Updates in the Treatment of

*Clostridium difficile* Colitis

Philip L Rosen, MD
Department of Surgery
SUNY Downstate / KCHC Resident
April 27, 2017
Disclosures

• None
Objectives

• Identify patients at risk for C diff

• Describe surgical options for C diff

• Describe the history of fecal transplants
2 Updates

• Loop ileostomy with colonic lavage
• Fecal Transplant
Clostridium difficile

- Anaerobic
- Gram Positive
- Spore-forming
- Toxin-producing
C. difficile

INTESTINAL FLORA IN NEW-BORN INFANTS
WITH A DESCRIPTION OF A NEW PATHOGENIC ANAEROBE,
BACILLUS DIFFICILIS

IVAN C. HALL, Ph.D.
AND
ELIZABETH O'TOOLE
DENVER

From the Department of Bacteriology and Public Health, University of Colorado School of Medicine and Hospitals.

John M. T. Finney, MD, FACS, 1863-1942

• Studied at Johns Hopkins Hospital
  • Halsted, Welch, Osler, and Kelly
• 1st President of ACS (1913-1916)
• 1893: first reported pseudomembranous colitis
  • Pre-Antibiotic era
  • Patient died after pyloric ulcer surgery from diffuse diarrhea
• “Can't see much sale for this, other than the fact that medical books do sell -- and the many friends to whom tribute is paid, may want to read the book. The book is full of very personal anecdotal material, but it is unquestionably dull, for the average reader, and makes little contribution to the layman's understanding of surgery. Dr. Finney's life followed more or less conventional lines, -- his father was a clergyman, he went to Princeton, Harvard Medical and Mass. General, chief consultant in surgery during the first World War, and has been at Johns Hopkins ever since. He devotes the last part of his book to brief biographies of his colleagues and to his rather low opinion of socialized medicine. He may be a grand person, but he has written a dull book, whose market will be largely local and professional.”
• Kirkus review
Pseudomembranous colitis
The link: 1978


**Role of Clostridium difficile in antibiotic-associated pseudomembranous colitis.**

Barlett JG, Moan N, Chang TV, Taylor N, Onderdonk AB.


**Identification of Clostridium difficile as a cause of pseudomembranous colitis.**

R H George, J M Symonds, F Dimock, J D Brown, Y Arabi, N Shinagawa, M R Keighley, J Alexander-Williams, and D W Burdon
Clostridium difficile colonization

- 3% of healthy adults are carriers
- 20-50% of adults in hospitals and long term care facilities are carriers
- 20% of patients with negative admission stool cultures become colonized during their hospitalization

Source: UpToDate
C Diff associated diarrhea (CDAD or CDI)

Risk Factors:

- Antibiotic use
- Hospitalization
- Advanced age
- Severe illness
- Gastric acid suppression (PPI, H2)
- GI surgery
- Obesity
- Chemotherapy
- Transplant patients
Antibiotic Use

- Broad spectrum antibiotics
- Multiple antibiotics
- Prolonged antibiotic duration
- Perioperative prophylaxis
- Herd effect

- Fluoroquinolones
- Clindamycin
- Penicillins
- Cephalosporins
- Metronidazole
- Vancomycin
Epidemics of Diarrhea Caused by a Clindamycin-Resistant Strain of Clostridium difficile in Four Hospitals

Stuart Johnson, M.D., Matthew H. Samore, M.D., Kylie A. Farrow, B.Sc., George E. Killgore, Dr.P.H., Fred C. Tenover, Ph.D., Dena Lytras, Ph.D., Julian I. Rood, Ph.D., Paola DeGirolami, M.D., Aldona L. Baltch, M.D., Mary Ellen Rafferty, R.N., Suzanne M. Pear, R.N., and Dale N. Gerding, M.D.


