Antimicrobial/Medication Stewardship and Prevention of 
*C. difficile* Infection

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Infectious Diseases Specialist  
Physician Lead, Infection Prevention and Control and Antimicrobial Stewardship  
*Lakeridge Health*
Disclosures

• Occasional speaking honoraria
• Some slides are repeated from previous presentations...
  – (And so I apologize for recycling jokes...)
Objectives

• Understand rationale for ASP
• Review evidence for ASP in CDI prevention
• Review other medications that should be used prudently
• Understand ways YOU can be an antimicrobial steward
Antimicrobial Stewardship: Definition

“Coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy, and route of administration.”

Policy Statement on Antimicrobial Stewardship by SHEA, IDSA, PIDS.
ICHE 2012; 33: 322-327
Antimicrobial Stewardship: Bottom Line

• Right drug
• Right dose
• Right time
• Right duration
• ....only when needed
Why Do We Need Antimicrobial Stewardship?

moxifloxacin IS CALLED A 'WONDER DRUG' BECAUSE ANY TIME THE DOCTOR WONDERS WHAT YOU'VE GOT, THAT'S WHAT YOU GET.
Evolution of Antimicrobial Prescriptions

- 2000 B.C.
  - “Here, eat this root.”
- 1000 A.D.
  - “This is not healthy. Here, say this prayer.”
- 1850 A.D
  - “That prayer is superstition. Drink this potion.”
- 1940 A.D
  - “That potion is poison. Here, take this penicillin. It is a miracle drug.”
- 1985 A.D.
  - “Penicillin is worthless. Here, take this new, bigger, better antibiotic.”
- 2012 A.D
  - “Those antibiotics don’t work anymore. Here, eat this root.”

Neil Fishman. SHEA Fellows’ Course 2011.
Antibiotic Utilization

• 30-50% of all hospitalized patients receive antibiotics
  – 70% of all ICU patients
• 30-50% of antimicrobial use is either unnecessary or inappropriate

Reimann, D’Ambola. JAMA 1968.
Antibiotic Utilization

• Overuse of antibiotics...
  – Increases adverse drug events
    • 5% of hospitalized patients who receive antibiotics experience an adverse event
  – Causes emergence of resistant bacteria
  – Contributes to rising cost of care
  – Resistant bacteria result in increase morbidity and mortality

Hidron et al Infect Control Hosp Epidemiol 2008;996-1011.
Global Risks 2013
Eighth Edition
The Dangers of Hubris on Human Health
The Dangers of Hubris on Human Health

“While viruses may capture more headlines, arguably the greatest risk of hubris to human health comes in the form of antibiotic-resistant bacteria. We live in a bacterial world where we will never be able to stay ahead of the mutation curve. A test of our resilience is how far behind the curve we allow ourselves to fall. “
Dramatic Drop in Development and Approval of Antimicrobial Agents

The discovery dates of distinct classes of antibiotics. No new classes have been discovered since 1987.
The Human Microbiome
Antimicrobial Stewardship: Bigger Picture

An Overview of Accreditation Canada’s Antimicrobial Stewardship ROP
Antimicrobial Stewardship Program (ASP)

PHO, in partnership with the Ontario Hospital Association, is developing an antimicrobial stewardship program (ASP) in Ontario. As of January 2013, all acute care hospitals undergoing accreditation must have an ASP in place in accordance with Accreditation Canada's Required Organizational Practices. There are any number of ways to initiate and sustain a stewardship program. How will you build your program? Share your story.

For more information email: asp@oahpp.ca.
Now the good stuff: *C. difficile*
C. difficile

- Antibiotic exposure is the single most important risk factor for the development of C. difficile infection
- ~85% of patients with CDI have antibiotic exposure in the 28 days before infection
- Crude CDI LOS 34 days vs. 8 days no CDI
  - HA-CDI increases median LOS ~6 days

Forster et al CMAJ 2011
Cumulative Antibiotic Exposures Over Time and the Risk of *Clostridium difficile* Infection

Vanessa Stevens,¹ ³ ⁴ Ghinwa Dumyati,² Lynn S. Fine,² Susan G. Fisher,³ and Edwin van Wijngaarden³

- Retrospective cohort study
- 10,154 hospitalizations; 241 cases of CDI
- Dose-dependent increases in risk of CDI with cumulative antibiotic exposure
- Highest risk antibiotics: FQs, clinda, B-lac/BLI

