



Antimicrobial Stewardship Workshop

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Bug Off, Prevention is Game On!
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Disclosure Statement

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Objectives

- Identify key stake holders needed to implement an antimicrobial stewardship program in their work setting
- Analyze their work setting and select one strategy for implementation.



Precious Drugs & Scary Bugs:
The 5 D's of Antimicrobial Stewardship



Conceptual Framework
RATIONAL FOR STEWARDSHIP

Mitigate the unintended consequences of antimicrobial use

- **Direct harms**
 - *C. difficile* & MDROs
 - Treatment failures
 - Adverse drug events, phlebitis
- **Indirect harms**
 - Increasing antimicrobial resistance
 - Increased colonization with MDROs
 - Excess costs
- **Regulatory burden**
 - Mandatory public reporting to CMS & IDPH



Conceptual Framework
OPERATIONAL GOALS

the 5 Ds

- *right* **D**agnosis
- *right* **D**rug selection
- *right* **D**ose
- *right* **D**uration
- *right* **D**e-escalation

Conceptual Framework
OPERATIONAL GOALS

the 5 Ds

- **Succinct way to market AMS aims**
- **Addresses frontline clinician's focus**
 - What is the best way to treat infections that are common in my practice?
- **Provides further justification/rationale when requesting additional support/resources from leadership**




Conceptual Framework
OPERATIONAL GOALS

Antimicrobial Mindfulness

- Umbrella concept for various methods employed to systematically assess and reassess the appropriateness of antimicrobial therapy
- Implement processes to review the 5 D's of Stewardship (Diagnosis, Drug, Dose, Duration, De-escalation)



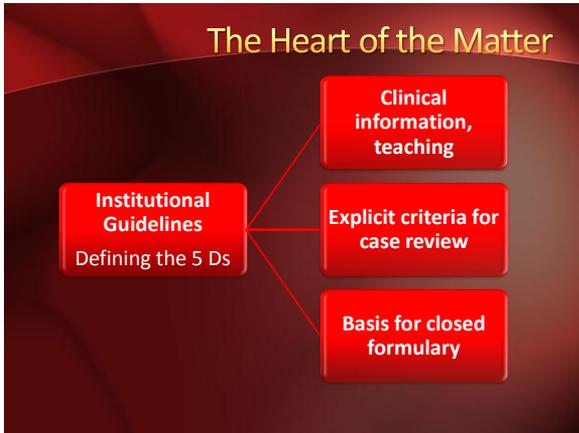
Conceptual Framework
ESSENTIALS FOR SUCCESS

- **Compelling rationale** & clear communication of purpose & goals: the 5 D's
- **Authority:** Leadership support & clinician buy-in
- **Financial impact:** AMS interventions are revenue neutral or cost saving
- **Feasibility:** Availability of resources & practicality of implementation – impact on workflow
- **Feedback:** Monitor progress toward goals by reporting measures back (clinical outcomes, process measure, abx use)

Conceptual Framework

MEASURES OF IMPACT

- **Clinical outcomes**
 - Treatment success
 - Rates of *C. difficile*, MDROs, SSIs, & adverse reactions
- **Process measures (monitor the 5 Ds)**
 - Rates of misdiagnosis
 - Pharmacist/AMS reviews & intervention outcomes
 - Inappropriate therapy (complex, redundant, or inadequate drugs/doses)
 - Excessive duration or failure to de-escalate
- **Antimicrobial utilization & costs**
- **Antimicrobial susceptibility prevalence trends**
 - Hospital wide & targeted patient care areas
 - Key bug-drug susceptibilities emphasized



How do we start the process of improvement?

- **Build on past successes**
 - HAI prevention efforts often “grow” as an extension of previous prevention efforts
 - Expansion from acute to long term care settings
 - *C. diff* → antimicrobial stewardship → CRE
- **Do what’s feasible**
 - Many small steps still get you closer to achieving your goals
- **Sustainability**
 - Build changes into the workflow
 - Engagement of partners & coordination of efforts

The Institute for Healthcare Improvement (IHI)
Model for Improvement

Start with a small test of change...
Then, build on and expand your efforts.