New York VA hospital (Upstate) 1989 – 174 cases

Arizona VA hospital 1990 – 101 cases

Florida community hospital 1991 – 106 cases

Massachusetts tertiary care hospital 1992 – 98 cases
Bacteria That Strike Elderly Spread in Canadian Hospitals

By CLIFFORD KRAUSS  AUG. 9, 2004

A type of bacteria that causes virulent diarrhea in the elderly has been spreading through hospitals in Quebec and Alberta and may have contributed to the deaths of 100 patients in one institution alone in the past 18 months, medical authorities said Sunday.
Wide Use of Antibiotics Allows C. Diff to Flourish

By JANE E. NUGENT
MAY 28, 2013 2:00 PM

You might say Jacob Epstein, a lean, healthy, 88-year-old Floridian, died in early May from a broken arm. Following surgery to reset the bone, he was given an antibiotic to prevent postoperative infection, a common hospital practice.
Hospital Infections With C. Difficile Level Off

By Nicholas Bakalar  October 1, 2014 12:08 pm

The incidence of the potentially deadly bacterial infection known as Clostridium difficile doubled in hospitals between 2001 and 2010, researchers report, and leveled off between 2008 and 2010.

C. difficile is a hospital-acquired infection linked to 14,000 deaths a year. According to the Centers for Disease Control and Prevention, the main cause is the overuse of antibiotics.

Using hospital discharge data on about 2.2 million people, average age 75, the scientists found that about a third had a principal diagnosis of C. difficile infection. Two thirds had other primary diagnoses. Incidence increased to 8.2 per thousand in 2008, the peak year, from 4.5 per thousand in 2001. It then decreased slightly through 2010.
Death Toll From C. Difficile Is Raised

By PAM BELLUCK  FEB 25, 2015

The deadly bacterial infection Clostridium difficile is estimated to have afflicted almost half a million Americans and caused 29,000 deaths in 2011, according to a study by the Centers for Disease Control and Prevention published Wednesday in The New England Journal of Medicine. The estimate is drawn from laboratory testing and reporting in 10 states and is larger than previous figures based on narrower data sources. C. difficile causes severe diarrhea and colon damage and is linked to overuse of antibiotics. The study estimated that 24 percent of cases occurred in hospitals and 40 percent began in nursing homes or community health care settings.

A version of this brief appears in print on February 26, 2015, on Page A16 of the New York edition with the headline: Death Toll From Bacteria Is Raised.
Downstate Data

**Hospital Acquired C-Difficile Infections**

- Jul-15: 1 in NS 62, 1 in NS 24 CTICU, 2 CO-HCFA
- Aug-15: 1 in NS 33 MICU, 1 in NS 61, 1 in NS 82
- Sep-15: 1 in NS 24, 1 in NS 33 (MICU)
- Oct-15: 1 in NS 62, 2 in NS 82
- Nov-15: 1 in NS 62 SD, 1 in NS 62
- Dec-15: 1 in NS 24, 1 in NS 62, 1 in NS 82
- Jan-16: 1 in NS 62, 2 in NS 82
- Feb-16: 1 in NS 33 MICU, 1 in NS 71/73, 2 CO-HCFA
- Mar-16: 1 in NS 71/73, 1 in NS 81 SD 607, 1 CO-HCFA
- Apr-16: 1 in NS 24, 1 in NS 71/73, 1 in NS 62
- May-16: 1 in NS 61, 1 in NS 62, 1 in NS 72

- Average
## Diagnosis

<table>
<thead>
<tr>
<th>Test</th>
<th>Reported Sensitivity</th>
<th>Reported Specificity</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enzyme immunoassay for toxin A and B (Tox A/Tox B EIA)</td>
<td>48%-96%</td>
<td>94%-100%</td>
<td>Commonly used; commercially available; 30-minute turnaround</td>
</tr>
<tr>
<td>Polymerase chain reaction (PCR) for toxins A/B genes</td>
<td>87%-100%</td>
<td>90%-100%</td>
<td>Emerging as test of choice because of improved sensitivity, 45-minute turnaround</td>
</tr>
<tr>
<td>PCR for the binary, cytolethal distending toxin (CDT)</td>
<td>95%-100%</td>
<td>95%-100%</td>
<td>Indicates likely hypervirulent strain if toxin A/toxin B PCR also positive</td>
</tr>
<tr>
<td>Glutaraldehyde dehydrogenase (GDH or common antigen)</td>
<td>99%-100%</td>
<td>60%</td>
<td>Less commonly used as a cheap, sensitive, but nonspecific screening test</td>
</tr>
</tbody>
</table>
Figure 1.
Cliff in detection dog outfit on one of the hospital wards.
A detection dog to identify patients with *Clostridium difficile* infection during a hospital outbreak