Stevens et al. CID 2011
**Cumulative Antibiotic Exposures Over Time and the Risk of *Clostridium difficile* Infection**

Vanessa Stevens,1,3,4 Ghinwa Dumlup,2 Lynn S. Fine,2 Susan G. Fisher,3 and Edwin van Wijngaarden3

- **Defined daily doses** (HR vs. DDD <3)

<table>
<thead>
<tr>
<th>DDD</th>
<th>Crude HR</th>
<th>Adjust HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-7.79</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>7.8-21</td>
<td>3*</td>
<td>3*</td>
</tr>
<tr>
<td>&gt;21</td>
<td>5*</td>
<td>5*</td>
</tr>
</tbody>
</table>

Stevens et al. CID 2011
Antibiotic days (HR vs. days <4)

<table>
<thead>
<tr>
<th>Abx days</th>
<th>Crude HR</th>
<th>Adjust HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-7</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>8-18</td>
<td>3*</td>
<td>3*</td>
</tr>
<tr>
<td>&gt;18</td>
<td>10*</td>
<td>8*</td>
</tr>
</tbody>
</table>
Cumulative Antibiotic Exposures Over Time and the Risk of *Clostridium difficile* Infection

Vanessa Stevens,¹,³,⁴ Ghinwa Dmyati,² Lynn S. Fine,² Susan G. Fisher,³ and Edwin van Wijngaarden³

- **Number of antibiotics** (HR vs. 1 antibiotic)

<table>
<thead>
<tr>
<th># Abx</th>
<th>Crude HR</th>
<th>Adjust HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>3*</td>
<td>3*</td>
</tr>
<tr>
<td>3-4</td>
<td>4*</td>
<td>3*</td>
</tr>
<tr>
<td>&gt;5</td>
<td>12*</td>
<td>10*</td>
</tr>
</tbody>
</table>

Stevens et al. CID 2011
What about other medications?

“We found a bunch of these clogging your arteries. They’re cholesterol pills.”
Acid Suppression and CDI Risk

“The hippies knew... acid is good, man.”
- Dr. Mark Crislip (edgydoc.com)
# Host and Pathogen Factors for *Clostridium difficile* Infection and Colonization

Vivian G. Loo, M.D., Anne-Marie Bourgault, M.D., Louise Poirier, M.D., François Lamothe, M.D., Sophie Michaud, M.D., M.P.H., Nathalie Turgeon, M.D., Baldwin Toye, M.D., Axelle Beaudoin, M.Sc., Eric H. Frost, Ph.D., Rodica Gilca, M.D., Ph.D., Paul Brassard, M.D., Nandini Dendukuri, Ph.D., Claire Béliveau, M.D., Matthew Oughton, M.D., Ivan Brukner, Ph.D., and Andre Dascal, M.D.

## Table 2. Odds Ratios for Health Care–Associated *Clostridium difficile* Infection and Colonization According to Various Patient and Pathogen Characteristics.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Health Care–Associated <em>C. difficile</em> Infection</th>
<th>Health Care–Associated <em>C. difficile</em> Colonization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic</td>
<td><img src="image" alt="Odds Ratio" /> 5.25 (2.15–12.82)</td>
<td>1.04 (0.61–1.78)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>1.33 (0.49–3.65)</td>
<td><img src="image" alt="Odds Ratio" /> 2.37 (1.09–5.14)</td>
</tr>
<tr>
<td>Proton-pump inhibitor</td>
<td><img src="image" alt="Odds Ratio" /> 2.64 (1.71–4.09)</td>
<td><img src="image" alt="Odds Ratio" /> 1.71 (1.15–2.53)</td>
</tr>
<tr>
<td>H₂ blocker</td>
<td>0.98 (0.55–1.73)</td>
<td><img src="image" alt="Odds Ratio" /> 2.14 (1.24–3.70)</td>
</tr>
<tr>
<td>Glucocorticoid</td>
<td>0.97 (0.48–1.97)</td>
<td><img src="image" alt="Odds Ratio" /> 1.33 (0.72–2.45)</td>
</tr>
<tr>
<td>NSAID</td>
<td>0.85 (0.55–1.30)</td>
<td>1.21 (0.79–1.84)</td>
</tr>
</tbody>
</table>
Proton Pump Inhibitors and Risk for Recurrent Clostridium difficile Infection

Amy Linsky, MD; Kalpana Gupta, MD, MPH; Elizabeth V. Lawler, DSc; Jennifer R. Fonda, MA; John A. Hermos, MD

Figure 2. Recurrence-free survival in those exposed vs unexposed to proton pump inhibitors (PPIs) during treatment for incident Clostridium difficile infection. Time to recurrence started from the incident toxin finding or the start of antibiotic treatment (≤3 days after the diagnosis).

