Antibiotic Stewardship

Nimalie D. Stone, MD/MS
Ambulatory and Long Term Care Team
Division of Healthcare Quality Promotion

AQAF Educational Conference
June 19, 2012

Presentation Outline

- Review basics about common bacteria which can develop antibiotic resistance in the healthcare setting
- Discuss mechanisms by which antibiotic resistance emerges in healthcare settings
- Identify opportunities for improving antibiotic stewardship using the example of urinary tract infection management

Basics on Bacteria

- Bacteria have different characteristics that allow us to identify them in the lab
  - Growth patterns, structure of the cell
  - We use these characteristics to develop antibiotics

| Gram Stain Positive (purple) | Gram Stain Negative (pink/red) |
Common types of Bacteria

Gram positive
- Most are cocci, “round bacteria”
  - Streptococcus, Staphylococcus, Enterococcus
- Clostridium difficile (C. diff) is a Gram positive rod

Gram negative
- Most are baccilli, “rod-shaped bacteria”
  - Enterobacteriaceae: E. coli, Klebsiella, Enterobacter, Proteus
- Pseudomonas

Normal Bacterial Carriage
- People have bacteria living in and on us all the time
- Some live on our skin, some in our nose and throats, others in our bowels
- Our bodies need these bacteria to help us
  - Some digest food/nutrients, others block bad bugs
- These “colonizing” bacteria aren’t harmful
- Only bacteria that invade our system and cause illness need to be treated

Antibiotics 101
- Antibiotics are drugs that treat and kill bacteria
- They are grouped into classes based on their structure and activity
  - Narrow-spectrum target a few specific bacteria
  - Broad-spectrum can kill a wide variety of bacteria
- Infection prevention programs track certain “bug-drug” combinations for evidence that the bacteria is getting resistant
  - Bacteria with resistance can cause patients to have more severe, costly infections which are harder to treat
Antibiotic Classes

Penicillins
- Examples: Penicillin, amoxicillin, ampicillin, methicillin
- Penicillins can be combined with a drug to help them overcome certain bacterial resistance
  - Amoxicillin + Clavulanate = Augmentin;
  - Piperacillin + tazobactam = Zosyn

Cephalosporins (cousins to penicillins)
- 1st generation (more gram positive activity): Cephalexin, Cefazolin
- 3rd/4th generation (more gram negative): Ceftriaxone, Ceftazidime

Antibiotic Classes (cont)

Carbapenems
- Examples: Imipenem, meropenem, ertapenem
- Extremely broad-spectrum, among the most powerful antibiotics we currently

Miscellaneous drugs with only gram positive activity: Vancomycin, linezolid, daptomycin
- Vancomycin is the primary treatment for Methicillin-resistant Staphylococcus aureus (MRSA)
  - Oral vancomycin is ONLY used to treat C difficile;
  - IV Vancomycin must be used to treat all other infections
- Enterococci that develop resistance to Vancomycin are called Vancomycin-resistant enterococci (VRE)

Antibiotic Classes (cont)

Fluoroquinolones
- 1st generation (Ciprofloxacin) mostly gram neg activity, often used for UTI treatment
- 2nd/3rd gen (Levofloxacin/Moxifloxacin) have broader activity, can cover Streptococcus pneumoniae and other respiratory/sinus bacteria

Aminoglycosides
- Examples: Gentamicin, Tobramycin, Amikacin
- Excellent gram negative drugs – especially for urinary tract
- Aren’t used as much because can be toxic to the kidneys, need to be monitored when used
Antibiotic Classes (cont)

Miscellaneous drugs
- Trimethoprim/Sulfamethoxazole (Bactrim): Considered by many to be narrow spectrum, but has Gram neg and Gram pos activity, used to treat UTIs, also good for MRSA skin infections
- Azithromycin ("Z-pack"): Also considered more narrow spectrum, good for respiratory/sinus infections
- Metronidazole (Flagyl): One of the main treatments for C. difficile infections
- Tigecycline: Structurally related to tetracyclines but with much broader spectrum of activity.
  - Active against common gram negative rods (except Proteus and Pseudomonas) and gram-positives organisms including MRSA, and VRE

Mechanisms of antibiotic resistance
- Production of proteins that destroy antibiotics
  - Beta-lactamases
  - Carbapenemases
- Change their cell structure so antibiotics can’t bind and block their function
- Reduce their antibiotic exposure
  - Pump drugs out
  - Increase cell barriers to keep drug out

http://bioinfo.bact.wisc.edu/themicrobialworld/bactresanti.html

It was an abstract cut through the hospital kitchen that Albert was first approached by a member of the Antibiotic Resistance.
Snapshot of resistance patterns: Facility antibiograms

