Appropriate Treatment of Common Infections in Primary Care

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Consulting Specialist, Acute Communicable Disease Control at the LA County Department of Public Health
“Antimicrobial stewardship is defined as a formalized program that provides advice, consent, and institutional guidance on appropriate selection, dosing, route and duration of antimicrobial usage.”
Outline

• Urinary Infections
  • Appropriate Selection of Antibiotics
  • Appropriate Duration of Antibiotics

• Respiratory Infections
  • Big Data can improve outcomes
UTI

Among 20-40 yo women, 35% have had a UTI

- 1.8 - 6.1 days of symptoms
- 0.6 - 1.2 days of missed work or classes
- 0.4 - 0.6 days in bed

US Expenditures

Women ($2.5B)  
Men ($1B)

UTI’s: Pathogenesis

Colonization of GI tract

- Vagina
- Periurethral
- Bladder

Hooton TM et al. *NEJM* 1996;335:468-474
Sobel JD et al. *Inf Dis Clin N Am* 1997; 11:531-47
Case #1

22 year old female presents with a chief complaint of burning when she pees. She reports frequency and urgency. No fever, no systemic symptoms. No CVA tenderness.
Cystitis

Symptoms from a Lower Tract Infection Result from Inflammation of the Bladder and Urethra

- Frequency, Urgency
- Pain
- Burning ("Ardor")
- Hematuria
Case #1

A: 22 year old female with cystitis, but no systemic symptoms. Physical Exam is unremarkable. UA is positive for LE and Nitrites, Umicro shows 15 WBC and 7 RBC.
P: No Culture Needed, Treat Empirically

Trimethoprim/Sulfamethoxazole po BID x 3 Days
• Wait ... Did this Guy Just Say Trimethoprim/Sulfamethoxazole?

• ...Is He Crazy?
IDSA Guidelines: Uncomplicated UTIs

• First Line Therapy
  • TMP-SMX DS BID x 3 Days
  • Nitrofurantoin 100mg BID x 5 Days
  • Fosfomycin 3 grams PO x 1 dose
  • Pivmecillinam – Not available in US

• Second Line Therapy
  • Fluoroquinolones -- Collateral Damage
  • β-lactams -- Less likely to be effective

Gupta K et al. Clin Infect Dis 2011:52:e103-120
Fluroquinolone Resistance is Here

**Figure 4**
Annual rates of *Enterobacteriaceae* co-resistant to fluoroquinolones and third-generation cephalosporins, Spain, 1999–2010

- **Enterobacter spp.**
- **Escherichia coli**
- **Klebsiella pneumoniae**

<table>
<thead>
<tr>
<th>Year of the survey</th>
<th>Percentage of co-resistant infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999</td>
<td>2.0</td>
</tr>
<tr>
<td>2000</td>
<td>4.0</td>
</tr>
<tr>
<td>2001</td>
<td>6.0</td>
</tr>
<tr>
<td>2002</td>
<td>8.0</td>
</tr>
<tr>
<td>2003</td>
<td>10.0</td>
</tr>
<tr>
<td>2004</td>
<td>12.0</td>
</tr>
<tr>
<td>2005</td>
<td>14.0</td>
</tr>
<tr>
<td>2006</td>
<td>16.0</td>
</tr>
<tr>
<td>2007</td>
<td>14.0</td>
</tr>
<tr>
<td>2008</td>
<td>12.0</td>
</tr>
<tr>
<td>2009</td>
<td>10.0</td>
</tr>
<tr>
<td>2010</td>
<td>8.0</td>
</tr>
</tbody>
</table>
The FDA first added a Boxed Warning to fluoroquinolones in July 2008 for the increased risk of tendinitis and tendon rupture. In February 2011, the risk of worsening symptoms for those with myasthenia gravis was added to the Boxed Warning. In August 2013, the agency required updates to the labels to describe the potential for irreversible peripheral neuropathy (serious nerve damage).

In November 2015, an FDA Advisory Committee discussed the risks and benefits of fluoroquinolones for the treatment of acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis and uncomplicated urinary tract infections based on new safety information. The new information focused on two or more side effects occurring at the same time and causing the potential for irreversible impairment. The advisory committee concluded that the serious risks associated with the use of fluoroquinolones for these types of uncomplicated infections generally outweighed the benefits for patients with other treatment options.