- PPI use associated with a 42% increased risk of recurrence
Iatrogenic Gastric Acid Suppression and the Risk of Nosocomial *Clostridium difficile* Infection

Michael D. Howell, MD, MPH; Victor Novack, MD, PhD; Philip Grgurich, PharmD; Diane Souliard, PharmD; Lena Novack, PhD; Michael Pencina, PhD; Daniel Talmor, MD, MPH

*Arch Intern Med.* 2010;170(9):784-790
• Study 1: Population based study of older adults in US.
• Study 2: Case-control study of hospitalized adults testing positive for CDI
• Depression increases odds of CDI
• Fluoxetine and mirtazapine associated with increased risk of CDI
Overall response to metronidazole 91.9%

Successful treatment associated with:
  • Absence of PPIs (OR 0.69)
  • Exposure to statins (OR 1.45)

Recurrence associated with:
  • No statin exposure (3% vs. 7.3%)
Do Antimicrobial Stewardship Programs Make a Difference?

YOU ARE THE NEXT CLASS OF DRUG-RESISTANT BACTERIA. AS HUMANS CONTINUE TO ABUSE AND OVERUSE ANTIBIOTICS, YOUR RANKS WILL SWELL. SO, GO OUT THERE AND MUTATE! AND REMEMBER: THAT WHICH DOES NOT KILL US MAKES US STRONGER!!

STRAIN OF 2000

[Image of cartoon characters in a classroom setting]
Evidence for ASP in CDI Prevention

• Change in fluoroquinolones associated with decreased CDI (Gaynes et al. CID 2004; Kellen et al. ICHE 2009)
• Overall decrease in antibiotic use associated with decreased CDI (Valiquette et al. CID 2007; Nuila et al. ICHE 2008)
• Decreased use of broad-spectrum cephalosporins associated with decreased CDI (McNulty et al. JAC 1997; Khan et al. J Hosp Infect 2003; Thomas et al. CID 2005)
**ASP: Evidence**

<table>
<thead>
<tr>
<th>Study, year, study</th>
<th>Location</th>
<th>Type of ASP Introduced</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elligsen 2012 Interrupted Time Series Analysis</td>
<td>University teaching hospital, Toronto, ON</td>
<td>Audit and feedback in Critical Care Units from: -3&lt;sup&gt;rd&lt;/sup&gt; gen cephalosporins, -β-lactam/β-lactamase inhibitors, -Carbapenems, -Fluoroquinolones, -Vancomycin</td>
<td>-Days of therapy, -AROs, -C. difficile, -Length of stay, -ICU mortality</td>
</tr>
</tbody>
</table>

ASP: Evidence

Monthly use of broad-spectrum antibiotics in critical care patients and control medical and surgical ward patients

ASP: Evidence

• Nosocomial C. difficile decreased 31%
  • 16 cases pre-intervention to 11 cases post-intervention
• Non-intervention (non-ICU) wards had a 33% increase in cases
  • 87 cases to 116 cases during the same time periods

### ASP: Evidence

<table>
<thead>
<tr>
<th>Study, year, design</th>
<th>Location</th>
<th>Type of ASP Introduced</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valiquette et al 2007</td>
<td>Secondary/tertiary care hospital, Quebec, Canada</td>
<td>Audit and feedback: -2&lt;sup&gt;nd&lt;/sup&gt; gen cephalosporins -3&lt;sup&gt;rd&lt;/sup&gt; gen cephalosporins -ciprofloxacin -clindamycin -macrolides</td>
<td>-Total antimicrobial use -Targeted antimicrobial use -C. difficile rates</td>
</tr>
</tbody>
</table>

Valiquette et al. Impact of a reduction in use of high-risk antibiotics on the course of an epidemic NAP1/027 strain. CID 2007; 45: S112-S121

Valiquette et al. Impact of a reduction in use of high-risk antibiotics on the course of an epidemic NAP1/027 strain. CID 2007; 45: S112-S121
## ASP: Evidence

