Antimicrobial Stewardship in the Hospital and Long-term Care Settings

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Outline

- Rationale for Antimicrobial Use Optimization in Acute care and Long-term Care
- Regulatory Messages, Oversight and Infrastructure
- Implementation
- Quality Measures
- Examples
- Conclusions
### Healthcare Continuum

- **Acute Care Facility**
- **Home Care**
- **Long Term Care**
- **Ambulatory Care**

### Resistant Organisms are Common in Long-Term Care Facilities

<table>
<thead>
<tr>
<th>Organism</th>
<th>RG</th>
<th>IP</th>
<th>n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA</td>
<td>26/123</td>
<td>29/136</td>
<td>(21)</td>
</tr>
<tr>
<td>ESBL-producing <em>Klebsiella pneumoniae</em></td>
<td>19/114</td>
<td>16/117</td>
<td>(14)</td>
</tr>
<tr>
<td>ESBL-producing <em>Escherichia coli</em></td>
<td>29/114</td>
<td>14/117</td>
<td>(12)</td>
</tr>
<tr>
<td>Vancomycin-resistant enterococci</td>
<td>22/114</td>
<td>16/117</td>
<td>(14)</td>
</tr>
</tbody>
</table>
**Antibiotic-Resistant *E. coli***

- LTCF strongest predictor of *E. coli* ST131 infection
  - LTCF residents had 8 times the risk of contracting *E. coli* ST131 compared with non-LTCF residents
- Risk factors in elderly:
  - Extensive antibiotic exposure, close contact with other antibiotic-exposed individuals, age and health-associated alterations in intestinal microbiota


**High Rates of Multidrug-Resistant Organisms in Long-Term Care**

- Frequent transfer from acute care hospitals
- Horizontal transmission of resistant organisms
- Widespread (often inappropriate) use of antimicrobials

Antibiotic Pressure from Hospital

<table>
<thead>
<tr>
<th>Variable</th>
<th>Relative Risk (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methicillin-resistant <em>Staphylococcus aureus</em></td>
<td></td>
</tr>
<tr>
<td>Levofloxacin receipt*</td>
<td>1.6 (1.1–2.2)</td>
</tr>
<tr>
<td>Third-generation cephalosporin receipt*</td>
<td>2.0 (1.0–4.0)</td>
</tr>
<tr>
<td>Vancomycin-resistant enterococci</td>
<td></td>
</tr>
<tr>
<td>Transfer to or from another OFH unit*</td>
<td>1.2 (1.1–1.4)</td>
</tr>
<tr>
<td>Levofloxacin*</td>
<td>1.2 (1.0–1.5)</td>
</tr>
<tr>
<td>ESBL-producing <em>Klebsiella pneumoniae</em></td>
<td></td>
</tr>
<tr>
<td>Gastrostomy tube</td>
<td>1.2 (1.0–1.4)</td>
</tr>
<tr>
<td>ESBL-producing <em>Escherichia coli</em></td>
<td></td>
</tr>
<tr>
<td>Total dependence for activities of daily living</td>
<td>1.2 (1.0–1.3)</td>
</tr>
<tr>
<td>Levofloxacin receipt*</td>
<td>1.2 (1.0–1.4)</td>
</tr>
<tr>
<td>Third-generation cephalosporin*</td>
<td>1.4 (0.9–2.2)</td>
</tr>
</tbody>
</table>

Horizontal Transmission

- LTTF today can promote antimicrobial resistant infections and transmission to other high-risk patients
  - Invasive devices and procedures increased
    - Central lines, chronic resp therapy, feeding tubes, dialysis, IV antibiotics
  - Population includes more acute and subacute patients treated previously in hospitals
    - Staff not given appropriate education
  - Changing infection control provider without expertise

Antimicrobial Use in Long-Term Care

- Antimicrobials prescribed frequently
  - 40% of all systemic drugs
  - 8% point prevalence
  - 50-70% likelihood resident will receive at least one course of systemic antimicrobials during one year period
  - Contributes to high costs