The Institute for Healthcare Improvement (IHI)
Model for Improvement

What are we trying to accomplish? → Shared goal

How will we know that a change is an improvement? → Measures to track progress/success
• Process
• Outcome

What changes can we make that will result in improvement? → Bundle Interventions & Innovations
• Multidisciplinary teams

The Breakthrough Series: IHI's Collaborative Model for Achieving Breakthrough Improvement. IHI Innovation Series white paper, Boston: Institute for Healthcare Improvement; 2003. (Available on www.IHI.org)

Objectives

1. State the primary goal of antimicrobial stewardship.
2. List alternate personnel who may be recruited to fulfill the roles of Infectious Diseases (ID)-trained physicians and pharmacists to spearhead antimicrobial stewardship initiatives.
3. State how application of each of the 5Ds is relevant to meeting the goal of antimicrobial stewardship.

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

Primary goal:

Optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including:

- toxicity
- the selection of pathogenic organisms (such as *Clostridium difficile*)
- and the emergence of resistance.

Dellit. *Clin Infect Dis* 2007; 44:159.

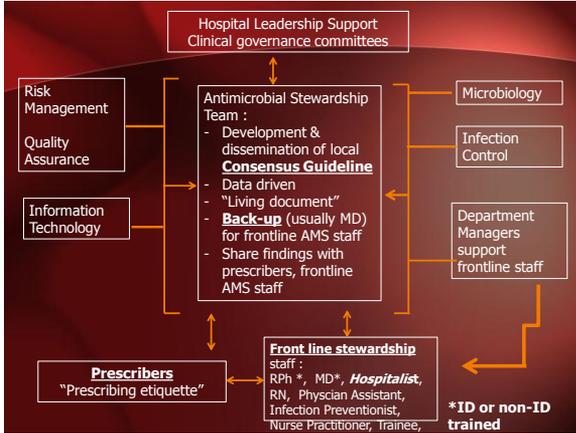
Core strategies

- **Formulary restriction and preauthorization**
- **Prospective audit with intervention and feedback by stewardship team**

Dellit. *Clin Infect Dis* 2007; 44:159

Many hospitals are already engaging in Supplemental Antimicrobial Stewardship Strategies

- **Education**
- **Guidelines and clinical pathways**
- **Antimicrobial order forms**
- **Combination therapy**
- **Streamlining or de-escalation of therapy**
- **Dose optimization**
- **Conversion from parenteral to oral therapy**
- **Antimicrobial cycling and scheduled antimicrobial switch**



Understanding the determinants of antimicrobial prescribing within hospitals: the role of "prescribing etiquette".

- "Unwritten but widely accepted cultural rules around prescribing....."
 - Hierarchy of prescribing....the senior doctors often decide what is prescribed.
 - Non-interference [reluctance to question] with the clinical decisions of others, [especially senior clinicians] despite the existence of local policies.
- Institutional guidelines may avert some of this [prescribing etiquette]...also need buy-in of senior doctors.
- Involve front-line & senior prescribers from the start.

Charani. Clin Infect Dis 2013; 57:188.

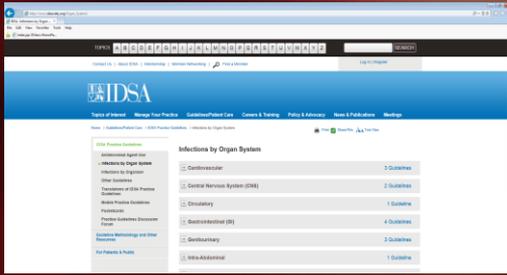
Developing an institution-specific consensus guideline....
Intranet guidelines...

Hospital Antibiotic Stewardship Programs – CDC Website

- [Barnes-Jewish Hospital](#)
- [The Cleveland Clinic Foundation](#)
- [Columbia University Medical Center](#)
- [The Johns Hopkins Hospital](#)
- [The Nebraska Medical Center](#)
- [University of California, San Francisco](#)
- [University of Kentucky Hospital](#)
- [University of Pennsylvania Health System](#)
- [University of Wisconsin Hospital and Clinics Antimicrobial Stewardship Program](#)
- [Wake Forest University](#)

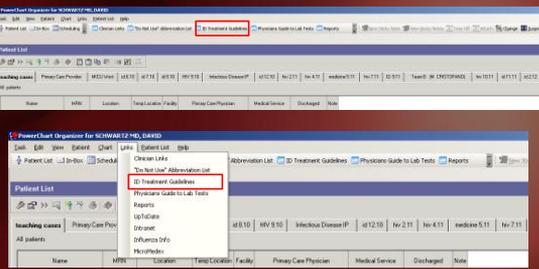
<http://www.cdc.gov/getsmart/healthcare/programs.html>