Today’s action also follows a May 12, 2016, drug safety communication advising that fluoroquinolones should be reserved for these conditions only when there are no other options available due to potentially permanent, disabling side effects occurring together. The drug safety communication also announced the required labeling updates to reflect this new safety information.
FDA Black Box Warning For

• Sinusitis

• COPD Exacerbation

• Uncomplicated Urinary Tract Infections
FQ Serious Adverse Effects

• Photosensitivity
• Hypersensitivity
• QT prolongation
• Peripheral neuropathy
• Tendinitis or tendon rupture
• CNS effects
• Myasthenia gravis exacerbation
Examining Fluoroquinolone Use through the Lens of Antimicrobial Stewardship

James A. McKinnell, M. D.
Case #2

22 year old female reports five days of frequency, urgency, and burning. Today, she reports back pain, fever, and emesis.
Pyelonephritis

Fevers, Chills, Nausea

Costovertebral-Angle Tenderness

Suppurative Necrosis of the Kidney
Case #2

A: 22 year old female with pyelonephritis evidenced by cystitis with systemic symptoms, CVA tenderness, positive LE and Nitrites.

P: Obtain Urine Culture and Initiate Empiric Antibiotics while awaiting Urine Culture Results

Trimethoprim/Sulfamethoxazole po BID x 7 Days
• Wait ... Did this Guy Just Say Seven Days for Pyelonephritis?

• ...Is He Crazy?
One Third of What You Learned in Medical School is Wrong…

The Trick is Figuring Out Which Third
• Several RCTs 5-7 days equal to 10-14 days

• Short course effective despite diabetes and GNB bacteremia

Community Associated Pneumonia

3-5 Days

- Multiple RCT showing 3-5 days NI to 7 - 10 days
- Includes pts with PORT IV and V
  (Uranga et al. JAMA IM)
- Reduced emergence of resistance

CELLULITIS/ABSCESS
5 DAYS

• Numerous trials show that 5-7 equal to 10-14 days

• Drainage of abscess is key

• When you drain and abscess, treat with antibiotics.

AECB/COPD
3-5 DAYS

• Dozens of Studies

• Meta-analysis show that 3-5 days of therapy equal to 7 or more days.

El Moussaoui 2008 Thorax 68:415-22
## Short Course Therapy!!!!

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Short (d)</th>
<th>Long (d)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAP</td>
<td>3 or 5</td>
<td>7, 8, or 10</td>
<td>Equal</td>
</tr>
<tr>
<td>HAP</td>
<td>7</td>
<td>10-15</td>
<td>Equal</td>
</tr>
<tr>
<td>VAP</td>
<td>8</td>
<td>15</td>
<td>Equal</td>
</tr>
<tr>
<td>Pyelo</td>
<td>7 or 5</td>
<td>14 or 10</td>
<td>Equal</td>
</tr>
<tr>
<td>Intra-abd</td>
<td>4</td>
<td>10</td>
<td>Equal</td>
</tr>
<tr>
<td>AECB</td>
<td>≤5</td>
<td>≥7</td>
<td>Equal</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>5-6</td>
<td>10</td>
<td>Equal</td>
</tr>
<tr>
<td>Osteo</td>
<td>42</td>
<td>84</td>
<td>Equal</td>
</tr>
</tbody>
</table>
Colonization or Infection?
One of the most dangerous results in modern medicine is a positive urine culture.

A positive culture is not the same as an infection
The diagnosis of a UTI requires Symptoms!
“Doctor, I’m calling you to let you know that the Urine Culture for HR Is Positive.”

“Read me the sensitivities.”

“Levofloxacin 500 mg po daily x 10 days.”
Table 2. Prevalence of asymptomatic bacteriuria in selected populations.

