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

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Minnesota Department of Health

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.”

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 Pneumonia¹</td>
<td>~35%</td>
<td>~10%</td>
<td>-25%</td>
</tr>
<tr>
<td>Hospital Pneumonia²</td>
<td>~60%</td>
<td>~30%</td>
<td>-30%</td>
</tr>
<tr>
<td>Heart Infection³</td>
<td>~100%</td>
<td>~25%</td>
<td>-75%</td>
</tr>
<tr>
<td>Brain Infection⁴</td>
<td>&gt;80%</td>
<td>&lt;20%</td>
<td>-60%</td>
</tr>
<tr>
<td>Skin Infection⁵</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 drugs⁶ -3%


B. Spellberg
Antibiotic Resistance

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

Emergence of Antimicrobial Resistance
Selective Pressure

- When bacteria are exposed to an antibiotic, susceptible cells die
- Those that are resistant (or acquire resistance through mutation, genetic rearrangement or acquisition of genes) survive
- With reduced competition from susceptible bacteria, resistant bacteria thrive and outcompete others
- Antibiotics also impact “normal flora” which otherwise could limit the expansion of pathogens
  - Non-pathogenic but resistant bacteria can impact the microbial niche by increasing the reservoir of resistance genes

Antibiotic Resistance

- Recent antibiotic use associated with colonization or infection with resistant bacteria (pneumococcus, S. aureus)
- Increasing resistance is both an individual and a public health issue
- Resistant infections
  - More difficult to treat
  - Broader spectrum therapy
  - May require parenteral therapy
  - Therapy may have increased toxicities and adverse effects
The new generation of resistant infections is almost impossible to treat

Jerome Groopman, August 11, 2008

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*
carbapenamase (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>Ciprofloxacin</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>Piperocillin/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*

![Bar chart showing mortality comparison]

**Overall Mortality**
- CRKP: 48%
- CSKP: 20%

**Attributable Mortality**
- CRKP: 38%
- CSKP: 12%

**OR 3.71 (1.97-7.01)**

A. Srinivasan, J. Patel – DHQP CDC

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**CP-CRE and Non CP-CRE Isolates by Patient Location, Minnesota, 2015**

![Bar chart showing distribution of isolates by location]

**CP-CRE**
- n = 41

**Non-CP-CRE**
- n = 202
**Clostridium difficile Infection**

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

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References:


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

Antibiotic Use in NHs

- Up to 70% of residents receive ≥1 systemic antibiotic/year
- 40–75% may 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

Castle, AJIC. 2012; 39:4

Antibiotic Use in NH (cont.)

- Ontario, Canada in 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 even 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: “the careful and responsible management of something entrusted to one’s care” – Merriam-Webster Dictionary
- Antimicrobial stewardship: responsible use of antimicrobials
  - Encompasses the appropriate diagnosis, drug, dose, de-escalation (switch from parenteral to po) 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
- Use of an 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
Summary of Core Elements for Antibiotic Stewardship in 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
Educate at least one pharmacist or other individual 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.

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.

<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>☐ 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 policies included in medical director 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>
CHECKLIST CONT.

ACCOUNTABILITY

2. Has your facility identified a leader for antibiotic stewardship activities? [ ] Yes [ ] No
   - [ ] Medical director
   - [ ] Director or assistant director of nursing services
   - [ ] Consultant pharmacist
   - [ ] Other: ____________________________

DRUG EXPERTISE

3. Does your facility have access to individual(s) with antibiotic stewardship expertise? [ ] Yes [ ] No
   - [ ] Consultant pharmacy has staff trained/semi-experienced in antibiotic stewardship
   - [ ] Partnering with a stewardship team at referral hospital
   - [ ] External infectious disease/stewardship consultant
   - [ ] Other: ____________________________

ACTIONS TO IMPROVE USE

4. Does your facility have policies to improve antibiotic prescribing/use? [ ] Yes [ ] No
   - [ ] Requires prescribers to document a dose, duration, and indication for all antibiotic prescriptions
   - [ ] Developed facility-specific algorithm for assessing residents
   - [ ] Developed facility-specific algorithms for appropriate diagnostic testing (e.g., obtaining cultures) for specific infections
   - [ ] Developed facility-specific treatment recommendations for infections
   - [ ] Reviews antibiotic agents listed on the medication formulary

CHECKLIST CONT.

