



Antimicrobial Stewardship: Is it Possible in our Hospital?

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Disclosure

- Speaker has nothing to disclose

Objectives

1. To review the rationale for antimicrobial stewardship
2. To provide an overview of the recommended components of an antibiotic stewardship program
3. To detect antibiotic use improvement opportunities from the analysis of utilization data
4. To explain the barriers for successful implementation of such a program

Stewardship

The conducting, supervising, or managing of something; especially the careful and responsible management of something entrusted to one's care.

Antimicrobial stewardship: what is it?

- *"The optimal selection, dosage, and duration of antimicrobial treatment that results in the best clinical outcome for the treatment or prevention of infection with minimal toxicity to the patient and minimal impact on subsequent resistance."*

Owens, RC Pharmacotherapy 2004

Goals of antimicrobial stewardship

- Primary goal:
 - To optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including:
 - Toxicity
 - Selection of pathogenic organisms (e.g., *Clostridium difficile*)
 - Emergence of resistance
 - Includes appropriate selection, dosing, route and duration of antimicrobial therapy
- Secondary goal:
 - To reduce health care costs without adversely impacting quality of care

Why are hospitals practicing antimicrobial stewardship?

- Antimicrobial resistance has both local and global health implications
- Antimicrobial resistance is associated with increased morbidity, mortality and healthcare costs
- Third parties may begin to not reimburse for “preventable nosocomial infections”
- 50% of antimicrobial use is inappropriate
- Antimicrobials account for 30% of the drug budget

Why are hospitals practicing antimicrobial stewardship?

- Mandate by law: SB 739
- Health and Safety Code 1288.8. (a) By January 1, 2008, the department shall take all of the following actions to protect against HAI in general acute care hospitals statewide:
 - (3) Require that general acute care hospitals develop a process for evaluating the judicious use of antibiotics, the results of which shall be monitored jointly by appropriate representatives and committees involved in quality improvement activities.

Why should we care about antimicrobial stewardship?

- Improve patient care
- Decrease drug costs
- Decrease overall hospital costs
- How we use antibiotics today affects the availability of antimicrobial choices and outcomes of tomorrow’s patients
- Antimicrobial resistance is steadily increasing
- No novel antibiotics in the pipeline for treating gram-negative infections!!!

Do antimicrobial stewardship programs work?

- Most of the data that supports this comes from:
 - Inpatients
 - Adults
 - ICU
- Comprehensive programs have consistently demonstrated:
 - Decrease in antimicrobial use (22%-36%)
 - Savings of \$200,000-\$900,000 per year
 - Success in diverse types of facilities: large academic institutions and small hospitals

McGowan, Finland, J. Infect. Dis. 1974;134:130-165
McGowan, Rev Infect Dis, 1983;5:1033-1048
Morone, Proc. Eur Soc Microbiology 2005;3:496-501
Coutrot et al. J. Antimicrob Chemother 1989;23:441-51
SHEA/ASPC Communication Network. Abstracts Presented at
March 2008 SHEA Annual Meeting
(www.apic.org/commnetwork)

Antimicrobial stewardship has been shown to:

- Increase infection cure rates
- Improve susceptibility patterns
- Reduce patient mortality and length of stay
- Reduce rate of CDAD
- Reduce hospital costs
- Reduce antibiotic resistance
- Reduce inappropriate prescribing

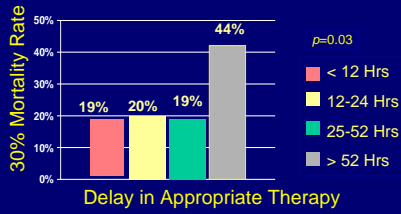
Bantar et al. CID 2003;27:180; Patel et al. Exp Rev Anti Infect Ther 2008; 6:209; Gentry et al. AJHSP 2000;57:268-74; MacDougall et al. Clin Micr Rev 2005;18:638; Davey et al. Cochrane 2005 CD003543

Antimicrobial stewardship: barriers

- Inappropriate/Unnecessary use of antimicrobials
- Inadequate use of antimicrobials
- Treating non-infectious conditions with antimicrobials
- Delay in appropriate therapy
- Patient non-compliance

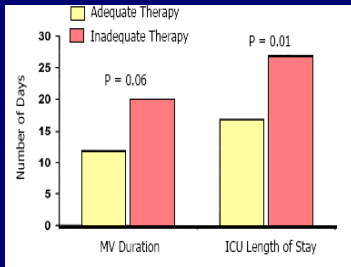


How much time do you have to correct the started therapy?



