Antibiotic Stewardship in Long-Term Care and the CDC Core Elements

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1928 – Alexander Fleming discovered a mold with bacteria killing properties
Introduction of Antibiotics

“For most of the infectious diseases on the wards of Boston City Hospital in 1937, there was nothing to be done beyond bed rest and good nursing care.”

Photo credit, LIFE

Lewis Thomas. The Youngest Science
Introduction of Antibiotics (cont.)

“I remember the astonishment when the first cases of pneumococcal and streptococcal septicemia were treated in Boston in 1937. The phenomenon was almost beyond belief. Here were moribund patients, who would surely have died without treatment, improving in their appearance within a matter of hours of being given the medicine and feeling entirely well within the next day or so….we became convinced, overnight, that nothing lay beyond reach for the future. Medicine was off and running.”

Lewis Thomas. The Youngest Science
## The Power of Effective Antibiotics

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pre-Antibiotic Death Rate</th>
<th>Death with Antibiotics</th>
<th>Change in Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community Pneumonia&lt;sup&gt;1&lt;/sup&gt;</td>
<td>~35%</td>
<td>~10%</td>
<td>-25%</td>
</tr>
<tr>
<td>Hospital Pneumonia&lt;sup&gt;2&lt;/sup&gt;</td>
<td>~60%</td>
<td>~30%</td>
<td>-30%</td>
</tr>
<tr>
<td>Heart Infection&lt;sup&gt;3&lt;/sup&gt;</td>
<td>~100%</td>
<td>~25%</td>
<td>-75%</td>
</tr>
<tr>
<td>Brain Infection&lt;sup&gt;4&lt;/sup&gt;</td>
<td>&gt;80%</td>
<td>&lt;20%</td>
<td>-60%</td>
</tr>
<tr>
<td>Skin Infection&lt;sup&gt;5&lt;/sup&gt;</td>
<td>11%</td>
<td>&lt;0.5%</td>
<td>-10%</td>
</tr>
</tbody>
</table>

*By comparison…treatment of heart attacks with aspirin or clot busting drugs*<sup>6</sup>  

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<sup>1</sup>IDSA Position Paper ‘08 Clin Infect Dis 47(S3):S249-65;  
<sup>2</sup>IDSA/ACCP/ATS/SCCM Position Paper ‘10 Clin Infect Dis In Press;  
<sup>6</sup>’88 Lancet 2:349-60
Antibiotic Resistance

- Ability of bacteria to withstand the effects of antibiotics
- Resistance may occur by a change in gene product(s)
  - Spontaneous point mutations
  - Genetic rearrangements on the bacterial chromosome
  - Acquisition of foreign DNA
Emergence of Antimicrobial Resistance

Resistant Bacteria → Resistance Gene Transfer → New Resistant Bacteria → Susceptible Bacteria → Mutations
Selective Pressure

- Bacteria exposed to antibiotic → susceptible cells die
  - Resistant bacteria survive
- Reduced competition from susceptible bacteria allows resistant bacteria to thrive and outcompete
- Antibiotics impact “normal flora”
  - Limit the space for pathogenic bacteria
- Non-pathogenic resistant bacteria impact antibiotic resistance
  - Increasing the reservoir of resistance genes
Antibiotic Resistance

• Antibiotic use is associated with colonization or infection with resistant bacteria (e.g., pneumococcus, *S. aureus*)
• Resistance is an individual and public health issue
• Resistant infections
  • More difficult to treat
  • Broader spectrum therapy
  • May require parenteral therapy
  • Therapy might increased toxicities and adverse effects
MRSA

Salmonella Typhimurium DT104

Resistant HIV

CARBAPENEM RESISTANT ENTEROBACTERIACEAE

Candida glabrata

quinolone resistant gonorrhea

XDR TB

multi-drug resistant malaria

C. difficile

MDR S. pneumoniae
The new generation of resistant infections is almost impossible to treat

In August, 2000, Dr. Roger Wetherbee, an infectious-disease expert at New York University’s Tisch Hospital, received a disturbing call from the hospital’s microbiology laboratory. At the time, Wetherbee was in charge of handling outbreaks of dangerous microbes in the hospital, and the laboratory had isolated a bacterium called *Klebsiella pneumoniae* from a patient in an intensive-care unit. “It was literally resistant to every meaningful antibiotic that we had”