- A yearly summary of the common bacteria from facility cultures and their susceptibility patterns to antibiotics
- Allows you to see trends in resistance over time
- Ask your microbiology lab about it

Defining Multidrug-resistance

- Resistant to treatment by several antibiotics from unrelated classes
- Sometimes just one key drug resistance will define an important MDRO, for example, Methicillin-resistance in Staph aureus
- Sometimes bacteria acquire resistance to several classes, often seen in gram negative rods
  - Cephalosporin-resistance is a big concern in bacteria like E coli/Klebsiella which often cause UTIs
  - Pseudomonas will be resistant to fluoroquinolones, penicillins, cephalosporins, and carbapenems

ABC's of MDROs

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Abbreviation</th>
<th>Antibiotic Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>MRSA</td>
<td>Methicillin-resistant</td>
</tr>
<tr>
<td>Enterococcus (faecalis/faecium)</td>
<td>VRE</td>
<td>Vancomycin-resistant</td>
</tr>
<tr>
<td>Enterobacteriaceae (E coli/Klebsiella, etc)</td>
<td>CRE (KPC)</td>
<td>Carbapenem-resistant</td>
</tr>
<tr>
<td>Pseudomonas/ Acinetobacter</td>
<td>MDR</td>
<td>Many drug classes</td>
</tr>
</tbody>
</table>
Case of an emerging MDRO....

Clinical Infectious Diseases 2010 50(12):1611-1616

Multidrug-Resistant Acinetobacter baumannii: An Emerging Pathogen among Older Adults in Community Hospitals and Nursing Homes

- Laboratory query for all Acinetobacter baumannii identified in clinical isolates from 4 community hospitals over a 5 year period
- Classified as nosocomial, NH-associated, or community-associated
- Analysis limited to individuals >60 yrs old and not presenting from any other hospital setting

Multidrug-resistance emerges quickly

- Over 5 year period, Acinetobacter resistance increased dramatically
- Culture sources: Respiratory secretions (56%); Wounds (22%); Urine (12%)

Healthcare facilities are the source of MDROs

**Critical message about care transitions**

The increase in prevalence of antibiotic-resistant strains in nursing homes and the degree of antibiotic resistance among these strains is extremely concerning. As the current study demonstrates, the degree of antibiotic resistance among “hospital-acquired” K. pneumoniae increased during the study period in parallel with the degree of resistance among Gram-negative bacteria from nursing home-dwelling patients. The co-identification of antibiotic-resistant strains from both clinical and environmental samples in this study indicates the existence of a hospital-residing K. pneumoniae. The ongoing support of a containment center that focuses on the dissemination of antibacterial resistance mechanisms due to ensure both types of healthcare facilities. Consequently, coordinated regional efforts are needed to control the spread of this pathogen. Long-term care facilities, despite their vulnerable populations, generally have few resources for infection surveillance and prevention.


---

**Transitions between healthcare settings**

- **Changing post-acute care population**
  - Acute care length of stay is decreasing
  - Patients are discharged with higher levels of medical complexity and care needs

- **Dynamic movement across healthcare settings**
  - Impacts where healthcare-associated infections and other adverse events manifest

---

**MDROs in the healthcare setting**

**DEVELOPMENT**

- Antibiotic pressure
  - Most common predictor of antibiotic resistance is prior exposure
- Device utilization
  - Biofilm formation on central lines, urinary catheters, etc.

**SPREAD**

- Patient to patient transmission via healthcare workers
- Environmental/equipment contamination
- Role of colonization pressure on acquisition
Resistance from antibiotic pressure

- At first most of the bacteria can be killed by the drug (green).
- But, once they are wiped out, the resistant bugs take over (red).

Antibiotic use drives resistance

![Graph showing antibiotic use drives resistance](https://www.ul.ie/elements/issue7/Biofilm%20Information.htm)

Biofilm formation on device surfaces

- Biofilm: An collection of bacteria within a sticky film that forms a community on the surface of a device. [Link](http://www.ul.ie/elements/issue7/Biofilm%20Information.htm)
Biofilm on an indwelling catheter

Resistance develops within biofilms

- Bacteria within a biofilm are grow every differently from those floating around freely
- These changes in their growth make our antibiotics less effective
- Antibiotics can’t penetrate the biofilm to get to the bacteria
- This leads to much less drug available to treat the bugs
- Bacteria within the biofilm can talk to each other and share the traits that allow some to be resistant
- Over time more and more of them become resistant as well