Lodise et al. AAC 2007;51:3510-3515

Inappropriate antimicrobial therapy: adversely impacts length of stay (LOS)



Inappropriate Empiric Therapy for Ventilator Associated Pneumonia

1. Longer mechanical ventilation (MV) duration
2. Longer ICU LOS

Dupont et al. Int Care Med. 2001;27(2):355-362

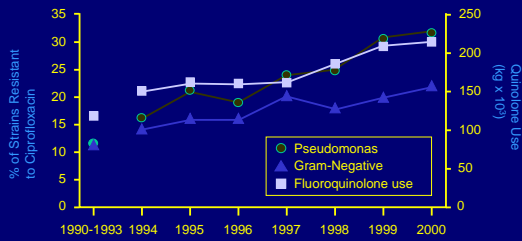
What is the impact of antibiotic use on resistance?

Causal associations between antimicrobial use and emergence of antimicrobial resistance

- Changes in antimicrobial use are paralleled by changes in prevalence of resistance
- Antimicrobial resistance is more prevalent in health care-associated infections
- Patients with health care-associated infections caused by resistant strains are more likely to have had prior antibiotic exposure than control patients
- Areas within hospitals with the highest rates of antimicrobial resistance also have the highest rates of antimicrobial use
- Increased length of exposure to antimicrobials increases the likelihood of colonization with resistant organisms

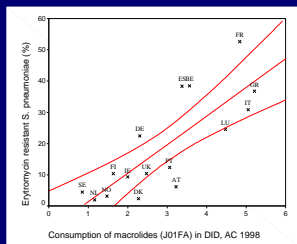
DeLitt TH et al. Clin Infect Dis. 2007;44:159-177.

Increased antibiotic use drives resistance



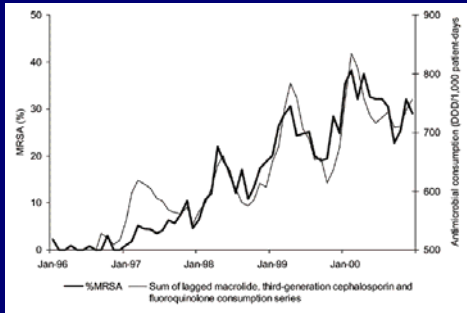
Increasing fluoroquinolone resistance in Gram-negative bacilli correlates with increased fluoroquinolone use in patients from 43 states (numbers of isolates from 1994-2000=35,790). The 1990 to 1993 data points represent composite susceptibility and quinolone use for those 4 years.
Adapted with permission from Neuhauser MM et al. JAMA. 2003;289:885-888.

Correlation between macrolide use and macrolide-resistant *S. pneumoniae*



Organism year of isolation (source of information)	Antibiotic resistance	Antibiotic use - ATC group (year of data)	No. of countries	Spearman correlation (r) (confidence interval)	P-value
<i>S. pneumoniae</i> 1999/2000 [8]	Erythromycin	Macrolides - J01FA (1998)	16	0.83 (0.67-0.94)	< 0.001

Antibiotic use and resistance in the hospital MRSA: temporal series (Aberdeen, 1996-2000)



Monnet et al. *Emerg Infect Dis* 2004; 10:1432-41

What is the impact of antibiotic resistance on morbidity, mortality, and cost of care?

MSSA vs. MRSA infections

- Cohort study, hospitalized patients with *Staphylococcus aureus* bacteremia, N=348
- Length of stay 7 vs 9 days (MSSA vs MRSA)
- Cost of treatment \$19,000 vs. \$26,000

ICHE 2005;26(2):166-74.

