LSU Health SHREVEPORT

*Clostridioides diff*icile and Fecal Microbial Transplantation

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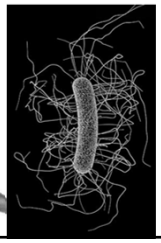
Objectives

1. Describe *Clostridioides difficile* infections, laboratory tests for identification and the toxins contributing to it.
2. Discuss treatments, prevention and control.
3. Describe the procedures, indications and testing required for fecal microbial transplantation.

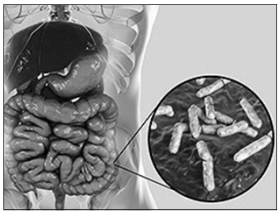
C. difficile Infection (CDI)

- Leading cause of hospital- and antibiotic-associated diarrhea globally
- > 500,000 infections each year in US hospitals
- > 29,000 deaths annually
- 2-5 excess hospital days
- 1% hospital admissions
- Costs the US ~$1.2- $5.9 billion a year
- Incidence—↑200% 1999-2011
- > double this decade

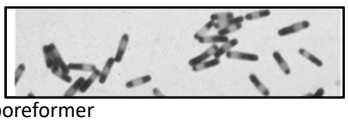


C. difficile Infection (CDI)

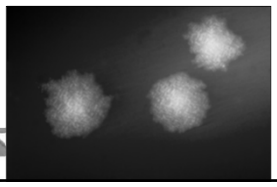
- Risk of recurrence within 8 weeks 15–25%
- Rises to 40–65% in patients with multiple recurrences
- Most common nosocomial pathogen
- >65 y.o. 26 times risk



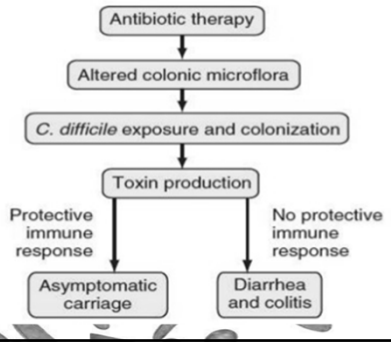
CDI



- Anaerobic gram positive sporeformer
- Disruption of the intestinal microbiota, colonization with the *C. difficile* and release of its two toxins; Toxin A (TcdA) and (TcdB)

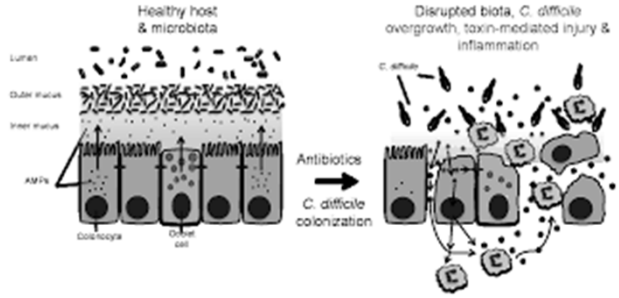


Pathogenesis

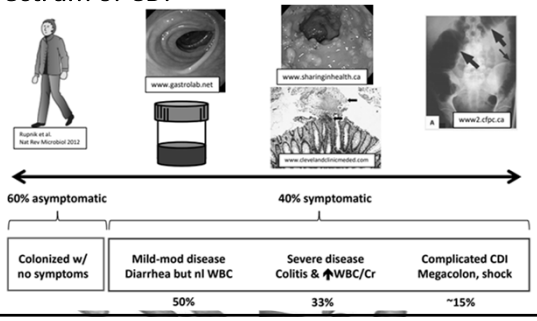


C. difficile Toxins

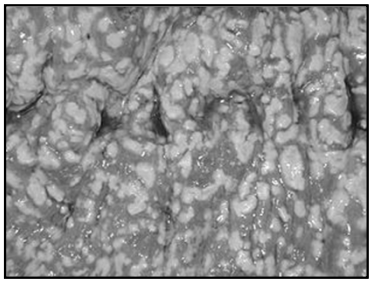
- Toxin A (TcdA) and Toxin B (TcdB)—Rho glucosyltranferases that irreversibly inactivate GTPases causing cell death
  - Massive fluid secretion
  - Colonic tissue necrosis
  - Inflammation
- CDT binary toxin—30% of hypervirulent strains—increased 30-d mortality independent of ribotype—inactivation of actin and microtubules increasing adherence to target cells
  - Hypervirulent BI/NAP/027 strain