Ways Resistance Spreads in Healthcare

<table>
<thead>
<tr>
<th>Unit A</th>
<th>Colonization pressure</th>
<th>X days in unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>VRE</td>
<td>++</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Unit B</th>
<th>Colonization pressure</th>
<th>X days in unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>VRE</td>
<td>-</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Source</th>
<th>Day(s)</th>
<th>Transmission Routes</th>
</tr>
</thead>
<tbody>
<tr>
<td>VRE</td>
<td>Staff</td>
<td>5</td>
<td>Direct/Indirect</td>
</tr>
<tr>
<td></td>
<td>Patient</td>
<td>5</td>
<td>Direct/Indirect</td>
</tr>
<tr>
<td></td>
<td>Patient</td>
<td>5</td>
<td>Direct/Indirect</td>
</tr>
<tr>
<td></td>
<td>Closed</td>
<td>-</td>
<td>Direct/Indirect</td>
</tr>
<tr>
<td></td>
<td>Closed</td>
<td>-</td>
<td>No direct/indirect</td>
</tr>
<tr>
<td></td>
<td>Closed</td>
<td>-</td>
<td>No direct/indirect</td>
</tr>
</tbody>
</table>


Key MDRO Prevention Strategies

- Assessing hand hygiene practices
- Implementing Contact Precautions
- Recognizing previously colonized patients
- Rapidly reporting MDRO lab results
- Environmental disinfection
- Careful device utilization
- Antibiotic stewardship
- Inter-facility communication

Case study #1: Care transitions

- A LCTF resident was transferred to a local ED for symptoms of worsening lower extremity swelling and shortness of breath
  - PMHx included h/x CAD, DM with neuropathy, BPH
  - No fever, focal complaints, or leukocytosis on admission
- Diagnosed with exacerbation of congestive heart failure admitted to ICU for cardiac monitoring and diuresis
- A urinary catheter was placed at the time of admission and a specimen was sent for UA/culture in ED.
  - Based on the UA, the patient was started on antibiotics

Case study (continued)

- After treatment for CHF and the positive urine culture, the patient was discharged back to the LTC facility with the catheter in place.
- Prior to removing the urinary catheter a repeat culture was sent which grew VRE
  - A second course of antibiotics was initiated
- Two weeks later the resident developed diarrhea, fever and hypotension resulting in transfer back to acute care hospital
  - Stool sample was positive C. Diff toxin test.
Issues raised by our case

- Is the practice of screening urine cultures on admission a valuable strategy?
  - What are the pros/cons
- Did the resident continue to need the urinary catheter once the CHF was managed?
- How is resident functionality communicated at time of transfer?
- How are antibiotics used in both acute/LTC facilities in this shared population?
- Who is accountable for the complications of antibiotic use?

Urinary Catheter Use

- 15-25% of hospitalized patients may receive a urinary catheter
  - 5% in long-stay population in LTCF
  - 10-12% in post-acute care population in LTCF
- Often placed/maintained for inappropriate indications
  - 28% of physicians unaware of catheter status
  - Documentation of indication/presence of catheter available for <50% of patients with device

Prevention Strategies: Careful Device Utilization

- Know the patients/residents with indwelling medical devices
  - May require focused infection surveillance
- Continually assess the ongoing need for devices
  - Develop a bladder protocol for urinary catheter removal
  - Make device use part of daily assessments
- Ensure staff are comfortable and trained on handling/maintenance of medical devices
  - Document device insertion/ maintenance practices
  - Standardize assessment of device functionality

References:
**Why we need to improve antibiotic use in healthcare**

- Antibiotics are misused in hospitals and nursing homes
- Antibiotic misuse adversely impacts patients and society
  - Adverse side effects, promotes resistance and secondary complications ([C. difficile](http://www.cdc.gov/getsmart/healthcare/inpatient-stewardship.html#Facts))
- Improving antibiotic use improves patient outcomes and has cost savings


**Antibiotics are misused in a variety of ways**

- Given when they are not needed
- Continued when they are no longer necessary
- Given at the wrong dose
- Broad spectrum agents are used to treat very susceptible bacteria
- The wrong antibiotic is given to treat an infection
  - Drug doesn't match the susceptibility of the bug


**Case study #2: Symptomatic UTI?**

- A family member states to the floor staff, "My mom is not acting right, I think she has a UTI"
- Patient JH is an 80 y/o female
  - Past medical history of diabetes mellitus, stroke, vancomycin-resistant enterococcus, Clostridium difficile.
  - Requires extensive assistance with mobility. In order to transfer from bed to wheelchair, she requires 2-person assistance
- Assessment:
  - CNA notes that patient’s urine is cloudy and foul-smelling; Vital signs are normal; no exam is documented
  - UA positive for leukocyte esterase/nitrite; Urine culture pending
- What do you want to know?
  - Do you think this resident would be given an antibiotic?
UTI in the Elderly: Diagnostic Dilemma