Marije K. Bomers a,*, Michiel A. van Agtmael a, Hotsche Luik b, Christina MJE. Vandenbroucke-Grauls c, Yvo M. Smulders a

a Department of Internal Medicine, VU University Medical Centre, PO BOX 7057, 1007 MB Amsterdam, Netherlands
b Animal Behaviour & Cognition, Scent Detection Research and Academy HL & Honden, Jan van Wallendalplein 7, 1135 WN Edam, Netherlands
c Department of Medical Microbiology and Infection Control, VU University Medical Centre, PO BOX 7057, 1007 MB Amsterdam, Netherlands

Accepted 11 May 2014
Available online 25 June 2014
Highlights

- Early and rapid identification of *Clostridium difficile* infections (CDI) is important to prevent transmission.
- A detection dog had high diagnostic accuracy (sensitivity 86%; specificity 97%) for bedside diagnosis of CDI patients. **And 100% adorable**
- For 2 CDI negative patients the dog repeatedly indicated a positive response; both did prove CDI positive weeks later.
- More research is needed to see if the use of sniffer dogs can lead to a quicker diagnosis, and improve outbreak management.
Treatment overview

- Confirm diagnosis
- Stop offending antibiotics
- Determine severity

If fail to improve

www.downstatesurgery.org
Box 23
Characteristics of Moderate, Severe, and Fulminant *Clostridium difficile* Infection

**Moderate Colitis**
- Pulse >90, SBP >100, Temp 100°F-101.5°F, WBC 12,000-15,000
- Pseudomembranes on colonoscopy
- Colonic thickening on CT
- Colon >6cm
- Oliguria responsive to volume
- Normal lactate
- Mild abdominal tenderness
- Mild tachypnea

**Severe Colitis**
- Moderate colitis and the following:
- Pulse >120, SBP <100, WBC >15,000
- Renal failure
- Respiratory distress or intubation
- Albumin <2.0
- Lactate >2.0
- Mental status changes
- Moderate abdominal tenderness

**Fulminant Colitis**
- Severe colitis and any of the following:
  - Unimproved after 48-72 hours of treatment
  - Need for vasopressors
  - Ventilator dependence
  - Abrupt rise in WBC

*CT*, computed tomography; *SBP*, systolic blood pressure; *WBC*, white blood cell count.
2 Updates

• Loop ileostomy with colonic lavage
• Fecal Transplant
Subtotal colectomy with ileostomy

BOOK CHAPTER
ACUTE FULMINATING COLITIS AND EMERGENCY COLECTOMY 🩸

Michael R B Keagley MS FRCS, Norman S Williams MS FRCS, James M Church BSc MB ChB MMedSci FRACS FACS, Lars Palmman MD PhD, John H Scholefield MB ChB FRCS ChM and Nigel A Scott MD FRCS

Surgery of the Anus, Rectum and Colon, 39, 1507-1569
• 159 VA hospitals
• 1997-2001
• 67 Patients had C. diff in colectomy specimen
  • 45% presented w/ SBP<90
  • 64% presented with an acute abdomen
  • WBC mean 27,000, 12% bands
  • 80% underwent total colectomy, 20% segmental resection
  • 58% had perforation and infarction
  • 48% mortality
Diverting Loop Ileostomy and Colonic Lavage

An Alternative to Total Abdominal Colectomy for the Treatment of Severe, Complicated Clostridium difficile Associated Disease

Matthew D. Neal, MD,* John C. Alverdy, MD,† Daniel E. Hall, MD,*‡
Richard L. Simmons, MD,* and Brian S. Zuckerbraun, MD*‡


(*)Department of Surgery, University of Pittsburgh School of Medicine, Pittsburgh, PA
(†)University of Chicago, Chicago, IL
(‡)VA Pittsburgh Healthcare System, Pittsburgh, PA
Diverting Loop Ileostomy with colonic lavage

1. Creation of diverting loop ileostomy.
2. Intraoperative antegrade colonic lavage with 8 liters of warmed PEG3350/electrolyte solution via ileostomy.
3. Postoperative antegrade colonic enemas with vancomycin (500 mg in 500 mL X 10 days) via ileostomy.
**TABLE 1. Indications for Operative Management in Patients With Severe, Complicated CDAD**

