Management of Common Infections in Long-Term Care

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Agenda

• Urinary Tract Infection (UTI)
  • Fluoroquinolone role in empiric therapy?
  • Nitrofurantoin: useful or malpractice?

• Upper Respiratory Tract Infection (URTI)
  • Back away from the prescription pad
  • Our addiction to macrolides

• Skin and Soft Tissue Infection (SSTI)
  • Non-purulent cellulitis
  • Purulent cellulitis

• Clostridium difficile (time permitting)
Urinary Tract Infections

- Account for 24% of all infections in older adults.
- Account for 12-25% of LTCF infections
- Most common cause of bacteremia in LTCF
- Responsible for 20-60% of antimicrobial use in LTCF
UTI is a Clinical Diagnosis

• **Non-Catheterized Patients:** Only residents with fever and/or localizing urinary symptoms should be treated for UTI
  • Dipstick can usually be used to ruled-out UTI
  • Dipstick should not be used as criteria for getting UCx

• **Catheterized Patients:**
  • Localizing symptoms often absent
  • Delirium plus fever/leukocytosis in absence of alternative explanation

• Cultures are used to guide *antibiotic selection* decisions not *treatment initiation* decisions
The Problem of Asymptomatic Bacteriuria

- Asymptomatic bacteriuria common
  - Community: 6 – 17%
  - Institutionalized: 19 – 57%

- Treatment of ASB
  - Does not reduce episodes of symptomatic UTI
  - Promotes resistance
  - Increases risk of *C. difficile*

Warren et al., *JAMA* 1982; 248(4): 454-8
Approach to Treatment

• **Always** get culture before starting therapy

• **Empiric therapy**
  • Base on regional/institutional susceptibility patterns
  • Review individual’s recent antibiotic use and culture results
  • NFT = TMP/SMX > fluoroquinolones
  • Fosfomycin with MDR/XDR

• **Follow-up on culture results and de-escalate to narrowest spectrum possible**

• **Avoid prolonged courses of antibiotics**
  • Females: 3-5d if **no catheter**, 7d if **catheter** or if NFT/BL used
  • Males: 7d regardless of catheter
  • Consider alternative diagnosis if symptoms not improving in 24-48 hours

NFT = nitrofurantoin; BL = beta-lactam antibiotic
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## Ecological Impact

<table>
<thead>
<tr>
<th></th>
<th>CP1</th>
<th>CP2</th>
<th>CP3</th>
<th>CTCP1</th>
<th>CTCP2</th>
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<th>CRL2</th>
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<tr>
<td>CRL3</td>
<td>0.4</td>
<td>0.004</td>
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<td>0.6</td>
<td>0.4</td>
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<td>1</td>
<td>1</td>
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<td>NF1</td>
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<td>0.5</td>
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<td>0.08</td>
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<td>0.6</td>
<td>0.2</td>
<td>0.2</td>
<td>0.1</td>
<td>0.06</td>
<td>1</td>
<td>0.9</td>
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</tbody>
</table>

*P <0.001*

*P <0.01*

*P <0.05*

*P <0.1*

C. difficile Risk Elevated
Empiric Efficacy Inferior

Variables Independently Associated with Risk of Inadequate Therapy Among 300 ED-Treated Patients with Confirmed *E. coli* Bacteriuria

<table>
<thead>
<tr>
<th></th>
<th>Relative Risk</th>
<th>95% Confidence Interval</th>
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<tbody>
<tr>
<td>Age</td>
<td>1.016</td>
<td>1.001 – 1.031</td>
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<tr>
<td>Male Gender</td>
<td>2.570</td>
<td>1.470 – 4.486</td>
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<tr>
<td>Fluoroquinolone</td>
<td>2.128</td>
<td>1.249 – 3.624</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>0.202</td>
<td>0.065 – 0.638</td>
</tr>
</tbody>
</table>

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NFT = nitrofurantoin; BL = beta-lactam antibiotic
Resistance Patterns in UTI