<table>
<thead>
<tr>
<th>Population</th>
<th>Prevalence, %</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy, premenopausal women</td>
<td>1.0–5.0</td>
<td>[31]</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>1.9–9.5</td>
<td>[31]</td>
</tr>
<tr>
<td>Postmenopausal women aged 50–70 years</td>
<td>2.8–8.6</td>
<td>[31]</td>
</tr>
<tr>
<td>Diabetic patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>9.0–27</td>
<td>[32]</td>
</tr>
<tr>
<td>Men</td>
<td>0.7–11</td>
<td>[32]</td>
</tr>
<tr>
<td>Elderly persons in the community(^a)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>10.8–16</td>
<td>[31]</td>
</tr>
<tr>
<td>Men</td>
<td>3.6–19</td>
<td>[31]</td>
</tr>
<tr>
<td>Elderly persons in a long-term care facility</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>25–50</td>
<td>[27]</td>
</tr>
<tr>
<td>Men</td>
<td>15–40</td>
<td>[27]</td>
</tr>
<tr>
<td>Patients with spinal cord injuries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermittent catheter use</td>
<td>23–89</td>
<td>[33]</td>
</tr>
<tr>
<td>Sphincterotomy and condom catheter in place</td>
<td>57</td>
<td>[34]</td>
</tr>
<tr>
<td>Patients undergoing hemodialysis</td>
<td>28</td>
<td>[28]</td>
</tr>
<tr>
<td>Patients with indwelling catheter use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-term</td>
<td>9–23</td>
<td>[35]</td>
</tr>
<tr>
<td>Long-term</td>
<td>100</td>
<td>[22]</td>
</tr>
</tbody>
</table>

\(^a\) Age, ≥70 years.
## Prospective Randomized Studies
### Treatment vs. No Treatment ASB

<table>
<thead>
<tr>
<th>Authors</th>
<th>Subjects</th>
<th>Intervention</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicolle LE, et al. NEJM</td>
<td>Men, NH, median age 80</td>
<td>Treated 16</td>
<td>No difference mortality or infectious morbidity 2 groups</td>
</tr>
<tr>
<td>1983;309:1420-5</td>
<td></td>
<td>Not treated 20</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Duration 2 years</td>
<td></td>
</tr>
<tr>
<td>1987;83:27-33</td>
<td></td>
<td>Not treated 24</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Duration 1 year</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>No difference mortality/GU</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>morbidity. Increase drug</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>reactions and AB resistance</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>treated group.</td>
<td></td>
</tr>
<tr>
<td>Abrutyn E, et al. Ann Intern</td>
<td>Women, ambulatory and NH</td>
<td>Treated 192</td>
<td>No survival benefit from treatment</td>
</tr>
<tr>
<td>Med 1994;120:827-33</td>
<td>Mean age 82</td>
<td>Not treated 166</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Duration 8 years</td>
<td></td>
</tr>
<tr>
<td>Ouslander JG Ann Intern Med</td>
<td>Women and men NH Mean age 85</td>
<td>Treated 33</td>
<td>No difference chronic urinary incontinence</td>
</tr>
<tr>
<td>1995;122:749-54</td>
<td></td>
<td>Not treated 38</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Duration 4 weeks</td>
<td></td>
</tr>
</tbody>
</table>
Proportion of Women with Diabetes Who Remained Free of Symptomatic Urinary Tract Infection, According to Whether They Received Antimicrobial Therapy or Placebo at Enrollment.

Outline

• Urinary Infections
  • Appropriate Selection of Antibiotics

• Appropriate Duration of Antibiotics
Resources for Antibiotic Selection

- Sanford Guide

- Project Aware (California Medical Foundation)

- ID Physicians

(Yes, I’ll take questions afterwards)
“Does Education Alone Change Provider Behavior?”
Effect of Behavioral Interventions on Inappropriate Antibiotic Prescribing Among Primary Care Practices
A Randomized Clinical Trial

Daniella Meeker, PhD; Jeffrey A. Linder, MD, MPH; Craig R. Fox, PhD; Mark W. Friedberg, MD, MPP;
Stephen D. Persell, MD, MPH; Noah J. Goldstein, PhD; Tara K. Knight, PhD; Joel W. Hay, PhD; Jason N. Doctor, PhD
Behavioral Interventions are Key!!!
Bill

48 year old male with no past medical history complaining of persistent cough x 2 weeks. Still able to perform ADLs, though cough is “annoying” and “Going on Forever”. “I need antibiotics”

T:98.6  P:116/62  R: 14  S:92%

CXR is Clear

•No Acute Distress

•Scattered Rhonchi
Acute URI - Bronchitis

- Cough --- by definition - 5 days
  1-3 week duration, mean 18 days

- Viruses represent about 60% of Acute Bronchitis

- Bacteria represent about 6% of Acute Bronchitis

- Sputum production can be seen with viral infections

UTDOL. “Acute Bronchitis in Adults” Accessed 2/7/2019
• “CDC, American College of Physicians, National Health Services of the UK, all recommend against treating acute bronchitis with antibiotics.”