VSE vs. VRE

- Blood stream infection (BSI) due to VRE associated with decreased survival (24% vs. 59%)
- Increased length of stay (35 vs. 17 days)
- Attributable cost \$27,190 per episode
- VRE BSI has attributable mortality of 30%

Arch Int Med 1998;158:522-7
CID 2005;41:327-33
ICHE 2003;24:690-8

The bitter truth

- 50% of antimicrobial use is either unnecessary or inappropriate

Antimicrobial Use

Carlos A. Diaz-Granados, MD, MS

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Antimicrobial Use

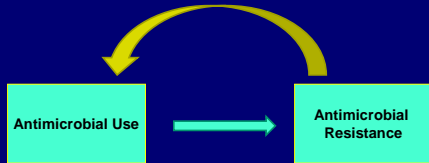


Antimicrobial Resistance

Carlos A. Diaz-Granados, MD, MS

The bitter truth

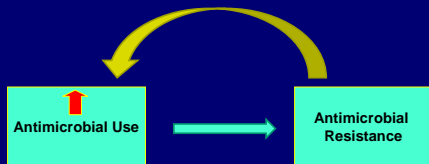
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The bitter truth

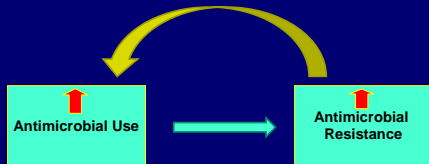
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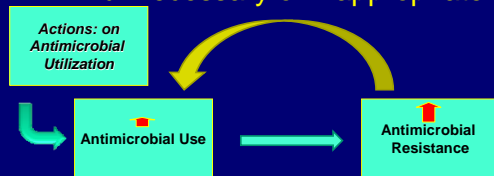
Consequences of antimicrobial resistance

- Excess morbidity and mortality
- Excess healthcare costs

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The bitter truth

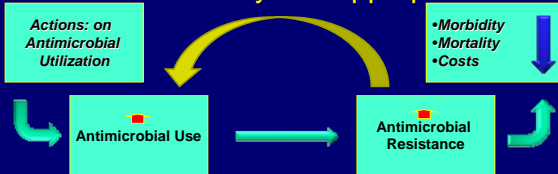
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The bitter truth

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What can hospitals do to manage resistance?

- Infection Prevention and Control measures
 - Hand washing!!!
 - Appropriate catheter management
 - Sepsis and VAP “Bundles”
 - Prospective isolation precautions
 - Environmental disinfection and cleaning
- Antimicrobial Stewardship
 - Appropriate antimicrobial use

What is appropriate antimicrobial use ?

- **Appropriate**
 - **Selection (according to the clinical syndrome)**
 - **Dosing/route**
 - **Streamlining/De-escalation**
 - **Duration**

1 - Appropriate selection

- Guidelines for empiric antibiotic selection available for download.
- Empirically, need to start broader spectrum antibiotics, according to the clinical syndrome, until cultures return.
- Maximize drawing cultures ideally before antibiotics are initiated.

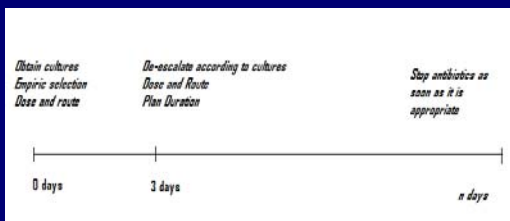
2 - Appropriate dosing & route

- For hemodynamically unstable patients, prefer IV route
- Maximizing dose for renal and hepatic function essential for safety of patient and also to prevent selection of resistant organisms
- Performing therapeutic drug monitoring "levels" to ensure target serum levels and preventing toxicities
- Pharmacist initiated IV to PO conversion programs in Non-ICU for highly bioavailable antimicrobials:
 - decrease cost & LOS

3 - Appropriate streamlining

- Modification of empiric antibiotics based on clinical information AND culture results.
- Usually takes places around **day 3** of empiric therapy.
- Requires the availability of reliable cultures (taken at time 0!!!).