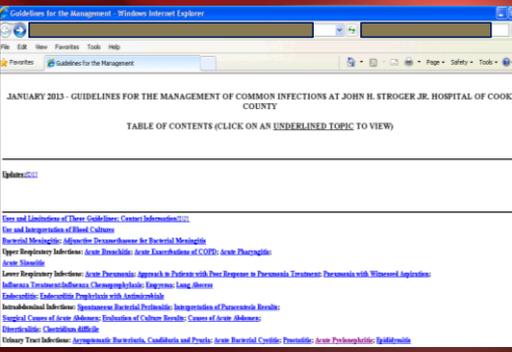
IDSA Website Practice Guidelines plus local resistance (antibiogram) patterns



http://www.idsociety.org/idsa_practice_guidelines/

Empower others... Easy access to guidelines Stroger Hospital ID Treatment Guidelines





RECOMMENDED DOSAGES FOR IV ANTIMICROBIAL DRUGS FOR ADULTS WITH RENAL INSUFFICIENCY

DRUG NAME	NORMAL DOSE	REGIMEN IF CREATININE CLEARANCE (DL/MIN):		
		49-29	19-19	<10 (DIALYSIS)
Levofloxacin (IV)	250mg q4h	No adjustment	250mg q4h ^b	250mg q4h
	300mg q4h	300mg LD ^a , then 250 mg q4	300mg LD ^a , then 250 mg q4h	300mg LD ^a , then 200mg q4h
	750mg q4h	750mg q4h	750mg LD ^a , then 300mg q4h	750mg LD ^a , then 300mg q4h

^a LD^a = loading dose.
^b If receiving hemodialysis (HD), then no dosage adjustment is required.

De-escalation opportunities

De-escalation process:
 Step 1: cultures before antimicrobials are started

Maximize pathogen identification

- Urinary tract infection
- Bloodstream/ intravascular – MSSA
 - beta-lactams better than vancomycin
- Long-term antibiotic therapy
 - osteomyelitis in stable patient, hold antibiotics until cultures obtained
- Ventilator-associated pneumonia

Kaye. *J Hosp Med* 2012; 7 (suppl 1):S13. Niederman. *Sem Respir Crit Care Med* 2006; 27:45.

De-escalation: Little Definitive Data

- Formulary
- Collateral damage
 - Risk for *C. difficile*, Extended-spectrum beta-lactamases, carbapenem-resistant *Enterobacteriaceae*
- Adverse drug reactions
- Convenience/cost
 - all things being equal, what's better?
 - Pencillin GK q4 hours vs Ceftriaxone q24h (*Streptococcal* endocardidits)

Antibiotic De-Escalation -- Making it work

- Prescribers need confidence that patients will not be harmed
- Protocols for specific infections are often lacking in the literature
- Stewardship Team back-up for frontline AMS staff
 - Dealing with equipoise – variable evidence to support recommendations
 - Many necessarily based on “expert opinion”

Masterson. *Crit Care Clin* 2011; 27:149.

Identifying Stewardship Opportunities
De-escalation

- Opinions of front-line stewardship staff, prescribers
- Pharmacy purchases / expenditures
- Publications on “stewardship opportunities”
- Surveillance snapshot at your site:
 - Diabetic foot infection at Stroger
 - Piperacillin/tazobactam plus vancomycin until discharge, despite availability of culture data

From Literature to Guideline for Common Syndromes

- Cellulitis
- Pneumonia

Simple Cellulitis. What would you suggest?

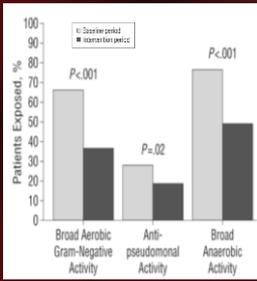
- 46 yo previously healthy male hospitalized for right lower extremity pain, multiple abrasions on arms, legs. No abscess or purulent drainage was described.
- Involved in a motor vehicle accident the day before. NKDA. Stable vital signs.
- A/P: RLE cellulitis. Start piperacillin/tazobactam plus vancomycin.
- What would you suggest regarding:
 - Gram-negative spectrum?
 - MRSA coverage?

Simple Cellulitis. Gram-negative spectrum?