A diagnosis of CDAD as determined by history of ongoing or recent diarrhea and one of the following:

1. Positive toxin assay
2. Endoscopic findings
3. CT scan findings consistent with *C. difficile* colitis (*pancolitis* +/− ascites)

Plus any one of the following criteria:

1. Peritonitis
2. Worsening abdominal distention/pain
3. Sepsis
4. New onset ventilatory failure
5. New or increasing vasopressor requirement
6. Mental status changes
7. Unexplained clinical deterioration
8. Nonimproving or worsening while blood cell count more than 20 or less than 3 despite appropriate antibiotic therapy for 96 hours
9. Nonimproving and worsening bandemia (>10%) despite appropriate antibiotic therapy for 96 hours
# Pre-op conditions

<table>
<thead>
<tr>
<th></th>
<th>Ileostomy/Lavage</th>
<th>Colectomy</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>65.3 ± 13</td>
<td>62.1 ± 14</td>
<td>0.28</td>
</tr>
<tr>
<td>Sex</td>
<td>45% women</td>
<td>45% women</td>
<td>1.0</td>
</tr>
<tr>
<td>APACHE-II (mean ± SD)</td>
<td>29.7 ± 5.5</td>
<td>28.5 ± 7.1</td>
<td>0.39</td>
</tr>
<tr>
<td>While blood cell count</td>
<td>25.4 ± 12.1</td>
<td>27.1 ± 13.2</td>
<td>0.54</td>
</tr>
<tr>
<td>Band count (mean ± SD)</td>
<td>21.4 ± 12.2</td>
<td>21.3 ± 12.9</td>
<td>0.97</td>
</tr>
<tr>
<td>Albumin (mean ± SD)</td>
<td>2.0 ± 0.8</td>
<td>2.2 ± 0.8</td>
<td>0.26</td>
</tr>
<tr>
<td>Intensive care unit</td>
<td>38/42 (90%)</td>
<td>38/42 (90%)</td>
<td>0.64</td>
</tr>
<tr>
<td>Intubated</td>
<td>27/42 (64%)</td>
<td>26/42 (62%)</td>
<td>0.82</td>
</tr>
<tr>
<td>Vasopressors</td>
<td>31/42 (74%)</td>
<td>32/42 (76%)</td>
<td>0.81</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>19/42 (45%)</td>
<td>17/42 (40%)</td>
<td>0.66</td>
</tr>
<tr>
<td>Postoperative death</td>
<td>8/42 (19%)</td>
<td>21/42 (50%)</td>
<td>0.006*</td>
</tr>
</tbody>
</table>

*Odds ratio = 0.24 (0.09–0.63).
49 patients with severe C diff

- 6 comfort care (no surgery)
- 43 patients
  - 1 planned total colectomy
  - 7 Laparoscopic converted to open ileostomy and colonic lavage
  - 35 Laparoscopic ileostomy and colonic lavage

- 2 POD0 total colectomy (compartment syndrome)
  - 1 POD 10 total colectomy (recurrent pressors)

- 42 Post op
  - 1) Vancomycin **anterograde** x 10 days
  - 2) Metronidazole IV x 10 days
• Results:
  
  • 30 Day deaths: 8 (19%)
  • >30 day deaths: 6 (14%)
  • Recurrent C. diff 1 (2%)
  
  • 79% reversal of ileostomy (for 6 month survivors)
Results:

30 Day deaths: 8 (19%)
>30 day deaths: 6 (14%)
Recurrent C. diff: 1 (2%)
79% reversal of ileostomy (for 6 month survivors)

Results:

30 Day deaths: 21 (50%)
>30 day deaths: Not reported
Recurrent C. diff: Not reported
19% reversal of ileostomy
# Post-op Morbidities

<table>
<thead>
<tr>
<th>Morbidity</th>
<th>Ileostomy/Colonic lavage No. (%)</th>
<th>Colectomy No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep venous thrombosis/pulmonary embolism</td>
<td>1 (2.4%)</td>
<td>3 (7.1%)</td>
</tr>
<tr>
<td>Surgical site infection</td>
<td>3 (7.1%)</td>
<td>9 (21%)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>3 (7.1%)</td>
<td>4 (9.5%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>4 (9.5%)</td>
<td>5 (12%)</td>
</tr>
<tr>
<td>Inadvertent enterotomy</td>
<td>1 (2.4%)</td>
<td>1 (2.4%)</td>
</tr>
<tr>
<td>Reoperation related to ileostomy</td>
<td>2 (4.8%)</td>
<td>4 (9.5%)</td>
</tr>
<tr>
<td>“Ileostomy tube” migration</td>
<td>1 (2.4%)</td>
<td>NA</td>
</tr>
</tbody>
</table>
Study Criticisms