Nitrofurantoin for Treatment of UTI in the Elderly

- Observational study of elderly females with UTI and low GFR (n = 9,223) or normal GFR (n = 182,634).
  - Outcome: 2nd Abx (14d) or ED/Hospitalization
  - Within strata comparison: NFT to cipro/norflox/TMP-SMX
  - Across strata comparison: NFT to NFT

Singh et al. CMAJ 2015; 187(9): 648-56
Prevention of UTIs

• Avoid the use of indwelling urinary catheters
  • Regularly evaluate and justify continued need for indwelling catheter
  • Consider use of incontinence pads, condom catheters, and intermittent straight catheterization
  • Catheter exchange (?)
  • Suprapubic catheter (for wound healing)

• Behavioral (peri-care, post-coital)
• Intra-uterine estrogen (if post-menopausal onset)
• Cranberry tablets (*E. coli*)
• Methenamine salts (?) Need acidic pH
• Acetic acid bladder instillations (?) straight cath or indwelling catheter
• Prophylactic antibiotics (if your goal is cultivating resistance)
• Probiotics (?)

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• Prophylactic antibiotics (if your goal is cultivating resistance)
• Probiotics (?)

Effectiveness of Cranberry Tablets in Older Adults

Unadjusted Rates and Rate Ratios for Secondary Study Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Event Rate (Per Pt. Year)</th>
<th>RR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cranberry</td>
<td>Placebo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Antimicrobials</td>
<td>17.0</td>
<td>22.4</td>
<td>0.76</td>
<td>0.46 – 1.25</td>
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<tr>
<td>Antibiotics for UTI</td>
<td>8.3</td>
<td>10.8</td>
<td>0.77</td>
<td>0.44 – 1.33</td>
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<tr>
<td>MDR GNB Bacteriuria</td>
<td>10.8</td>
<td>28.6</td>
<td>0.38</td>
<td>0.10 – 1.46</td>
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<tr>
<td>Hospitalization</td>
<td>39.7</td>
<td>59.6</td>
<td>0.67</td>
<td>0.32 – 1.40</td>
</tr>
<tr>
<td>Mortality</td>
<td>20.4</td>
<td>19.1</td>
<td>1.07</td>
<td>0.54 – 2.12</td>
</tr>
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</table>

Juthani-Mehta et al. JAMA 2016; 316(18): 1879-87
Respiratory Conditions Most Sensitive to Unnecessary Prescribing

- Acute rhinosinusitis
- Acute bronchitis
- Pharyngitis
- AECB in patients with mild-moderate COPD (Gold stage I, II)


- 46% of older adults presenting with these conditions are prescribed antibiotics
- 70% of prescriptions involved broad-spectrum agents (macrolides [49%), cephalosporins [11.4%], fluoroquinolones [9.6%])
- Prescribing more common with senior providers, non-Canadian/US training and high patient volume
Drug-Resistant Pneumococcus

- 1,200,000 drug-resistant cases/year
- 19,000 attributable hospitalizations
- 7,000 attributable deaths
- $96,000,000 excess healthcare costs

CDC. Antibiotic Resistant Threats in the United States, 2013
Conditions Most Sensitive to Unnecessary Prescribing

• Acute rhinosinusitis
• Acute bronchitis
• Pharyngitis
• AECB in patients with mild-moderate COPD (Gold stage I, II)

>90% are viral
Purulence ≠ bacteria
Reserve Abx for patients with severe symptoms or double-sickening

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• Acute bronchitis

• Pharyngitis

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Conditions Most Sensitive to Unnecessary Prescribing

• Acute rhinosinusitis

• Acute bronchitis

• Pharyngitis
  - GAS causative pathogen in ~10% of adults
  - Abx Rx reduces sxs by 1-2 days
  - Test(+) before treatment (Centor 2/3)
  - Consider fusobacterium (Age = 15-25; Centor 4/5)

• AECB in patients with mild-moderate COPD (Gold stage I, II)

Centor & Samlowski. *Am Fam Phys* 2011; 83(1): 26-8
Conditions Most Sensitive to Unnecessary Prescribing

- Acute rhinosinusitis
- Acute bronchitis
- Pharyngitis
- AECB in patients with mild-moderate COPD (Gold stage I, II)

Pyogenic infxns. seen in Gold III/IV
Abxs of limited benefit in outpatients
PCT may help guide Rx in ED/Hosp.