30% of antimicrobial use in acute care is either inappropriate or suboptimal


**Take Home Message**

Antibiotic exposures and infection control measures in the hospital influence residents’ health at LTCFs.
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
**Schwartz, DN et al., J Am Geriatr Soc 2007;55:1236-1242

Regulatory Messages, Oversight and Infrastructure
Dept HHS: Antimicrobial Review in Long-Term Care

- With Center for Medicare and Medicaid Services (CMS)
- Effective September 30, 2009
- Interpretive Guidelines for Long-Term Care Facilities
  - “It is the physician’s responsibility to prescribe appropriate antibiotics and to establish the indication for use of specific medications. As part of the medication regimen review, the consultant pharmacist can assist with the oversight by identifying antibiotics prescribed for resistant organisms or for situations with questionable indications, and reporting such findings…”


California Senate Bill 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) (2006)

What does §1288.8(a)(4) mean to the CDPH HAI Program?

- Each California acute care hospital should have an Antimicrobial Stewardship Program
  - 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
### Infection Control Oversight Differs

<table>
<thead>
<tr>
<th>Acute Care Hospitals</th>
<th>Non-Acute Care Settings</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Must meet CMS Infection Control Standards</td>
<td>• Few are accredited by the Joint Commission or other Accrediting Organizations</td>
</tr>
</tbody>
</table>
| • Most are accredited by the Joint Commission  
  – Survey every 3 years | • Certain types must be Medicare-certified (e.g., most nursing homes, dialysis clinics, and ASCs) |
| • Also subject to complaint or validation survey by State Survey Agencies (on behalf of CMS) | • Variable state requirements re licensing. Many outpatient settings operate primarily under MD license, with limited oversight |

### Infection Control Infrastructure Differs

<table>
<thead>
<tr>
<th>Acute Care Hospitals</th>
<th>Non-Acute Care Settings</th>
</tr>
</thead>
</table>
| • Infection Control Program  
  – Hospital Epidemiologist  
  – Full-time Infection Preventionists | • ? |
| • Infection Control Committee | • Staff member with or without infection control training |
Implementation

Differences in ASP Implementation

• Many acute care hospitals have developed ASPs due to:
  – Increasing prevalence of HAIs coupled with decreased reimbursement and public reporting
  – Lack of new antimicrobials under development

• LTCFs have been slower to adopt ASPs due to:
  – Lack of necessary personnel
  – Funding
  – Paucity of well-validated strategies specific to LTCFs

Antimicrobial Movement in the Healthcare Setting

**Patient Evaluation**

**Choice of Antimicrobial**

**Prescription Ordering**

**Dispensing Antimicrobial**

Difficulties in Patient Evaluation in Long-Term Care

- Clinical diagnosis of infection is imprecise
  - Symptoms not expressed or misinterpreted
    - Hearing and cognition impairment
    - Comorbid medical illness may obscure infection
  - Febrile response may be relatively impaired
  - Fever without source is frequent
  - Limitations in resources to support clinical assessment

Difficulties in Patient Evaluation in Long-Term Care

• Limited availability and use of laboratory and radiological testing
  – Leads to empiric treatment
• Evidenced-based recommendations on use of antimicrobials in LTCFs are limited
  – Based on clinical criteria targeted for younger populations with less complex problems
  – Optimal treatment regimens have not been defined


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
## Stewardship Hierarchy in LTCF

<table>
<thead>
<tr>
<th>Most Intrusive</th>
<th>Least Intrusive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Requires most expertise, effort and expertise.</td>
<td>Requires least expertise, effort and expense.</td>
</tr>
</tbody>
</table>

### "Back End" approach – Review of already prescribed antibiotics
Individual cases are concurrently reviewed for appropriateness, usually by an expert, with feedback to the provider. Individual use data with comparators and benchmarks is provided to prescribers regarding appropriate use.

