Prudent Use of Antibiotics in Long Term Care Residents with Suspected UTI

Shira Doron, MD
Assistant Professor of Medicine
Division of Geographic Medicine and Infectious Diseases
Tufts Medical Center
Boston, MA

Consultant to Massachusetts Partnership Collaborative:
Improving Antibiotic Stewardship for UTI
Antibiotics in Long Term Care: why do we care?

• Antibiotics are among the most commonly prescribed classes of medications in long-term care facilities

• Up to 70% of residents in long-term care facilities per year receive an antibiotic

• It is estimated that between $38 million and $137 million are spent each year on antibiotics for long-term care residents

• As much as half of antibiotic use in long term care may be inappropriate or unnecessary
The importance of prudent use of antibiotics

![Increase in Antibiotic Resistance](image)

- MRSA
- VRE
- FQRCP
Bad Bugs No Drugs

DECLINING ANTIBACTERIAL APPROVALS (PAST 25 YEARS)

1983-1987: 16
1988-1992: 14
1993-1997: 10
1998-2002: 6
2003-2007: 2
2008-2009: 1

Spellberg, CID 2004, Modified
The drug development pipeline for antibacterials
• 12 studies in North America:
  – 1.8-13.5 infections per 1000 resident-care days
  – Rate of death from infection 0.04-0.71 per 1000 resident-care days
The burden of infection in long-term care

27,000 nursing home residents have antibiotic-resistant infections \(^1\)

2 out of 3 nursing home residents receive at least one course of antibiotics annually \(^2\)

250,000 nursing home residents have infections \(^3\)

1.6 million people live in nursing homes \(^4\)

\(^1\) Centers for Medicare and Medicaid Services, Long Term Care Minimum Data Set, Resident profile table as of 05/02/2005, Baltimore, MD.


\(^3\) Centers for Disease Control and Prevention, National Center for Health statistics, 1999 National Nursing Home Survey. Nursing Home Residents, number, percent distribution, and rate per 10,000, by age at interview, according to sex, race, and region: United States, 1999.
Antibiotic resistance in long-term care is associated with:
- Increased risk of hospitalization
- Increased cost of treatments
- Increased risk of death
Appropriate initial antibiotic while improving patient outcomes and healthcare

Unnecessary Antibiotics, adverse patient outcomes and increased cost

A Balancing Act
What is Antimicrobial Stewardship?

• Antimicrobial stewardship involves the **optimal selection, dose and duration** of an antibiotic resulting in the cure or prevention of infection with **minimal unintended consequences** to the patient including emergence of resistance, adverse drug events, and cost.

Ultimate goal is improved patient care and healthcare outcomes

Dellit TH, et al. CID 2007;44:159-77,
Why focus on long term care?

- Many long-term care residents are colonized with bacteria that live in an on the patient without causing harm
- Protocols are not readily available or consistently used to distinguish between colonization and true infection
- So, patients are regularly treated for infection when they have none
  - 30-50% of elderly long-term care residents have a positive urine culture in the absence of infection
Why focus on long term care?

• When patients are transferred from acute to long-term care, potential for miscommunication can lead to inappropriate antibiotic use.

• Elderly or debilitated long-term care residents are at particularly high risk for complications due to the adverse effects of antibiotics, including *Clostridium difficile* infection.
Antibiotic misuse adversely impacts patients

Getting an antibiotic increases a patient’s chance of becoming colonized or infected with a resistant organism.
Association of vancomycin use with resistance

(JID 1999;179:163)
Annual prevalence of imipenem resistance in *P. aeruginosa* vs. carbapenem use rate

\[ r = 0.41, \ p = .004 \]
(Pearson correlation coefficient)

45 LTACHs, 2002-03 (59 LTACH years)

Gould et al. ICHE 2006;27:923-5
Case

- An 82-year-old long-term care resident has fever and a productive cough
- He has no urinary or other symptoms, and a chronic venous stasis ulcer on the lower extremity is unchanged
- A “pan-culture” is initiated in which urine is sent for UA and culture, sputum and blood are sent for culture, and the ulcer on the leg is swabbed.
• A CXR is done and is negative
• The urinalysis has 3 white blood cells
• Urine culture is positive for >100,000 CFU of E coli
• Sputum gram stain has no PMNs, no organisms
• Sputum grows 1+ Candida albicans
• Wound culture grows VRE
• The patient is started on cipro for the E coli in the urine, linezolid for the VRE in the wound, and fluconazole for the Candida in the sputum

• Two weeks later the patient has diarrhea and *C. diff* toxin assay is positive
• The only infection this patient ever had was a viral URI
Colonized or Infected: What is the Difference?

• People who carry bacteria or fungi without evidence of infection are **colonized**

• If an infection develops, it is usually from bacteria or fungi that colonize patients

• Bacteria or fungi that colonize patients can be transmitted from one patient to another by the hands of healthcare workers

• There is no need to treat for colonization
The Iceberg Effect

Infected

Colonized
What could have been done differently?

