Managing *Clostridium difficile* Infection and an Overview of Antimicrobial Stewardship

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Colorado Hospital Association

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Department of Pharmacy Services  
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Housekeeping

- Please mute your phone (*6) if there is background noise
- *Please do NOT put your phone on hold*
- Questions: type into the chat box or ask at the end of the webinar
Objectives

At the close of this discussion, attendees should be able to:

- Summarize the increasing frequency of *Clostridium difficile* infection (CDI) and influence on certain patient populations;
- List 2 elements of a CDI bundle employed to limit institutional outbreaks;
- Describe and identify 2 antimicrobial stewardship (AMS) interventions that can positively impact the rate of CDI.
So why a focus on *Clostridium difficile*?
Urgent Threat

**Clostridium Difficile**

- 250,000 infections per year
- 14,000 deaths

**Threat Level: URGENT**

- This bacteria is an immediate public health threat that requires urgent and aggressive action.

**In excess medical costs per year:** $1,000,000,000
Recent Burden of CDI Hospitalizations

Deaths Caused by *C. difficile Infections*

Deaths related to *C. difficile* increased 400% between 2000 and 2007, partly due to a more virulent strain.

*Age-adjusted Rate of *C. difficile* as the Primary (Underlying) Cause of Death.

CDC National Center for Health Statistics, 2012
The Clinical and Economic Burden

In 2009 CDI resulted in:
- Approximately 337,000 hospitalizations
- 30,000 deaths
- $8.2 billion in costs associated with *C. difficile*-related stays in the hospital

Leading cause of HA infectious diarrhea in US
- 1 in 10 HAIs caused by CDI
- Ranks 3rd among HAIs behind CAUTI, SSI

Changes in Age-Specific CDI Incidence Rate, U.S, 2000–2005

Special Populations

Among hospitalized patients

- Medical patients are at increased risk compared to surgical patients

*C. diff* is the most common cause of acute diarrheal illness in LTCF

- Population is older, receive more medications known to increase risk of *C. diff*

Neonates may be colonized with *C. diff*

- Up to 70% colonized with toxigenic strains
- Neonates may lack toxin receptors in their immature enterocytes
- Less likely than adults to develop symptomatic disease
- *Colonized neonates can shed* → *transmission*

31 yo woman 14 weeks pregnant with twins developed 3 weeks of intermittent diarrhea- stool specimens positive for *C. diff*

Only ABX exposure was TMP-SXT 3 mo prior

Treated but ultimately developed severe disease hospitalized for 18 days

Had recurrent disease 4 days after discharge, spontaneously aborted her fetuses, developed sepsis and died

CDC and Philadelphia Department of Public Health launched investigation
HRET C. Diff Change Package
No laboratory test can diagnose Clostridium difficile infection (CDI)
Important Information Sharing

Inter-facility Infection Control Transfer Form

This form must be filled out for transfer to accepting facility with information communicated prior to or with transfer. Please attach copies of latest culture reports with susceptibilities if available.

<table>
<thead>
<tr>
<th>Sending Healthcare Facility:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient/Resident Last Name</td>
</tr>
<tr>
<td>------------------------------</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name/Address of Sending Facility</th>
<th>Sending Unit</th>
<th>Sending Facility phone</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Sending Facility Contacts</th>
<th>NAME</th>
<th>PHONE</th>
<th>E-mail</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case Manager/Admin/SW</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection Prevention</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Is the patient currently in isolation? □ NO □ YES
Type of Isolation (check all that apply) □ Contact □ Droplet □ Airborne □ Other:

<table>
<thead>
<tr>
<th>Does patient currently have an infection, colonization OR a history of positive culture of a multidrug-resistant organism (MDRO) or other organism of epidemiological significance?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methicillin-resistant Staphylococcus aureus (MRSA)</td>
</tr>
<tr>
<td>Vancomycin-resistant Enterococcus (VRE)</td>
</tr>
<tr>
<td>Colonization or history</td>
</tr>
<tr>
<td>Active infection on Treatment</td>
</tr>
</tbody>
</table>

http://www.cdc.gov/hai/pdfs/toolkits/InfectionControlTransferFormExample1.pdf
Recommended Elements of a CDI bundle