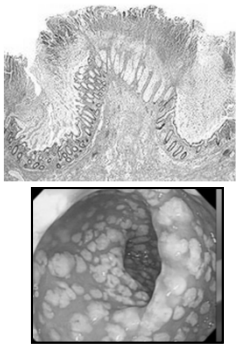


Spectrum of CDI



Pseudomembranous Colitis





Carriers 5: 1 CDI Patients

80-90% Diarrhea non-infectious causes

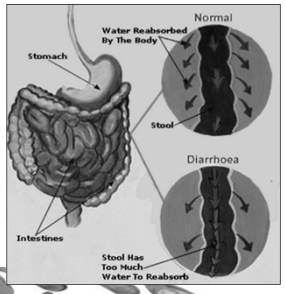
Most Diarrhea Noninfectious

	Patients on antibiotics	ICU patients	Solid Organ Transplant patients	Onc/HSCT patients
Prevalence of diarrhea overall	**5-25%**	**15-40%**	**10-20%**	**50-80%**
• **Percent of total diarrhea due to infection**	**10-20%**	**10-20%**	**≥20%**	**6-20%**
• Percent of total diarrhea due to C. difficile	10-20%	10-20%	5-10%	4-13%
• Percent of total diarrhea due to other infection	3-8%	unknown	5-10%	5-10%
• **Percent of diarrhea due to** non-infectious cause	**80-90%**	**80-90%**	**≤80%**	**80-95%**

Polage et al. CID 2012

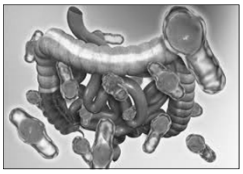
CDI

- Mild to severe diarrhea
- Pseudomembranous colitis--30% develop
- 25% to 30% of antibiotic-associated diarrhea
- 15-25% healthcare associated diarrhea
- >95% of pseudomembranous colitis cases



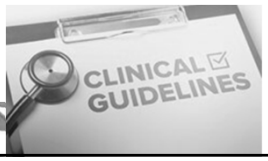
Typical Symptoms

- Mild to moderate watery diarrhea rarely bloody
- Cramping abdominal pain
- Anorexia
- Malaise
- Fever especially severe cases
- Dehydration
- Abdominal tenderness



SHEA-IDSA CDI Classification Guidelines

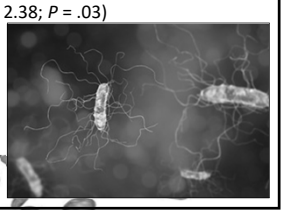
- Community associated (CA)
- Healthcare facility onset (HFO)—cases per 10000 pt days
- Community onset with exposure to healthcare facilities in last 4 weeks (CO)—cases per 1000 admissions
  - Day surgery
  - Dialysis
  - Chemotherapy suites
  - Long-term care facilities



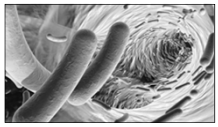
Risk Factors for HFO

- Length of stay, roommate
- Multiple classes of antimicrobials
  - Beta-lactam with beta-lactamase inhibitors (OR = 3.65; *P* < .001)
  - First-generation cephalosporins (OR = 2.38; *P* = .03)
  - Carbapenems (OR = 2.44; *P* = .03)
- Opiod use
- Cirrhosis
- Age >60

Pointer D et al. *Clin Infect Dis.* 2019. doi. 10.1093/cid/ciz626



More CDI Risk Factors



- Inflammatory bowel disease (IBD)
- Similar disruptions to the intestinal microbiome found in IBD and in obesity
- Of 132 patients, 43% had community onset, 30% had health care facility onset, and 23% had community onset after exposure to a health care facility
- Community onset had > BMIs

Risk in Pediatric Patients

- Prior antimicrobial use 2X
  - Carbapenems
  - Aminoglycosides and cephalosporins
- PPI—3X

Infect Control & Hosp Epi. 40(4):420-6. 2019
https://doi.org/10.1017/ice.2019.23

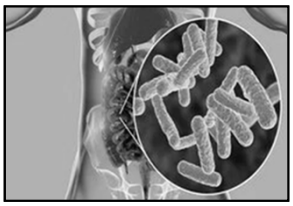
Distribution in China

- 3699 healthy Chinese over 1 year
- 25% < 1 year—20% toxin forming genes
- 13.6% of children
- 6.3% of healthcare workers
- 5.5% healthy adults—65% toxin
- Susceptible to all but ciprofloxacin (98.3% resistant)

Molecular Characterization of *Clostridium difficile* Isolates from Human Subjects and the Environment (2016) PLOS.org
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0151964

Resistance to Colonization

- Intestinal microbiota
- Convert bile acids to secondary bile acids
- Inhibit grow by depriving important germinant
- Increasing concentration toxic to vegetative form



