Antimicrobial Stewardship in Acute and Long Term Healthcare Facilities: Design, Implementation and Challenges

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Antimicrobial Stewardship: Design, Implementation and Efficacy

- Background
- Conceptual framework for use of antibiotics
- Strategies to improve antibiotic use
- Can antimicrobial stewardship limit resistance?
- The Future

MAGNITUDE OF ANTIMICROBIAL USE

- Antibiotics are the second most commonly used class of drugs in the United States
- More than 8.5 billion dollars are spent on anti -infectives annually
  - 200-300 million antimicrobials prescribed annually
  - 45% for outpatient use
- 30-50% of all hospitalized patients receive antibiotics

Anti-Infective Use in US Hospitals

Table 5.
Top 10 Therapeutic Classes by Expenditures for Nonfederal Hospitals[1]

Therapeutic Class	Total 2005 Expenditure ($ Thousands)	Percentage of Total 2005 Nonfederal Hospital Expenditures	Percent Increase over 2004	2006 Expenditures (through Sep 2006) ($ Thousands)
Systemic antiinfectives	3,101,632	12.0	7.1	2,229,846
Hemostatic modifiers	3,035,120	11.8	9.5	2,364,684
Antineoplastic agents	2,781,424	10.8	7.8	2,308,742
Blood growth factors	2,642,378	10.2	7.7	2,120,270
Diagnostic aids	1,386,260	5.4	5.6	1,106,555
Hospital solutions	1,172,584	4.5	3.5	863,330
Psychotherapeutics	1,128,637	4.4	1.3	841,730
Anesthetics	1,125,912	4.4	3.8	711,932
Biologicals	1,064,736	4.1	24.1	821,578
Gastrointestinal agents	967,189	3.7	1.1	784,028

Hoffman, et al. Am J Health Syst Pharm 2007;64:258-314

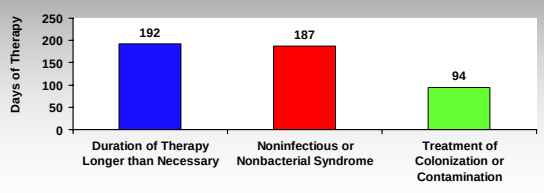
Causal Association Between Antimicrobial Use and Resistance In Healthcare: Lines of Evidence

- Changes on antimicrobial use are paralleled by changes in prevalence of resistance
- Resistance more prevalent in healthcare associated infections compared with community-acquired infections
- Patients with infections caused by resistant strains more likely to have received prior antimicrobials
- Areas in hospitals with highest rates of antimicrobial use have highest rates of resistance
- Increased duration of antimicrobial exposure increases risk of colonization with resistant organisms

Unnecessary Use of Antimicrobials in Hospitalized Patients

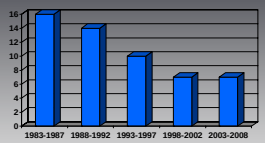
- **Prospective observational study in ICU**
- **576 (30%) of 1941 antimicrobial days of therapy deemed unnecessary**

Most Common Reasons for Unnecessary Days of Therapy



Hecker MT et al. *Arch Intern Med.* 2003;163:972-978.

New Antibacterial Drugs Approved By FDA



Spellberg, *CID* 2004, Modified

Antimicrobial Stewardship Goals

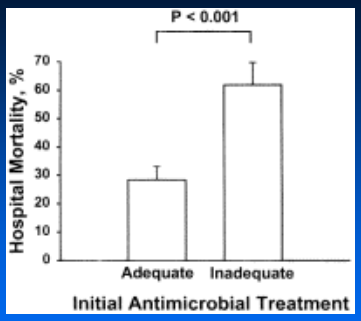
- Ensure the proper use of antimicrobials
  - To optimize clinical outcomes
  - Decrease the risk of adverse effects
  - Reduce or stabilize resistance
- Promote cost effectiveness

Dellit TH, Owens RC, McGowan JE, et al. CID 2007;44:159-77.
MacDougall CM and Polk RE. Clinical Microbiology Reviews 2005;18(4):638-56.

From the Prescriber's Perspective, How Should Antibiotic Stewardship Be Prioritized Relative to Clinical Outcomes In Individual Patients?

What Are the Consequences of Failing to Prescribe an Antibiotic When The Patient Needs It?