- Most are caused by beta-hemolytic streptococci (mostly Group A strep, but also Groups B, C, G).
 - *S. aureus* – rarely causes cellulitis, unless associated with abscess, furunculitis or ulcer.
 - Drug: dicloxacillin, cephalexin, clindamycin
 - Duration:
 - Outpatient: 5-10 days
 - Hospitalized: 7-10 days
- } According to clinical response

Stevens et al. *Clin Infect Dis* 2014; 59:147.

Decreased Antibiotic Utilization After Implementation of a Guideline for Inpatient Cellulitis and Cutaneous Abscess



- Decrease in broad-spectrum antibiotic exposure.
 - Decrease median tx duration (13 to 10 days; p<.001).
 - Clinical failure unchanged.
- Jenkins. Arch Intern Med 2011; 171:1072.

Public safety net health care system.
Retrospective pre- / post-intervention study

Multidisciplinary committee:

- Guideline development & dissemination
- Antibiotics & **diagnostics**
- Electronic admission order set for cellulitis and abscess to facilitate guideline adherence

Education:

- **Key attending physician peer champions**
- Representatives from the departments that routinely manage patients with cellulitis and abscess

Audit & feedback:

- Quarterly review of cases
- **Feedback to peer champions** who shared data with their faculty & housestaff
- Reinforce management concepts to prescribers

Jenkins. Arch Intern Med 2011; 171:1072.

Simple Cellulitis.
What would you suggest?

- What would you suggest regarding:
 - Gram-negative spectrum → unnecessary for most cases of cellulitis, abscess
 - MRSA coverage?

IDSA Clinical practice guidelines

- Hospitalized patients:
 - beta-lactam (eg: cefazolin) may be considered for nonpurulent cellulitis
 - modification to MRSA-active therapy if there is no clinical response

Stevens et al. *Clin Infect Dis* 2014; 59:147.

ERYSIPELAS/CELLULITIS/LYMPHANGITIS not associated with venous catheter or chronic ulcer

- Erysipelas: superficial inflammatory process with sharply demarcated borders usually affecting the extremities, face, scalp and genitalia
- Uncomplicated cellulitis: erythema, induration, warmth, pain. Deeper infection extending into the subcutaneous tissue with less distinct demarcation
- Lymphangitis: Painful, tender erythematous linear streak on the skin progressing towards draining regional lymph nodes. Tender lymphadenopathy commonly seen with fever, chills and malaise
- Cellulitis with cutaneous abscess: superficial abscess (fluctuant mass or, if opened, purulent drainage) with associated cellulitis. Frequently caused by MRSA, even in community-acquired cases. **SEND PUS FOR GRAM STAIN AND CULTURE.**

INFECTION	ETIOLOGY	RECOMMENDED EMPIRIC REGIMENS	
		DRUG OF CHOICE (DAILY DRUG COST)	PCN-ALLERGIC/ ALTERNATIVE
<i>A = ID APPROVAL REQUIRED, I = DRUG INTERACTION, R = DOSAGE REDUCTION FOR RENAL INSUFFICIENCY</i>			
ERYSIPELAS UNCOMPLICATED CELLULITIS LYMPHANGITIS	ERYSIPELAS: Group A streptococcus ^a is almost always the cause	PARENTERAL^b cefazolin 1-2g IV q8h (\$68-108) OR cefazolin 8-12 g q8h (\$17)	PARENTERAL ^{b,c} clindamycin 600mg IV q8h (\$44)
	CELLULITIS: <i>S. aureus</i> and <i>S. pneumoniae</i>	ORAL^d dicloxacillin 500mg PO q6h (\$0-28)	ORAL^{b,e} clindamycin 300mg PO q8h (\$0-86)
	LYMPHANGITIS: Group A streptococcus, family <i>S. aureus</i>	PARENTERAL	PARENTERAL
Cellulitis with cutaneous abscess	Methicillin-resistant and susceptible <i>S. aureus</i>	Vancomycin R 1 gm IV q12h (\$7)	PARENTERAL Vancomycin R 1 gm IV q12h (\$7)
		ORAL^d MRSA: doxycycline 100 mg PO q12h (\$0-08) OR TRIMETHOPRIM-sulfamethoxazole PO q12h	ORAL^d MRSA: doxycycline 100 mg PO q12h (\$0-08)

Clinical Trial: Comparative Effectiveness of Cephalexin Plus Trimethoprim-Sulfamethoxazole Versus Cephalexin Alone for Treatment of Uncomplicated Cellulitis: A Randomized Controlled Trial

