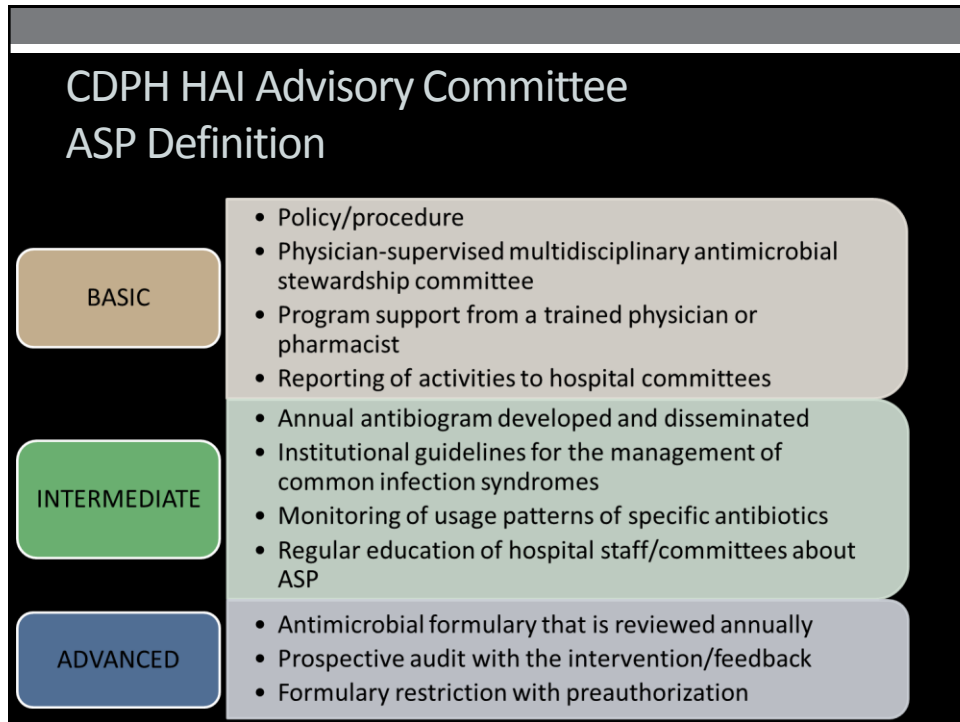
- Antimicrobial resistance is recognized as one of the greatest threats to human health worldwide
 - MRSA kills more Americans every year than emphysema, AIDS, Parkinson's, and homicide combined
 - Drug-resistant pathogens cost \$21-34 billion to treat and contribute to more than 8 million additional hospital days
 - We need multifaceted approach to prevent, detect, and control the emergence of resistance

IDSA. Clin Infect Dis. (2011) 52 (suppl 5): S397-S428.

Antimicrobial Stewardship Program (ASP)

- The concept of ASP is not new (1970s)
- Recent IDSA policy paper: calls to strengthen US efforts to improve prevention and control efforts, including adoption of ASP in *all* US healthcare facilities
- ASP is an intervention-based program to:
 1. Improve patient safety and optimize clinical outcomes
 2. Curb spread of antimicrobial resistance
 3. Promote cost effectiveness

SHEA, IDSA, PIDS. Infect Control Hosp Epidemiol. 2012 April.



California Senate Bill 1311

- Signed into law September 2014
- 1288.85. Each general acute care hospital, shall do all of the following by **July 1, 2015**:
 1. Requires hospitals to adopt and implement as ASP in accordance with guidelines established by federal government and professional organizations
 2. Establish a physician-supervised multidisciplinary antimicrobial stewardship committee with at least one physician or pharmacist who has undergone specific training related to stewardship
 3. Report ASP activities to appropriate hospital quality improvement committee

http://leginfo.legislature.ca.gov/faces/billNavClient.xhtml?bill_id=201320140SB1311

Many Targets of ASP

For every patient

- Right drug, right time, right duration, right disease state
- De-escalation
- Feedback to providers

Institution/Health System level

- Utilizing resistance concepts
- Minimizing collateral damage
- Maximizing PK/PD of antibiotics
- Developing procedures to improve outcomes and prevent adverse events