- Preventable morbidity, possibly mortality occurs
- Physician bears sole responsibility-personal impact high

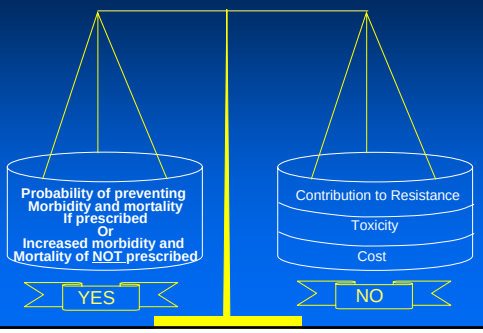


Ibrahim EH et. al. Chest 2000;118:146-155

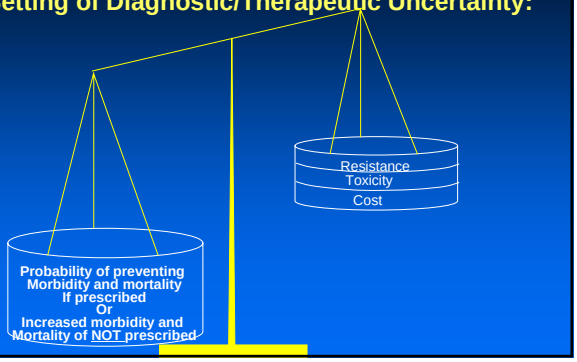
What Are the Consequences of Prescribing an Antibiotic When The Patient Does Not Need It?

- Small, incremental contribution to ecology of resistance
- Small, incremental contribution to cost of care
- Responsibility shared equally by all prescribing physicians-personal impact small
- Small chance of toxicity

Should This Antimicrobial Agent Be Prescribed To This Patient At This Time?



The Default Condition for Most Prescribers In The Setting of Diagnostic/Therapeutic Uncertainty:

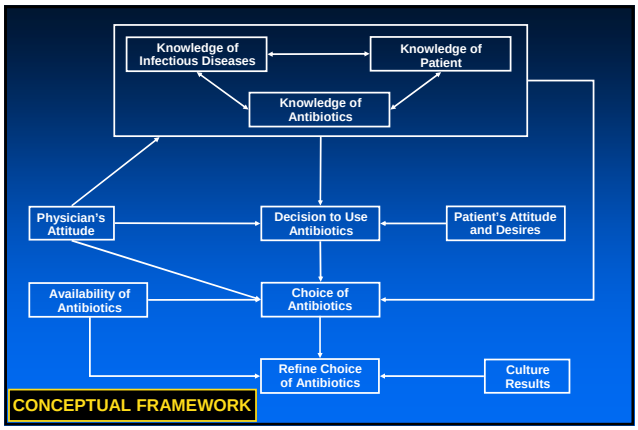


"The Tragedy of the Commons"

Hardin G. *Science* 1968;162:1243-8

Antimicrobial Stewardship Interventions

- Education
- Formulary restriction
- Prior approval
- Prospective Audit with Feedback (Streamlining)
- Cycling/rotation
- Computer-assisted programs
- Comprehensive programs



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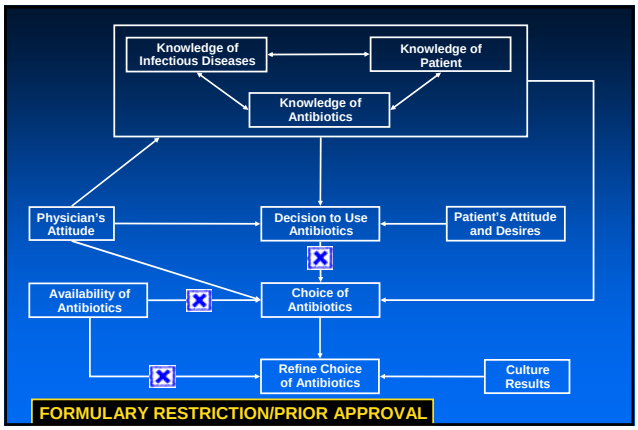

FORMULARY RESTRICTION/PRIOR APPROVAL PROGRAMS

- Multiple approaches
  - Phone approval
  - Antibiotic order forms
  - Automatic stop orders
  - Direct interaction
  - Simple chart entry
- Most onerous to physicians
- Most effective single intervention to decrease use of specific antimicrobials
  - McGowan and Finland. J Infect Dis 1974;130:165-8
  - Recco et al. JAMA 1979;241:2283-6
  - Coleman et al. Am J Med 1991;90:439-44

Antimicrobial restriction: unintended consequences?