Recommended Laboratory Tests

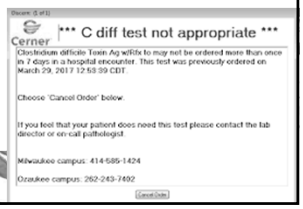
- CBC-leukocytosis may be high
- Electrolytes, creatinine
- Albumin—low
- Lactate-->5 mmol.L
- Stool positive for blood but not grossly bloody; fecal leukocytes in half

ASM Testing Guideline

- **≥3 episodes of non-formed stool within 24 hours or 6 in 48 hours**
- Adults: Recent or current antibiotic use
- Unexplained and new onset diarrhea
- Children ages 1 to 3 with diarrhea, consider viruses first
- No routine testing in children <1 (high carriage rates)
- Children >3 same as for adults

Do Not Test

- On asymptomatic patients, unless it's for use in an epidemiological study
- Repeat tests during the same episode of diarrhea that takes place within a week's time
- Do not test for cure



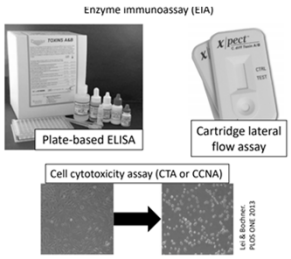
CDI Laboratory Tests

- Culture: Performed for research to ensure viable organisms
- Toxigenic culture & cell cytotoxicity—reference methods
- Glutamate dehydrogenase (GDH) EIA
  - Very sensitive but not specific
  - Rules out CDI
  - Must be confirmed
  - Can be automated and gives numerical result

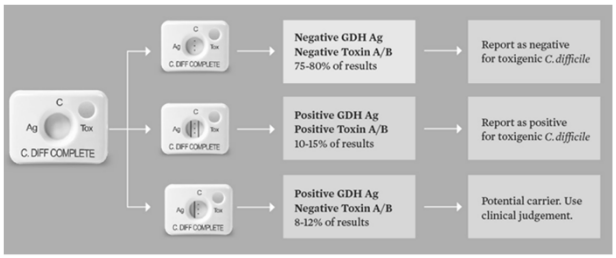
- C. Diff Toxin EIA-- enzyme immunoassay for toxin A & B—not as sensitive as NAAT

Examples of Toxin Tests

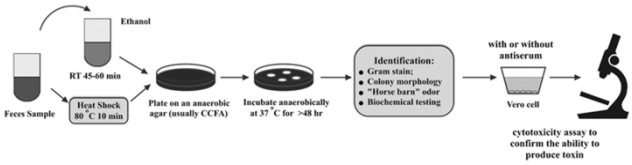
Name	Type
Abbott (TechLab) Tox A/B Quik Chek	EIA
Abbott C.difficile Tox A/B II	EIA
Abbott C. difficile Tox-B Test	CCNA
Meridian Toxins A/B EIA	EIA
Meridian Immunocard Toxins A/B	EIA
Remel Xpect C.diff Toxin A/B	EIA



C. DIFF QUIK CHEK COMPLETE



Culture



Laboratory Tests

- NAAT—
  - PCR
    - Presence of ribotype O27 strain
  - Highly sensitive but false positives
  - Overdiagnose due to colonization, presence of genes but not producing toxin
  - Add toxin test to improve specificity

FDA Approved PCR Assays (Not Complete)

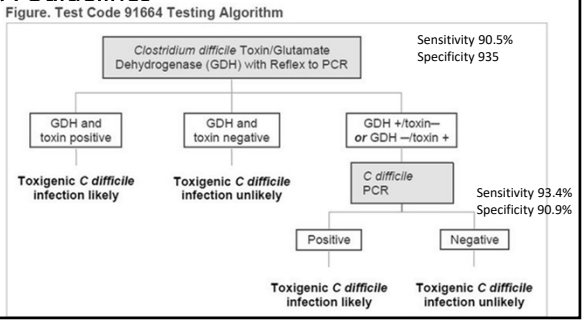
Assay	Target Gene	Instrument	TAT (minutes)
BD Gene-Ohm	*tcdB*	Smart Cycler and Amplification or new Automated Version	75-120
Gen-Probe (Hologics) proGastro	*tcdB*	Extraction Smart Cycler/Amp	180-200
Cepheid Xpert	*tcdB* *tcdC* deletion Binary Toxin	GeneXpert	30-45
Great Basin Portrait	*tcdB*	Incubator Ind. Cartridge	90
Focus DX Simplexa	*tcdB*	3M Integrated Cycler	60-90