- No blinding
- No randomization
- Single institution
- Broad inclusion criteria
- 42 cases compared to 42 prior SURGICAL controls
Me:

“Were there any patients who met criteria for surgery in your novel approach but were not sufficiently sick for surgery in your prior chart review?”

Dr. Zuckerbraun:

“There was a retrospective review reported at EAST this year. Comparing colectomy to loop. No statistical significant difference between demographics or severity of illness”… “We have now done 105 of them. Outcomes are very similar to what was published in our initial paper...We have not change[d] your criteria for operating overall.”
The Surgical Management of Complicated *Clostridium difficile* Infection: Alternatives to Colectomy

To cite this article: Kautza Ben and Zuckerbraun Erien S.. Surgical Infections. May 2016, 17(3): 337-342. doi:10.1089/sur.2016.006.

Published in Volume: 17 Issue 3: May 20, 2016

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**FIG. 1.** Operative management strategy for complicated *Clostridium difficile* infection (CDI).
Questions on the study?
University of Virginia

Retrospective chart review

2011-2015 (51 months)

Severe, complicated C. difficile

For all patients treated surgically

Excluded IBD

Excluded final path not showing pseudomembranous colitis
All with severe, complicated C. difficile

4 Excluded (IBD or not pseudomembranous colitis)

27 patients

23 patients

13 Total Colectomy

7 LAPAROSCOPIC Loop ileostomy and colonic lavage

3 OPEN Loop ileostomy and colonic lavage

51 months Retrospective Chart Review

NOT RANDOMIZED

www.downstatesurgery.org
An institutional comparison of total abdominal colectomy and diverting loop ileostomy and colonic lavage in the treatment of severe, complicated Clostridium difficile infections.

Fashandi AZ¹, Martin AN¹, Wang PT², Hedrick TL¹, Friel CM¹, Smith PW¹, Hays RA², Hallowell PT³.

Table 1
Preoperative risk factors stratified by procedure.

<table>
<thead>
<tr>
<th></th>
<th>TAC, N = 13</th>
<th>Loop ileostomy, N = 10</th>
<th>P-value³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years), Median (IQR)</td>
<td>63.2 (59.4–72.4)</td>
<td>59.7 (56.4–63.4)</td>
<td>0.54</td>
</tr>
<tr>
<td>Female sex, N (%)</td>
<td>7 (54)</td>
<td>7 (70)</td>
<td>0.67</td>
</tr>
<tr>
<td>Preoperative WBC, Median (IQR)</td>
<td>21 (9.8–43.4)</td>
<td>39.3 (24.5–49.5)</td>
<td>0.35</td>
</tr>
<tr>
<td>Preoperative albumin, Median (IQR)</td>
<td>2.2 (1.9–2.8)</td>
<td>2.0 (1.8–2.7)</td>
<td>0.44</td>
</tr>
<tr>
<td>Preoperative ICU, N (%)</td>
<td>11 (85)</td>
<td>9 (90)</td>
<td>1.00</td>
</tr>
<tr>
<td>Preoperative intubation, N (%)</td>
<td>6 (46)</td>
<td>2 (20)</td>
<td>0.38</td>
</tr>
<tr>
<td>Preoperative vasopressor use, N (%)</td>
<td>6 (46)</td>
<td>5 (50)</td>
<td>0.86</td>
</tr>
<tr>
<td>Immunosuppression, N (%)</td>
<td>2 (15)</td>
<td>2 (20)</td>
<td>1.00</td>
</tr>
<tr>
<td>Treated with metronidazole and/or oral vancomycin, N (%)</td>
<td>13 (100)</td>
<td>10 (100)</td>
<td>N/A</td>
</tr>
<tr>
<td>Treated with rectal vancomycin, N (%)</td>
<td>6 (46)</td>
<td>7 (70)</td>
<td>0.40</td>
</tr>
</tbody>
</table>

TAC = total abdominal colectomy; IQR = interquartile range; ICU = intensive care unit.