- Early recognition of CDI
- Implementation of contact precautions
- Establishment and monitoring of adherence to proper environmental controls
- Hand Hygiene
- Patient and family education
- Antimicrobial stewardship
- Education of healthcare workers
- Administrative support

APIC Guide to the Elimination of *Clostridium difficile* in Healthcare Settings 2008
Effects of a CDI “bundle”

To Test or Not to Test ...

Treat the patient, not the test:

**No laboratory test can** diagnose *Clostridium difficile* infection (CDI)

- CDI is a **clinical diagnosis** that can be supported by laboratory data.

- While a diagnostic assay may indicate the absence or presence of the organism or its toxins, the **test by itself does not determine who does or does not have CDI**
Current Guidelines Say ...

Strategies to Prevent *Clostridium difficile* Infections in Acute Care Hospitals: 2014 Update

Erik R. Dubberke, MD, MSPH; Philip Carling, MD; Ruth Carrico, PhD, RN; Curtis J. Donskey, MD; Vivian G. Loo, MD, MSc; L. Clifford McDonald, MD; Lisa L. Maragakis, MD, MPH; Thomas J. Sandora, MD, MPH; David J. Weber, MD, MPH; Deborah S. Yokoe, MD, MPH; Dale N. Gerding, MD

**PURPOSE**

Previously published guidelines are available that provide comprehensive recommendations for detecting and preventing healthcare-associated infections (HAIs). The intent of this document is to highlight practical recommendations in a concise format designed to assist acute care hospitals in implementing them.

**Classification of Diseases, Ninth Revision, Clinical Modification** discharge diagnosis code for CDI more than doubled between 2000 and 2009. CDI rates may have leveled off, but they remain at historically high levels. These increases have been seen in inpatient and adult populations, but the elderly are particularly affected. CDI is...

(b) *Area of controversy.* Asymptomatically colonized patients who have not had CDI can shed *C. difficile* spores, but the number of spores and degree of contamination is not as great as for patients with active CDI. There are currently no data to support detection or isolation of these asymptomatic patients.
# Emerging Diagnostics

## C. difficile Testing

<table>
<thead>
<tr>
<th>Parameter</th>
<th>EIA Only</th>
<th>GDH+EIA</th>
<th>GDH+EIA+ cytotoxin</th>
<th>GDH+PCR</th>
<th>PCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Specimens</td>
<td>432</td>
<td>432</td>
<td>431</td>
<td>432</td>
<td>428</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>58.3%</td>
<td>55.6%</td>
<td>83.1%</td>
<td>86.1%</td>
<td>94.4%</td>
</tr>
<tr>
<td>Specificity</td>
<td>94.7%</td>
<td>98.3%</td>
<td>96.7%</td>
<td>97.8%</td>
<td>96.3%</td>
</tr>
<tr>
<td>Accuracy</td>
<td>88.7%</td>
<td>91.2%</td>
<td>94.4%</td>
<td>95.8%</td>
<td>96%</td>
</tr>
<tr>
<td>PPV</td>
<td>68.9%</td>
<td>87%</td>
<td>83.1%</td>
<td>88.6%</td>
<td>84%</td>
</tr>
<tr>
<td>NPV</td>
<td>91.9%</td>
<td>91.7%</td>
<td>96.7%</td>
<td>97.2%</td>
<td>98.8%</td>
</tr>
</tbody>
</table>

EIA, enzyme immunoassay; GDH, glutamate dehydrogenase; PCR, polymerase chain reaction; PPV, positive predictive value; NPV, negative predictive value

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During an endoscopy, a versed patient kept on calling the gastroenterologist, "Captain Kirk." After the procedure, the doctor asked why he was being called the Star Trek name. "Well," explained the patient, "you just went where no man has gone before."
CDC’s Bacterial Threats

