Clostridium difficile infections: Challenges and Scenarios

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Background

- *Clostridium difficile*: anaerobic, gram positive, spore forming, bacillus

- Estimated $3.2 billion/year in expenditures

- Mortality estimated to be ~4-8%

- Surgical Treatment In Complicated Cases

Courtesy of American College of Surgeons Division of Education Clinical Congress 2015
58 yo female calls your office after being discharged from the hospital from laparoscopic hysterectomy. Now POD 6, states she has diarrhea for one day (17 loose BM) and feels lousy.
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B. Send her for C diff testing and start therapy if positive.
C. Tell her to eat yogurt with live active cultures as well as probiotics and follow her progress.
D. Treat her with a course of vancomycin

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67 yo female in the hospital on the medical service for community acquired pneumonia treated with ceftriaxone 1 g IV q24h plus azithromycin 500 mg IV q24h for past 4 days, now with WBC increase to 15 and diarrhea. No abdominal tenderness, normal creatinine and labs otherwise WNL. C diff PCR +
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A. Stop or change antibiotics for pneumonia if possible and start treatment with metronidazole 500 PO q8h.
B. Stop or change antibiotics for pneumonia if possible and start treatment with vancomycin 125 mg IV q6h.
C. Start vancomycin 125 mg po q6h.
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Courtesy of American College of Surgeons Division of Education Clinical Congress 2015
Practice Guidelines

The American Journal of Gastroenterology, (26 February 2013) | doi:10.1038/ajg.2013.4

Guidelines for Diagnosis, Treatment, and Prevention of Clostridium difficile Infections

Christina M Surawicz, Lawrence J Brandt, David G Binion, Ashwin N Ananthakrishnan, Scott R Curry, Peter H Gilligan, Lynne V McFarland, Mark Mellow and Brian S Zuckerbraun

Courtesy of American College of Surgeons Division of Education
Clinical Congress 2015
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### ACG Severity Scoring and Treatment

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Metronidazole v. Vancomycin

Metronidazole
- effective as intravenous or enteral form
- Does not reach colon at effective MIC unless diarrhea
- Both dosing regimens dependent upon GI motility

Vancomycin
- Intravenous not effective
- Enteral (oral, tube, rectal) reaches colon at effective MIC in both diarrheal and non-diarrheal stool

Courtesy of American College of Surgeons Division of Education
Clinical Congress 2015
Metronidazole v. Vancomycin

-No antimicrobial agent is clearly superior for the initial cure of C. difficile infection

-Three randomized control trials have compared metronidazole to vancomycin

*One trial demonstrated vanco superior in severe disease (Zar et al, Clinical Infectious Disease, 2007)
(evidence considered insufficient)

Courtesy of American College of Surgeons Division of Education
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- Non-inferior to vancomycin for cure rate
- Lower recurrence rate compared to vanco
- Expensive
- Use in setting of recurrences
Probiotics

Data does not support the use of probiotics as a treatment for C Diff infection.

Studies suggest a trend for prevention or to limit recurrences.

Courtesy of American College of Surgeons Division of Education Clinical Congress 2015
72 yo male s/p total hip whose post-op course was complicated by the development of C diff infection treated with a 10 day course of vancomycin 125 mg PO q6h X 10 days. Was discharged 4 days into the course with clinical resolution of diarrhea. Initial post-op visit was doing well. Calls 3 weeks later (POD 38) with new onset diarrhea. “Just like in hospital.” No fevers, mild cramping.
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A. Treat with second course vancomycin for 10 days
B. Treat with 7 week pulse and taper of vanc
C. Treat with fidaxomicin for 10 day course.
D. Treat with metronidazole and followed by probiotics.
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D. Treat with metronidazole and followed by probiotics.
Recommended for recurrent disease

1\textsuperscript{st} Recurrence: Vancomycin

2\textsuperscript{nd} Recurrence: Vancomycin 7 week taper

3\textsuperscript{rd} Recurrence: Fecal Microbiota Therapy
Duodenal Infusion of Donor Feces for Recurrent *Clostridium difficile*