- Pre-approval policy for cephalosporins in response to increased incidence of cephalosporin-resistant *Klebsiella*
  - 80% reduction in cephalosporin use
  - 44% hospital-wide reduction in incidence of cephalosporin-resistance *Klebsiella*
  - Imipenem use increased 141%
  - 69% increase of carbapenem-resistant *Pseudomonas*

Rahal et al. JAMA 1998;280:1233-7

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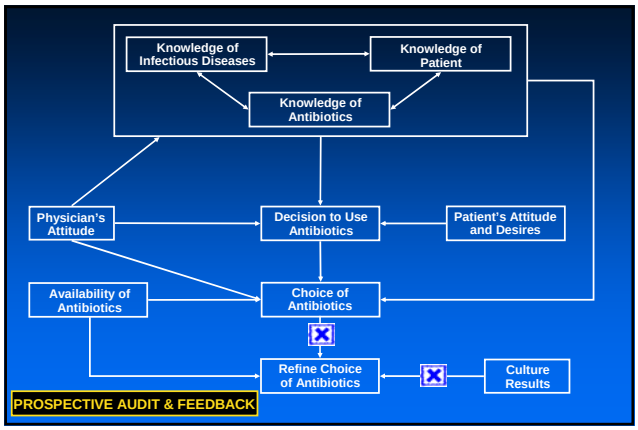
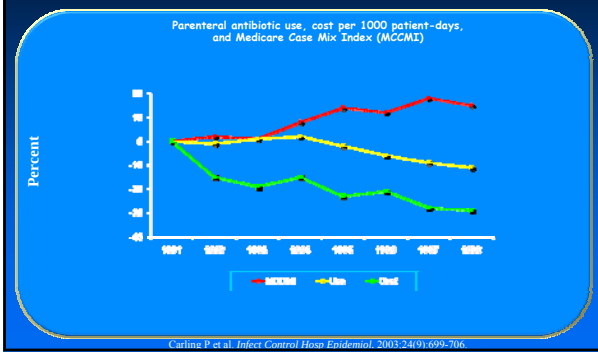


Prospective Audit & Feedback Example



Carling P et al. *Infect Control Hosp Epidemiol.* 2003;24(9):699-706.

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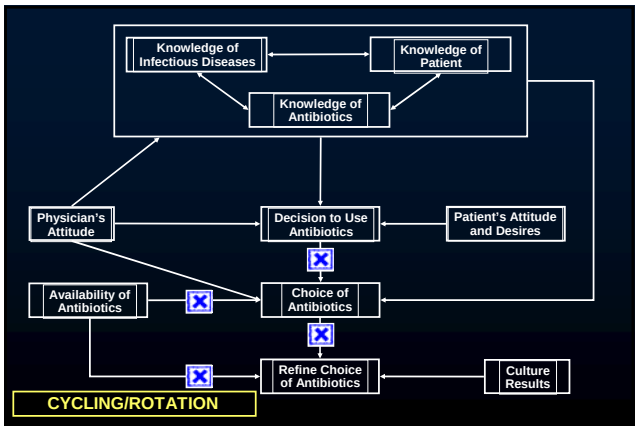
ANTIMICROBIAL CYCLING

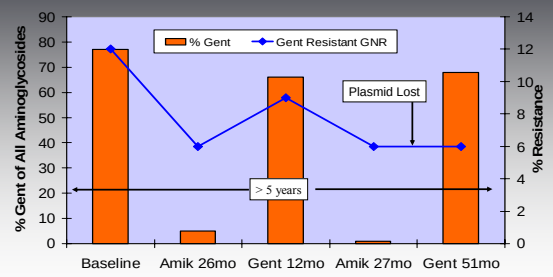
- Withdrawal of an antibiotic or antibiotic class from general use (either within a patient care ward or institution) for a designated period of time, and then substituting it with antibiotics from a different class possessing comparable spectrum of activity but different mechanisms of antimicrobial resistance. The process is repeated at scheduled intervals

RATIONALE FOR ANTIMICROBIAL CYCLING

- "It's hard to hit a moving target"
- Resistance will decline or emerge at a slower rate by limiting bacterial exposure to specific agents
- Frequent switching will decrease resistance to any single agent

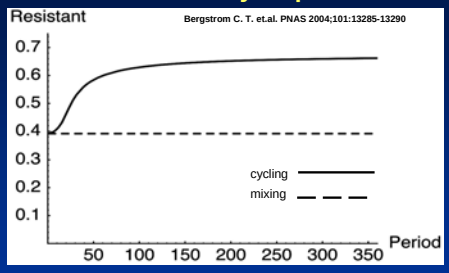


AMINOGLYCOSIDE CYCLING



Gerding D. ICHE 2000:21 (Suppl):S12-S17.