• One recent study documented that "UTI" was incorrectly diagnosed in approximately 40% of cases among patients aged 75 years and over.
  – One reason for this may be the atypical presentation of disease in this age group.
    • A consequence is that a large number of patients inappropriately receive antibiotics
    • 46% had no clinical evidence of sepsis, others may have received inappropriate antibiotics for a different infection unrelated to bacteriuria


UTIs drive Antibiotic Use in NHs

• 73 LTCF followed over 6 months:
• 42% of residents received antibiotic (3,392 prescriptions)

Benoit S. et al. JAGS 2008; 56:2039-44

"UTI" presentation in LTC residents

• Multiple comorbid illnesses
  – May present w/ symptoms similar to symptomatic bacteriuria
  – Cognitive impairment
    • May not be able to report their symptoms
    • Laboratory confirmation with significant bacteriuria should be present
    • But not sufficient for diagnosis of Symptomatic UTI in this population
Alterations in GU Tract Increases Susceptibility to Infection

- Loss of normal periurethral bacterial flora
- Alterations in environment of the bladder
- Changes in bladder functioning
- Disruptions in the flow of urine
  - Obstruction
- Foreign Bodies
  - Healthcare devices (catheters, stents)
  - Renal stones

Asymptomatic Bacteriuria (ASB)

Clinical Infectious Diseases 2006;42:643-54

Infectious Disease Society of America Guidelines
for the Diagnosis and Treatment of Asymptomatic Bacteriuria in Adults

Prevalence of Asymptomatic Bacteriuria

<table>
<thead>
<tr>
<th>Population</th>
<th>Prevalence, %</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy, noninstitutional women</td>
<td>1.5-7.5</td>
<td>(251)</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>1.2-4.9</td>
<td>(251)</td>
</tr>
<tr>
<td>Postmenopausal women aged 60-70 years</td>
<td>2.0-4.9</td>
<td>(251)</td>
</tr>
<tr>
<td>Diabetic patients</td>
<td>9.0-47</td>
<td>(252)</td>
</tr>
<tr>
<td>Women</td>
<td>5.9-11</td>
<td>(253)</td>
</tr>
<tr>
<td>Resident patients in the community*</td>
<td>0-6.1-10</td>
<td>(251)</td>
</tr>
<tr>
<td>Men</td>
<td>2.5-10</td>
<td>(251)</td>
</tr>
<tr>
<td>Elderly persons in a long-term care facility</td>
<td>2.5-10</td>
<td>(251)</td>
</tr>
<tr>
<td>Women</td>
<td>5-10</td>
<td>(251)</td>
</tr>
<tr>
<td>Men</td>
<td>0.1% - 4.7%</td>
<td>(251)</td>
</tr>
</tbody>
</table>

* Patients with special risk factors:
  - Transplantation or kidney/renal disease (previous or present)
  - Diabetes mellitus
  - Immunosuppression
  - Active or recent cancer
  - Patients undergoing hemodialysis
  - Patients with other underlying conditions

Special Note: 5-10% prevalence in institutional settings.

IDSA Guidelines C32 2008

14
Pyuria and ASB

Prevalence of pyuria in different populations with asymptomatic bacteriuria

<table>
<thead>
<tr>
<th>Population</th>
<th>Bacteriuria (%)</th>
<th>Pyuria with bacteriuria (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy adult women</td>
<td>7-5</td>
<td>0-2</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>2-11</td>
<td>50</td>
</tr>
<tr>
<td>Diabetic women</td>
<td>7-9</td>
<td>70</td>
</tr>
<tr>
<td>Elderly, nursing home</td>
<td>5-50</td>
<td>90</td>
</tr>
<tr>
<td>Spinal-cord injury patients</td>
<td>50</td>
<td>23-86</td>
</tr>
<tr>
<td>Indwelling urinary catheter</td>
<td>100</td>
<td>70</td>
</tr>
</tbody>
</table>

- Pyuria accompanying bacteriuria is NOT an indication for antimicrobial treatment

ICSA Guidelines CID 2005

Pyuria in the elderly – not useful

- Over 90% of older adults with positive urine cultures (bacteriuria) have pyuria
  - No evidence of poor clinical outcomes with high levels
- If LE and Nitrite negative, then strongly predictive that a urinary tract infection is not present
- Bottom line: Don’t get the test unless you know how to interpret AND plan on acting on the results