5. Has your facility implemented practices to improve antibiotic use? [ ] Yes [ ] No
   - [ ] Utilizes a standard assessment and communication tool for residents suspected of having an infection
   - [ ] Implemented process for communicating or receiving antibiotic use information when residents are transferred to/from other healthcare facilities
   - [ ] Developed reports summarizing the antibiotic susceptibility patterns (e.g., facility antibiogram)
   - [ ] Implemented an antibiotic review process (“antibiotic time out”)
   - [ ] Implemented an infection specific intervention to improve antibiotic use
   - [ ] Indicates which condition(s) ____________________________

6. Does your consultant pharmacist support antibiotic stewardship activities? [ ] Yes [ ] No
   - [ ] Indications performed by the consultant pharmacist (select all that apply)
   - [ ] Reviews antibiotic courses for appropriateness of administration and/or indication
   - [ ] Establishes standards for clinical/laboratory monitoring for adverse drug events from antibiotic use
   - [ ] Reviews microbiology culture data to assess and guide antibiotic selection

TRACKING: MONITORING ANTIBIOTIC PRESCRIBING, USE, AND RESISTANCE

7. Does your facility monitor one or more measures of antibiotic use? [ ] Yes [ ] No
   - [ ] Adherence to clinical assessment documentation (signs/symptoms, vital signs, physical exam findings)
   - [ ] Adherence to prescribing documentation (dose, duration, indication)
   - [ ] Adherence to facility-specific treatment recommendations
   - [ ] Performs point prevalence surveys of antibiotic use
   - [ ] Monitors rates of new antibiotic starts/1,000 resident-days
   - [ ] Monitors antibiotic days of therapy/1,000 resident-days
   - [ ] Other: ____________________________
### Checklist cont.

8. Does your facility monitor one or more outcomes of antibiotic use?  
   [ ] Yes  [ ] No  
   - Monitors rates of C. difficile infection  
   - Monitors rates of antibiotic-resistant organisms  
   - Monitors rates of adverse drug events due to antibiotics  
   - Other: __________________________

### REPORTING INFORMATION TO STAFF ON IMPROVING ANTIBIOTIC USE AND RESISTANCE

9. Does your facility provide facility-specific reports on antibiotic use and outcomes with clinical providers and nursing staff?  
   [ ] Yes  [ ] No  
   - Measures of antibiotic use at the facility  
   - Measures of outcomes related to antibiotic use (i.e., C. difficile rates)  
   - Report of facility antibiotic susceptibility patterns (within last 12 months)  
   - Personalized feedback on antibiotic prescribing practices (to clinical providers)  
   - Other: __________________________

### EDUCATION

10. Does your facility provide educational resources and materials about antibiotic resistance and opportunity for improving antibiotic use?  
    [ ] Yes  [ ] No  
    - Clinical providers (e.g., MDs, NPs, PAs, PharmD)  
    - Nursing staff (e.g., RNs, LPNs, CNA)  
    - Residents and families  
    - Other: __________________________

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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


