Guideline Updates
Change is Inevitable – Especially in Infectious Diseases!

Vicky Shah, PharmD, BCPS
Assistant Professor of Pharmacy Practice
Wilkes University Nesbitt School of Pharmacy
Vicky Shah has no potential or actual conflicts of interest to disclose.
Objectives

- Describe first line therapies for the treatment of Clostridium difficile
- Apply new pneumonia guidelines to your place of practice
- Evaluate antimicrobial stewardship at your institution
Clostridium Difficile

Guidelines Update 2017/2018
The Infectious Diseases Society of America (IDSA)

The Society for Healthcare Epidemiology of America (SHEA)

New 2017/2018 Guidelines
Major Guideline Updates

- Inclusion of specific pediatric guidelines
- Discussion on laboratory guided diagnosis in adults
- Removal of metronidazole for 1st line therapy in adults
- Discussion on fecal transplantation utilization
- Consideration of prophylaxis techniques
Clostridium difficile

- Gram-positive, anaerobic, spore-forming bacillus
- Infection is a result of a disturbance of the normal flora of the colon
- Responsible for development of antibiotic-associated diarrhea and colitis
- Incidence and severity of infection is increasing

Epidemiology

Normal fecal flora

2% of healthy adults

How long will Clostridium difficile pathogens live on a dry surface?
Pathophysiology

Antibiotic Therapy

Alteration of colonic microorganisms

C. difficile exposure and colonization

Release of Toxins A and B

Binding to enterocyte receptors

Colonic mucosal injury and acute inflammation

Diarrhea and colitis

Symptoms

- Asymptomatic Colonization
- Diarrhea
- Abdominal Pain/Distension
- Fever
- Pseudomembranous Colitis
- Toxic Megacolon
- Death

References:
Risk Factors

- Hospitalization
- Chronic Care Facility
- Antibiotics
- Age
- Surgery
- Chemotherapy
- Intestinal Obstruction
- PPIs

# Antibiotic Related Risk

<table>
<thead>
<tr>
<th>High Risk</th>
<th>Medium Risk</th>
<th>Low Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clindamycin</td>
<td>Macrolides</td>
<td>Aminoglycosides</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Tetracyclines</td>
<td>Metronidazole</td>
</tr>
<tr>
<td>Ampicillin/Amoxicillin</td>
<td>Fluoroquinolones</td>
<td>Anti-pseudomonas Penicillin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vancomycin</td>
</tr>
</tbody>
</table>

Inclusion of Specific Pediatric Guidelines

Major Update
Pediatric Additions

Surveillance

Diagnosis

Treatment

Pediatric Surveillance

Epidemiology of pediatric cases will be tracked and reported in the same manner as adult cases.

Patients under the age of 2 weeks will not be included in the surveillance.

Pediatric Diagnosis

Neonates or infants ≤12 months of age with diarrhea
• Testing is not recommended due to high prevalence of asymptomatic carriage

Ages 1-2
• Testing is not recommended UNLESS other infectious or noninfectious causes have been excluded

Children 3 and older
• Testing is recommended for patients with prolonged or worsening diarrhea WITH risk factors (underlying inflammatory bowel disease, immunocompromising condition, recent contact with the healthcare system or recent antibiotic use)

# Pediatric Treatment

<table>
<thead>
<tr>
<th>Clinical Definition</th>
<th>Recommended Treatment</th>
<th>Pediatric Dose</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-severe (initial episode)</strong></td>
<td>Metronidazole PO x 10 days</td>
<td>7.5mg/kg/dose TID or QID</td>
<td>500mg TID or QID</td>
</tr>
<tr>
<td></td>
<td>Vancomycin PO x 10 days</td>
<td>10mg/kg/dose QID</td>
<td>125mg QID</td>
</tr>
<tr>
<td><strong>Severe/Fulminant (initial episode)</strong></td>
<td>Vancomycin PO x 10 days</td>
<td>10mg/kg/dose QID</td>
<td>500mg QID</td>
</tr>
<tr>
<td></td>
<td>WITH OR WITHOUT</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metronidazole IV x 10 days</td>
<td>10mg/kg/dose TID</td>
<td>500mg TID</td>
</tr>
<tr>
<td><strong>Non-severe (1st recurrence)</strong></td>
<td>Metronidazole PO x 10 days</td>
<td>7.5mg/kg/dose TID or QID</td>
<td>500mg TID or QID</td>
</tr>
<tr>
<td></td>
<td>Vancomycin PO x 10 days</td>
<td>10mg/kg/dose QID</td>
<td>125mg QID</td>
</tr>
<tr>
<td><strong>Second or subsequent recurrence</strong></td>
<td>Vancomycin Taper/Pulse Dose</td>
<td>10mg/kg/dose QID</td>
<td>125mg QID</td>
</tr>
<tr>
<td></td>
<td>Vancomycin PO x 10 days followed by</td>
<td>No pediatric dosing for Rifaximin</td>
<td>Vancomycin – 500mg QID Rifaximin – 400mg TID</td>
</tr>
<tr>
<td></td>
<td>Rifaximin PO x 20 days</td>
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<td></td>
</tr>
</tbody>
</table>