• Among otherwise healthy individuals, antibiotics have not demonstrated any consistent benefit in the symptomatology or natural history of acute bronchitis.

• Healthcare Effectiveness Data and Information Set for NCQA and National Quality Forum quality measure.

• In Real World Clinical Practice, Bronchitis and Cough can be fairly complex and may actually be a wobbler for when you might need antibiotics.

UTDOL. “Acute Bronchitis in Adults” Accessed 2/7/2019
Acute URI - Do Not Treat

• Early in the Course of a Clear Viral Syndrome

• Post Nasal Drip - Allergic Rhinitis or Viral

• Sore Throat - Viral

• Undiagnosed Asthma - 65% of patients with two or more episodes of bronchitis in a 5 year period have mild asthma that has simply not been diagnosed

• CHF, PE, GERD

Acute URI - Bronchitis --- TREAT

• Acute Exacerbation of COPD - Absolutely Treat!

• Fever, Tachycardia, Tachypnea - Admit to Hospital?

• Post viral Complication

• Non-Healthy Adults: Immunosuppressed Patients, *Streptococcus* infection, mycobacterial infections, cystic fibrosis, diseases of the spleen, Crohn’s disease, bacterial pneumonia - Maybe Treat
LADPH TAP OUT Program

• Initiative from the LAC DPH to help support Antimicrobial Stewardship Activities

• Specifically targeting inappropriate prescribing for Bronchitis, acute URI
LA DPH TAP OUT Program

EHR extracted for encounters with URI ICD-10 codes

Encounters excluded if have comorbidity, immunosuppressed

Overall and individual rates calculated

For Example:
• Bronchitis (J20)
• URI (J069)
• Influenza (J10)
• Nasopharyngitis (J00)
• Allergic Rhinitis (J30)
• Cough (R05)

For Example:
• COPD (J44)
• Immunosuppressed
• Streptococcus (B95)
• Disease of spleen (D73)
• Bacterial pneumonia (J15)
• Crohn’s disease (K50)

Baseline results

• October 1, 2016 through March 31, 2017
• 4,651 Total number encounters
  • Cough (2488)
  • Acute upper respiratory infection, unspecified (382)
  • Allergic rhinitis, unspecified (380)

• 615 Encounters (13%) Resulted in an Antibiotic Prescription
  • Cough (487)
  • Bronchitis (89)
  • Acute upper respiratory infection, unspecified (46)
Baseline Utilization was Low!!!

![Graph showing baseline utilization comparison over days relative to intervention start. The graph indicates a decrease in utilization over time, with the peer comparison group showing a steeper decline compared to the control group.](image)
Histogram of internal medicine provider antibiotic prescribing rate for acute URI, October 2016-March 2017

Antibiotic prescribing rate for acute URI (%)

Number of providers

0 1-10 11-20 21-30 31+

58 25 20 6 11
LA County DPH
Tap Out Program Components

- Public commitment posters in waiting areas
- Communication skills training
- Clinical education on treatment guidelines
- Monthly peer comparison reports emailed to each provider
Commitment Poster’s and Guidelines

When do you need antibiotics?

**You NEED antibiotics if you have ...**
- Whooping Cough
- Strep Throat
- Urinary Tract Infection

**You DON’T need antibiotics if you have ...**
- Cold/Runny Nose
- Bronchitis/Chest Cold
- Fluid in the Middle Ear
- Flu
- Sore Throat

Antibiotics only fight infections caused by bacteria and will not relieve symptoms caused by a viral infection, such as a cold or flu. Unneeded antibiotics can cause diarrhea, rashes or yeast infections and make future infections more difficult to treat.

As your healthcare provider, we are dedicated to practicing safe and effective antibiotic use. Ask us about alternative treatment plans.
Tap Out Program Components

- Public commitment posters in waiting areas
- Communication skills training
- Clinical education on treatment guidelines
- Monthly peer comparison reports emailed to each provider
Communication Skills Training

The Primary Care Office Visit: Antibiotics

Play as a Patient
Talk to a virtual physician and learn about the proper use of antibiotics, how to make sure you get answers to your questions, and leave the office with a plan that works for you.