### "Front End" approach—Active direction of antibiotic selection
Preauthorization of antibiotics based upon predetermined criteria. Review of case and immediate feedback on choice of antibiotics at initiation.

### "Front End" approach—Passive direction of antibiotic selection
Guidelines, treatment algorithms, antibiotic formulary, antimicrobial order forms

### Education
Classes or training sessions regarding antibiotic resistance, stewardship practices, etc. offered to LTCF employees or staff. Small group sessions with prescriber feedback and case discussions.

### Passive monitoring
Measuring types and quantities of antibiotics used in the facility, and the presence of antimicrobial resistance in cumulative laboratory culture and sensitivity reports.

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### Criteria for Selecting Cases for ASP Review

- High cost agents
- Broad-spectrum agents (eg. FQs, Pip/Tazo)
- Site of infection (eg. CLABSI)
- Resistance profiles (eg. MDROs, MRSA)
- High risk of adverse effects (eg. Amphotericin)
- Novel agents
- Syndromic approach (eg. asymptomatic bacteriuria)
- High use agents (facility dependent)
- Double coverage of organisms (eg. anaerobes)
Syndromic Approach

• Useful in LTCFs to identify problem area and focus interventions:
  – Asymptomatic bacteriuria: positive urine cultures in absence of clinical signs/symptoms
    • Treatment indicated in pregnancy and after GU tract manipulation only
    • Multiple treatments often given in elderly
      – RCTs have shown no benefit
      – Does not decrease occurrence of symptomatic infection, chronic symptoms or alter mortality
      – Can lead to unnecessary adverse drug effects and colonization with MDROs


Asymptomatic Bacteriuria in Elderly

• 5-50% of elderly patients in LTCFs have bacteriuria
• Over 90% of elderly with bacteriuria have pyuria
  – No evidence of poor clinical outcomes with high levels of pyuria
    • Some individuals: high levels of pyuria >1000 WBCs/mm³ of urine
      – May persist for months or years
Management of Asymptomatic Bacteriuria

• No need to treat asymptomatic bacteriuria with or without pyuria
  – For elderly or institutionalized
    • Remove indwelling catheter – replace with straight or condom catheter
    • No treatment unless clinical scenario warrants
    • Prevention measures important

Syndromic Approach

• An example of a criteria for selecting cases for ASP review
  – Target every case of patient being treated for “asymptomatic bacteriuria”
  – Couple with education for clinical staff
  – “Low hanging fruit”
Quality Measures

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”

Antibiotic Use Quality Measures on CMS IC Worksheet

1. C.2.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.

2. C.2.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).

3. C.2.c Antibiotic orders include an indication for use.

4. C.2.d There is a mechanism in place to prompt clinicians to review antibiotic courses of therapy after 72 hours of treatment.

5. C.2.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
• Few CMS survey agencies have begun pilot testing
• Goal of revising worksheet

Proposed National Quality Measure: Time Out

• All antimicrobial orders need:
  • Dose
  • Duration (stop date)
  • Indication
• Get cultures
• Once the culture data comes back, take an antimicrobial time-out: Reassess therapy

http://blogs.cdc.gov/safehealthcare/?p=1026; accessed 3/2/11
Examples

Hospital ASPs: Improved Antibiotic Use

- Cluster randomized trial over 10 months
  - 6 IM teams received academic detailing regarding appropriate use of vancomycin, levofloxacin, piperacillin/tazobactam
  - 6 IM teams received guidelines only