<table>
<thead>
<tr>
<th>HAI and AU Prevalence by Resident Characteristic</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>11.7</td>
<td>(9.4 – 12.9)</td>
</tr>
<tr>
<td>Age:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-84</td>
<td>4.5</td>
<td>0.143</td>
<td>12.5</td>
<td>0.2186</td>
</tr>
<tr>
<td>85 +</td>
<td>6.3</td>
<td></td>
<td>10.4</td>
<td></td>
</tr>
<tr>
<td>Gender:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5.3</td>
<td>1.000</td>
<td>11.7</td>
<td>0.788</td>
</tr>
<tr>
<td>Female</td>
<td>5.2</td>
<td></td>
<td>11.2</td>
<td></td>
</tr>
<tr>
<td>Diabetes:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>5.7</td>
<td>0.270</td>
<td>11.3</td>
<td>0.8834</td>
</tr>
<tr>
<td>Yes</td>
<td>4.1</td>
<td></td>
<td>11.6</td>
<td></td>
</tr>
<tr>
<td>Stay:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long</td>
<td>4.7</td>
<td>0.031</td>
<td>10.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>Short</td>
<td>8.7</td>
<td></td>
<td>21.2</td>
<td></td>
</tr>
<tr>
<td>Device*:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4.8</td>
<td>0.018</td>
<td>10.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>Yes</td>
<td>10.8</td>
<td></td>
<td>23.5</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Type of Infections</th>
<th>Percent</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI infections</td>
<td>36%</td>
<td>7 of 20 GI infections were CDI</td>
</tr>
<tr>
<td>Skin and soft tissue infections</td>
<td>27%</td>
<td>But, 50 residents received antibiotic for UTI</td>
</tr>
<tr>
<td>Respiratory infections</td>
<td>22%</td>
<td></td>
</tr>
<tr>
<td>Urinary tract infections</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>Other HAIs</td>
<td>4%</td>
<td></td>
</tr>
</tbody>
</table>

Top 10 Antimicrobials Administered in 9 US Nursing Homes

Evaluation of Antibiotic Appropriateness Measures for UTI

**AGS “Choosing Wisely®” campaign 2013: Don’t use antimicrobials to treat bacteriuria in older adults unless specific urinary tract symptoms are present**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Prophylaxis n=16 (32%)</th>
<th>Therapeutic n=33 (67%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>McGeer</td>
<td>5 (15%)</td>
<td></td>
</tr>
<tr>
<td>Loeb</td>
<td>?*</td>
<td>10 (30%)</td>
</tr>
<tr>
<td>Crnich</td>
<td>15 (45%)</td>
<td></td>
</tr>
</tbody>
</table>


- <50% appropriate → opportunities for improving prescribing
- AU for UTI prophylaxis → likely unnecessary, but additional evaluation needed

**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

**Collaborations for LTC**

- MDH partners with other 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

Released Summer 2014
Other Important Components in Combating Antibiotic Resistance

• Infection Control: prevent transmission of resistant organisms

Vaccination of residents and health care workers
• Surveillance for infections, including antibiotic resistant infections
CMS Rules

• Infection Prevention and Control Program (IPCP) incorporate preventing and controlling infections and communicable diseases, and an antibiotic stewardship program
  • Antibiotic use protocols (November 2017)
  • System to monitor antibiotic use (November 2017)
  • Recording incidents identified under the facility's IPCP and corrective actions taken by the facility (November 2016)

CMS Rules

• Pharmacist conduct monthly drug regimen review which includes medical record review for residents taking antibiotics (and admission/transfer) (November 2017)
  • Facility must designate one or more infection preventionists who are responsible for the IPCP and have specialized training; also IP part of QAA committee (November 2019)
  • Annual Review of IPCP (November 2016)
  • Infection control training for staff (November 2019)
  • Influenza and pneumococcal vaccinations (November 2016)
“…. 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

**Antibiotics Research Subsidies Weighed by U.S.**

By Andrew Pollack Published: November 5, 2010

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,
Acknowledgements

MDH:
- Amanda Beaudoin
- Pam Gahr
- Jane Harper
- Janet Lilleberg
- Claudia Miller
- Jean Rainbow
- Sara Tomczyk
- Linn Warnke
- Jacy Walters

CDC:
- Lauren Epstein
- Lauri Hicks
- Sarah Kabbani
- Nimalie Stone
- Nicola Thompson