Play as a Physician
Talk to a virtual patient and see how well you do in building trust, collaborating on a treatment plan, and addressing the patient's request for antibiotics.

Created by Kognito with the generous support of the Robert Wood Johnson Foundation
Tap Out Program Components

- Public commitment posters in waiting areas
- Communication skills training
- Clinical education on treatment guidelines
- Monthly peer comparison reports emailed to each provider
Peer Comparison

February 16, 2018;

Dear,

Below you will find data regarding your antibiotic prescribing practices for acute viral respiratory infections. You are a top performer for the period of January 2018, compared to your peers in Cedars-Sinai Medical Group primary care. Based on your recent activity, you wrote 0 prescriptions out of 23 acute upper respiratory infection cases that did not warrant antibiotics. These data are based on documentation in CS-Link.

Antibiotic Prescribing Rate for January 2018

| Rate of Top Performing Prescribers | 0 |
| Rate of all Prescribers in CSMG | 5.7 |
| Your Percent | 0 |

Your prescribing rate depends on the number of antibiotics dispensed for eligible patients with visits to your practice. Eligible patients are those who have a diagnosis of a respiratory illness that is generally non-bacterial in nature.

• Began sending peer comparison reports in October
Peer Comparison

The graph below shows how your current performance compares to your performance during the baseline period, which is the entire cold/flu season last year (October 2016 through March 2017). You can also see how your baseline and current performance compare to all primary care prescribers in the Cedars-Sinai Medical Group.

Antibiotic Prescribing Rate, by Month, Compared to Baseline Period

- Began sending peer comparison reports in October

Acute upper respiratory infection treatment guidelines can be found at:
http://www.thecmafoundation.org/Portals/0/assets/docs/Physician-Resources/AWARE/compendium-adult-2016-11x17-final-web.pdf?ver=2016-12-14-090913-470

If you would like to discuss any part of this feedback, please contact Hayden Lowenstein, MD, or Neel Joshi, MD (Co-Chairs, Infection Prevention Committee).
Tap Out Program Components

- Public commitment posters in waiting areas
- Communication skills training
- Clinical education on treatment guidelines
- Monthly peer comparison reports emailed to each provider
Over 45% Reduction in Inappropriate Use

ITS model of percent of URI encounters with antibiotics prescribed inappropriately by month, May 2016 - June 2018

<table>
<thead>
<tr>
<th>Period</th>
<th>Actual Encounters Inappropriately Prescribed Antibiotics</th>
<th>Model Encounters Inappropriately Prescribed Antibiotics</th>
<th>Percent change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (May’16-Oct’17)</td>
<td>1710/15056 (11.36)</td>
<td>658/10947 (6.00)</td>
<td>-47.2%</td>
</tr>
<tr>
<td>Intervention (Nov’17-Jun ’18)</td>
<td>658/10947 (6.00)</td>
<td>658/10947 (6.00)</td>
<td>-47.2%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IM</td>
<td>925/9212 (10.04)</td>
<td>386/6997 (5.52)</td>
<td>-45.0%</td>
</tr>
<tr>
<td>UC</td>
<td>785/5844 (13.43)</td>
<td>271/3950 (6.86)</td>
<td>-48.9%</td>
</tr>
</tbody>
</table>
Public Commitment Poster

• Helpful in communicating to patients
  18/21 (86%)

• Reinforced their commitment to prescribe appropriately
  11/21 (52%)
Communication Skills Training

- Only 7% completed the online communication skills training.
In Person Educational Sessions

- Useful in understanding stewardship or reinforcing existing knowledge
  12/21 (55%)
- Enhancing knowledge of antibiotic choice and duration
  7/21 (33%)
Peer Reports

- Monthly peer comparison reports were useful in understanding their prescribing habits (6.3 out of 10)

- Reactions ranged
  - Feeling proud of their prescribing rates (45%)
  - Realizing the rates could improve (35%)
  - Reviewing individual encounters (28%)
  - Useless (14%)
## Value of 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 myocardial infarction with aspirin or fibrinolytic drugs⁶* -3%

Thank you for your time...