Daniel J. Pallin,^{1,2} William D. Binder,² Matthew B. Allen,^{3,4} Molly Lederman,^{1,5} Siddharth Parmar,¹ Michael R. Filbin,² David C. Hooper,² and Carlos A. Camargo Jr.²

¹Department of Emergency Medicine, Brigham and Women's Hospital, ²Division of Emergency Medicine, Boston Children's Hospital, and ³Department of Emergency Medicine, Massachusetts General Hospital, Boston; ⁴Perelman School of Medicine at the University of Pennsylvania, Philadelphia; ⁵Department of Pediatrics, and ⁶Division of Infectious Diseases, Department of Medicine, Massachusetts General Hospital, Boston

- High prevalence of MRSA.
- Outpatients diagnosed with cellulitis without abscess
- Addition of trimethoprim-sulfamethoxazole to cephalexin did not improve outcomes

Clin Infect Dis 2013; 56:1754.

Back to the question: Simple cellulitis, unknown microbiologic etiology – what to do?

- A. Continue vancomycin & piperacillin/tazobactam.
- B. Continue vancomycin only.
- C. Stop vancomycin (and piperacillin/tazobactam, start cefazolin or oxacillin).

Pneumonia

CMS Core Measures & Initial *Antibiotic Selection* for

- CAP in Immunocompetent –ICU patient
- CAP Immunocompetent – Non-ICU patient

What is the Role of Antimicrobial Stewardship in Improving Outcomes of Patients with CAP?

Veronique Nussenblatt, MD, MHS
Edina Avdic, PharmD, MBA
Sara Cosgrove, MD, Ms

Includes summary of publications supporting short-course therapy for community-acquired pneumonia.

Infect Dis Clin N Am 2013; 27:211.

MAJOR ARTICLE

Impact of an Antimicrobial Stewardship Intervention on Shortening the Duration of Therapy for Community-Acquired Pneumonia

Edina Avdic,¹ Lisa A. Coshimoto,² Andrew H. Hughes,³ Amanda R. Hansen,⁴ Leigh E. Elrod,⁵ John G. Bartlett,^{1,2} and Sara E. Cosgrove^{1,2}

¹Department of Pharmacy, The Johns Hopkins Hospital, and the ²Department of Medicine and ³Division of Infectious Diseases, Johns Hopkins University School of Medicine, Baltimore, Maryland; ⁴Department of Pharmacy, Bryn Mawr Hospital, Main Line Health System, Pennsylvania; and ⁵Department of Pharmacy, Carilion Roanoke Memorial Hospital, Virginia

“The duration of therapy for CAP was excessive at our institution”.... But with a stewardship intervention decreased from 10 to 7 days.

Avdic. *Clin Infect Dis* 2012; 54:1581.

Additional findings...

CAP guideline	Pre-	Post -	
30 day readmission	9 (14.5%)	5 (7.7%)	P = .22
<i>C. difficile</i> infection	3 (4.8%)	1 (1.5%)	P=.28

Narrowing of antibiotic regimen in patients with positive cultures increased by 47%

Avdic. *Clin Infect Dis* 2012; 54:1581.

Culture-directed therapy

Organism	Drug
S. pneumoniae (penicillin-nonresistant)	penicillin, amoxicillin
H. Influenzae (beta-lactamase negative) (beta-lactamase positive)	amoxicillin amoxicillin/clavulanate
Legionella	azithromycin or fluoroquinolone
Others	

Mandell. *Clin Infect Dis* 2007; 44:S27.

Prospective, 925 bed tertiary care facility



Avdic. *Clin Infect Dis* 2012; 54:1581.

Comparison of 8 vs 15 Days of Antibiotic Therapy for Ventilator-Associated Pneumonia in Adults

Chastre. *JAMA* 2003; 290:2588.

A Randomized Trial

Jean Chastre, MD
 Michel Wolff, MD
 Jean-Yves Fagon, MD
 Sylvie Chevret, MD

Context The optimal duration of antimicrobial treatment for ventilator-associated pneumonia (VAP) is unknown. Shortening the length of treatment may help to contain the emergence of multiresistant bacteria in the intensive care unit (ICU).

Objective To determine whether 8 days is as effective as 15 days of antibiotic treatment of patients with microbiologically proven VAP.

- For patients who received appropriate initial empiric therapy
- Comparable clinical effectiveness for VAP,
- Except patients with infection from non-fermenting gram-negative bacilli who experienced more recurrence of infection with 8-day course

Chastre. *JAMA* 2003; 290:2588.