## Susceptibility Profile of *Klebsiella pneumoniae* carbapenemase (KPC) Producing K. pneumoniae

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Interpretation</th>
<th>Antimicrobial</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>I</td>
<td>Chloramphenicol</td>
<td>R</td>
</tr>
<tr>
<td>Amox/clav</td>
<td>R</td>
<td>Ciprofloxacan</td>
<td>R</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>R</td>
<td>Ertapenem</td>
<td>R</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>R</td>
<td>Gentamicin</td>
<td>R</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>R</td>
<td>Imipenem</td>
<td>R</td>
</tr>
<tr>
<td>Cefpodoxime</td>
<td>R</td>
<td>Meropenem</td>
<td>R</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>R</td>
<td>Pipercillin/Tazo</td>
<td>R</td>
</tr>
<tr>
<td>Cetotetan</td>
<td>R</td>
<td>Tobramycin</td>
<td>R</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>R</td>
<td>Trimeth/Sulfa</td>
<td>R</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>R</td>
<td>Polymyxin B</td>
<td>MIC &gt;4μg/ml</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>R</td>
<td>Colistin</td>
<td>MIC &gt;4μg/ml</td>
</tr>
<tr>
<td>Cefepime</td>
<td>R</td>
<td>Tigecycline</td>
<td>S</td>
</tr>
</tbody>
</table>
Mortality: Carbapenem Resistant vs. Susceptible *Klebsiella pneumoniae*

Overall Mortality

<table>
<thead>
<tr>
<th>CRKP</th>
<th>CSKP</th>
</tr>
</thead>
<tbody>
<tr>
<td>48%</td>
<td>20%</td>
</tr>
</tbody>
</table>

Attributable Mortality

<table>
<thead>
<tr>
<th>CRKP</th>
<th>CSKP</th>
</tr>
</thead>
<tbody>
<tr>
<td>38%</td>
<td>12%</td>
</tr>
</tbody>
</table>

OR 3.71 (1.97-7.01)

p<0.001

OR 4.5 (2.16-9.35)

A. Srinivasan, J. Patel – DHQP CDC
Antibiotic exposure is the most important risk factor for the development of *Clostridium difficile*-associated disease.
Estimated Burden of Healthcare-Associated C. difficile in U.S.

- **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


HAIs in Nursing Homes

- 1.8-3.6 million HAIs in NHs/year
  - 150,000 hospitalizations, 388,000 deaths
  - $673 million - $2 billion in excess healthcare costs

Issues:
- Residents have co-morbidities, functional impairments, frail, multiple medications
- Faster discharge from acute care
  - Residents often have invasive devices (ventilators, central lines, feeding tubes) and greater medical needs
  - Multiple providers
- Nursing home also their home

Castle, AJIC. 2012; 39:4
Antibiotic Use in NHs

• Up to 70% of residents receive ≥1 systemic antibiotic/year
• 40–75% might be unnecessary or inappropriate
• Adverse consequences
  • *C. difficile*
  • Adverse drug events and drug interactions
  • Colonization and/or infection with antibiotic-resistant organisms
  • Increased costs of care
• Common misuse: treating asymptomatic bacteriuria, viral respiratory infection (acute bronchitis), colonization instead of infection

NH Antibiotic Use, Ontario 2010

- 630 LTCFs (66,900 residents)
- Approximately 20% of prescribers prescribed 80% of the antibiotics
- Long duration of antibiotics (>7 days) was associated with individual prescribers, though patient characteristics were similar

Daneman N, JAMA Int Med 2013
Antibiotic Misuse in LTC

**Resident Factors**
- Chronic medical conditions, debilitation
- Impaired communication
- Difficulty obtaining specimens
- Family concerns

**System Factors**
- Lack of care continuity
- Time constraints and limited staffing
- Limited diagnostic resources
- Staff turnover

**Provider Factors**
- Telephone ordering
- Limited direct evaluation
- Lack of access to information at time of decision making
Antibiotic Stewardship Program (ASP)

- Stewardship: “careful and responsible management of something entrusted to one's care” – Merriam-Webster Dictionary
- Antimicrobial stewardship: improving use of antimicrobials through coordinated interventions
  - Appropriate diagnosis, drug, dose, de-escalation, and duration of treatment using evidence-based guidelines
  - Assist residents in managing symptoms of non-bacterial infections
- In order to be effective, must include all levels of healthcare workers and education to residents and family members
- Infectious Disease consult-supported ASP in LTC has led to decreased antibiotic use and decrease in *C. difficile* infections*

*Jump. ICHE 2012; 33:1185-92*
Putting Stewardship into Practice

**Core Elements of Antibiotic Stewardship for Nursing Homes**

**Leadership Commitment**
Demonstrate support and commitment to safe and appropriate antibiotic use in your facility.

**Accountability**
Identify physician, nursing, and pharmacy leads responsible for promoting and overseeing antibiotic stewardship activities in your facility.

