Diagnosis & Treatment of *Clostridium difficile* Infection (CDI)

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**First Step: Make Diagnosis**

Making the diagnosis: diarrhea plus positive fecal test for *C. difficile* toxin(s):
- EIA lacks sensitivity;
- Toxicgenic culture and Tissue culture cytotoxicity assay takes 3 days
- PCR overly sensitive and picks up carriage
- Two step methods have been developed (e.g. glutamate dehydrogenase + EIA or PCR)
- Fecal CD toxin test plus finding inflammatory markers in stool suggests; Finding pseudomembranous colitis by endoscopy confirms the diagnosis

**Make an Early Diagnosis of CDI, Consider Stopping Current Antibiotics and Start CDI Treatment**

**Oral Vancomycin vs Metronidazole in Mild and Severe CDI**

- 172 patients enrolled and 150 completed the trial
- Clinical Cure in Mild Disease (n=81)
- Clinical Cure in Severe Disease (n=69)

**Relative Cost of Various CDI Treatments**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Average Wholesale Price for 10 Days</th>
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<tbody>
<tr>
<td>Metronidazole 500 mg</td>
<td>PO TID $25.00</td>
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<tr>
<td>Vancomycin 125 mg</td>
<td>PO QID Capsules $1,300 Oral liquid &lt;$200</td>
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<tr>
<td>Fidaxomicin 200 mg</td>
<td>PO BID $2,500</td>
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Is 10% 1% recurrence w/ fidaxomicin worthwhile? Additional cost? If yes factor in prevention of recurrence as may be! Before prescribing fidaxomicin, be sure patient is willing to accept all the conditions of drug as important

**Immune Response in *C. difficile* Infection and Diarrhea**

- Antitoxin A IgG antibody rises most common in subclinical infection; both subclinical infection and serum antibodies are protective against *C. difficile* diarrhea
- Development of a serum antitoxin A IgG or IgM antibody response predicts those who will not relapse

**Vancomycin Versus Metronidazole**

- In a double-blind randomized trial vancomycin was superior to metronidazole for all cases from mild to severe


Treatment Strategies for Recurrent CDI

- 1st recurrence - initial therapy can be repeated (not metronidazole)
- Oral vancomycin
  - Tapered dose (125 mg 4 times a day down to 125 mg once every 3 days over 6 weeks)
  - Pulse dose (125 mg or 500 mg every 3 days for 3 weeks)
  - Saccharomyces boulardi 500 mg bid x 14 days after oral vancomycin
- Fidaxomicin 200 mg twice a day for 10-20 days
- Rifaximin 550 mg twice a day for 4 weeks alone or followed by 2 weeks of S. boulardi (above dose)
- Fecal microbiota transplant (FMT) most effective treatment for ≥3 bouts of CDI

DuPont HL. Diagnosis and management of Clostridium difficile infection. Clinical Gastro Hepatol 2013;11:1216-23

For Depletion of Diversity of Microflora - Fecal Microbiota Transplantation (FMT)

- 50 g of stool is collected from healthy donor
- CDI patients are randomized to receive fresh, frozen or lyophilized fecal bacteria
- 120 patients treated so far in two studies with >90% cure rates
- We have moved to enteric coated capsules & enemas for administration

C. difficile Diarrhea (CDI)
Directions of Future Research

To Determine:
- Optimal methods to diagnose CDI that differentiates between disease & colonization
- Treatment of primary and recurrent CDI (for cure without future recurrence)
- Development of novel therapeutic drugs and biologic agents (advanced probiotics)
- Prevention of CDI in high risk people

C. difficile Research Team at Baylor St. Luke's