Vollenweider et al. *Cochrane Database Syst* 2012; vol. 12
Biomarker-Aided Diagnosis

## Abx Prescribing for URTI: Impact on Outcomes

<table>
<thead>
<tr>
<th></th>
<th>No Antibiotic</th>
<th>Immediate Antibiotic</th>
<th>Delayed Antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hospitalization or Death</strong></td>
<td>26/7332 (0.3%)</td>
<td>156/17,628 (0.9%)</td>
<td>14/3819 (0.4%)</td>
</tr>
<tr>
<td><strong>Re-Consult</strong></td>
<td>1443/7332 (19.7%)</td>
<td>4445/17,628 (25.3%)</td>
<td>538/3819 (14.1%)*</td>
</tr>
</tbody>
</table>

* RR = 0.64 (95% CI 0.57 – 0.72)

Management Issues for LRTI

• AECB
  • Gold Class A-B: No antibiotics
  • Admitted or Gold Class C-D: Antibiotics
    • Amox/Clav (875/125 BID) for 5-7 days
    • Amox/clav (2000/125 BID) for 5-7 days
    • Doxycycline (200mg load, 100mg BID) for 5-7 days

• Pneumonia
  • Macrolide monotherapy not recommended
  • Macro-aspiration a possibility
    • Amox-clav (875/125 or 2000/125 BID) for 5-7 days
    • Ceftriaxone
    • Moxifloxacin (400mg QD) if PCN allergic
  • Macro-aspiration unlikely
    • Amoxicillin (500mg or 1000mg TID) for 5-7 days
    • Standard or high dose amox/clav for 5-7 days
    • Doxycycline (200mg load, 100mg BID) for 5-7 days
Skin and Soft Tissue Infections
General Approach

• Redness or presence of a wound alone are not sufficient for starting empiric Abx

• Redness ≠ cellulitis
  • Consider venous insufficiency, DVT, gout
  • Start Abx only if resident has two or more of: 1) fever*; 2) tenderness; 3) warmth; or 4) new or increasing swelling

• Ulcer ≠ infection
  • Focus should be on vascular/mechanical issues
  • Start Abx only if resident has two or more of: 1) fever*; 2) redness; 3) tenderness; 4) warmth; or 5) new or increasing swelling
Figures 1A and 1B: Notice the integrity of the skin, the ill-described border of the lesion as well as the extension of erythema up medial aspect of the leg (figures courtesy of DermNetNZ.org).
Treatment of Cellulitis


Moran et al. *JAMA* 2017; 317(20): 2088
Management Approach

• Intact skin (i.e., cellulitis)
  • Non-purulent $\rightarrow$ target streptococci (diclox or cephalexin)
  • Purulent $\rightarrow$ target MRSA
  • Be patient $\rightarrow$ it often takes 72 hours for redness to recede
  • Expect some post-cellulitis capillaritis (no fever, no WBC/CRP, plus dependent rubor)

• Non-intact skin
  • Get cultures before treatment (Curettage or Levine technique)
  • NPV of cultures for MRSA and PSAE is high $\rightarrow$ target streptococci, MSSA, and Enterobacteriaceae if cultures are negative for these pathogens
  • I&D plus Abx for lesions $\geq$ 2cm

Recurrent Cellulitis

• Control edema
  • Edema lowering therapy (PT referral)
  • Compression stockings
  • Scheduled elevation
  • Compressive dressings with skin breakdown or dermatitis flare

• Maintain skin hydration
• Treat tinea pedis and onychomycosis
• Prophylactic penicillin
Recurrent Cellulitis