URGENT

- Clostridium difficile
- Carbapenem-resistant Enterobacteriaceae (CRE)
- Drug-resistant Neisseria gonorrhoeae (cephalosporin resistance)

SERIOUS

- Multidrug resistant (MDR) Acinetobacter
- Drug-resistant Campylobacter
- Fluconazole-resistant Candida
- Extended-spectrum β-lactamase producing Enterobacteriaceae (ESBLs)
- Vancomycin-resistant Enterococcus (VRE)
- Multidrug-resistant Pseudomonas aeruginosa
- Drug-resistant Non-typhoidal Salmonella
- Drug-resistant Salmonella Typhi
- Drug-resistant Shigella
- Methicillin-resistant Staphylococcus aureus (MRSA)
- Drug-resistant Streptococcus pneumoniae
- Drug-resistant tuberculosis (MDR and XDR)

CONCERNING

- Vancomycin-resistant S. aureus (VRSA)
- Erythromycin-resistant Streptococcus Group A
- Clindamycin-resistant Streptococcus Group B

CDC=Centers for Disease Control and Prevention; XDR=extensively drug resistant.

Approaches to treatment of CDI

1. Evaluate patient with risk factors for CDI for the presence of the following symptoms: diarrhea, fever, or colonic distention.

   - Symptoms present?
     - Yes: Perform C. difficile stool testing and stop precipitating antibiotics if possible. Start empirical therapy (indicated below) if high suspicion of CDI or patient critically ill.
     - No: C. difficile testing positive?
       - Yes: Assess severity of disease and risk of recurrence (Table 3) and continue or start therapy based on disease severity.
       - No: Stop therapy if initiated.

   - Severity of disease and risk of recurrence:
     - Mild to moderate CDI: Metronidazole, 500 mg by mouth, 3 times daily, for 10-14 days. Or Vancomycin, 1.25 mg by mouth, 4 times daily, for 10-14 days if intolerance, contraindication, or lack of response to metronidazole. If significant risk of recurrence, Vancomycin, 1.25 mg by mouth, 4 times daily, for 10-14 days, or Fidaxomicin, 200 mg by mouth, twice daily, for 10 days.
     - Severe CDI: Vancomycin, 1.25 mg by mouth, 4 times daily, for 10-14 days. If significant risk of recurrence, Vancomycin, 1.25 mg by mouth, 4 times daily, for 10-14 days, or Fidaxomicin, 200 mg by mouth, twice daily, for 10 days.
     - Severe, complicated CDI: Vancomycin, 1.25-5.00 mg by mouth, 4 times daily and/or Vancomycin, per rectum (500 mg in 500 mL saline as enema), 4 times daily and/or Metronidazole, 500 mg intravenously every 8 hours.

2. Stop therapy and evaluate for clinical signs of recurrence. No need for “test of cure.”

   - Recurrence present?
     - Yes: Continue to monitor clinically for signs of recurrence.
     - No: First recurrence of uncomplicated CDI: Repeat initial therapy or Fidaxomicin, 200 mg by mouth, twice daily, for 10 days.

   - Recurrence of uncomplicated CDI:
     - Two or more recurrences of uncomplicated CDI: Fidaxomicin, 200 mg by mouth, twice daily, for 10 days.

   - Recurrence of severe, complicated CDI:
     - Expert consultation for fecal microbiota transplantation.
Antimicrobial Stewardship

“...the optimal selection, dose, & duration of an antimicrobial

that results in

the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient & minimal impact on subsequent resistance.”

- Dale Gerding
Why Stewardship?

- What is it about the CDI disease state that calls for AMS?

- As with other disease states:
  - Quality – now a CMS measure
  - Safety
  - Cost reduction
    - Immediate – decrease in ABX expenditures
    - Future – if resistance can be reduced or minimized
Spectrum of *Clostridium difficile*-Induced Disease/Complications

- Asymptomatic (colonized, carrier state)
- *Clostridium difficile*-associated diarrhea/colitis (CDAD)
- Pseudomembranous colitis (PMC)
- Toxic megacolon
- Hyperpyrexia
- Leukemoid reaction
- Relapse: 20% - 30%
ABX as Risk Factors for CDI

Given through practically all routes, nearly all ABX have been associated with CDAD.