Mean resistance levels as a function of cycle period



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COMPUTERIZED ANTIBIOTIC ASSISTANT: LDS HOSPITAL

Clinical Outcomes

- Significant reductions in:
  - Orders for drugs with reported allergies (35 vs. 146)
  - Excess drug dosages (87 vs.405)
  - Antibiotic-susceptibility mismatches (12 vs. 206)
  - Mean number of days of excessive dosages (2.7 vs. 5.9)
  - Adverse events (4 vs. 28)

Evans et al. N Engl J Med 1998; 338:232-8

COMPUTERIZED ANTIBIOTIC ASSISTANT: LDS HOSPITAL

Institutional Outcomes

VARIABLE	PREINTERVENTION PERIOD	INTERVENTION PERIOD	
		Regimen Followed	Regimen Overridden
LOS - ICU (days)	4.9	2.7	8.3
Total LOS (days)	12.9	10.0	16.7
Cost of antiinfective ($)	340	102	427
Total cost ($)	35,283	26,315	44,865

Evans et al. N Engl J Med 1998; 338:232-8

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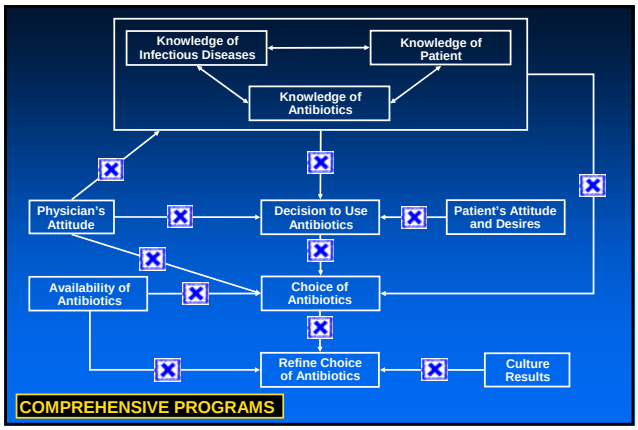


Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

Timothy H. Dellit,[1] Robert C. Owens,[2] John E. McGowan, Jr.,[3] Dale N. Gerding,[4] Robert A. Weinstein,[5] John P. Burke,[6] W. Charles Huskins,[7] David L. Paterson,[8] Neil O. Fishman,[9] Christopher F. Carpenter,[10] P. J. Brennan,[9] Marianne Billeter,[11] and Thomas M. Hooton[12]

[1]Harborview Medical Center and the University of Washington, Seattle; [2]Maine Medical Center, Portland; [3]Emory University, Atlanta, Georgia; [4]Hines Veterans Affairs Hospital and Loyola University Stritch School of Medicine, Hines, and [5]Stroger (Cook County) Hospital and Rush University Medical Center, Chicago, Illinois; [6]University of Utah, Salt Lake City; [7]Mayo Clinic College of Medicine, Rochester, Minnesota; [8]University of Pittsburgh Medical Center, Pittsburgh, and [9]University of Pennsylvania, Philadelphia, Pennsylvania; [10]William Beaumont Hospital, Royal Oak, Michigan; [11]Ochsner Health System, New Orleans, Louisiana; and [12]University of Miami, Miami, Florida

CID 2007; 44:159

IDSA/SHEA Guidelines: Specific Language

- **Core members: (A-II)**
  - ✓ **infectious diseases physician**
  - ✓ **clinical pharmacist with ID Training**
  - ✓ **Optimally to also Include:infection control professionals, hospital epidemiologists, clinical microbiologists, and information specialists when available (A-III)**
- **Close collaboration with the Pharmacy and Therapeutics Committee (A-III)**
- **Development with the support administration and the collaboration with quality assurance and patient safety teams or their equivalents (A-III)**
- **Intervention and feedback critical to success**

Dellit TH, et al. Clin Infect Dis 2007;44:159-77.