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  • Compression stockings
  • Scheduled elevation
  • Compressive dressings with skin breakdown or dermatitis flare
• Maintain skin hydration
• Treat tinea pedis and onychomycosis
• **Prophylactic penicillin**
Penicillin to Prevent Recurrent Leg Cellulitis

Table 3. Factors Predictive of Prophylaxis Failure.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
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<tbody>
<tr>
<td>No. of previous cellulitis episodes</td>
<td>≥3 3.23 (1.82–5.73)</td>
<td>&lt;0.001</td>
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<td></td>
<td>&lt;3 1</td>
<td></td>
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<tr>
<td>Edema</td>
<td>Preexisting edema</td>
<td>1.83 (0.97–3.47)</td>
</tr>
<tr>
<td></td>
<td>No evidence of edema</td>
<td>1</td>
</tr>
<tr>
<td>BMI</td>
<td>≥33 2.05 (1.16–3.64)</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>&lt;33 1</td>
<td></td>
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</table>

No. of previous cellulitis episodes

- ≥3: 3.23 (1.82–5.73), <0.001
- <3: 1

Preexisting edema
- Odds Ratio: 1.83 (0.97–3.47), P = 0.06
- No evidence of edema: 1

BMI
- ≥33: 2.05 (1.16–3.64), P = 0.01
- <33: 1

The new england journal of medicine

Clostridium difficile
Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA)

L. Clifford McDonald,1 Dale N. Gerding,2 Stuart Johnson,2,3 Johan S. Bakken,4 Karen C. Carroll,5 Susan E. Coffin,6 Erik R. Dubberke,7 Kevin W. Garey,8 Carolyn V. Gould,1 Ciaran Kelly,3 Vivian Loo,10 Julia Shaklee Sammons,8 Thomas J. Sandora,11 and Mark H. Wilcox12

1Centers for Disease Control and Prevention, Atlanta, Georgia; 2Edward Hines Jr Veterans Administration Hospital, Hines, and 3Loyola University Medical Center, Maywood, Illinois; 4St Luke’s Hospital, Duluth, Minnesota; 5Johns Hopkins University School of Medicine, Baltimore, Maryland; 6Children’s Hospital of Philadelphia, Pennsylvania; 7Washington University School of Medicine, St Louis, Missouri; 8University of Houston College of Pharmacy, Texas; 9Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts; 10McGill University Health Centre, McGill University, Montréal, Québec, Canada; 11Boston Children’s Hospital, Massachusetts; and 12Leeds Teaching Hospitals NHS Trust, United Kingdom

Testing (Major Change)

- Do not perform repeat testing (within 7 days) during the same episode of diarrhea
- Do not test patients without symptoms
- Fecal leukocyte testing is not recommended

Clinicians and laboratory personnel agree at the institutional level to not submit stool specimens on patients receiving laxatives and to submit stool specimens only from patients with unexplained and new onset ≥3 unformed stools in 24 h for testing for CDI.

*Approved stool ELA toxin tests vary widely in sensitivity. Laboratories should choose a toxin test with sensitivity in the upper range of sensitivity as reported in the literature [146-149, 156].

Infection Prevention (Minor Changes)

• Private room or cohorting with other patients with CDI
• Gown and gloves for all direct cares
• Dedicated equipment

• Soap & water OR alcohol-based hand rub (unless epidemic)

• Cleaning issues
  • Use a sporicidal cleaning agent for cleaning & reprocessing of reusable equipment
  • Assess adequacy of cleaning
  • Daily cleaning if outbreaks

• Duration of isolation = 48 (unless outbreak then continue until discharge → silent on long-term care implications)

Other Prevention Activities (Moderate Changes)

- Minimize exposure to agents with higher risk of CDI
- Implement ASPs
- Discontinue unnecessary PPI
- Probiotics not routinely recommended
- No recommendation for pre-emptive anti-C. diff therapy