**Mechanism:** Alteration of normal GI microflora

- Spectrum of activity
- Other pharmacologic characteristics

<table>
<thead>
<tr>
<th>Associated with <em>C. difficile</em> Infection</th>
<th>Some Normal Colonic Microflora</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequently</td>
<td>Infrequently</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Tetracycline</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>Macrolides</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Sulfonamides</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>Zosyn</td>
</tr>
<tr>
<td>Quinolones</td>
<td>Aminoglycosides</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>Metronidazole</td>
</tr>
<tr>
<td></td>
<td>Vancomycin</td>
</tr>
<tr>
<td></td>
<td>Bacteroides spp.</td>
</tr>
<tr>
<td></td>
<td><em>Clostridium</em> spp.</td>
</tr>
<tr>
<td></td>
<td>ESCO</td>
</tr>
<tr>
<td></td>
<td>Enterococci</td>
</tr>
<tr>
<td></td>
<td><em>Lactobacillus</em> spp.</td>
</tr>
<tr>
<td></td>
<td>Others</td>
</tr>
</tbody>
</table>
2000 – 2003; Six states, 8 healthcare facilities
Current NAP1 strain resistant to FQs (100% vs. Hx isolates, 42% \( P < 0.0001 \))
“\( \uparrow \) WBC’s, more severity of disease among NAP1 vs. non-NAP1...”
“CT hospital reports \( \uparrow \) cases severe disease necessitating colectomy”
“However PA hospital finds no assoc. of NAP1 to severe disease”
Epidemic Strain  Typed BI/NAP1/027

- Has a *tcdC* gene deletion

- Highly virulent
  - Produces 16-fold higher levels of Toxin A and 23-fold higher levels of Toxin B
  - Produces binary toxin CDT
  - ↑ sporulation + / - robust toxin production ➔ severe dx ??

- High resistance to fluoroquinolones

Quebec: Attributable M&M due to CDI*

* Predominantly NAP1 strains

Why stewardship?

- What kind of interventions might work?
Effect of antibiotic stewardship programmes on *Clostridium difficile* incidence: a systematic review and meta-analysis

Leah M. Feazel¹, Ashish Malhotra¹,², Eli N. Perencevich¹,², Peter Kaboli¹,², Daniel J. Diekema¹ and Marin L. Schweizer¹,²*

