Antibiotics and Duration

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Acute Communicable Disease Control Unit
Appreciation

- Brad Spellberg
- Phil Robinson
Disclosures

• I have received Government Research Funding from NIH, AHRQ, CDC, and CTSI

• I have served as a consultant for Achaogen, Allergan, Cempra, Science 37, Theravance, and ThermoFisher

• I have no commercial/financial relationships related to decolonization, CHG, mupirocin, or iodophor products
Disclosures

One Third of What you Learned in Medical School and Residency is Wrong .... The Trick is Learning Which Third!!
Objectives

- Understand the Value of Antibiotics
- Understand Where Current Durations of Antibiotics were developed
- Review Current Indications of Antibiotic Duration
## 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 Pneumonia</td>
<td>~35%</td>
<td>~10%</td>
<td>-25%</td>
</tr>
<tr>
<td>Hospital Pneumonia</td>
<td>~60%</td>
<td>~30%</td>
<td>-30%</td>
</tr>
<tr>
<td>Heart Infection</td>
<td>~100%</td>
<td>~25%</td>
<td>-75%</td>
</tr>
<tr>
<td>Brain Infection</td>
<td>&gt;80%</td>
<td>&lt;20%</td>
<td>-60%</td>
</tr>
<tr>
<td>Skin Infection</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 drugs*

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Inadequate antimicrobial therapy associated with higher mortality

Prospective study (n=2000: 655 with infections)
25% of patients received inadequate treatment

Prospective study (n=2000: 655 with infections)
25% of patients received inadequate treatment

Relationship between survival and time to effective antimicrobial treatment among patients with septic shock

“The more we use them, the more we lose them…”

By courtesy of Dr. Liselotte Diaz Högberg
“Make sure you take every dose of your prescribed antibiotic, even after you feel better.”
Antibiotic Duration as Football Scores

- Community Associated Pneumonia 7-10
- HAP/VAP 10-14
- Pyelonephritis 10-14
- Cellulitis 7-10
- Bacteremia 14-42
Standard Abx durations: 1-2 Constantine units—based on 1695 year old decree

In AD 321, Roman Emperor Constantine the Great codified that there would be 7 days in a week. Even in the modern era of evidence-based-medicine, this 1695-year-old decree remains a primary reference for duration of antibiotic therapy: it leads physicians to treat infections in intervals of 7 days. Thus, it is gratifying when clinical trials challenge the standard antibiotic duration of 7 to 14 days.

The New Antibiotic Mantra—“Shorter Is Better”

Brad Spellberg, MD

JAMA Internal Medicine
## Short Course Therapy!!!!

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Short (d)</th>
<th>Long (d)</th>
<th>Result</th>
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<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>(\leq 5)</td>
<td>(\geq 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>
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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

Several RCTs 7-8 days equal to 10-15 days

Reduced emergence of resistance

MRSA and Pseudomonas infections may require longer therapy

PYELONEPHRITIS
5-7 DAYS

• Several RCTs 5-7 days equal to 10-14 days
• Short course effective despite diabetes and GNB bacteremia

INTRA-ABDOMINAL INFECTION
4-5 DAYS

• Recent Trial 4 Days Equal to 10 days
• Assuming Adequate Source Control

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
CELLULITIS/ABSCESS
3-5 DAYS

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

• Drainage of abscess is key

• When you drain and abscess, treat especially if surrounding cellulitis.

EXCEPTIONS

• Short Course TB trials underway
• Chronic infections still require prolonged therapy - e.g. prosthetic hip infections
• Data on Endocarditis is evolving
• Rheumatic fever may require 5 days of cephalosporins but 10 days of penicillin - data not clear
# Short Course Therapy!!!!

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“The most viable strategy for reducing antimicrobial selective pressure is to treat infections only for as long as is necessary.”

Dr. Lou Rice, Executive Chair of Medicine, Warren Alpert School of Medicine of Brown University. 2008 Maxwell Finland Lecture at IDSA Annual Meeting
Longer Therapy Actually Hurts the Patient

- Longer therapy causes more selective pressure—off-target in microbiome and in the environment

- Even at the site of infection, studies of short vs. long-course therapy have found greater emergence of resistance with longer therapy (Chastre ‘03 JAMA 290:2588-9; Singh ‘00 Am J Resp Crit Care Med 162:505-11)
Fight the Errors of our Forebearers

- Stop telling patients to complete course of Abx even if their symptoms are gone
- Taking antibiotics after symptom resolution provides no efficacy but selects for resistant among microbiome
- If patients feel better, they should call their doctor to ask to stop early
LAC - DPH to the Rescue

Healthcare Associated Infection Antibiotic Resistance Control Task Force

Epidemiology, Infectious Disease Physicians, Infectious Disease Pharmacists, Microbiologists, Infection Prevention Specialists, and Others
Antibiotic Stewardship in Nursing Homes

