The Role of Antimicrobial Stewardship in Decreasing *Clostridium Difficile* Infections

Hospital Council of Northern and Central California  
June 28, 2013

Kavita K. Trivedi, MD  
Lead, California Antimicrobial Stewardship Program Initiative  
Healthcare Associated Infections Program  
California Department of Public Health
Outline

• Rationale for Improved Antimicrobial Use
• Regulatory Messages, Mandates and Quality Measures
• Antimicrobial Stewardship Program Implementation
• How Antimicrobial Stewardship can Decrease *Clostridium difficile* infections
Rationale for Improved Antimicrobial Use
30% of antimicrobial use in acute care is either inappropriate or suboptimal

Rationale for Antimicrobial Use Optimization

• Antimicrobial resistance
  – Inherent
  – Antimicrobial exposure

• Patient safety
  – Arrhythmias, rhabdomyolysis, nephrotoxicity, *Clostridium difficile* infections, death

• Cost
  – Unnecessary use, switching from IV to PO, broad-spectrum to pathogen-directed therapy
Rationale for Antimicrobial Use Optimization

• Antimicrobial resistance
  – Inherent
  – Antimicrobial exposure

• Patient safety
  – Arrhythmias, rhabdomyolysis, nephrotoxicity, *Clostridium difficile* infections, death

• Cost
  – Unnecessary use, switching from IV to PO, broad-spectrum to pathogen-directed therapy
“The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and, by exposing his microbes to non-lethal quantities of the drug, educate them to resist penicillin.”

Nobel lecture, 1945
Geographical Distribution of Carbapenemase-producing *Enterobacteriaceae*

November 2006

CDC, unpublished data
Geographical Distribution of Carbapenemase-producing *Enterobacteriaceae*

February 2013

CDC, unpublished data
Rationale for Antimicrobial Use Optimization

- **Antimicrobial resistance**
  - Inherent
  - Antimicrobial exposure

- **Patient safety**
  - Arrhythmias, rhabdomyolysis, nephrotoxicity, *Clostridium difficile* infections, death

- **Cost**
  - Unnecessary use, switching from IV to PO, broad-spectrum to pathogen-directed therapy

- ED visits for antibiotic-related adverse effects
  - Estimated 142,000 per year (116K-168K)
  - Most prescriptions for URI, COPD, Otitis media and sinusitis
  - 78% due to allergic reactions (PCN)
  - Sulfas – highest rate of serious allergic reactions
  - 50% overall due to Sulfas and Clindamycin
  - Sulfas and quinolones associated with highest rate of neurological events

Shehab et al., *CID* 2008:47-735-43
Rationale for Antimicrobial Use Optimization

• Antimicrobial resistance
  – Inherent
  – Antimicrobial exposure

• Patient safety
  – Arrhythmias, rhabdomyolysis, nephrotoxicity, *Clostridium difficile* infections, death

• Cost
  – Unnecessary use, switching from IV to PO, broad-spectrum to pathogen-directed therapy
# Cost of Antimicrobial-Resistant Infections (ARI)

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>Patients with ARI</th>
<th>Patients without ARI</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>1391</td>
<td>188 (13.5)</td>
<td>1203 (86.5)</td>
</tr>
<tr>
<td>APACHE II score</td>
<td>42.1</td>
<td>54.8*</td>
<td>40.1*</td>
</tr>
<tr>
<td>LOS (days)</td>
<td>10.2</td>
<td>24.2*</td>
<td>8.0*</td>
</tr>
<tr>
<td>HAI (n)</td>
<td>260</td>
<td>135*</td>
<td>125*</td>
</tr>
<tr>
<td>Cost per day ($)</td>
<td>1651</td>
<td>2098*</td>
<td>1581*</td>
</tr>
<tr>
<td>Total cost ($)</td>
<td>19,267</td>
<td>58,029*</td>
<td>13,210*</td>
</tr>
<tr>
<td>Death [n (%)]</td>
<td>70</td>
<td>34 (18.1)*</td>
<td>36 (3.0)*</td>
</tr>
</tbody>
</table>