<table>
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<th>Location</th>
<th>Type of ASP Introduced</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schabas et al.</td>
<td>Small Community Hospital, Campbellford</td>
<td>• Restriction of fluoroquinolone use</td>
<td><em>Clostridium difficile</em> infection</td>
</tr>
</tbody>
</table>

• Restriction and prior authorization of FQs

• 71% of CDI cases had prior FQ exposure

• Pre-implementation: 55 cases in 15 months

• After implementation: 1 case in 24 months
ASP: Lakeridge Health
ASP: Lakeridge Health

OG5 & OC7
Targeted Anti-Infectives (DOT per 1000 pt. days)

~40% decrease
ASP: Lakeridge Health

~50% decrease  
(p=0.02)
ASP: Lakeridge Health

*C difficile*: confirmed cases 2009 - 2013 (Oct 21)
Lakeridge Health and Community

- **Healthcare associated Lakeridge** (onset of symptoms > 72 hours after admission)
- **All cases presenting to Lakeridge** (e.g., from Long Term Care, other Hospitals, Community Acquired, Relapses)
What Constitutes an Antimicrobial Stewardship Program?
ASP CORE TEAM

**(ID) Pharmacist**
**(ID) Physician**
ASP Goals

• Improve individual patient outcomes
  – Best treatment for their infection
  – Decrease HAI w/ ARO (especially C. diff)
  – Minimize adverse drug reactions

• Improve “local” antibiotic resistance profile

• Do the above in a cost effective way
LH ASP Activities

Antimicrobial Usage
- Audit-Feedback
- IV→PO stepdown
- Formulary Restriction
- Education

IPAC/Quality
- CAUTI Prevention
- Probiotics/PPI
- CLI/VAP Prevention
- Blood Culture Contamination

ID Management
- CDI treatment
- Pre-printed Orders
- Optimized dosing
- AE Monitoring
Specific ASP Strategies

- Prospective audit and feedback
  - Streamlining/de-escalation of therapy
  - Dose optimization
  - Minimum effective duration
  - Drug allergy/interaction review
- Targets:
  - Specific drugs
  - Duration
  - Bug/drug mismatch
- Education/discussion/raise awareness

IDSA/SHEA Guidelines for Development of an Institutional Program to Enhance Antimicrobial Stewardship. CID 2007; 44: 159-177
SLOW IDEAS
Some innovations spread fast. How do you speed the ones that don’t?
BY ATUL GAWANDE
JULY 29, 2013
LH ASP

• Daily audit-feedback: Critical Care
  – Since November 1, 2011

• Weekly audit-feedback: LH-Whitby Rehab
  – March 1, 2012

• Daily audit-feedback: Medicine wards (OG5, OC7)
  – Since August 27, 2012

• Daily audit-feedback: Medicine wards (OG9, OC6)
  – Since September 1, 2013
CrCU Targeted Antibiotics

CRITCARE Targeted Antimicrobials
(DOT per 1000 pt days)

~35% decrease
ASP: Lakeridge Health

OG5 & OC7 Targeted Antimicrobials
(DOT per 1000 pt. days)

~40% decrease
OC6 Targeted Antibiotics

OC6 Targeted Antimicrobials (DOT per 1000 pt. days)

~40% decrease

DOT per 1000 Patient Days
Median
How to Be an Antibiotic Steward...

“Be sure to keep taking the medication until it’s all finished – even if you begin to look better.”
Lesson 1:

Don’t Do Something; Just Sit There
Don’t Do Something; Just Sit There

By ABIGAIL ZUGER, M.D.

“The art of doing nothing is learning to help by not doing or advising,” he wrote. “The evaluation is the treatment.”

Our Obsession with Dental Antibiotic Prophylaxis and an E-mail from Mom

Paul Sax • March 30th, 2012
Categories: Health Care. Patient Care

It’s broadly misconceived by dentists and orthopedists alike that the risk of antibiotics is lower than the risk of “seeding” an artificial joint or plate by the dental work. Clearly wrong.

But that doesn’t stop them. And it’s because surgeons are much more worried about passive errors (not doing something) than they are about harming someone with an active error (medication side effect).

They’re surgeons, after all. Maddening.