The continuum of appropriate antimicrobial use



3 - Appropriate streamlining

- De-escalate based on cultures from **broad to narrow** spectrum agents.
- De-escalation decreases ecological pressure from the broad spectrum antibiotic and therefore can have a favorable impact on the emergence of resistance.
- Streamlining usually results in decreased antibiotic cost (not always)

4 - Appropriate duration

- Most infections: 7 – 14 days
- Many experts recommend *Staphylococcus aureus* bacteremia to be treated for at least: 28 days.
- Osteomyelitis, endocarditis, endovascular infection: **6-8 weeks**
- Trend towards drug trials of shorter courses for:
 - community acquired pneumonias (CAP): 5-7 days
 - UTIs: 3 days for uncomplicated; 5-14 days for complicated
- CAP: Levofloxacin 750 mg x 5 days = 500 mg x 10 days
- VAP (HCAP, HAP): 8 days.

How to start an antimicrobial stewardship program?

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.,² Dale N. Gerding,³ Robert A. Weinstein,⁴ John P. Burke,⁵ W. Charles Huskins,⁶ David L. Paterson,⁷ Neil O. Fishman,⁸ Christopher F. Carpenter,⁹ P. J. Brennan,¹⁰ Marianne Billeter,¹¹ and Thomas M. Hootes¹²

CID 2007;44 (15 January) • 159

IDSA/SHEA Antimicrobial Stewardship Guidelines

- A comprehensive evidence-based antimicrobial stewardship program:
 - Includes elements chosen from among 11 recommendations
 - Based on local antimicrobial use and resistance problems
 - Resources, programs, surveillance, assessment are all key components to a program

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

Antimicrobial Stewardship

- There are National Guidelines published by Infectious Diseases Society of America (IDSA) in 2007
- Many facilities doing elements of stewardship:
 - Not under one umbrella
 - Not dedicated team
 - Less formal ongoing program, tracking processes or outcomes
- Guidelines, they don't tell you how to do this in your facility



IDSA and SHEA Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship. CID 2007;44: 159-177.

Getting started

- Identify the problems with the old system
- Creating a policy: "Antimicrobial Stewardship & Restricted Anti-infective Agents"
- Generate a list to flag the "restricted antibiotics"
 - 20 restricted agents
 - spectrum of activity, potential for emergence of resistance, adverse effect profiles and cost
- Establish interventions
 - 11 interventions
- Develop monitoring tool
- Create antibiotic guidelines for each agent

Keys Components

- ✓ Written hospital Guideline
- ✓ Educational efforts
- ✓ Providing clinical consultations
- ✓ Ongoing surveillance of antimicrobial susceptibility
- . Restriction of hospital formulary
- . Antimicrobial utilization review
- . Ongoing monitoring and analysis of antimicrobial agents usage
- . Monitoring adherence
- . Usage feedback

Components of antimicrobial stewardship programs

Core activities

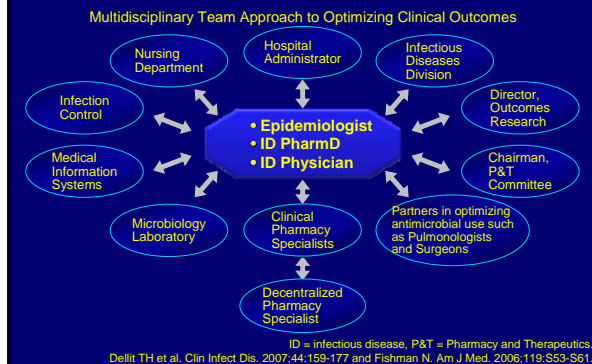
- Stewardship team-multidisciplinary*
- Formulary restrictions and preauthorization*
- Prospective audit with intervention and feedback*

Supplemental strategies

- Streamlining or timely de-escalation of therapy*
- Dose optimization*
- Parenteral to oral conversion*
- Antimicrobial order forms
- Avoid therapeutic duplication
- Combination therapy
- Guideline and clinical pathways*
- Education

*Activities with the strongest data and support by IDSA
• IDSA and SHEA Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship CID 2007;44: 159-177.