*p<0.001

Antimicrobial Approvals

DECLINING ANTIBACTERIAL APPROVALS (PAST 25 YEARS)

Total # New Antibacterial Agents


Spellberg, C/D 2004, Modified
The Pipeline is Dry

- Only 15-16 antibiotics are in development
- Only 8 of these have activity against key Gram negative bacteria
- None have activity against bacteria resistant to all current drugs

European Centre for Disease Prevention and Control/European Medicines Agency Joint Technical Report
Antimicrobial Use Optimization

• Widely accepted in acute care settings*:  
  – Improve antimicrobial resistance patterns 
  – Decrease patient toxicity 
  – Decrease costs 

• Limited literature and few studies in LTCFs 
  – Efforts are necessary**

*SHEA/IDSA Guidelines, *CID* 2007 Jan;44(2):159-77
Regulatory Messages, Mandates and Quality Measures
California Senate Bill 739

- Health & Safety Code §§ 1288.5 to 1288.9 (2006)

- Established Healthcare Associated Infections (HAI) Program at CDPH
  - HAI surveillance, prevention and annual reporting in all general acute care hospitals

- Mandatory public reporting of process measures
  - CLIP, SCIP, and influenza vaccination

- Later legislation mandated HAI-specific public reporting (2008)
California SB 739

“By January 1, 2008, [CDPH] shall take all of the following actions to protect against health care associated infections (HAI) in general acute care hospitals statewide:

– (4) 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.”

Health & Safety Code § 1288.8(a)
What does § 1288.8(a)(4) mean to the HAI Program?

• Each California acute care hospital should have an Antimicrobial Stewardship Program (ASP)
  – California is the only state with this type of legislation
Antimicrobial Stewardship Program (ASP)

• Promotes appropriate use of antimicrobials by selecting the appropriate agent, dose, duration and route of administration

• Objective:
  – Optimize the utilization of antimicrobial agents in order to:
    • Minimize acquired resistance
    • Improve patient outcomes and toxicity
    • Reduce treatment costs
CDPH Licensing and Certification Surveys

• To determine compliance of CA acute-care hospitals with SB 739:
  – How do you monitor the judicious use of antibiotics?
  – Do you have a policy and procedure on the judicious use of antibiotics?
  – What committees review and approve the policy on the judicious use of antibiotics?
  – Who monitors the judicious use of antibiotics and prepares reports on the monitoring?

National Quality Forum

• Core Measures
  – Pneumonia: Optimize empiric antibiotic therapy
  – Surgical Care Infection Prevention (SCIP): Right drug, right dose, right duration
  – Proposed measure under discussion to include antimicrobial utilization measurement
The Joint Commission

• National Patient Safety Goal 07.03.01
  – Implement evidence-based practices to prevent HAIs due to MDROs in acute care hospitals
  – Defines process interventions and outcomes measurements
CMS Inpatient Infection Control Worksheet

- Used by surveyors to ensure compliance with CMS Conditions of Participation
- Includes quality measures on antibiotic use in “Section 1: Systems to prevent transmission of MDROs and promote antibiotic stewardship, Surveillance”

1. C.3.a Facility has a multidisciplinary process in place to review antimicrobial utilization, local susceptibility patterns and antimicrobial agents in the formulary and there is evidence that the process is followed.

- C.3.b Systems are in place to prompt clinicians to use appropriate antimicrobial agents (e.g. CPOE, comments in microbiology susceptibility reports, notifications from clinical pharmacist, formulary restrictions, evidence based guidelines and recommendations)
Antibiotic Use Quality Measures on CMS IC Worksheet

1. C.3.c Antibiotic orders include an indication for use.
   - C.3.d There is a mechanism in place to prompt clinicians to review antibiotic courses of therapy after 72 hours of treatment.
   - C.3.e The facility has a system in place to identify patients currently receiving IV antibiotics who might be eligible to receive PO treatment.
CMS Inpatient Infection Control Worksheet