Paul
Effects of Clinical Pathways for Common Outpatient Infections on Antibiotic Prescribing

Timothy C. Jenkins, MD, a,b,e,f Amy Irwin, DNP, RN, a Leotynia Coombs, EdD, g Lauren DeAlleaume, MD, c,g Stephen E. Ross, MD, e Jeanne Rozwadowski, MD, MPH, c,e Brian Webster, MD, h L. Miriam Dickinson, PhD, g Allison L. Sabel, MD, PhD, MPH, d,i Thomas D. MacKenzie, MD, MSPH, c,d,e David R. West, PhD, e,g Connie S. Price, MD a,b,e,f

a Department of Medicine, b Division of Infectious Diseases, c Department of Community Health Services, d Department of Patient Safety and Quality, Denver Health Medical Center, Denver, Colo; e Department of Medicine, f Division of Infectious Diseases, g Department of Family Medicine, University of Colorado Denver, Aurora; h Wilmington Health, Wilmington, NC; i Department of Biostatistics and Informatics, Colorado School of Public Health, Aurora.

Table 4 Antibiotic Prescriptions for Non-pneumonia Acute Respiratory Infections*

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Baseline Period N = 15,114</th>
<th>Intervention Period N = 7897</th>
<th>P</th>
<th>Control Group</th>
<th>Baseline Period N = 7650</th>
<th>Intervention Period N = 4052</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotic prescribed for acute respiratory infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory infection</td>
<td>1135 (21.6)</td>
<td>468 (15.6)</td>
<td></td>
<td>371 (12.8)</td>
<td>182 (14.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute bronchitis</td>
<td>1773 (60.5)</td>
<td>737 (54.9)</td>
<td></td>
<td>625 (57.2)</td>
<td>289 (51.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>715 (29.9)</td>
<td>426 (31.5)</td>
<td></td>
<td>565 (40.6)</td>
<td>364 (37.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute rhinosinusitis</td>
<td>2242 (66.5)</td>
<td>1060 (65.9)</td>
<td></td>
<td>999 (70.2)</td>
<td>524 (65.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute otitis media</td>
<td>595 (50.6)</td>
<td>300 (51.2)</td>
<td></td>
<td>485 (57.5)</td>
<td>210 (48.5)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The American Journal of Medicine, Vol 126, No 4, April 2013
Effects of Clinical Pathways for Common Outpatient Infections on Antibiotic Prescribing

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1Department of Medicine, 2Division of Infectious Diseases, 3Department of Community Health Services, 4Department of Patient Safety and Quality, Denver Health Medical Center, Denver, Colo; 5Department of Medicine, 6Division of Infectious Diseases, 7Department of Family Medicine, University of Colorado Denver, Aurora; 8Wilmington Health, Wilmington, NC; 9Department of Biostatistics and Informatics, Colorado School of Public Health, Aurora.

Table 5  Broad-Spectrum Antibiotic Prescriptions for All Clinical Pathway Conditions*

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline Period</td>
</tr>
<tr>
<td>N = 21,351</td>
<td>N = 11,619</td>
</tr>
<tr>
<td>Broad-spectrum antibiotic prescribed</td>
<td>5645 (26.4)</td>
</tr>
<tr>
<td>Upper respiratory infection</td>
<td>771 (14.7)</td>
</tr>
<tr>
<td>Acute bronchitis</td>
<td>1333 (45.5)</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>337 (14.1)</td>
</tr>
<tr>
<td>Acute rhinosinusitis</td>
<td>1429 (42.4)</td>
</tr>
<tr>
<td>Acute otitis media</td>
<td>333 (28.3)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>963 (29.2)</td>
</tr>
<tr>
<td>Skin and soft tissue infection</td>
<td>283 (13.3)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>196 (24.2)</td>
</tr>
</tbody>
</table>

The American Journal of Medicine, Vol 126, No 4, April 2013
UTI/ASB

- **Do not send** urine samples unless patients have definite signs or symptoms of UTI
- **Remove** (or don’t insert) the urinary catheter

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**Urinary Tract Infections**

*Does the Smell Really Tell?*

_Urine odor may be misleading in detecting urinary tract infections in elderly nursing home residents._

Susan J. Midthun, MS, RN, Ruth Paur, MS, MT (ASCP), and Glenda Lindseth, PhD, RN, FADA
Catheter-Associated Urinary Tract Infection Is Rarely Symptomatic

A Prospective Study of 1497 Catheterized Patients

Paul A. Tambyah, MBBS; Dennis G. Maki, MD

Background: Catheter-associated urinary tract infection (CAUTI) is the most common nosocomial infection, accounting for more than 1 million cases each year in US hospitals and nursing homes.