McDonald et al. *Infect Clin Infect Dis* 2018; 66(7): 987-994


Preventing Dysbiosis to Prevent *C. difficile*

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Experimental (n)</th>
<th>Control (n)</th>
<th>Weight (%)</th>
<th>Relative Risk (95% CI)</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Johnston et al. 2012</td>
<td>Probiotic</td>
<td>Placebo</td>
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<tr>
<td></td>
<td>Antibiotic-Associated Diarrhea</td>
<td>159/1470 (10.8%)</td>
<td>153/1471 (10.4%)</td>
<td>1.04 (0.83 – 1.32)</td>
<td>0.72</td>
</tr>
<tr>
<td></td>
<td>C. difficile diarrhea</td>
<td>12/1470 (0.8%)</td>
<td>17/1471 (1.2%)</td>
<td>0.70 (0.34 – 1.48)</td>
<td>0.35</td>
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### SHEA/IDSA Treatment Guideline

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Clinical Findings</th>
<th>Treatment</th>
<th>Evidence Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild/Moderate</td>
<td>WBC ≤ 15,000 Cr &lt; 1.5 x baseline</td>
<td>Metronidazole 500mg PO/IV TID x 10-14 days</td>
<td>A-I</td>
</tr>
<tr>
<td>Severe</td>
<td>WBC &gt; 15,000 Cr &gt; 1.5 x baseline</td>
<td>Vancomycin 125mg QID x 10-14 days</td>
<td>B-I</td>
</tr>
<tr>
<td>Severe/Complicated</td>
<td>Hypotension or shock, ileus, megacolon</td>
<td>Vancomycin 500mg PO/PNG QID plus Metronidazole 500mg IV Q8</td>
<td>C-III</td>
</tr>
</tbody>
</table>

(consider rectal instillation of vancomycin if ileus present)

Cohen et al. *Infect Control Hosp Epidemiol* 2010; 31(5): 431-55
Metronidazole... A drug for your mother-in-law, not your mother?

• Sherwood Gorbach, 1992
## Treatment (Major Changes)

### Table 1. Recommendations for the Treatment of *Clostridium difficile* Infection in Adults

<table>
<thead>
<tr>
<th>Clinical Definition</th>
<th>Supportive Clinical Data</th>
<th>Recommended Treatment**</th>
<th>Strength of Recommendation/Quality of Evidence</th>
</tr>
</thead>
</table>
| Initial episode, non-severe | Leukocytosis with a white blood cell count of ≤15,000 cells/mL and a serum creatinine level <1.5 mg/dL | - VAN 125 mg given 4 times daily for 10 days, OR  
  - FDX 200 mg given twice daily for 10 days  
  - Alternate if above agents are unavailable: metronidazole, 500 mg 3 times per day by mouth for 10 days | Strong/High  
  Strong/High  
  Weak/High |
| Initial episode, severe     | Leukocytosis with a white blood cell count of ≥15,000 cells/mL or a serum creatinine level >1.5 mg/dL | - VAN, 125 mg 4 times per day by mouth for 10 days, OR  
  - FDX 200 mg given twice daily for 10 days | Strong/High  
  Strong/High |
| Initial episode, fulminant  | Hypotension or shock, ileus, megacolon          | - VAN, 500 mg 4 times per day by mouth or by nasogastric tube. If ileus, consider adding rectal installation of VAN. Intravenously administered metronidazole (500 mg every 8 hours) should be administered together with oral or rectal VAN, particularly if ileus is present. | Strong/Moderate (oral VAN);  
Weak/Low (rectal VAN);  
Strong/Moderate (intravenous metronidazole) |

**Note:** VAN = Vancomycin, FDX = Fidaxomicin.
Fidaxomicin versus Vancomycin for Clostridium difficile Infection

Thomas J. Louie, M.D., Mark A. Miller, M.D., Kathleen M. Mullane, D.O., Karl Weiss, M.D., Arnold Lentnek, M.D., Yoav Golan, M.D., Sherwood Gorbach, M.D., Pamela Sears, Ph.D., and Youe-Kong Shue, Ph.D., for the OPT-80-003 Clinical Study Group*

ABSTRACT

BACKGROUND
Fidaxomicin vs. Vancomycin

Figure 2. Rates of Primary and Secondary End Points.
For the primary outcome of clinical cure, the lower boundary of the 97.5% confidence interval for the difference in cure rates between fidaxomicin and vancomycin was −3.1 percentage points in the modified intention-to-treat (mITT) analysis and −2.6 percentage points in the per-protocol (PP) analysis.