**Drug Expertise**
Establish access to consultant pharmacists or other individuals with experience or training in antibiotic stewardship for your facility.

**Action**
Implement at least one policy or practice to improve antibiotic use.

**Tracking**
Monitor at least one process measure of antibiotic use and at least one outcome from antibiotic use in your facility.

**Reporting**
Provide regular feedback on antibiotic use and resistance to prescribing clinicians, nursing staff, and other relevant staff.

**Education**
Provide resources to clinicians, nursing staff, residents, and families about antibiotic resistance and opportunities for improving antibiotic use.
1: Administrative Leadership and Commitment

- Identify relevant administrative leadership
  - Communicate the importance of antibiotic stewardship commitment
  - Outline CMS rules and other applicable requirements
  - Consider discussing costs associated with treating resistant and *C. difficile* infections

- Establish how commitment to antibiotic stewardship will be communicated to staff, residents, and families
  - Posters in the facility
  - Family and resident discussions at admission, at regular intervals, and when illness occurs
  - Annual staff communication about commitment and expectations

- Consider engaging administrative leadership to identify facility ASP leader

- Begin plans to draft an antibiotic stewardship policy
  - Include facility goals and objectives
2: Accountability

- Often a physician, prescriber, or pharmacist will lead the antibiotic stewardship team (AST)
- Define the team’s overall purpose and responsibilities
- Identify staff members and tasks
- Use CDC’s Core Elements of Antibiotic Stewardship for Nursing Homes document to guide AST discussion
  - Medical, nursing, pharmacist, infection prevention, laboratory roles
- Consider how often the AST will review data (e.g., monthly, quarterly)
Team Responsibilities

• Policy and procedure development
• Tracking and reporting protocols and reports for antibiotic use and outcomes
  • Internal review
  • Consulting pharmacist review
• Nursing responsibilities
  • Standardized documentation and sharing of patient information
  • Communication protocols
  • Practice protocols (e.g., antibiotic time-outs, urine testing)
3: Drug Expertise

- Nursing homes should establish access to individuals with antibiotic expertise
  - Within referral network
  - New relationships with consultants in community
- Support from consultants can help reduce antibiotic use and adverse outcomes like *C. difficile* infection
  - Infectious disease physicians
  - Pharmacists with infectious disease or antibiotic stewardship training
- This provides an opportunity to establish relationships with other facilities connected to you through referrals or transfers
4: Action

- Implementation of policies and practices to improve antibiotic use
- Identify priority interventions on which to focus first
- Actions can be implemented with stepwise approach
- Consider identifying actions for this year and proposed actions for next year
Action Examples

• Baseline actions
  • Record-keeping requirements
  • Regular antibiotic use tracking and reporting
  • Standardized nursing communication protocols (SBAR)
  • Antibiotic “time-outs” to review antibiotic appropriateness, need for de-escalation
  • Protocols to improve management of asymptomatic bacteriuria/urinary tract infections

• More advanced actions
  • Tracking of antibiotic use appropriateness (e.g., Loeb minimum criteria for antibiotic use)*
  • Pharmacy-level interventions
  • Policies limiting use of specific antibiotics (e.g., fluoroquinolones)
  • Establishment of facility-specific first-line prescribing guidelines
  • Additional syndrome-specific interventions
  • Use of facility/regional antibiogram to guide prescribing

*Loeb et al. Inf Control Hosp Epi. 2001
5-6. Tracking and reporting

• Monitor antibiotic use practices, outcomes
  • Track progress
  • Guide changes to protocol

• Reporting facilitates awareness and accountability among administration, staff

• Feedback can drive prescribing improvement if communicated in ways acceptable to prescribers

• Measurement types:
  • Process measures
  • Antibiotic use measures
  • Outcome measures
Process Measures

• Tracking processes that influence how antibiotics are prescribed

• Use of nursing communication protocols

• Compliance with antibiotic initiation protocols

• Completeness of prescription documentation (dose, duration, route, indication)
Antibiotic Use Measures