Antimicrobial stewardship team



Role of the antimicrobial stewardship team

- Daily rounds with medicine and surgery
- Tuesday/Thursday rounds with Pediatrics
- Review all patient data and antimicrobials
 - Do restricted agents meet the guidelines for use?
- Verbal and written recommendations
 - Talk to the primary teams
- Follow up in 24 hours that recommendation were accepted
 - If not, address the issue with the teams
 - Pharmacist and ID Physician discuss with Primary team Staff

Formulary restrictions and preauthorization with justification

PRO

- Is the most effective method of controlling antimicrobial use
- May be useful in healthcare associated outbreaks



John, Fishman, CID. 1997;24:471-485
 Pfaller et al. Ann Intern Med. 1994;120:272-277
 Bamberg et al. Arch Intern Med. 1992;152:554-557
 French et al. CID. 1999;23:1270-1271

CON

- The effectiveness depends on who makes the recommendations
- Mainly effects initial regimen
 - Less control over length of use
- Prescribers have less control ("antibiotic police")

Prospective audit with intervention and feedback

PRO

- Has been shown to improve ATM use in facilities of differing sizes
- Data that decreased:
 - *C. difficile*
 - Cost
 - Resistant gram negative infections
- Benefits in hospital where daily review not feasible

CON

- Labor Intensive
- Have to identify opportunities to intervene
- The need for a computer surveillance software



Solomon et al Arch Intern Med 2001;161:807-802
 Foster et al Arch Intern Med 1997;157:2441-2444
 Caring et al JCHE 2003;24:699-706
 LaRocca, CID, 2003; 37:742-743

Supplementary activities

De-escalation of therapy

- When culture results become available to move to more targeted therapy
- Discontinuation of empiric therapy (including redundant) based on clinical status and negative cultures
- Good data to support

Kollef, Chest, 2005;128:2706-2013
 Brodzinski, Arch Intern Med, 1998; 148:2019-2022

Dose optimization

- Optimization of dosing based on:
 - Patient (age, renal function, wt)
 - Causal organism
 - Site of infection
 - Pharmacokinetics and pharmacodynamics of the drug
- Greater involvement on behalf of PharmD
- Good data to support

ISAS/SHEA, CID 2007;44: 159-177.

Supplementary activities

Parenteral to oral conversion

- Enhanced bioavailability of certain antimicrobials allows conversion (or initiation) to oral therapy
 - Quinolones
 - Fluconazole
 - Metronidazole
- Studies have shown reduced LOS and cost

Chan et al. BMJ, 1995;310:1360-1362
 Przybylski et al. Pharmacotherapy, 1997;17:271-276

Guidelines and Clinical pathways

- Taking national guidelines, incorporating local microbiology and resistance
- Multidisciplinary development
- Successes with Community Acquired Pneumonia

Marrin et al. JAMA, 2000;282:749-756
 MacDougall C. Polk RE, Clin Microbiol Rev, 2005;18:638-656

Supplementary activities

Education

- Essential
- Education alone without intervention has a marginal effect

Giratt et al. Can J Surg. 1990;33:385-388.

Antimicrobial order forms

- Can be effective
- Coupled with practice guidelines
 - Specially studied perioperative prophylaxis orders with automatic discontinuation

Durbin et al. JAMA. 1981;26:1798-1800

Supplementary activities

Combination therapy

- Role in certain clinical context/organisms
- Just redundant in usual circumstance
- Insufficient evidence to recommend routine use

DSAS/SHCA. CID 2007;44: 159-177.