³ P-value for continuous variables calculated using Mann-Whitney U test; p-value for categorical variables calculated using Chi-squared or Fisher’s exact tests, where appropriate.

Note: Apache II not recorded.
Table 2
Outcomes following total abdominal colectomy versus loop ileostomy for CDI.

<table>
<thead>
<tr>
<th></th>
<th>TAC, N = 13</th>
<th>Loop ileostomy, N = 10</th>
<th>P-value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-day mortality, N (%)</td>
<td>3 (23)</td>
<td>3 (30)</td>
<td>1.00&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>1-year mortality, N (%)</td>
<td>6 (46)</td>
<td>4 (40)</td>
<td>1.00&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>CDI recurrence, N (%)</td>
<td>3 (23)</td>
<td>4 (40)</td>
<td>0.57</td>
</tr>
<tr>
<td>CDI recurrence in &gt;30-day survivors, N (%)</td>
<td>3 (30)</td>
<td>4 (57)</td>
<td>0.35</td>
</tr>
<tr>
<td>Colon preservation in &gt;1-year survivors, N (%)</td>
<td>—</td>
<td>6 (100)</td>
<td>—</td>
</tr>
<tr>
<td>Return of intestinal continuity in &gt;1-year survivors, N (%)</td>
<td>3 (43)</td>
<td>5 (83)</td>
<td>0.27</td>
</tr>
</tbody>
</table>

TAC = total abdominal colectomy; CDI = *Clostridium difficile* infection.

<sup>a</sup> P-value for continuous variables calculated using Mann-Whitney *U* test; p-value for categorical variables calculated using Chi-squared or Fisher’s exact tests, where appropriate.

<sup>b</sup> Odds ratio = 0.70, 95% CI: 0.11–4.54, *p* = 0.71.

<sup>c</sup> Odds ratio = 1.29, 95% CI: 0.24–6.83, *p* = 0.77.
Conclusions:

• Similar preop characteristics
• Similar morbidity/mortality
• Only 23 patients
• More data needed
Questions on anterograde colonic lavage?
“Lou, why aren’t there millions of zebras in the jungle?”
Fecal Microbiota Transplants (FMT)

- 1958
- Long Island College Hospital
- Outbreak of Staphylococcal enterocolitis
1st Patient

• Robert Kelleher
• 65M
• Colon resection for malignancy
• Preoperative Sulfasuxidine and neomycin
• Post op right lung pneumonia
  • Penicillin, streptomycin, Achromycin
  • POD 15 watery diarrhea
  • Stool grew Staphylococcus aureus
    • Resistant to ALL antibiotics
Two surgery residents eating dinner

• PGY2:
  “Why aren’t there millions of zebras in the jungle?”

• PGY5:
  “Why aren’t there?”

• PGY2:
  “because there are millions of lions in the jungle and the lions kill lots of the zebras”
1\textsuperscript{st} Patient

- Needed healthy donor
- Orthopedic fracture patients in traction
- Mixed feces with gelatin capsule
- “Crapsule” x8 days
- Concurrent post pyloric NG and yogurt-mixed enema
- Diarrhea resolved in 48 hours
- Expired POD 96
- Autopsy: normal colon flora, absence of staphylococcus
Fecal Feedings as a Therapy in Staphylococcus Enterocolitis

LOUIS C. CUTOLO, M.D., NOEL H. KLEPPH, M.D., H. ROBERT FREUND, M.D., AND JEANNE HOLKER, M.S., BROOKLYN, NEW YORK

(From the State University of New York Downstate Medical Center, Department of Surgery of The Long Island College Hospital)

In the treatment of a patient with staphylococcus enterocolitis, a disease resulting from replacement of the usual bacterial flora of the intestinal tract by this organism, conventional therapy has been the administration of the antibiotic demonstrated by sensitivity tests to be the most effective in combating the microorganism. In a review of the literature1–18 no example of staphylococcus enteritis resistant to all available antibiotics has been found. Recently a patient with a staphylococcus enterocolitis due to an organism resistant to all antimicrobial agents tested in vitro was en-
Fecal Microbiota Transplant (FMT) for C diff
No Randomized Controlled Trials

“Studies that used FMT via any delivery modality for laboratory or endoscopically proven CDI with clinical resolution as primary outcome were included. A sample size of 10 or more patients was a further criterion.”