Targets must be tailored to the specific institution's needs

ASP ACTIVITIES TARGETING DECREASE IN CDI

Costs Associated with Treating HA-CDI

Antimicrobial Stewardship Strategies in CDI

Prevention of CDI

- Minimizing risk factors
- ?Probiotics

Appropriate Management

- Rapid identification
- Maximizing antibiotic therapy of CDI therapy
- Prevent recurrence

Prevention of CDI

Greatest risk factors for acquiring CDI

- **Exposure to antibiotics**
- Recent exposure to healthcare
- Use of Proton Pump Inhibitors (PPI's)
- Gastrointestinal Manipulation/Surgery
- Length of stay in healthcare facilities
- Serious underlying conditions
- Immunocompromised patients
- Advanced age

1 Antibiotic Resistance Threats in the United States, 2013. Access: <http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf>.

2. Jarvis, WR et al. National point prevalence of Clostridium difficile in US health care facility inpatients, 2008. AJIC; May 2009. 263-270.

3 CDC Vital Signs. Making Health Care Safer: Stopping C. difficile infections. March 2012.

Antibiotics and associated CDI risk

Biguardi GE. J Hosp Infect. 1998 Sep;40(1):1-15.

Successful Interventions at secondary/tertiary care hospital

- Local guidelines developed by ID physicians and pharmacists and publicized initially by distributing a letter to all house staff
 - No formal restriction
 - Recommendations reinforced through telephone feedback to recommend alternatives as applicable
 - Shortening duration of therapy in accordance with IDSA guidelines
- Oral presentations to selected services
- Pocket-sized antibiotic guide focusing on empirical treatment of common infections
 - Aimed at decreasing use of target antibiotics: 2nd-3rd gen cephalosporins, ciprofloxacin, clindamycin, and macrolides
 - Examples:
 - Gentamicin instead of cipro for pyelonephritis
 - Cotrimoxazole instead of cipro for cystitis
 - Levofloxacin or moxifloxacin instead of cephalosporin/azithro for CAP

Valiquette L, et al. Clin Infect Dis. (2007) 45 (Supplement 2): S112-S121.

Success of ASP targeted at CDI Reduction

ASP interventions targeted at CDI

Setting	Intervention	Impact
683-bed secondary/ tertiary care hospital Canada	<ul style="list-style-type: none"> • Development of guidelines • Educational materials • Shorter treatment durations 	CDI decreased 60% and overall decrease in targeted abx consumption by 54%
834-bed tertiary care urban teaching hospital Pittsburgh	<ul style="list-style-type: none"> • Education material for providers • Active surveillance for CDI • Expanded infection control measures • Targeted abx restriction (clindamycin, ceftriaxone, levofloxacin, other broad spectrum) 	Targeted abx use decreased by 41%. Decrease in CDI from 7.2/1000 discharges to 3/1000
1200-bed tertiary care teaching hospital London	<ul style="list-style-type: none"> • Narrow spectrum abx policy • Prospective feedback on CDI and MRSA infection every 8-12 wks. 	Significant reduction in targeted abx use. Decrease in CDI IRR 0.35 (0.17, 0.73)
174-bed community teaching hospital Boston	<ul style="list-style-type: none"> • Multidisciplinary-prospective abx monitoring (inappropriate use) • Program use guidelines • Pharmacy restrictions • Abx detailing with individual prescriber education 	22% decrease in use of broad spectrum abx Decrease in CDI 2.2/1000 pt days to 1.4/1000 pt days (p=0.002) Same trend in nosocomial MDR gram negative infections

Utilization of Specific Probiotic to Prevent *C. difficile* Overgrowth: B-1 recommendations

“Consuming *L. acidophilus* CL1285 and *L. casei* LBC80R can decrease CDI incidence. Probiotics should be added in bundle of preventive measures to control CDI.”

Clin Infect Dis. (2015) 60 (suppl 2): S148-S158.