<table>
<thead>
<tr>
<th>Variable</th>
<th>Proportion (%) of prescriptions</th>
<th>Risk ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention group</td>
<td>Control group</td>
<td></td>
</tr>
<tr>
<td>Antibiotic use deemed appropriate</td>
<td>305/390 (78)</td>
<td>229/394 (58)</td>
<td>1.35 (1.22–1.49)</td>
</tr>
<tr>
<td>Empirical</td>
<td>242/294 (82)</td>
<td>211/291 (73)</td>
<td>1.14 (1.04–1.24)</td>
</tr>
<tr>
<td>Definitive</td>
<td>92/112 (82)</td>
<td>60/138 (43)</td>
<td>1.89 (1.53–2.33)</td>
</tr>
<tr>
<td>Appropriate cultures obtained</td>
<td>188/270 (70)</td>
<td>193/286 (67)</td>
<td>1.03 (0.92–1.15)</td>
</tr>
<tr>
<td>Changed to recommended antibiotics</td>
<td>168/186 (90)</td>
<td>85/199 (43)</td>
<td>2.11 (1.79–2.50)</td>
</tr>
<tr>
<td>Appropriate end antimicrobial usage</td>
<td>367/390 (94)</td>
<td>277/394 (70)</td>
<td>1.34 (1.25–1.43)</td>
</tr>
</tbody>
</table>

Hospital ASPs: Improved Resistance, Decreased Costs

<table>
<thead>
<tr>
<th>Hospital Size</th>
<th>ID MD</th>
<th>Microbiologist</th>
<th>Data analyst</th>
<th>IP</th>
<th>Antimicrobial Cost Savings</th>
<th>Drug Resistance &amp; Infectious Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>174 beds</td>
<td>×</td>
<td>×</td>
<td></td>
<td></td>
<td>Annual cost reduction: $200,000-$250,000</td>
<td>Reduced rate of nosocomial Clostridium difficile</td>
</tr>
<tr>
<td>250 beds</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td></td>
<td>Cost-savings during 18-month study: $913,236</td>
<td>Decreased resistance rates</td>
</tr>
<tr>
<td>650 beds</td>
<td>×</td>
<td></td>
<td>×</td>
<td></td>
<td>Net savings for 1 year: $189,318</td>
<td>Reduced rate of VRE colonization and bloodstream infections</td>
</tr>
</tbody>
</table>

McQuillen DP, et al. CID 2008;47: 1051-1063

Hospital ASPs: Optimized Patient Safety

• Improved surgical prophylaxis
  – Intervention: Simplify drug options, standardize dosing, improve timing
    • All doses correct
    • Reduction in dosing after incision (20% to 7%)
    • Annual cost savings $112,000

• Improved renal dosing
  – Intervention: Clinical decision support system and academic detailing
    • Appropriate dosing of gentamicin increased from 63% to 87%
    • Appropriate dosing of vancomycin increased from 47% to 77%
    • Appropriate use of gentamicin therapeutic monitoring increased from 70% to 90%

LTCAFs: Education Can Work to Reduce Treatment of Asymptomatic Bacteriuria

<table>
<thead>
<tr>
<th></th>
<th>3-Months Pre-intervention</th>
<th>7 to 30 Months Post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total urine cultures sent/1000 patient days</td>
<td>3.7 (2.8 – 4.9)</td>
<td>1.3 (1.1 – 1.5)</td>
</tr>
<tr>
<td>Inappropriate cultures, n (%)</td>
<td>34 (69%)</td>
<td>75 (46%)</td>
</tr>
<tr>
<td>ASB treated, n. (%)</td>
<td>23 (68%)</td>
<td>33 (44%)</td>
</tr>
<tr>
<td>ASB treated/1000 patient days</td>
<td>1.7 (1.1 – 2.6)</td>
<td>0.3 (0.2 – 0.4)</td>
</tr>
<tr>
<td>Antimicrobial days of therapy/1000 patient days</td>
<td>167.7</td>
<td>109</td>
</tr>
</tbody>
</table>

CDPH Investigation in LTCF: 2010

• Point prevalence study in LTCF with high rate of MDR Acinetobacter baumannii
  – Baseline colonization rate 19%
    • 36% colonized residents MDR (resistant to cephalosporins, FQ, aminoglycosides)
  – Implemented strict infection control practices
    • HH, cohorting, contact precautions
  – Enhanced environmental cleaning
  – Follow-up six month colonization rate remained 19%
    • 36% colonized residents negative 6 months previous
    • 71% colonized residents MDR