- Tracking how many antibiotics are prescribed
  - Antibiotic starts
  - Days of therapy
  - Cost
  - Length of therapy
  - Point prevalence

- Manual or electronic tracking can be used

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Mylotte J. *J Am Med Dir Assoc* 2016; 17(7): e13-8
Outcome Measures

• Tracking outcomes that might be related to or influenced by antibiotic use
  • Urinary tract infections
  • *Clostridium difficile* infection rates by using CDC’s NHSN criteria
  • Infections with antibiotic-resistant organisms
  • Adverse drug events
7: Education

• Antibiotic stewardship education is needed for clinicians, nursing staff, residents, and families

• Platforms for education can include:
  • Fliers and newsletters
  • Trainings, conferences, workshops

• CDC suggests linking professional education to feedback on prescribing practices

• Spending time to explain why the facility has a commitment to stewardship will help to change resident and family member expectations
Education Tools for Residents, Families

AHRQ AS Education Toolkit for Long-term Care

Centers for Disease Control and Prevention
https://www.cdc.gov/longtermcare/prevention/antibiotic-stewardship.html
# Checklist for Core Elements of Antibiotic Stewardship in Nursing Homes

The following checklist is a companion to the Core Elements of Antibiotic Stewardship in Nursing Homes. The CDC recommends that all nursing homes take steps to implement antibiotic stewardship activities. Before getting started, use this checklist as a baseline assessment of policies and practices which are in place. Then use the checklist to review progress in expanding stewardship activities on a regular basis (e.g., annually). Over time, implement activities for each element in a step-wise fashion.

## Leadership Support

<table>
<thead>
<tr>
<th>LEADERSHIP SUPPORT</th>
<th>ESTABLISHED AT FACILITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Can your facility demonstrate leadership support for antibiotic stewardship through one or more of the following actions?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td>If yes, indicate which of the following are in place (select all that apply)</td>
<td></td>
</tr>
<tr>
<td>☐ Written statement of leadership support to improve antibiotic use</td>
<td></td>
</tr>
<tr>
<td>☐ Antibiotic stewardship duties included in medical director position description</td>
<td></td>
</tr>
<tr>
<td>☐ Antibiotic stewardship duties included in director of nursing position description</td>
<td></td>
</tr>
<tr>
<td>☐ Leadership monitors whether antibiotic stewardship policies are followed</td>
<td></td>
</tr>
<tr>
<td>☐ Antibiotic use and resistance data is reviewed in quality assurance meetings</td>
<td></td>
</tr>
</tbody>
</table>
How are we doing in Minnesota?
CDC Nursing Home Prevalence Pilot, 2013-14

- Single day HAI and AU prevalence survey pilot
  - 9 NHs in 4 EIP sites: CT, MN, NM, NY
  - Eligibility: CMS certified nursing facilities, >100 licensed beds, voluntary participation
- Enrolled, completed data collection at 9 NHs
  - Median licensed beds 130 (range 104 – 229)
  - Total of 1272 eligible residents (98% of all residents)
    - Median age 85 years (22 – 91)
    - 14% short stay

## HAI and AU Prevalence by Resident Characteristic

<table>
<thead>
<tr>
<th></th>
<th>HAI Prev.</th>
<th>(95% CI)</th>
<th>AU Prev.</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>5.3</td>
<td>(4.6 – 6.6)</td>
<td>11.1</td>
<td>(9.4 – 12.9)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>HAI Prev.</th>
<th>AU Prev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-84</td>
<td>4.5</td>
<td>12.5</td>
</tr>
<tr>
<td>85 +</td>
<td>6.3</td>
<td>10.4</td>
</tr>
<tr>
<td>Gender:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5.3</td>
<td>11.7</td>
</tr>
<tr>
<td>Female</td>
<td>5.2</td>
<td>11.2</td>
</tr>
<tr>
<td>Diabetes:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>5.7</td>
<td>11.3</td>
</tr>
<tr>
<td>Yes</td>
<td>4.1</td>
<td>11.6</td>
</tr>
<tr>
<td>Stay:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long</td>
<td>4.7</td>
<td>9.7</td>
</tr>
<tr>
<td>Short</td>
<td>8.7</td>
<td>21.2</td>
</tr>
<tr>
<td>Device*:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4.8</td>
<td>10.3</td>
</tr>
<tr>
<td>Yes</td>
<td>10.8</td>
<td>23.5</td>
</tr>
</tbody>
</table>