11 Studies
273 Patients
<table>
<thead>
<tr>
<th>Author (reference)</th>
<th>Sample size</th>
<th>Patient type (in-patient, out-patient, mixed)</th>
<th>CDI type (recurrent, refractory, both)</th>
<th>Donor (patient selected, anonymous, both)</th>
<th>Delivery modality</th>
<th>Stool sample dose/solution</th>
<th>Follow-up data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kassam et al. (47)</td>
<td>27</td>
<td>Mixed</td>
<td>Both</td>
<td>Anonymous</td>
<td>Enema</td>
<td>150g Stool/300ml sterile water</td>
<td>Mean “427.3 days”</td>
</tr>
<tr>
<td>Mattila et al. (37)</td>
<td>70</td>
<td>Mixed</td>
<td>Both</td>
<td>Both</td>
<td>Colonoscopy</td>
<td>20–30ml Stool/ 100ml water</td>
<td>Mean “10.7 months (range 2–30 months)”</td>
</tr>
<tr>
<td>Kelly et al. (43)</td>
<td>26</td>
<td>Out-patient</td>
<td>Recurrent</td>
<td>Patient selected</td>
<td>Colonoscopy</td>
<td>6–8 Tablespoon stool/1,000 ml sterile water or saline; total aliquoted dose 500–960ml</td>
<td></td>
</tr>
<tr>
<td>Polak et al. (44)</td>
<td>15</td>
<td>NR</td>
<td>Recurrent</td>
<td>Patient selected</td>
<td>Nasojejunal tube</td>
<td>20–50g Stool/dilute in 50ml saline</td>
<td>NR</td>
</tr>
<tr>
<td>Mellows et al. (39)</td>
<td>13</td>
<td>Mixed</td>
<td>Both</td>
<td>Patient selected</td>
<td>Colonoscopy</td>
<td>Stool amount NR/saline (amount NR); Total aliquoted dose 300–600cc</td>
<td>Mean “5 months (range 1–10 months)”</td>
</tr>
<tr>
<td>Garborg et al. (40)</td>
<td>40</td>
<td>Mixed</td>
<td>Recurrent</td>
<td>Patient selected</td>
<td>Gastroscopy, Colonoscopy</td>
<td>50–100g Stool/ 250ml saline; total aliquoted dose ~200ml</td>
<td>NR</td>
</tr>
<tr>
<td>Rohike et al. (38)</td>
<td>19</td>
<td>Out-patient</td>
<td>Recurrent</td>
<td>Patient selected</td>
<td>Colonoscopy</td>
<td>Variable (full quantity-“several ounces”)/saline (amount: NR); total aliquoted dose 200–300cc</td>
<td>Mean “27.2 months (range 6–65 months)”</td>
</tr>
<tr>
<td>Yoon et al. (45)</td>
<td>12</td>
<td>NR</td>
<td>Both</td>
<td>Patient selected</td>
<td>Colonoscopy</td>
<td>Stool amount NR/1,000ml saline; total aliquoted dose ~250–400cc</td>
<td>Mean NR; range “3 weeks to 6 years”</td>
</tr>
<tr>
<td>MacConnachie et al. (41)</td>
<td>15</td>
<td>Mixed</td>
<td>Recurrent</td>
<td>Patient selected</td>
<td>Nasogastric tube</td>
<td>30g Stool/150ml saline; total aliquoted dose 30ml</td>
<td>Mean NR; median 16 weeks (range 4–24 weeks)</td>
</tr>
<tr>
<td>Aas et al. (46)</td>
<td>18</td>
<td>Mixed</td>
<td>Recurrent</td>
<td>Both</td>
<td>Nasogastric tube</td>
<td>30g Stool/50–70ml saline; total aliquoted dose 25ml 5–10g Stool/milk (amount: NR)</td>
<td>“2–3 Weeks”</td>
</tr>
<tr>
<td>Lund-Tonnesen et al. (42)</td>
<td>18</td>
<td>In-patient</td>
<td>Unclear</td>
<td>Anonymous</td>
<td>Colonoscopy, Gastrostomy tube</td>
<td>30g Stool/50–70ml saline; total aliquoted dose 25ml 5–10g Stool/milk (amount: NR)</td>
<td></td>
</tr>
</tbody>
</table>