4.1 MILLION
Americans are admitted to or reside in nursing homes during a year

UP TO 70%
of nursing home residents received antibiotics during a year

UP TO 75%
of antibiotics are prescribed incorrectly

CDC (http://www.cdc.gov/media/releases/2015/p0915-nursing-home-antibiotics.html)
New Requirements

• “By the end of 2017, CMS and CA require long-term care and nursing home facilities to develop and implement robust ASPs that adhere to best practices”
Basic ASP Tier Elements for SNFs: Less Challenging Components

1. Antimicrobial stewardship (AS) policy/procedure
2. Written statement in support of ASP with evidence for necessary budget/staffing
3. AS activities reported to facility’s Quality Assurance-Performance Improvement (QAPI) program.
4. Establish physician-supervised, multidisciplinary antimicrobial stewardship committee
Basic ASP Tier Elements for SNF: More Challenging Components

4. Program support from a physician or pharmacist with specific training on antimicrobial stewardship

5. AS education provided to nursing staff, medical staff, residents, and visitors
LA County Antimicrobial Resistance Network (ARN)

- Support acute care hospitals (ACHs) in engaging their network SNFs to meet upcoming ASP requirements
- Improve inter-facility communication to reduce spread of multidrug-resistant organisms (MDROs)
LA County Department of Public Health Antibiotic Resistance Network
UTI

Estimates for Outpatient UTI in the US in 1995:

- 11.3 million Rx with $1.6 Billion in costs

US Expenditures

25-35% women 20-40 y/o 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

GN Resistance

• **Fluroquinolone Resistance was High**
  Among E. Coli it was 32%

  TMP/SMX resistance not included

Nitrofurantoin resistance not included
<table>
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<tr>
<th>Description</th>
<th>Probability</th>
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<tr>
<td>TMP-SMX resistance</td>
<td>0.15</td>
</tr>
<tr>
<td>Fluoroquinolone resistance</td>
<td>0.025</td>
</tr>
<tr>
<td>Nitrofurantoin resistance</td>
<td>0.012</td>
</tr>
<tr>
<td>Clinical cure of TMP-SMX--resistant infection treated with TMP-SMX</td>
<td>0.55</td>
</tr>
<tr>
<td>Clinical cure of TMP-SMX--sensitive infection treated with TMP-SMX</td>
<td></td>
</tr>
<tr>
<td>Clinical cure of fluoroquinolone--resistant infection treated with</td>
<td>0.91</td>
</tr>
<tr>
<td>fluoroquinolone</td>
<td></td>
</tr>
<tr>
<td>Clinical cure of fluoroquinolone--sensitive infection treated with</td>
<td>0.78</td>
</tr>
<tr>
<td>fluoroquinolone</td>
<td></td>
</tr>
<tr>
<td>Clinical cure of nitrofurantoin--resistant infection treated with nitrofurantoin</td>
<td>0.94</td>
</tr>
<tr>
<td>Clinical cure of nitrofurantoin--sensitive infection treated with nitrofurantoin</td>
<td>0.67</td>
</tr>
<tr>
<td>Hospitalization for pyelonephritis</td>
<td>0.89</td>
</tr>
<tr>
<td>Pyelonephritis if initial empirical therapy unsuccessful</td>
<td>0.04</td>
</tr>
<tr>
<td>Vaginal yeast infection after ≤3 d of therapy</td>
<td>0.05</td>
</tr>
<tr>
<td>Vaginal yeast infection after &gt;3 d of therapy</td>
<td>0.07</td>
</tr>
<tr>
<td>Medical visit for vaginal yeast infection</td>
<td></td>
</tr>
<tr>
<td>Change of therapy due to lack of clinical response to TMP-SMX</td>
<td>0.25</td>
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<td>Change of therapy due to lack of clinical response to fluoroquinolone</td>
<td>0.75</td>
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<td>Change of therapy due to lack of clinical response to nitrofurantoin</td>
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LAC DPH Outpatient Stewardship Project

- LAC DPH Healthcare Outreach Unit is planning a multi-faceted intervention to improve provider prescribing in outpatient settings
- Intervention includes a core package:
  - Poster commitment
  - Treatment guidelines
  - Communication skills training
  - Additional strategies tailored to facility’s needs
LAC DPH Outpatient Stewardship Project, cont.

• Benefits to participation:
  • Tailored assistance in implementation of CDC Core Elements
  • Improved provider knowledge of resistance and appropriate prescribing for upper respiratory infections
  • Free resources to support providers in improving antibiotic prescribing
  • Increased coordination and exchange of antibiotic stewardship best practices
LAC DPH Outpatient Stewardship Project, cont.

- Seeking volunteer primary care clinics to participate
  - Ability to collect/report prescribing data
  - Identify stewardship champion in facility

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(213) 240-7941