*p*-value: \( \chi^2 \)

*Indwelling urinary catheter, vascular device, ventilator or tracheostomy, PEG/J tube*

HAI in Nursing Homes (N=70 infections, 67 residents)

Type of Infections

- GI infections
- Skin and soft tissue infections
- Respiratory infections
- Urinary tract infections
- Other HAIs

Percent

HAI in Nursing Homes
(N=70 infections, 67 residents)

- 7 of 26 (27%) GI infections were CDI
- But, 50 residents received antibiotic for UTI

Top 10 Antimicrobials Administered in 9 US Nursing Homes

- **OSELTAMIVIR**
- **TMP-SMX**
- **DOXYCYCLINE**
- **CEPHALEXIN**
- **NITROFURANTOIN**
- **CIPROFLOXACIN**
- **LEVOFLOXACIN**
- **METRONIDAZOLE**
- **VANCOMYCIN**
- **NYSTATIN**

Number administered

Thompson ND. AMDA. 2016;17:1151-3.
Documentation of Antimicrobial Prescribing Practices

Thompson ND. AMDA. 2016;17:1151-3.
Evaluation of Antibiotic Appropriateness Measures for UTI

- Study assessed appropriateness of initiating antibiotics for NH residents in 4 states (n=49)
  - 3 published algorithms: Loeb, McGreer, Crnich
- 33/49 received treatment
  - Appropriateness varied: 15–45%
  - Opportunities exist for improving prescribing
- 16/49 (32%) received prophylaxis
  - Antibiotic prophylaxis for UTI is likely unnecessary
  - Additional evaluation is needed
- Improvement of antibiotic use for UTI could have large impact on overall use

MN ASP for Long-Term Care
Core Tools

• Action steps and strategies:
  • How to implement ASP

• Gap analysis:
  • Readiness for ASP

• Surveys:
  • Attitudes and beliefs of nursing staff, providers on antibiotic-use
  • Who gets antibiotics and why

• Evaluation tool:
  • Improve quality of nursing assessment, communication, documentation of resident symptoms

Released Summer 2014
Collaborations for LTC

- MDH partners with groups working on LTC stewardship
  - Quality improvement organization (QIO)
  - Hospital association
  - Aging services professional organizations
  - Medical directors
  - Infection preventionists
- LTC stewardship workgroup developed to work on informatics and on prescribing issues
  - E-health experts
  - Consulting pharmacists
Fighting Resistance

According to Centers for Disease Control and Prevention, *four core actions* can help fight resistance.

1. Prevent infections
2. Track infections
3. Improve prescribing (stewardship)
4. Develop new drugs and diagnostics

http://www.cdc.gov/drugresistance/about.html
Infection Control

- Prevent transmission of resistant organisms
Vaccination and Surveillance

- Vaccination of residents and health care workers
- Surveillance for infections, including antibiotic resistant infections
CMS and Stewardship

Final CMS rule changes in long-term care (including § 483.80 Infection Control)

- First comprehensive change to conditions of participation since 1991
- **November 28, 2016:** IPC program and quality assurance programs must be in place
- **November 28, 2017:** Antibiotic stewardship program must be in place
- **November 28, 2019:** Infection preventionist with specialized training in IPC must be on staff

For **November 28, 2017**, infection prevention and control program must include:

- Antibiotic use protocols
- System to monitor antibiotic use
Maintaining a Stewardship Program

“Implementing and sustaining antibiotic stewardship in nursing homes requires an organizational commitment and a strategy based on goal setting, process and outcome measurement, and continuous quality improvement.”

“…. the microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out… In such cases the thoughtless person playing with penicillin is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted.”

- Sir Alexander Fleming, June 1945
Margaret A. Hamburg, commissioner of the Food and Drug Administration, said at a news conference last month. The world’s weakening arsenal against “superbugs” has prompted scientists to warn that **everyday infections could again become a major cause of death just as they were before the advent of penicillin around 1940.**

“For these infections, we’re back to dancing around a bubbling cauldron while rubbing two chicken bones together,” said Dr. Brad Spellberg, an infectious disease specialist at Harbor-U.C.L.A. Medical Center in Torrance.
Post-Antibiotic Era
Acknowledgements

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