NICE, National Institute of Clinical Excellence; NR, not reported.
<table>
<thead>
<tr>
<th>Subgroups</th>
<th>Unweighted rate n/N (percentage)</th>
<th>Weighted rate (95% CI)</th>
<th>Proportion difference of unweighted rate (95% CI, P value)</th>
<th>Proportion difference of weighted rate (95% CI, P value)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Delivery modality</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower gastrointestinal delivery (colonoscopy, enema)</td>
<td>203/222 (91.4%)</td>
<td>91.2 % (86.0%, 95.2%)</td>
<td>9.1% (-0.1%, 22.1%), P=0.046</td>
<td>10.6% (-0.6%, 21.8%), NS</td>
</tr>
<tr>
<td>Upper gastrointestinal delivery (nasogastric/nasojugal tube, gastroscopy, gastrostomy tube)</td>
<td>42/51 (82.3%)</td>
<td>80.6% (69.3%, 89.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Donor type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients selected (related family member, partner, spouse, close friend)</td>
<td>195/219 (89.5%)</td>
<td>89.2% (83.2%, 94.0%)</td>
<td>-1.2% (-8.5%, 9.9%), NS</td>
<td>-0.7% (-10.5%, 9.1%), NS</td>
</tr>
<tr>
<td>Anonymous</td>
<td>49/54 (90.7%)</td>
<td>89.9% (80.3%, 96.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Methodological quality</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher (total NICE score ≥4)</td>
<td>173/185 (93.5%)</td>
<td>92.9% (88.8%, 96.1%)</td>
<td>11.7% (3.7%, 21.5%), P=0.003</td>
<td>12.3% (3.5%, 21.1%), P&lt;0.05</td>
</tr>
<tr>
<td>Lower (total NICE score &lt;4)</td>
<td>72/88 (81.8%)</td>
<td>80.6% (72.0%, 88.0%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI, confidence interval; NICE, National Institute of Clinical Excellence, NS, non-significant.
Proposed screening for Fecal Transplants

- **Donor blood**
  - Hepatitis A, B, C
  - HIV-1, HIV-2, syphilis

- **Stool tests**
  - Giardia antigen
  - Cryptosporidium
  - Cyclospora, Isospora, Dientamoeba, Blastocystis
  - Norovirus, rotavirus
  - H pylori
  - Ova and parasites
  - C diff

- **No antibiotics in the past 6 months**
- **Healthy donor**
- **Live together?**
Unanswered Questions for Fecal transplants in C diff

• During initial illness or recurrence?

• Mild, moderate, or severe disease?

• Delivery method?

• Single dose or repeated?

• Anonymous donor?
Resident Questions - #1

• Which of the following is/are considered risk factors for developing C diff associated diarrhea?
  • A) Clindamycin use
  • B) PPI use
  • C) Immunosuppression
  • D) Metronidazole use
  • E) All of the Above
Resident Questions - #1

• Which of the following is/are considered risk factors for developing C diff associated diarrhea?
  • A) Clindamycin use
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  • C) Immunosuppression
  • D) Metronidazole use
  • E) All of the Above
Resident Questions - #2

• Which is a **contraindication** for loop ileostomy and anterograde colonic lavage?

• A) Sepsis
• B) Immunosuppresion
• C) Ventilatory failure
• D) Recent abdominal surgery
• E) Abdominal compartment syndrome
Resident Questions - #2

• Which is a contraindication for loop ileostomy and anterograde colonic lavage?
  • A) Sepsis
  • B) Immunosuppression
  • C) Ventilatory failure
  • D) Recent abdominal surgery
  • E) Abdominal compartment syndrome
Conclusions

• Loop ileostomy and anterograde colonic lavage is an emerging alternative for surgical management of severe/fulminant C diff associated diarrhea

• Fecal transplants (FMT) show significant promise in C diff but require standardization and have yet to be proven in RCTs


Current Surgical Therapy, Cameron's 11th edition

Sabiston Textbook of Surgery

UpToDate

New York Times
Thank you

Figure 1.
Cliff in detection dog outfit on one of the hospital wards.