<table>
<thead>
<tr>
<th>Study of subgroup</th>
<th>log [Risk ratio]</th>
<th>SE</th>
<th>Weight</th>
<th>Risk ratio IV, Random, 95% CI</th>
<th>Risk ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elligson 2012</td>
<td>-0.37</td>
<td>0.393</td>
<td>5.0%</td>
<td>0.69 [0.32, 1.49]</td>
<td></td>
</tr>
<tr>
<td>Fowler 2007</td>
<td>-1.05</td>
<td>0.372</td>
<td>5.3%</td>
<td>0.35 [0.17, 0.73]</td>
<td></td>
</tr>
<tr>
<td>Frank 1997</td>
<td>0.029</td>
<td>0.522</td>
<td>3.6%</td>
<td>1.03 [0.37, 2.86]</td>
<td></td>
</tr>
<tr>
<td>Gulhar 2009</td>
<td>-1.65</td>
<td>0.522</td>
<td>3.6%</td>
<td>0.19 [0.07, 0.53]</td>
<td></td>
</tr>
<tr>
<td>Jones 1997</td>
<td>-0.4</td>
<td>0.205</td>
<td>8.1%</td>
<td>0.67 [0.45, 1.00]</td>
<td></td>
</tr>
<tr>
<td>Ludlam 1999</td>
<td>-0.721</td>
<td>0.177</td>
<td>8.7%</td>
<td>0.49 [0.34, 0.69]</td>
<td></td>
</tr>
<tr>
<td>Malani 2013</td>
<td>-0.755</td>
<td>0.257</td>
<td>7.2%</td>
<td>0.47 [0.28, 0.78]</td>
<td></td>
</tr>
<tr>
<td>Miller 2009</td>
<td>-1.341</td>
<td>0.341</td>
<td>5.8%</td>
<td>0.26 [0.13, 0.51]</td>
<td></td>
</tr>
<tr>
<td>O’Connor 2004</td>
<td>-1.164</td>
<td>0.567</td>
<td>3.2%</td>
<td>0.31 [0.10, 0.95]</td>
<td></td>
</tr>
<tr>
<td>Price 2010</td>
<td>-0.661</td>
<td>0.082</td>
<td>10.1%</td>
<td>0.52 [0.44, 0.61]</td>
<td></td>
</tr>
<tr>
<td>Reinoso 2002</td>
<td>-3.372</td>
<td>1.438</td>
<td>0.7%</td>
<td>0.03 [0.00, 0.57]</td>
<td></td>
</tr>
<tr>
<td>Schön 2011</td>
<td>0.034</td>
<td>0.103</td>
<td>9.8%</td>
<td>1.03 [0.85, 1.27]</td>
<td></td>
</tr>
<tr>
<td>Starks 2008</td>
<td>-0.984</td>
<td>0.309</td>
<td>6.3%</td>
<td>0.37 [0.20, 0.68]</td>
<td></td>
</tr>
<tr>
<td>Stone 1998</td>
<td>-0.546</td>
<td>0.251</td>
<td>7.3%</td>
<td>0.58 [0.35, 0.95]</td>
<td></td>
</tr>
<tr>
<td>Talpae 2011</td>
<td>-1.079</td>
<td>0.272</td>
<td>6.9%</td>
<td>0.34 [0.20, 0.58]</td>
<td></td>
</tr>
<tr>
<td>Thomas 2002</td>
<td>-0.78</td>
<td>0.19864</td>
<td>8.3%</td>
<td>0.46 [0.31, 0.68]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td>100.0%</td>
<td>0.48 [0.38, 0.62]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.14$; $\chi^2 = 61.27$, df = 15 ($P < 0.00001$); $I^2 = 76\%$
Test for overall effect: $Z = 5.94$ ($P < 0.00001$)

- 16 studies selected
- Hi heterogeneity, *but...*
- Spectrum allows choice
  - Education
  - Restriction
  - ABX removal
  - Prior approval
  - Post-Rx review
- Quins, cephalosporins
- ASPs effective on CDI
- Best performers
  - Sust’d programs
  - Geriatrics

Forest plot of all included studies. IV, inverse variance.
Reduce Risk of CDI Acquisition: Antimicrobial Stewardship

- Reduce use of “high risk” antimicrobials
- Reduce unnecessary antimicrobial use
- Effective in outbreak & non-outbreak settings

Effect of ABX Restriction Policy on CDI & MDRO

A cardiothoracic surgeon “is interested” in using ceftriaxone for AMP in open-heart cases.

Is this appropriate; can CTS start using it?

- CTRX use detected in ABX surveillance reports

The Society of Thoracic Surgeons Practice Guideline Series: Antibiotic Prophylaxis in Cardiac Surgery, Part II: Antibiotic Choice*

Richard Engelman, MD, David Shahian, MD, Richard Shemin, MD, T. Sloane Guy, MD, Dale Bratzler, DO, MPH, Fred Edwards, MD, Marshall Jacobs, MD, Hiran Fernando, MD, and Charles Bridges, MD, ScD

Baystate Medical Center, Springfield, Massachusetts; Tufts University School of Medicine, Boston, Massachusetts; Boston Medical Center, Boston, Massachusetts; University of California, San Francisco, California; Oklahoma Foundation for Medical Quality, Oklahoma City, Oklahoma; University of Florida, Shands Jacksonville, Jacksonville, Florida; St. Christopher’s Hospital for Children, Philadelphia, Pennsylvania; and University of Pennsylvania Medical Center, Philadelphia, Pennsylvania

- “...our predominant organism for cardiac surgical infections is a Staphylococcus sp.;”
- “...earlier generation cephalosporins are...preferred for prophylaxis;”
- “In fact, published data would support that conclusion.”