Els van Nood, M.D., Anne Vrieze, M.D., Max Nieuwdorp, M.D., Ph.D., Susana Fuentes, Ph.D., Erwin G. Zoetendal, Ph.D., Willem M. de Vos, Ph.D., Caroline E. Visser, M.D., Ph.D., Ed J. Kuijper, M.D., Ph.D., Joep F.W.M. Bartelsman, M.D., Jan G.P. Tijssen, Ph.D., Peter Speelman, M.D., Ph.D., Marcel G.W. Dijkgraaf, Ph.D., and Josbert J. Keller, M.D., Ph.D.

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U.S.’s first stool bank supplies hospitals with fecal transplants for C. difficile treatment

February 22, 2014 8:00 am by Deanna Pogorelc | 1 Comments
81 yo transferred to MICU from another institution with known c diff infection treated for 5 days with vancomycin on norepinephrine at 0.4mcg/kg/min, creatinine 3.2, intubated and ventilated. Next step...
81 yo transferred to MICU from another institution with known c diff infection treated for 5 days with vancomycin on norepinephrine at 0.4mcg/kg/min, creatinine 3.2, intubated and ventilated. Next step...

A. Resuscitate, add metronidazole and watch clinical response.
B. Resuscitate, add vancomycin enemas and watch clinical response.
C. Resuscitate, add metronidazole, vanc enemas, and give patient 24 hours to improve.
D. Immediate surgical consultation and immediate operative intervention.

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*Courtesy of American College of Surgeons Division of Education Clinical Congress 2015*

A diagnosis of CDAD as determined by one of the following:

1. Positive C Diff test
2. Endoscopic findings
3. CT scan consistent with CDAD

Plus any one of the following criteria:

1. Peritonitis
2. Perforation
3. Worsening abdominal distention/pain
4. Severe Sepsis
5. Intubation
6. Ongoing Vasopressor requirement
7. Mental status changes
8. Unexplained clinical deterioration
9. Renal Failure
10. Lactate > 5mmol/L
11. White blood cell count greater or equal to 50,000
12. Abdominal compartment syndrome
13. Not improving after ? Days
Hypothesis: Therapy to decrease bacterial counts and toxin levels throughout the whole colon will adequately treat severe, complicated CDAD.

Not C Diff Colon

Diverting Loop Ileostomy and Colonic Lavage: An Alternative to Total Abdominal Colectomy for the Treatment of Severe, Complicated Clostridium difficile Associated Disease

Neal MD, Alverdy JC, Hall DE, Simmons RL, Zuckerbraun BS


Courtesy of American College of Surgeons Division of Education Clinical Congress 2015
Methods

1. Exploratory laparoscopy/laparotomy
2. Creation of diverting loop ileostomy
3. Colonic lavage with 8 liters of warm PEG3350/balanced electrolyte solution (Go-Lightly™) via ileostomy
4. Post-op antegrade vancomycin flushes via ileostomy (500mg in 500ml tid) for 10 days

Courtesy of American College of Surgeons Division of Education Clinical Congress 2015
Loop ileostomy/colonic lavage patients have improved survival compared to total abdominal colectomy (historical controls) for severe, complicated *C. Diff.*

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<td>29.7±10.8</td>
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<td><strong>Post-Operative Death</strong></td>
<td>22/100* (22%)</td>
<td>49/100 (49%)</td>
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-3 patients not offered this therapy and offered colectomy

-7/100 had subsequent colectomy.

Courtesy of American College of Surgeons Division of Education Clinical Congress 2015
Loop ileostomy/colonic lavage has an improved one-year survival and restoration of GI continuity in patients that were discharged to home following surgery.

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<td>Alive at 1 year</td>
<td>58/67 (87%)</td>
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<td>Restoration of GI continuity*</td>
<td>49/58 (84%)</td>
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*Data for patients followed for greater than 12 months
Loop ileostomy/lavage patients had similar APACHE-II scores as colectomy patients, however there was earlier consultation & surgical management compared to historical colectomy controls.