Mortensen, E et al., unpublished data; Trivedi, K et al., unpublished data
CDPH: ASP in LTCF Study 2011-2012

- Goal: characterize the benefit of implementing a formal ASP in LTCF
- Establish ASP in three LTCFs
  - Post-prescriptive review and feedback with pharmacist and ID physician
  - Establish feasibility and effectiveness
  - Specify effects of ASP on antimicrobial utilization, susceptibility patterns and rates of *Clostridium difficile* over time

Doernberg, S et al., unpublished

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CDPH: ASP in LTCF Study Results

- Urinary catheters were uncommon
- Patients rarely had signs/symptoms consistent with UTI
- Rare empiric therapy
- Pressure from RNs and families to send UA/Ucx for “soft” indications
- Pressure to treat positive cultures regardless of symptoms
- Antibiotic use was most often inappropriate
  - Indicated in only 18% of cases

Doernberg, S et al., unpublished
NY Antimicrobial Stewardship Project 2009

- Greater NY Hospital Association, United Hospital Fund, NY State Department of Health
- Objectives:
  - Establish ASPs in 3 LTCFs using existing personnel through collaboration with acute care hospital partners
    - Emphasis on implementing strategies without expending significant new resources
  - Develop and pilot tools and materials for ASP development and implementation

Calfee DP, et al. SHEA Annual Meeting. 2011; poster presentation

NY Antimicrobial Stewardship Project 2009

- Project sponsors provided LTCFs with access to ID and Pharmacy consultants, technical support and tool kit materials
  - Monthly conference calls and site visits x 8 months
- Each LTCF created
  - ASP team
  - Assessed baseline practices
  - Identified 1-2 areas of intervention
  - Implemented strategies to reach goals

Calfee DP, et al. SHEA Annual Meeting. 2011; poster presentation
NY Antimicrobial Stewardship Project 2009

• All LTCFs identified inappropriate treatment of asymptomatic bacteriuria
• 2/3 LTCFs reported qualitative improvement
• Successful ASP implementation associated with:
  – Motivated team, support from administration and medical leadership, collaboration with hospital partner, ability to provide antimicrobial use and resistance data

Calfee DP, et al. SHEA Annual Meeting. 2011; poster presentation

NY Antimicrobial Stewardship Project 2009

• ASPs were developed in LTCFs with existing resources with access to
  – Basic tools (data collection forms, surveys, educational materials)
  – Expert advice
  – Forum to discuss barriers and best practices

Calfee DP, et al. SHEA Annual Meeting. 2011; poster presentation
Conclusions

ASPs in Acute Care Settings

• ASPs appearance will differ
  – View strategies as a menu of interventions and tailor to your resources
• Process and outcomes should be measured and monitored over time
• Essential elements:
  – Administrative buy-in
  – Well-respected physician champion
  – Multi-disciplinary approach
ASPs in Long-Term Care

• Essential:
  – High rates of resistance, variable infection control, overuse of antimicrobials

• CMS established regulatory guidance to prioritize optimizing antimicrobials

• Implementation of ASPs difficult
  – Elderly population complex
  – Patient evaluation, diagnosis difficult
  – Guidelines sparse

ASPs in LTCF

• Criteria such as syndromic approach may be “low hanging fruit”
  – E.g., Pneumonia or UTI

• Education strategies must include nurses, patients, and their families

• ASP interventions must be tailored to the environment
Recommendations: Partnership

• Acute care and long-term care should work together
  • Improve interfacility communication
    – Interfacility transfer form
  • Share resources
    – ID, infection control and PharmD expertise
  • Goal is a standardized regional approach to ASP implementation and infection control

Keep ASPs in Perspective…

• Minimizing antimicrobial resistance:
  – ASP
  – Infection control
  – Environmental services
Questions/Comments

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