From QI Services

Examples of Intra- and Extramural Benchmarking

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Prophylactic ABX Received Within One Hour Prior to Surgical Incision-Cardiac Sx</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>12</td>
<td>16</td>
<td>13</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td>Prophylactic ABX Selection For Surgical Patients-Cardiac Sx</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>86%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>10</td>
<td>15</td>
<td>14</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td>Prophylactic ABX Discontinued Within 48 hours after Surgery End Time-Cardiac Sx</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>92%</td>
<td>93%</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>UHC Top 10 Percent</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>
“Third generation cephalosporins, even when administered as short-term perioperative prophylaxis, but not ureidopenicillins, are significantly associated with C. difficile-related diseases.”

De Lalla, et. al. 1989. JAC;23:623-31
### Dr. Z: 3 SSI cases over 20 months

<table>
<thead>
<tr>
<th>Pt Demo</th>
<th>Procedure</th>
<th>SSI Site</th>
<th>Cx Result</th>
<th>Sensi’s</th>
</tr>
</thead>
<tbody>
<tr>
<td>M 31y</td>
<td>Aor Root replace; St. J mech valve conduit; replace ascending aorta</td>
<td>Sternum Organ / Space</td>
<td>S = Cefz (66%)</td>
<td></td>
</tr>
<tr>
<td>F 71y</td>
<td>CABG x 3; L leg SV graft</td>
<td>LLE graft Superficial</td>
<td>S = Cefz (93%)</td>
<td>S = Cefz (91%)</td>
</tr>
<tr>
<td>M 72y</td>
<td>CABG x 4; R leg SV graft</td>
<td>Sternum Organ / Space</td>
<td>R = Cefz (43%)</td>
<td></td>
</tr>
</tbody>
</table>
Effecting Change

**Key Elements:**

- Face-to-face education
- Use of key opinion leaders (ie Dept. Chairs)
- Implementing instantaneous reminders to prevent prescribing mishaps *before* they occur

---

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# UCH Empiric Antibiotic Guidance for Common Conditions

Target antibiotics toward microbiologic data when available.

Outpatient transition only for uncomplicated cases with clinical improvement.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Inpatient Therapy</th>
<th>Transition to Outpatient Therapy</th>
<th>Total Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Purulent Cellulitis</td>
<td>Cefazolin 2g IV q8h</td>
<td>Cephalexin 1000mg TID</td>
<td>5 days</td>
</tr>
<tr>
<td></td>
<td><strong>Severe B-lactam allergy:</strong> Vancomycin IV. PO step down: clindamycin 300mg TID</td>
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</tr>
<tr>
<td>Purulent Cellulitis/Cutaneous Abscess</td>
<td><strong>Incision &amp; drainage</strong></td>
<td>Doxycycline 100mg PO BID OR Bactrim DS 1 tab PO BID (&gt;80kg, 2 DS tab BID)</td>
<td>5 days w/ adequate drainage</td>
</tr>
<tr>
<td>Diabetic Foot</td>
<td>See UCH Empiric Antibiotic Guidance for Complicated Infections (next page)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Community-Acquired Pneumonia</td>
<td>Ceftriaxone 1-2g IV qday + Azithromycin 500mg IV/PO qday</td>
<td>Azithromycin 250-500mg PO daily</td>
<td>5 days</td>
</tr>
<tr>
<td></td>
<td><strong>Severe B-lactam allergy:</strong> Levofloxacin 750 mg IV/PO daily</td>
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<tr>
<td>HAP/HCAP/VAP</td>
<td>Ceftazidime 2g IV q8h + Vancomycin IV</td>
<td>Levofloxacin 750mg PO daily</td>
<td>7 days</td>
</tr>
<tr>
<td></td>
<td><strong>Severe B-lactam allergy:</strong> Aztreonam 2g IV q8h + Vancomycin IV</td>
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<tr>
<td>Aspiration Pneumonia (non-ventilator associated)</td>
<td>Unasyn 3g IV q6h OR ceftriaxone 1g IV qday + metronidazole 500mg q8h OR Clindamycin 600mg IV q8h (or 300mg PO q8h)</td>
<td>Amox/clav 875mg PO BID OR clindamycin 300mg PO TID</td>
<td>7 days</td>
</tr>
<tr>
<td></td>
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<tr>
<td><strong>Highly resistant gram negative pathogens suspected:</strong></td>
<td>Zosyn 4.5 g IV q6h</td>
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</table>
RENAL DOSING