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<td><strong>Time from presentation to surgical consultation</strong></td>
<td>11±9 hours</td>
<td>32±12 hours</td>
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<td><strong>Time from surgical consultation to operative intervention</strong></td>
<td>9±6 hours</td>
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*Courtesy of American College of Surgeons Division of Education Clinical Congress 2015*
Figure 1.

Diarrhea and confirmed or suspected CDI

- Fluid and electrolyte resuscitation as necessary
- Infection control measures
- Stop inciting antibiotics if possible

Mild/moderate Disease
- Metronidazole 500 mg PO tid for 10 days

Severe Disease
- Vancomycin 125 mg PO qid For 10 days

Severe, Complicated Disease
- Surgical consultation
- CT scan abdomen/pelvis
- vaspressors, intubation, mental status changes, peritonitis, or end organ failure?

- no
  - If symptoms not resolving within 6 days:
    - Surgical consultation, CT scan

- yes
  - Metronidazole 500 mg IV tid
    - Plus
    - Vancomycin 125 mg PO qid
      - Plus
    - Vancomycin 500 mg in 500 mL enema

If worsening clinical symptoms or deterioration, worsening WBC, cardiopulmonary compromise, or end organ failure

OPERATIVE MANAGEMENT
OPERATIVE MANAGEMENT STRATEGY FOR CDAD

Does the patient have abdominal compartment syndrome?

(∼5% incidence) yes

Exploratory laparotomy, subtotal abdominal colectomy with end ileostomy.

No

Exploratory laparoscopy (convert to laparotomy as necessary)

Colonic perforation/necrosis?

Yes (rare)

Loop ileostomy/intraoperative colonic lavage

No

Development of abdominal compartment syndrome post-op?

Yes (∼7% incidence; Usually within 48 hours)

No

Monitor for continued improvement

Courtesy of American College of Surgeons Division of Education
Clinical Congress 2015
72 yo male 3 weeks s/p an esophagectomy readmitted to the thoracic service with abdominal pain and diarrhea (15 per day for 3 days). Admitted to ICU.

- Abdomen mildly tender and distended.
- WBC 23
- Cr 2.7 (baseline 1.1)
- Albumin 2.4
- SBP 90.
- Started on fluids (total of 5 liters)
- Initially on NE gtts, but weaned off
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-C diff testing sent off
-Started on metronidazole 500 mg IV q8h and vancomycin 500 mg PO q6h
-General Surgery team consulted
72 yo male 3 weeks s/p an esophagectomy readmitted to the thoracic service with abdominal pain and diarrhea (15 per day for 3 days). Admitted to ICU.

Next day...

- Continued diarrhea
- No hypotension
- WBC down to 15 (23)
- Cr down to 1.6 (2.7)
Was making continued progress until 3 days later...

- Mild increase in pain and tenderness
- Continue 10 BM per day
- No hypotension
- WBC back up to 21, 42% bands
- Good urine output, hemodynamics normal, normal MS
Was making continued progress until 3 days later...

- Mild increase in pain and tenderness
- Continue 10 BM per day
- No hypotension
- WBC back up to 21, 42% bands
- Good urine output, hemodynamics normal, normal MS

- Added vancomycin enemas (500 mg in 500 mL q8)
- Increased frequency of serial exams
Pain and tenderness improved by next day. Still with 8-10 BM/day. WBC 20 (14% bands).
Pain and tenderness improved by next day. Still with 8-10 BM/day. WBC 20 (14% bands). Until the next day.

- Increased pain, distention, and tenderness
- No hypotension
- WBC 22
Pain and tenderness improved by next day. Still with 8-10 BM/day. WBC 20 (14% bands). Until next day.

- Increased pain, distention, and tenderness
- No hypotension
- WBC 22

Took to OR for laparoscopy, diverting loop ileostomy/colonic lavage. D/C to SNF after 8 days.