- Not “citation level” events
- Not currently part of CMS Conditions of Participation
- For quality improvement
ASP Implementation
Acute Care Hospitals and ASP Implementation

- Many have developed ASPs due to:
  - Increasing prevalence of HAIs coupled with decreased reimbursement and public reporting
  - Lack of new antimicrobials under development

Antimicrobial Movement in the Healthcare Setting

Patient Evaluation

Choice of Antimicrobial

Prescription Ordering

Dispensing Antimicrobial
ASP Strategies

- Patient Evaluation
  - Choice of Antimicrobial
    - Prescription Ordering
      - Dispensing Antimicrobial
  - Education/Guideline
    - Formulary Restriction and Pre-authorization
      - Computer-assisted strategies
        - Review and Feedback
ASP Strategy Selection

• Facility dependent
  – Beds and acuity of care
  – Dedicated personnel
  – Funds
  – Pharmacy support
  – Electronic systems
  – Laboratory support
Antimicrobial Stewardship Program

- Infection Control Department
- Pharmacy
- Microbiology
- Infectious Diseases Division
- Director, Information Systems
- P&T Committee
- Patient Safety
- Hospital Leadership
Clostridium difficile Infection (CDI) and ASPs
C. difficile Incidence and Mortality Are Increasing


Estimated burden of Healthcare-Associated CDI

- Hospital-acquired, hospital-onset: 165,000 cases, $1.3 billion in excess costs, and 9,000 deaths annually
- Hospital-acquired, post-discharge (up to 4 weeks): 50,000 cases, $0.3 billion in excess costs, and 3,000 deaths annually
- Nursing home-onset: 263,000 cases, $2.2 billion in excess costs, and 16,500 deaths annually

Antibiotic misuse adversely impacts patients - *C. difficile*

- Antibiotic exposure is the single most important risk factor for the development of *Clostridium difficile* associated disease (CDAD)
  - Up to 85% of patients with CDAD have antibiotic exposure in the 28 days before infection

Antibiotic misuse adversely impacts patients - *C. difficile*

- Emergence of the NAP-1/BI or “epidemic” strain of *C. difficile* has intensified the risks associated with antibiotic exposure
  - This strain is resistant to fluoroquinolones, which confers a selective advantage.
  - Associated with increased risk of morbidity and mortality
Unnecessary Antimicrobial Use in Current or Recent CDI

- Up to 20% of CDI patients will have a recurrence
- At MN VAMC – 246 patients with new-onset CDI, 57% received additional antibiotics during CDI treatment
  - Antimicrobials assessed for appropriateness:
    - 26% unnecessary totaling 45% non-CDI antimicrobial days
- Providers should be more cautious with treating recent CDI patients with antibiotics due to increased risk of recurrence

Shaughnessy, MK, WH Amundson, MA Kuskowski et al.; Infection Control and Hospital Epidemiology, Vol. 34, No. 2 (February 2013), pp. 109-116
Impact of Fluoroquinolone Restriction on Rates of Hospital-Onset *C. difficile* Infection

![Graph showing the impact of fluoroquinolone restriction on rates of hospital-onset *C. difficile* infection.]
ASP Can Make a Difference with Hospital-Associated CDI

Tertiary Care Hospital; Québec, Canada (2003-2006)

Conclusions

• Antimicrobial resistance is increasing – especially in HAIs
• Antimicrobial stewardship programs can improve antimicrobial use and decrease development of resistance
• Hospital-onset and hospital-associated CDI is also on the rise
  – Antimicrobial stewardship strategies can decrease rate of CDI
You are the next class of drug-resistant bacteria. As humans continue to abuse and overuse antibiotics, your ranks will swell. So, go out there and mutate! And remember: that which does not kill us makes us stronger!
Keep ASPs in Perspective...

- Minimizing antimicrobial resistance:
  - ASP
  - Infection control
  - Environmental services
Questions

Kavita K. Trivedi, MD
Healthcare Associated Infections Program
Center for Health Care Quality
California Department of Public Health
850 Marina Bay Parkway
Richmond, CA  94804
KTrivedi@cdph.ca.gov