Renal Dose Adjustment per Pharmacy Protocol will be available for the following agents:

- All medications on this protocol will be evaluated for appropriateness of dosing by a pharmacist on initial verification and at least every 72 hours.
- Cockcroft-Gault equation will be used to determine CrCl, using adjusted body weight in obese individuals, and the UCH Antimicrobial Stewardship Handbook and/or Lexi comp® Drug Information Handbook will be utilized for medication dosing.
- Progress notes will be written when medication doses are renally adjusted.
- Provider will be contacted in the following situations: (1) medication is contraindicated based on renal function, (2) medication is not on the renal dose protocol, or (3) original ordered dose is not appropriate for the indication.

Antimicrobial dosing during continuous renal replacement therapy (CRRT)

CRRT therapy fluid/dialysate fluid rates vary from 2-10 L/hr and can change on a daily basis.

*Per the University of Colorado Hospital policy, these agents are not recommended for patients with a CrCl < 30 ml/min since this population was not studied in the clinical trials.
RPh-Initiated, IV – PO Switch

- Worthwhile Reward

**Patient Benefits:**

- Increased comfort
- Increased mobility
- Decreased likelihood of IV-related AEs
- Decreased LOS

**Institution Benefits:**

- Improves MD IV → PO compliance
- Reduced med admin times
- Reduced med prep times
- Reduced materials
- Reduced dose form expenses

*Arch Intern Med* 1999;159:2449-54.
UCH - Other AMS Activities

RPh-Initiated Contact Precautions
- Many CDI occurring as OP
  - IS “flag/alert” not enacted for a + patient
- RPh can denote *C. diff* meds with high specificity
- Can help IP, RNs by selecting “Contact Precautions” status
  - Tip sheets for IT engagement
  - Support of IPs & IP MDs

IV ABX Desensitization
- Enables 1\textsuperscript{st}-line ABX regimens
- Minimize anti-PSAE carbapenems
- Std’ize order sets
  - Initially 9 IV ABX
  - Improve safety of tedious cpd’ing
  - Improve RN admin/proper sequence
- Statis significant decreases
  - ICU bed time
  - Med errors

Standardized Order Sets – Surgical Prophylaxis

Provides opportunity for:

- Uniformity
- Correct timing of pre-op ABX doses to incision
- Appropriate ABX agent; alternatives for allergy
- Appropriate dosing (favor: weight-based dosing)
- Intra-op dosing for lengthy cases, EBL/repletion
- Limit duration of post-op dosing
Case: Standardized Order Sets – Surgical Prophylaxis Colon Bundle

DUKE COLON BUNDLE: ERTAPENEM D.O.C.