Fidaxomicin guidelines for CDI at UWHC

Restricted to:

- Documented (PCR positive or colonoscopy proven) recurrent CDI requiring hospitalization (B-I)
- Relapse during current hospitalization (B-I).
- Patients with documented low levels of neutralizing antibodies to *C. difficile* (since this test is not available with rapid turnaround time, use under this indication would likely take 10-14 days) (B-II).
- Outpatients with 1 or more relapse of disease not requiring hospitalization (B-I).
- Fidaxomicin generally will NOT be prescribed because a patient may fall into a “high risk/severe disease/likely antibody deficient”
  - Do not use beyond 10 days of treatment.
  - $2800 = cost of 10 day course
Recurrent CDI

• Threefold increase in incidence of multi-recurrent CDI from 2001 – 2012

• Risk Factors
  • Age: 1.25 (1.21 – 1.29)
  • Female Gender: 1.24 (1.11 – 1.38)
  • Repeat Antibiotics: 1.79 (1.59 – 2.01)
  • PPI: 1.14 (1.01 – 1.29)
  • Steroids: 1.15 (1.00 – 1.32)
  • CKD: 1.49 (1.24 – 1.80)
  • SNF: 1.99 (1.34 – 2.93)

Ma et al. Ann Intern Med 2017; 167(3): 152
### Treatment (Major Changes)

**Table 1. Recommendations for the Treatment of Clostridium difficile Infection in Adults**

<table>
<thead>
<tr>
<th>Clinical Definition</th>
<th>Supportive Clinical Data</th>
<th>Recommended Treatment*</th>
<th>Strength of Recommendation/Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>First recurrence</td>
<td></td>
<td>VAN 125 mg given 4 times daily for 10 days if metronidazole was used for the initial episode, OR</td>
<td>Weak/Low</td>
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<tr>
<td></td>
<td></td>
<td>Use a prolonged tapered and pulsed VAN regimen if a standard regimen was used for the initial episode (e.g., 125 mg 4 times per day for 10–14 days, 2 times per day for a week, once per day for a week, and then every 2 or 3 days for 2–3 weeks), OR</td>
<td>Weak/Low</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FDX 200 mg given twice daily for 10 days if VAN was used for the initial episode</td>
<td>Weak/Moderate</td>
</tr>
<tr>
<td>Second or subsequent recurrence</td>
<td></td>
<td>VAN in a tapered and pulsed regimen, OR</td>
<td>Weak/Low</td>
</tr>
<tr>
<td></td>
<td></td>
<td>VAN, 125 mg 4 times per day by mouth for 10 days followed by rifaximin 400 mg 3 times daily for 20 days, OR</td>
<td>Weak/Low</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FDX 200 mg given twice daily for 10 days, OR</td>
<td>Weak/Low</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fecal microbiota transplantation&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Strong/Moderate</td>
</tr>
</tbody>
</table>

*McDonald et al. Infect Clin Infect Dis 2018; 66(7): 987-994*
Fecal Transplant

Bacteriotherapy

Intestinal Microbiota Transplant

Brown Gold
Reversing Dysbiosis to Treat *C. difficile*

Staggered and Tapered Antibiotic Withdrawal With Administration of Kefir for Recurrent *Clostridium difficile* Infection

Johan S. Bakken
Section of Infectious Disease, St Luke’s Hospital, Duluth, Minnesota

Daily administration of the probiotic kefir given in combination with a staggered and tapered antibiotic withdrawal regimen may resolve recurrent *Clostridium difficile* infection as effectively as fecal microbiota transplantation.

Bakken JS. *Clin Infect Dis* 2014; 59(6): 858-61
Thank You