“Only 1 of the 235 episodes of CAUTI (0.4%) ... Was associated with secondary bloodstream infection”

Results: There were 235 new cases of nosocomial CAUTI during the study period. More than 90% of the infected patients were asymptomatic; only 123 infections (52%) were associated with symptoms, and 22 of the infections (9%) were associated with the development of bloodstream infection.

Conclusions: Whereas CAUTIs are a major reservoir of antibiotic-resistant organisms in the hospital, they are rarely symptomatic and infrequently cause bloodstream infection. Symptoms referable to the urinary tract, fever, or peripheral leukocytosis have little predictive value for the diagnosis of CAUTI.

Arch Intern Med. 2000;160:678-682
“Three episodes of (308 patients with) bacteriuria developed bacteremia (0.7%).”

“CAUTI rather than CAABU was associated with bacteremia, but neither predicted mortality.”

“Use of antimicrobials was not associated with bacteremia or mortality.”
UTI

• **Do not treat** asymptomatic bacteriuria
  – Except pregnancy, pre-TURP
  – Beware of blaming behavioural symptoms alone on cystitis
    • They probably had bacteriuria when feeling fine as well

• Negative urinalysis has high NLR

• Positive urinalysis has low PLR
Lesson 2:
Minimize Harm
Community-associated *Clostridium difficile* infection and antibiotics: a meta-analysis

Abhishek Deshpande¹†, Vinay Pasupuleti¹†, Priyaleela Thota¹, Chaitanya Pant², David D. K. Rolston³, Thomas J. Sferra⁴, Adrian V. Hernandez⁵ and Curtis J. Donskey¹,⁶

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>OR of CDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>clindamycin</td>
<td>20</td>
</tr>
<tr>
<td>fluoroquinolones</td>
<td>6</td>
</tr>
<tr>
<td>cephalosporins</td>
<td>5</td>
</tr>
<tr>
<td>penicillins</td>
<td>3</td>
</tr>
<tr>
<td>macrolides</td>
<td>3</td>
</tr>
<tr>
<td>SMZ/TMP</td>
<td>2</td>
</tr>
<tr>
<td>tetracyclines</td>
<td>1</td>
</tr>
</tbody>
</table>
Does Doxycycline Protect Against Development of *Clostridium difficile* Infection?

Sarah B. Doernberg,¹ Lisa G. Winston,¹ Daniel H. Deck,² and Henry F. Chambers¹

- 2734 hospitalizations
- 5.6 per 10,000 pt. days if received ceftriaxone
- 1.6 per 10,000 pt. days if ceftriaxone/doxycycline
- 8.11 per 10,000 pt days if ceftriaxone without doxycycline
LH ASP: CAP Experience

OG5 & OC7
Moxifloxacin

~65% decrease
LH ASP: CAP Experience

O5G & OC7
Doxycycline

DOT per 1000 Patient Days
Median
LH ASP: CAP Experience

Ceftriaxone
OG5 & OC7

DOT per 1000 Patient Days
Median
Lesson 3:
Duration: Use Evidence not “experience”
How to Figure Out the Length of an Antibiotic

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Editor-in-Chief
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- Choose a multiple of 5 (fingers of the hand) or 7 (days of the week).
- Is it an outpatient problem that is relatively mild? If so, choose something less than 10 days. After application of our multiples rule, this should be 5 or 7 days.
- Is it really mild, so much so that antibiotics probably aren’t needed at all but clinician or patient are insistent? Break the 5/7 rule and go with 3 days. Ditto uncomplicated cystitis in young women.
How to Figure Out the Length of an Antibiotic

• Is it a serious problem that occurs in the hospital or could end up leading to hospitalization? With the exception of community-acquired pneumonia (5 or 7 days), 10 days is the minimum.
• Patient not doing better at the end of some course of therapy? Extend treatment, again using a multiple of 5 or 7 days.
• Does the infection involve a bone or a heart valve? Four weeks (28 days) at least, often 6 weeks (42 days). Note that 5 weeks (35 days) is not an option — here the 5’s and 7’s cancel each other out, and chaos ensues.
• The following lengths of therapy are inherently weird, and should generally be avoided: 2, 4, 6, 8, 9, 11, 12, 13 days.
Evidence-based Durations