Fecal Microbiota Transplantation

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Discussion on Laboratory Guided Diagnosis in Adults

Major Update
Diagnosis

Past medical history of the patient

Laboratory results

Symptoms (number of unformed stools in a 24 hour period)

Diagnosis

If the institution uses only specimens from patients who are not taking laxatives and have at least 3 or more unformed stools in a 24 hour period:

- Nucleic Acid Amplification Test (NAAT) alone is satisfactory!
- Stool toxin test may be recommended to confirm the diagnosis

Glutamate dehydrogenase (GDH) followed by a stool toxin test:

- If GDH comes back negative, follow-up with the NAAT
Nonpharmacological Treatments

- Discontinue antibiotics
- Fluid and electrolyte replacement
- Isolation
- Avoid antimotility agents
- Fecal Microbiota Transplantations (FMT)

Severity Classification

Non-Severe
- WBC Count <15,000

Severe
- WBC Count >15,000
- SCr > 1.5mg/dL

Fulminant
- WBC Count >15,000
- SCr > 1.5mg/dL
- Signs of Complications
  - Hypotension/shock
  - Ileus
  - Toxic Megacolon

Removal of Metronidazole for 1st Line Therapy in Adults

Major Update
<table>
<thead>
<tr>
<th>Clinical Definition</th>
<th>Recommended Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-severe (initial episode)</td>
<td>Vancomycin PO 125mg QID x 10 days</td>
</tr>
<tr>
<td></td>
<td>Fidaxomicin 200mg BID x 10 days</td>
</tr>
<tr>
<td></td>
<td>Metronidazole 500mg BID x 10 days (only if Vancomycin and Fidaxomicin are unavailable)</td>
</tr>
<tr>
<td>Severe (initial episode)</td>
<td>Vancomycin PO 125mg QID x 10 days</td>
</tr>
<tr>
<td></td>
<td>Fidaxomicin 200mg BID x 10 days</td>
</tr>
<tr>
<td>Fulminant (initial episode)</td>
<td>Vancomycin PO 500mg QID x 10 days</td>
</tr>
<tr>
<td></td>
<td>WITH</td>
</tr>
<tr>
<td></td>
<td>Metronidazole IV 500mg TID x 10 days</td>
</tr>
</tbody>
</table>

## Treatment

<table>
<thead>
<tr>
<th>Clinical Definition</th>
<th>Recommended Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First recurrence</strong></td>
<td>If Metronidazole used during 1&lt;sup&gt;st&lt;/sup&gt; episode → Vancomycin PO 125mg QID x 10 days</td>
</tr>
<tr>
<td></td>
<td>If Vancomycin used during 1&lt;sup&gt;st&lt;/sup&gt; episode → Vancomycin Taper/Pulse Dose</td>
</tr>
<tr>
<td></td>
<td>If Vancomycin used during 1&lt;sup&gt;st&lt;/sup&gt; episode → Fidaxomicin 200mg BID x 10 days</td>
</tr>
<tr>
<td><strong>Second recurrence</strong></td>
<td>Vancomycin Taper/Pulse Dose</td>
</tr>
<tr>
<td></td>
<td>Vancomycin PO 125mg QID x 10 days following by Rifaximin 400mg TID x 20 days</td>
</tr>
<tr>
<td></td>
<td>Fidaxomicin 200mg BID x 10 days</td>
</tr>
<tr>
<td></td>
<td>Fecal Microbiota Transplantation</td>
</tr>
</tbody>
</table>

Discussion on Fecal Transplantation Utilization

Major Update
Fecal Microbiota Transplantation (FMT)