Mandell: Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 7th ed. 2009

ASB in the Elderly

<table>
<thead>
<tr>
<th>Population</th>
<th>Day 1-3</th>
<th>Day 7</th>
<th>Outcome</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambulatory and hospitalized women</td>
<td>12-24</td>
<td>24</td>
<td>Improvement, improved</td>
<td>[129]</td>
</tr>
<tr>
<td>Nursing home women</td>
<td>0-3</td>
<td>7</td>
<td>Improvement</td>
<td>[14]</td>
</tr>
<tr>
<td>Institutionalized women</td>
<td>0-3</td>
<td>7</td>
<td>Improvement</td>
<td>[14]</td>
</tr>
</tbody>
</table>
Management of ASB:
DON'T screen/treat

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening for, and treatment of, asymptomatic bacteriuria (2)</td>
<td></td>
</tr>
<tr>
<td>Recommendations against screening for, and treatment of, asymptomatic bacteriuria (2)</td>
<td></td>
</tr>
<tr>
<td>Screening for, and treatment of, asymptomatic bacteriuria is not recommended for:</td>
<td></td>
</tr>
<tr>
<td>1. Postmenopausal, nonpregnant women</td>
<td>A-I</td>
</tr>
<tr>
<td>2. Diabetic women</td>
<td>A-I</td>
</tr>
<tr>
<td>3. Older people living in the community</td>
<td>A-II</td>
</tr>
<tr>
<td>4. Elderly, institutionalized people</td>
<td>A-I</td>
</tr>
<tr>
<td>5. People with spinal cord injury</td>
<td>A-I</td>
</tr>
<tr>
<td>6. Patients with indwelling catheters</td>
<td>A-I</td>
</tr>
</tbody>
</table>


Diagnosis of "UTI" in LTC residents

- Applying standard criteria for surveillance, diagnosis, and treatment can help improve antibiotic use
- Several guidance documents for NH residents developed by ID/geriatrics consensus panels
  - McGeer criteria for surveillance (1991)
  - Loeb minimum criteria for antibiotic use (2001)
  - IDSA clinical practice guidelines for assessing fever and infection (2009)
  - Updated McGeer infection surveillance definitions (coming soon, Fall 2012)

Infection surveillance definitions for LTC: McGeer criteria

- First published infection surveillance definitions for LTC
  - Consensus definitions lead by a Canadian researcher, Allison McGeer in the early 1990's
  - Adapted from CDC hospital infection surveillance definitions by a group of experts in the field
Guidelines for Infection diagnosis and management in LTCF

Clinical Practice Guideline for the Evaluation of Fever and Infection in Older Adult Residents of Long-Term Care Facilities, 2009 Update. By the Infectious Diseases Society of America

Infect Control Hosp Epidemiol 2001; 22:120-124

Updated Infection surveillance definitions for LTC: Coming soon

- Three year project, co-led by CDC and SHEA Long-term care interest group, to update the infection surveillance definitions for LTC
- Revisions based on a structured review of evidence and consensus opinion of experts in the field
- Significant changes to criteria for UTI and Respiratory tract infection; Added new definitions for norovirus gastroenteritis and C. difficile infection
- Endorsed by multiple LTC and infection prevention partners including APIC
- In press at the journal Infection Control and Hospital Epidemiology with planned release in September 2012

Prevention Strategies:
Inter-facility Communication

- Mechanism for communicating MDRO carriage and other risk factors at time of transfer between facilities
- Critical components:
  - MDRO history of current infection or carriage
  - Device utilization
  - Current antibiotic treatments (indication/duration)
  - Bedside care issues (wounds, continence, etc)
Antibiotic Stewardship: Keys for Success

- Identify a Physician and Nurse Champions
  - Must be influential among peers
- Enlist support from leadership
- Tailor efforts to address local problems
- Include residents and family in educational efforts around antibiotic stewardship
- Identify outcome measurements to track impact
  - Examples: Antibiotic costs, adverse side effects, C difficile rates

http://www.cdc.gov/getsmart/healthcare/improve-efforts/keys.html

Antibiotic Stewardship

- Careful antibiotic use is a critical component in the control of MDROs
- Know the frequency/indications for antibiotic use by medical providers in your facility
  - Apply criteria to assess utilization in a standard way
- Develop mechanisms for communicating rationale and plan for antibiotic courses when person leaves your facility
  - Ensure documentation of drug, indication and duration is available

Thank you!!

Email: nstone@cdc.gov with questions/comments

For more information please contact Centers for Disease Control and Prevention

For more information please contact Centers for Disease Control and Prevention

Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov Web: www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

National Center for Emerging and Zoonotic Infectious Diseases
Division of Healthcare Quality Promotion