- CAP: <7 days (usually 5)
- VAP: 8 days
- Cellulitis: 7 days
- UTI: 3 days
- UTI in men: <7 days
- Pyelonephritis: 7 days
- Even with bacteremia? 7 days
Evidence-based Durations

Evidence-Based Summaries for Short-Course Antimicrobial Therapy

- Acute Exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD)
- Community-Acquired Pneumonia
- Surgical Prophylaxis
- Uncomplicated Urinary Tract Infection
- Ventilator-Associated Pneumonia
Duration of antibiotic treatment for acute pyelonephritis and septic urinary tract infection—7 days or less versus longer treatment: systematic review and meta-analysis of randomized controlled trials

Noa Eliakim-Raz¹,²*, Dafna Yahav²,³, Mical Paul²,³ and Leonard Leibovici¹,²

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Short Events</th>
<th>Total Events</th>
<th>Long Events</th>
<th>Total</th>
<th>Weight</th>
<th>RR M-H, Random, 95% CI</th>
<th>RR M-H, Random, 95% CI</th>
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<tbody>
<tr>
<td>Peterson 2008</td>
<td>23</td>
<td>265</td>
<td>31</td>
<td>241</td>
<td>38.9%</td>
<td>0.67 [0.41–1.12]</td>
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<tr>
<td>Sandberg 2012</td>
<td>2</td>
<td>73</td>
<td>3</td>
<td>83</td>
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<td>Talan 2000</td>
<td>4</td>
<td>113</td>
<td>19</td>
<td>111</td>
<td>21.5%</td>
<td>0.21 [0.07–0.59]</td>
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<td>de Gier 1995</td>
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<td>18</td>
<td>5</td>
<td>16</td>
<td>24.5%</td>
<td>1.24 [0.49–3.15]</td>
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<td>Klausner 2007</td>
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<td>1</td>
<td>76</td>
<td>4.8%</td>
<td>0.95 [0.06–14.92]</td>
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<tr>
<td>Total (95% CI)</td>
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<td></td>
<td>100.0%</td>
<td>0.63 [0.33–1.18]</td>
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<td>59</td>
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</table>

Heterogeneity: τ² = 0.20; χ² = 6.83, df = 4 (P = 0.15); I² = 41%
Test for overall effect: Z = 1.45 (P = 0.15)

Figure 2. Clinical failure at EOT in patients treated for pyelonephritis, comparing short versus long treatment. EOT was defined as a lack of resolution of fever or signs and symptoms of UTI, or antibiotic modification at the end of the long-treatment arm. Clinical failure was significantly lower in the short-treatment arm. Studies are identified by the name of the first author and year of publication. FE meta-analysis was used for estimation of combined RR (95% CI). The diamond indicates the overall summary estimate for the analysis. Tx, treatment; M-H, Mantel-Haenszel.

Less Is More

Urinary Tract Infection in Male Veterans

Treatment Patterns and Outcomes

Dimitri M. Drekonja, MD, MS; Thomas S. Rector, PhD; Andrea Cutting, MA; James R. Johnson, MD

Conclusion: Longer-duration treatment (>7 days) for male UTI in the outpatient setting was associated with no reduction in early or late recurrence.
Future Directions

• Target antibiotic use in the community
  – EDs; WICs; PCP office
• Target antibiotic use in LTCFs
• Beyond antibiotics
  – Prudent PPI use etc.
Questions?
E. coli Antibiotic Resistance
2011 to 2012

- Ampicillin: 70% (2011), 60% (2012)
- Cefazolin: 40% (2011), 30% (2012)
- Ceftriaxone: 30% (2011), 20% (2012)
- Ciprofloxacin: 20% (2011), 10% (2012)
- TMP/SMX: 10% (2011), 10% (2012)
- Piptazosin: 5% (2011), 5% (2012)
Pseudomonas Antibiotic Resistance
2011 vs 2012

<table>
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<tr>
<th>Antibiotic</th>
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<tr>
<td>Gentamicin</td>
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<td>Tobramycin</td>
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<tr>
<td>Ceftazidime</td>
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<tr>
<td>Ciprofloxacin</td>
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<td>Meropenem</td>
<td>5%</td>
<td>2.5%</td>
</tr>
<tr>
<td>Pip-tazo</td>
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<td>2.5%</td>
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