• Understanding the difference between colonization and infection
  – No (or few) WBCs in a UA= no UTI
  – In the absence of dyspnea, hypoxia and CXR changes, pneumonia is unlikely
  – Candida is an exceedingly rare cause of pneumonia
  – Wounds will grow organisms when cultured-infection can only be determined clinically
10 clinical situations in long term care in which antibiotics are often prescribed but rarely necessary

Khandelwal et al. Annals of Long Term Care 2012: 20 (4)
Urinary tract conditions

1. Positive urine culture in an asymptomatic patient
2. Urinalysis or culture for cloudy or malodorous urine
3. Non-specific symptoms or signs not referable to the urinary tract
– 4. Upper respiratory tract conditions
– 5. Bronchitis absent of COPD
– 6. Suspected or proven influenza without a secondary infection
– 7. Respiratory symptoms in a terminal patient with dementia
Skin wounds

- 8. Skin wounds without cellulitis, sepsis or osteomyelitis
- 9. Small localized abscess without significant cellulitis
- 10. Decubitus ulcer in a terminal patient
UTIs in Long Term Care Residents
Microbiology in Nursing Homes

- New Haven, CT
- 5 Nursing Homes May 2005-2007
- 551 patients, presumed UTI

Antimicrobial Susceptibilities from Nursing Home Residents in New Haven, CT

Antibiogram

- Helps to determine best choices for empiric therapy

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<tr>
<th>JANUARY - DECEMBER 2010</th>
<th>AMPICILLIN</th>
<th>CEPFEPIME</th>
<th>CEFTRIAXONE</th>
<th>CEFAZOLIN</th>
<th>CIPROFLOXACIN</th>
<th>GENTAMICIN</th>
<th>IMIPENEM</th>
<th>LEVOFLOXACIN</th>
<th>MEROPENEM</th>
<th>NITROFURANTOIN*</th>
<th>PIP/TAZO</th>
<th>TRIM/SULFA</th>
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na = not applicable

*NITROFURANTOIN reported only on urinary isolates
Antimicrobial Prescribing

Empiric

• Initial administration of an antibiotic regimen
  – Goal: improve outcome while minimizing potential to promote resistance

Defined or Targeted

• Modification of antimicrobial therapy once the cause of infection is identified.
  – Goal: select the narrowest spectrum agent possible

• Therapy may also be discontinued if the diagnosis of infection becomes unlikely.
Targeting, de-escalating and discontinuing antibiotics

• The empiric regimen is very often NOT the regimen that should be continued for the full treatment course

• GET CULTURES and use the data to target therapy using the most narrow spectrum agent possible.

• Take an “Antibiotic Time Out” – reassess after 48-72 hours
Culture Data

Collect date: 04/15/12 08:35
Result Date: 04/17/12 09:33

SPECIMEN DESCRIPTION : URINE CLEAN CATCH/MIDSTREAM

CULTURE : >100,000 COL/ML ESCHERICHIA COLI

ORGANISM >100,000 COL/ML ESCHERICHIA COLI

AMPICILLIN RESISTANT
AMPICILLIN/SULBACTAM INTERMEDIATE
AMOXICILLIN/CLAVULAN SUSCEPTIBLE
CEFAZOLIN SUSCEPTIBLE
CEFEPIME SUSCEPTIBLE
CEFTRIAXONE SUSCEPTIBLE
CIPROFLOXACIN SUSCEPTIBLE
ERTAPENEM SUSCEPTIBLE
GENTAMICIN SUSCEPTIBLE
LEVOFLOXACIN SUSCEPTIBLE
MEROPENEM SUSCEPTIBLE
NITROFURANTOIN SUSCEPTIBLE
PIPERACILLIN/TAZOBAC SUSCEPTIBLE
TRIMETH/SULFAMETHOX SUSCEPTIBLE
TETRACYCLINE SUSCEPTIBLE
Choosing the perfect antibiotic…

• Empiric:
  – Needs to get into urinary tract
    • And sometimes the prostate
  – Patient’s microbiology and antibiotic history
  – Minimize adverse effects
    • Other medical problems (renal insufficiency, *C. diff*, etc)
  – Avoid drug interactions
  – Allergy
  – Threshold for failure
  – Antibiogram
Choosing the perfect antibiotic…

• Targeted
  – Treat specific organism
  – Narrowest spectrum possible
  – Compliance
  – Cost
  – Oral option?
Recommendations from the Guidelines

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

Lindsay E. Nicod, Suzanne Bradley, Richar

SUMMARY OF RECOMMENDATIONS
1. The diagnosis of asymptomatic bacteriuria is based on results of culture of a urine sample collected in a manner that minimizes contamination (table 1).
   - For asymptomatic women, bacteriuria as 2 consecutive voided urine specimens with an identical bacterial strain is considered positive (B-II).
   - A single, clean-catch voided urine specimen with 1 bacterial species isolated in a quantitative concentration of ≥10^5 CFU/mL identifies bacteriuria if it is positive (B-II).
   - A single catheterized urine specimen with 1 bacterial species isolated in a quantitative concentration of ≥10^5 CFU/mL identifies bacteriuria in men (A-II).
2. Pyuria accompanying asymptomatic bacteriuria is not an indication for antimicrobial treatment.
3. Pregnant women should be screened for asymptomatic bacteriuria at least once in early pregnancy and should be treated if the results are positive (A-I).
4. The duration of antimicrobial therapy is not specified.