Antimicrobial cycling and scheduled switch

- Scheduled removal and substitution of a specific antimicrobial
- Studies are limited and vary
- Insufficient evidence to recommend routine use

Martinez et al. Crit Care Med. 2008; 34:329-336

Status of stewardship activities at RCRMC

- Efforts are directed at inpatient use (ICU and Non-ICU)
- Established a stewardship team
- Extensive assessment of the formulary and preauthorization practices ("approvals")
- Aggregated baseline data of ATM use, costs, resistance and some adverse events (*C. difficile*)

Status of stewardship activities at RCRM

- Assisting with Guidelines
 - Community Acquired Pneumonia
 - Flu (shared by intranet, educational sessions)
- Formal tracking, auditing/feedback/de-escalation systems
- Increasing IV to PO
- Dose optimization- focus on vancomycin
- Working with microbiology
 - *C. difficile* testing, resistant Gram negatives (KPC), H1N1 testing, review/promoting use of antibiograms
- Educational opportunities
- Research initiatives

$$^{\dagger}\text{DDD per 1000 patient-days} = \frac{\text{DDD of specific agent used}}{\text{Total number of patient-days}} \times 1000$$

Antimicrobial agent	Medical-surgical ICU (n = 61)		Percentile				
	No. DDD ^a	Pooled mean	10%	25%	50% (median)	75%	90%
Penicillin group	21,837	46.5	0.0	2.3	13.6	38.7	113.4
Ampicillin group	94,546	201.4	33.1	79.1	185.0	200.8	276.9
Antipseudomonal penicillins	33,471	75.5	18.2	37.2	61.7	95.4	115.5
Axistat/phycozoccal penicillins	12,079	25.7	1.4	4.8	13.8	29.3	49.0
First-generation cephalosporins	48,242	102.8	23.9	53.5	76.7	126.6	209.2
Second-generation cephalosporins	14,107	34.3	2.6	6.4	19.0	42.5	91.7
Third-generation cephalosporins	67,688	144.1	61.2	80.4	116.4	163.4	200.6
Carbapenem group	17,727	37.8	3.4	8.2	26.8	47.0	62.9
Aztreonam	4785	10.2	0.0	1.9	6.2	14.0	23.9
Fluoroquinolones	94,695	205.9	55.4	92.8	147.5	201.2	260.1
Trenethopren/sulfamethoxazole	31,448	67.0	0.0	11.5	24.2	48.6	203.4
Vancomycin (oral)	2848	6.1	0.0	0.0	2.4	5.9	9.3
Vancomycin (parenteral)	40,303	85.8	33.1	53.2	66.7	122.9	143.0

Our successes

- Visibility and credibility (Don't want to just be the "Abx police")
- Getting baseline data to start to attack the issues
- Results:
 - More ID consults: 294 formal ID/PharmID interventions made in the two quarters.
 - Approval with conditions (consult, shorter duration, dosing)
 - Sustained reduction of drug consumption was shown during this period. In comparison between 1st and 3rd Quarter 2009, we observed a use's reduction of antipseudomonal penicillins: 11%, fluoroquinolones: 37.8%, and vancomycin: 12.8%.
 - In the ICU ward alone, we saw a total cost savings in the antipseudomonal group of \$7,333.89 between the first quarter and third quarter. In the fluoroquinolone group, we saw a total cost saving of \$5,138.61.

Opportunities in this region to take the lead on stewardship

- Strong hospitals systems (diverse)
- Strong Pharmacy and Infectious Diseases
- Large patient populations
- Existence of emerging pathogens
 - *C. difficile*
 - MDR Gram negatives (KPC), MRSA
- Ongoing initiatives:
 - Southern California Patient Safety Collaborative

OVERUSE

“The desire to ingest medicines is one of the principal features which distinguish man from the animals”



Osler W. Aecquanimitas, 1920

Acknowledgements

- Team members:
 - Pharm. Madiha Mushtaq
 - Dr. Madé Sutjita
 - Pharm. Chengqing Li
 - AO Christopher Johnson
 - Dr. Arnold Tabuenca



Antimicrobial stewardship is important, but remember, it's all about the patient.

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