Previously not recommended in 2010 guidelines as not much data was available

77-94% efficacy rate for treating and reducing reoccurrences

Recommended for patients with multiple recurrences with failure of appropriate antibiotic treatments

What makes someone a good candidate to be a DONOR?
Donor Requirements

Healthy individual

- No history of irritable bowel diseases, crohn’s disease, gastrointestinal cancer, etc.
- No active autoimmune disorders
- No antibiotic use in the last 90 days

Not an asymptomatic carrier of Clostridium difficile

Best candidate is someone with a similar diet as the recipient

Consideration of Prophylaxis Techniques

Major Update
Prophylaxis

Probiotics may be effective at preventing infections when given to patients on antibiotics who do not have a history of Clostridium difficile.

Probiotic use is NOT currently supported due to lack of significant results in controlled trials.

Lactobacillus and Saccharomyces boulardii have been associated with some reduction in recurrence.

Prophylaxis

Patients who complete appropriate treatment for Clostridium difficile requiring antibiotic therapy for other infections may be provided prophylaxis treatment with Vancomycin 125mg daily or Fidaxomicin 200mg daily.

Treatment duration of their Clostridium difficile treatment may also be extended beyond 10 days until completion of their new antibiotic for other infections.

Guidelines do not fully support prophylaxis but initial studies have shown reduction in recurrences when prophylaxis or extended therapy is administered.

HAP/VAP

Guidelines Update 2016
Major Guideline Updates

- Removal of the concept of Health Care Associated Pneumonia (HCAP)
- Larger emphasis on local institutions collecting data and creating antibiogram
- Decrease the unnecessary use of dual gram-negative and empiric MRSA coverage
- Shorter duration of therapy
Removal of the Concept of Health Care Associated Pneumonia (HCAP)

Major Update
<table>
<thead>
<tr>
<th>Type of Pneumonia</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community Acquired Pneumonia (CAP)</td>
<td>Pneumonia developing in patients with no contact to a medical facility</td>
</tr>
</tbody>
</table>
| Healthcare Associated Pneumonia (HCAP)| Pneumonia developing in patients not in medical facility but two or more risk factors for multidrug resistant pathogens:  
  • Recent hospitalization ≥ 2 days within past 90 days  
  • Nursing home or long-term care patients  
  • Recent antibiotic use, IV therapy, wound care, or chemotherapy within past 30 days  
  • Hemodialysis patient within past 30 days  
  • Contact with family member who has multidrug resistant pathogen infection |
| Hospital Acquired Pneumonia (HAP)      | Pneumonia developing ≥ 48 hours after admission                              |
| Ventilator Associated Pneumonia (VAP)  | Pneumonia developing ≥ 48 hours after intubation and mechanical ventilation  |
| Aspiration Pneumonia (AP)              | Pneumonia developing in alcoholic patients or patients who have trouble swallowing |
Healthcare Associated Pneumonia

New IDSA 2016 guidelines recommend treating HCAP similar to CAP

Older guidelines treated closer to HAP/VAP but newer guidelines reduce resistance and overuse of antibiotics
Larger Emphasis on Local Institutions
Collecting Data and Creating Antibiogram

Major Update
Antibiogram Example

**Gram-Positive Organisms**

<table>
<thead>
<tr>
<th></th>
<th>Penicillins</th>
<th>Cephalosporins</th>
<th>Quinolones</th>
<th>Tetracyclines</th>
<th>Other Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Percent Susceptible</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Number of isolates</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tested)</td>
<td></td>
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<tr>
<td><strong>Enterococcus sp.</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>(unsuspected)</td>
<td>92 (3,112)</td>
<td></td>
<td>81 (816)</td>
<td>75 (100)</td>
<td>99 (2,865)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Enterococcus</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>faecalis</td>
<td>99 (2,046)</td>
<td></td>
<td>82 (1,699)</td>
<td>32 (461)</td>
<td>100 (1,396)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Enterococcus</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>faecium</td>
<td>25 (161)</td>
<td></td>
<td>14 (163)</td>
<td>68 (163)</td>
<td>100 (166)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methicillin-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>resistant Staphylococcus</td>
<td>0 (4,658)</td>
<td></td>
<td>44 (4,669)</td>
<td>100 (1,739)</td>
<td>99 (7,426)</td>
</tr>
<tr>
<td>aureus (MRSA)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>100 (11,841)</td>
<td></td>
<td>95 (6,748)</td>
<td>96 (12,028)</td>
<td>86 (7,447)</td>
</tr>
<tr>
<td>Methicillin-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>susceptible Staphylococcus</td>
<td>100 (8,459)</td>
<td></td>
<td>100 (6,141)</td>
<td>83 (11,935)</td>
<td>100 (11,825)</td>
</tr>
<tr>
<td>aureus (MSSA)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>362</td>
<td></td>
<td>86 (329)</td>
<td>99 (362)</td>
<td>85 (341)</td>
</tr>
</tbody>
</table>