International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women: A 2010 Update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases

Kolpana Gupta, Thomas M. Hooton, Kurt G. Naber, Bjar

Gregory J. Moran, Lindsay E. Nicod, Paul Raz

A Panel of International Experts was convened by the European Society for Microbiology and Infectious Diseases (ESMoC) to update the 1999 Uncomplicated Urinary Tract Infection Guideline. The focus of this work is to provide recommendations for the diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America.

Uncomplicated UTI: Lower Tract

Can one of the recommended antimicrobials* below be used considering:
Availability
Allergy history
Tolerance

- Nitrofurantoin monohydrate/macrodystals 100 mg bid X 5 days
  (avoid if early pyelonephritis suspected)

- Trimethoprim-sulfamethoxazole 160/800 mg (one DS tablet) bid X 3 days
  (avoid if resistance prevalence is known to exceed 20% or if used for UTI in previous 3 months)

- Fosfomycin trometamol 3 gm single dose
  (lower efficacy than some other recommended agents; avoid if early pyelonephritis suspected)

- Pivmecillinam 400 mg bid X 5 days
  (lower efficacy than some other recommended agents; avoid if early pyelonephritis suspected)

*The choice between these agents should be individualized and based on patient allergy and compliance history, local practice patterns, local community resistance prevalence, availability, cost, and patient and provider threshold for failure (see Table 4)

Fluoroquinolones
(resistance prevalence high in some areas)

OR

β-lactams
(avoid ampicillin or amoxicillin alone; lower efficacy than other available agents; requires close follow-up)

Prescribe a recommended antimicrobial

Gupta K et al. Clinical Infectious Diseases 2011;52(5):e103-120.
Nitrofurantoin (Macrobid, Macrodantin)

- **DRUG INTERACTIONS**
  - Minimal
  - Concomitant administration of a magnesium trisilicate antacid may decrease the absorption of nitrofurantoin
  - Nitrofurantoin may reduce the effect of quinolone antibiotics
  - Fluconazole: increased risk of pulmonary and hepatic toxicity

- Not for systemic infection
- Avoid if creatinine clearance less than 60
  - Due to potentiation of adverse effects
- Common side effects: nausea, headache
- Other serious adverse effects:
  - Peripheral neuropathy
  - Pulmonary hypersensitivity
  - Hepatotoxicity
  - Decreased renal function
  - Hemolytic anemia
Fosfomycin

- Minimal resistance
- Minimal collateral damage
- High urinary levels
- Prolonged bactericidal effect
- Minimal drug interactions
- Not always available
- Susceptibility data not routinely available
- Role for treatment of resistant organisms such as ESBLs, VRE, MRSA
- May be less effective than other short-course regimens
- Not for systemic infections
Trimethoprim/Sulfamethoxazole
TMP/SMX (Bactrim)

- **DRUG INTERACTIONS**
  - Warfarin
  - Methotrexate
  - Fluconazole (incr QT)
  - TCA, antipsychotics, antiarrhythmics
  - Antihyperglycemics

- Common side effects: nausea, vomiting, rash

- Other serious adverse effects:
  - Bone marrow suppression
  - Hepatic necrosis
  - Severe rash
  - Hyperkalemia
  - Hypoglycemia (esp with renal and liver disease)

- Increased creatinine…may be falsely elevated
Quinolones: Ciprofloxacin and Levofloxacin

- Highly efficacious in a 3-day regimen
- Numerous issues with collateral damage: *C. difficile* and resistance
- Save for other uses
- Black Box Warning: tendonitis/tendon rupture esp. over age 60, steroids, transplant

- Interactions:
  - calcium, aluminum, magnesium, iron, and zinc (antacids, nutritional supplements, multivitamin and mineral supplements), sucralfate
  - Warfarin
  - Antihyperglycemics

- Other issues:
  - QT prolongation esp. in elderly
  - Decreased seizure threshold
Alternatives

- Amoxicillin-clavulanate
- Cefdinir (Omnicef)
- Cefpodoxime-proxetil (Vantin)
- Cefaclor (Ceclor)

- Not for **empiric** therapy due to poor efficacy and resistance: amoxicillin and ampicillin
Alternatives to antibiotics

• Fluids to promote a dilute urine flow
• Topical estrogen
  – In some postmenopausal women it can normalize the vaginal flora and reduce recurrent UTI
• Methenamine
• Adhesion blockers (D-mannose)
  – Not evaluated in clinical trials
• Drinking cranberry juice or cranberry tablets
  – Clinical Data Cochrane Review 2008
  – Recent studies
  – Pilot Study in LTC
Take Home Points

• Antibiotics are a shared resource… and becoming a scare resource
• Appropriate antibiotic use is a patient safety priority
• Know the difference between colonization and infection
• To combat resistance: Think globally, act locally