CAN ANTIMICROBIAL STEWARDSHIP LIMIT THE EMERGENCE OF RESISTANCE?

Best Evidence

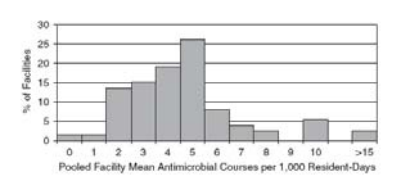
- Decreased CDI
- Decreased resistant GNB
- Decreased VRE

Carling et al. ICHE 2003;24:699-706
Climo et al. Ann Intern Med 1998;128:989-95
Khan et al. J Hosp Infect 2004;54:104-8
Meyer et al. Ann Intern Med 1993;119:353-8
Pear et al. Ann Intern Med 1994;120:272-7
Bradley et al. J Antimicrob Chemother 1997;40:707-11
de Man et al. Lancet 2000;355:973-8
Singh et al. Am J Respir Crit Care Med 2000;162:505-11

POOR STUDY DESIGN ISSUES

- Selection biases
- Insufficient power
- Varying duration of intervention
- Failure to deal with confounders
  - Cause of resistance is multifactorial
  - Community vs. nosocomial pathogens
  - Multiple concurrent control measures
  - Colonization pressure
- Generalizability
  - Bug/drug combinations
  - Setting

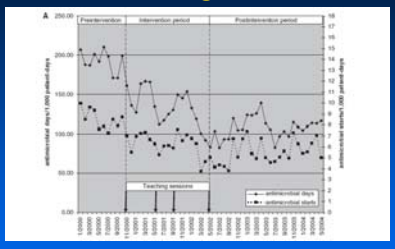
Distribution of Antimicrobial Use Between Nursing Homes, September 2001 to February 2002, (N=73 facilities in 4 States)



42% of resisdents recieived antibiotics during the six month study

Benoit et al. J Am Geriatr Soc 2008;56:2039-44

Successful Intervention in a Chicago Nursing Home



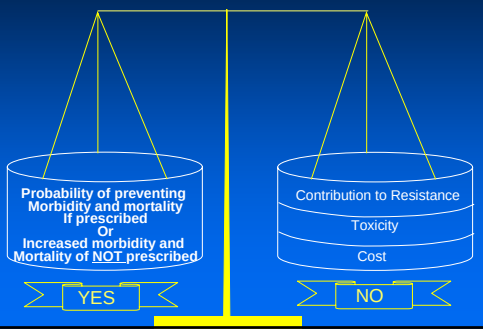
•Developed diagnostic and treatment algorithms in collaboration with clinicians
•Education sessions which included case reviews and feedback

Schwartz et al. J Am Geriatr Soc 2007;55:1236–1242

The Future of Antimicrobial Stewardship?

- Improved Medical Informatics
  - Better computerized decision support
  - Standardized measurement of use with comparative feedback
    - Individual prescriber
    - Unit
    - Service
    - Hospital

Should This Antimicrobial Agent Be Prescribed To This Patient At This Time?



Ease of Prioritizing Antibiotic Stewardship Relative to Clinical Outcome In Individual Patients

The Future?

- Randomized controlled trials that inform antibiotic use
  - Sort course empiric antibiotic therapy for patients with pulmonary infiltrate in the intensive care unit. Singh et. al. Am J Respir Crit Care Med 2000;162:505-11
    - Randomized patients with suspected pneumonia, but with low CPIS (<6)
      Intervention group-discontinue abx at day 3 if CPIS remains low
      Control group-per clinician preference
    - Significant decrease in duration of therapy (3 vs 9.8 days)
    - Lower rates of bacterial superinfection and recovery of resistant organisms in intervention group
  - Comparison of 8 vs 15 days of antibiotic therapy for ventilator associated pneumonia in adults. Chastre et al. JAMA 2003;290:2588-98
    - No difference in mortality
    - More antimicrobial free days in 8 day group
    - Decreased antimicrobial resistance among those with recurrence of pulmonary infection

The Future?

- Better Epidemiologic studies of inpatient antimicrobial use
  - Who, what, when, and where?
  - Will help target efforts
- Behavioral interventions
- Antimicrobial use optimization collaboratives
  - Multiple facilities sharing stewardship strategies and comparative rates of antimicrobial use
- Better Diagnostics