**Comparison to 2014 susceptibility**: 10% or greater increase, 5-9% increase, 5-9% decrease, 10% or greater decrease

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Decrease the Unnecessary Use of Dual Gram-Negative and Empiric MRSA Coverage

Major Update
Minimum Empiric Treatment for HAP/VAP

Staphylococcus aureus

- MSSA coverage if MRSA negative

Pseudomonas auroginosa coverage

- Single agent is appropriate

MRSA Treatment

Greater than 10-20% MRSA in hospital Staphylococcus aureus isolates or unknown MRSA prevalence

Aggressive Anti-Pseudomonas Coverage

HAP
- Ventilator support
- Septic shock
- Prior IV antibiotic use within 90 days

VAP
- Prior IV antibiotic use within 90 days
  - Septic Shock at time of VAP
  - Acute Respiratory Distress Syndrome preceding VAP
- Five or more days of hospitalization prior to the occurrence of VAP
  - Acute renal replacement therapy prior to VAP onset

Structural Lung Disease

>10% Pseudomonas Resistance

Abundance of GNB on Gram Stain

Pneumonia develops ≥ 48 hours following

Hospitalization [HAP] ← Intubation [VAP]

Patient has any of:
- Ventilatory support
- Septic Shock
- IV Antibiotics within 90 days

*guidelines recommend 10%-20% cutoff for VAP and 20% cutoff for HAP

Is there > 10-20%* MRSA in hospital S. aureus isolates or unknown MRSA prevalence?

- Does the patient have structural lung disease?
- Is there > 10% pseudomonal resistance to anti-pseudomonal therapy under consideration?
- Is there an abundance of GNB on gram stain?

MRSA coverage & 2 anti-pseudomonal antimicrobial agents of different classes

1 anti-pseudomonal antimicrobial agent with activity against MSSA [if MRSA not covered]

2 anti-pseudomonal antimicrobial agents
One of which with activity against MSSA [if MRSA not covered]

If dual pseudomonas coverage is needed, which of the following combinations would you recommend?

A. Cefepime PLUS Zosyn
B. Levofloxacin PLUS Zosyn
C. Ceftriaxone PLUS Imipenem
D. Cefepime PLUS Ertapenem
## Empiric Therapy

<table>
<thead>
<tr>
<th>Not at high risk of mortality and no factors increasing likelihood of MRSA</th>
<th>Not at high risk of mortality but with factors increasing likelihood of MRSA</th>
<th>High risk of mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zosyn OR Cefepime OR Levofloxacin OR Carbapenem</td>
<td>Zosyn OR Cefepime or Ceftazidime OR Levofloxacin or Ciprofloxacin OR Carbapenem OR Aztreonam</td>
<td>Zosyn OR Cefepime or Ceftazidime OR Carbapenem OR Aztreonam</td>
</tr>
<tr>
<td>PLUS</td>
<td>PLUS</td>
<td>PLUS</td>
</tr>
<tr>
<td>Vancomycin OR Linezolid</td>
<td>Levofloxacin or Ciprofloxacin OR Aminoglycoside</td>
<td>Vancomycin OR Linezolid OR MSSA Coverage</td>
</tr>
</tbody>
</table>

Shorter Duration of Therapy

Major Update
Duration of Therapy

7 days

Role of Antibiotic Stewardship
Antibiotic Stewardship

Minimize the frequency and duration of high risk antibiotic therapy and the number of antibiotic agents prescribed

Implement an antibiotic stewardship program!

- Encourage in ALL IDSA/SHEA guidelines

Target treatment based on local epidemiology and institution specific resistance rates.

Restriction of fluoroquinolones, clindamycin and cephalosporin antibiotics may be considered (especially for Clostridium difficile risk patients)
What Questions Do You Have?

vicky.shah@wilkes.edu