Maximizing Management of CDI

Rapid Diagnostics

- Early detection of toxigenic *C. difficile* leads to earlier treatment and more timely isolation
- Nucleic acid amplification assays are rapid and have high sensitivity and specificity
 - rPCR tests available to shorten time to diagnosis from 2-3d → hours
- Education on appropriate interpretation and limitations of tests important
 - Limit the frequency of tests that can be sent by provider
- Key: Antimicrobial stewardship intervention needed
 - Calling prescriber with results and recommendations for appropriate management

Goff DA, et al. Pharmacotherapy. 2012 Aug;32(8):677-87

2010 IDSA guidelines Treatment Guidelines

Clinical definition	Clinical symptoms	Recommended Therapy
Initial episode, mild or mod	WBC <15,000 cells/microL Scr < 1.5x premorbid lvl	MTZ 500mg PO TID x 10-14d
Initial episode, severe	WBC > 15,000 cells/microL Scr ≥ 1.5x premorbid lvl	Vancomycin 125mg PO QID x 10-14d
Initial episode, severe complicated	Hypotension or shock, ileus, megacolon	Vanco 500mg PO QID + MTZ 500mg IV q8h
First recurrence	--	Same as initial episode
Second recurrence	--	Vanco PO (tapered/pulsed regimen)

What about newer modalities and where do they fall in this algorithm?

Cohen SH, et al. Infect Control Hosp Epidemiol. 2010 May.

Newer Available Management of CDI

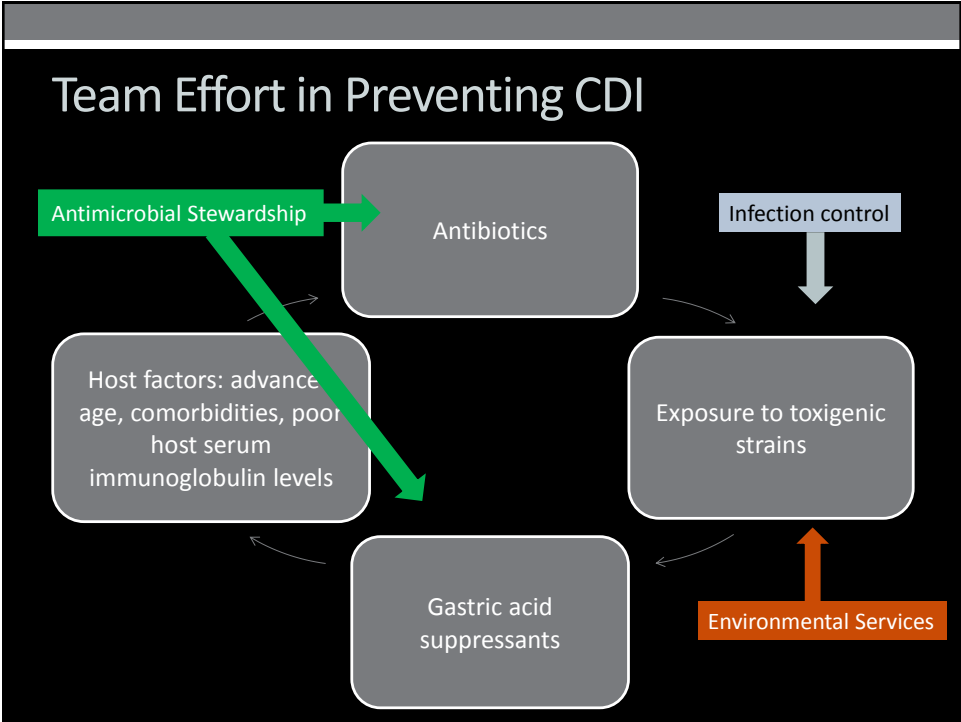
1. Fidaxomicin (Dificid)

- **Benefit:** more specific for *C. diff* compared to others → less disturbance of normal GI flora
- **Benefit:** inhibits spore formation
- Recurrence rate: Non-BI/NAP1/027: 7.8% (fidaxomicin) vs. 25.5% (vanco), $p < 0.001$
- ~\$4000 (fidaxomicin) vs \$15 (vancomycin) per course

2. Fecal microbiota transplant

- Recolonization of GI flora with stool from donor
- Oral, Capsulized, Frozen FMT for relapsing *C. difficile* Infection
 - 90% rate of clinical resolution of diarrhea
 - 70% resolved after 1 round of treatment

Louie TJ, et al. *N Engl J Med.* 2011;364(5):422-431
Babakhani F, et al. *CID* 2012;55(S2):S162-169



THANK YOU!