**Sounds great:**
- Broad spectrum
  - *Enterobacteriaceae*
- Strong anaerobe coverage
- Omits PSAE
- Potent activity
- Easy for PCN allergies
- Long duration; q 24 hr

**But...**
- False sense of protection
  - Long duration; q 24 hr
  - ↑EBL → ABX in vacutainer at foot of bed
- Fluids → conc. at site
- Re-dosing?
  - At what interval?
  - ↑seizure risk, ADR?
- RFs for CRE?
Case: Standardized Order Sets – Surgical Prophylaxis Colon Bundle

OUTCOME:

- Cefazolin, wt.-based dosing + metronidazole 500mg
  Within 1-hr prior to initial incision:
  - < 50 kg = cefazolin 1g
  - ≥ 50 kg – 119 kg = cefazolin 2g
  - ≥ 120 kg = cefazolin 3g

- Intra-op 1g (< 50kg) or 2g q3-4h

- Alternatives for severe PCN allergy provided

- Single doses post-op, if at all

Community-Associated CDI

2009-2011: 984 patients with community-associated CDI

- 41% (400) had low-level outpatient health care exposure
  - i.e. dental, physician, or other outpatient appointments
- 18% (177) had no outpatient health care exposure
- 35% (353) did not receive antibiotics
  - 31% of the 353 patients *did receive PPIs*

Chitnis AS, et al. *JAMA Intern Med.* (Published online June 17, 2013)
Outcomes and Collaborative Targets

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<th>Sites Like Yours</th>
<th>All Sites</th>
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<tr>
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<td>4 days</td>
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<td>Rehospitalized within 30 days</td>
<td>13 (17%)</td>
<td>64 (16%)</td>
<td>218 (13%)</td>
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<td>Rehospitalized within 30 days due to UTI</td>
<td>6 (8%)</td>
<td>20 (31%)</td>
<td>56/218</td>
</tr>
<tr>
<td><em>Clostridium difficile</em> infection</td>
<td>1 (1%)</td>
<td>6 (1%)</td>
<td>37 (2%)</td>
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## CHA Baseline Data, UCH (Metro Denver)

### Outcomes and Collaborative Targets

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# CHA Baseline Data, UCH (Metro Denver)

## Antimicrobial Treatment Data

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<td><strong>Most common inpatient antibiotics</strong></td>
<td></td>
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</tr>
<tr>
<td>Higher-generation IV cephalosporin</td>
<td>57 (73%)</td>
<td>244 (60%)</td>
<td>889 (53%)</td>
</tr>
<tr>
<td>Fluoroquinolone (IV or PO)</td>
<td>15 (19%)</td>
<td>142 (35%)</td>
<td>679 (41%)</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>11 (14%)</td>
<td>63 (15%)</td>
<td>194 (12%)</td>
</tr>
<tr>
<td><strong>Most common discharge antibiotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PO Fluoroquinolone</td>
<td>18 (23%)</td>
<td>113 (28%)</td>
<td>456 (27%)</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>7 (9%)</td>
<td>32 (8%)</td>
<td>146 (9%)</td>
</tr>
<tr>
<td>Trimethoprim-Sulfamethoxasole</td>
<td>11 (14%)</td>
<td>29 (7%)</td>
<td>100 (6%)</td>
</tr>
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</table>
Summary

- Rising rates & increasing severity of CDI are associated with ↑ LOS, patient M&M, costs, elevating CDI to “Urgent Threat” status
- Last 10 yrs: traditional patient profiles such as elderly, super-aged appear exquisitely susceptible
- New patient profiles are emerging in changing healthcare settings
- Vigilance for influence of “new” RFs such as PPIs
- Hypervirulent *C. difficile* strains assoc with severe presentations & ABX resistance
Summary Continued

- ABX exposure remains strongest influence for inducing CDI (Prevention = Best Medicine)
- AMS programs have shown a temporal association of ↓ ABX use to ↓ rates of CDI. Winning!!!
- Prevention: IP, AMS, industrial & personal hygiene best for ↓ environmental prevalence & density
- Please WASH YOUR HANDS!!
80% of all antibiotics are used on farm animals.
I was getting sick, and you came at once,
Together with a hundred students,
O Symmachus;
A hundred frosty fingers probed me;
I had no fever, O Symmachus; now I have.

Wash These Frequently
What Can Be Done in the Community?

"EAT A STEAK, THERE ARE SO MANY ANTIBIOTICS IN IT, YOU'LL BE CURED."
Questions?
Contacts

Have any more questions? Contact Teri and Gerry!

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