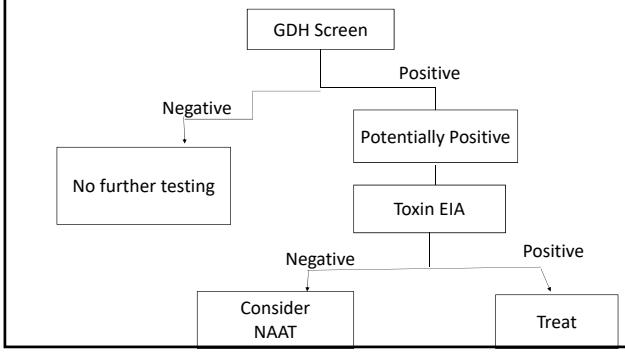
Available Tests

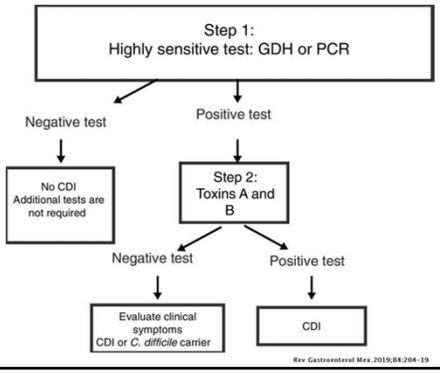
Test	Sensitivity	Specificity	Substance Detected
Toxigenic culture	High	Low	Vegetative cells or spores
NAAT	High	Low - moderate	Toxin genes
GDH	High	Low	Common antigen
Cell culture toxicity neutralization	High	High	Free toxins
Toxin A, B EIA	Low	Moderate	Free toxins

https://www.guidelinecentral.com/share/pocketcard/53c97d6970546/

IDSA Guidelines







Meta-analysis

- NAAT alone Sensitivity $P < 0.001$ Specificity $P < 0.001$
- NAAT + glutamate dehydrogenase Sensitivity $P < 0.02$ Specificity $P < 0.16$
- NAAT + glutamate dehydrogenase + toxin enzyme immunoassay Sensitivity $P < 0.001$ Specificity $P < 0.58$
- Align with ASM recommendations

Clin Micro Rev. http://cmr.asm.org 2019

Practice Category	Practice recommendations
NAAT only	Best Practice for detection of gene
GDH/NAAT algorithm	Best Practice for detection of organism, toxin or gene
GDH, toxin/NAAT algorithm	Best Practice for detection of organism, toxin or gene
Repeated testing using NAAT	Insufficient evidence

Clin Micro Rev. http://cmr.asm.org 8-23-2019

Toxin Negative NAAT Positive Causes

- Colonization
  - Borderline symptoms
  - Alternative cause (laxatives, meds)
- Prior antibiotic treatment
  - Metronicazole for non-CDI
  - Prior therapy
- Pre-analytical toxin degradation

2015 prospective study w/ outcomes

Polage et al. JAMA Intern Med 2015

	C. difficile positive		*C. difficile* negative	
Outcome	Tox+/PCR+ (n=131)	Tox-/PCR+ (n=162)	Tox-/PCR- (n=1123)	*P*-value
Complication[a]	10 (7.6%)	0	3 (0.3%)	<0.001
Death[b, c]	11 (8.4%)	1 (0.6%)	0	<0.001
Complication or death	18 (13.7%)	1 (0.6%)	3 (0.3%)	<0.001

[a]ICU care, megacolon, colectomy related to CDI
[b]Death within 30 days related to CDI
[c]All-cause 30 day mortality: 14 (10.7%); 23 (14.2%); 98 (8.7%); *P*=0.08

Toxin - /NAAT + Patients

- Shorter duration of symptoms
- 14 of 18 studies better outcomes
- Few or no complications
- Toxin – complicated CDI rare
- Similar outcomes to Toxin -/NAAT - patients

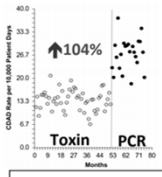
Diagnostic changes have contributed to the rise

1999-2008: True epidemic
- Novel hypervirulent strain
- 95% labs used toxin tests
- Toxin+ = CDI
- Toxin-/*C. difficile*+ not detected
- Occasional missed CDI cases

2009-2015: Test-related epidemic
- First FDA-cleared PCR test
- Labs switch to PCR/NAAT tests
- Toxin+ & Toxin-/*C. difficile*+ detected
- CDI Rates ↑ 1.5-2X

PCR-related CDI increases

Institution-Level



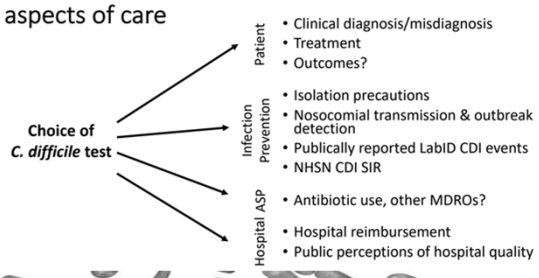
Population-Level	
California	↑52%
Colorado	↑43%
Georgia	↑67%

Gould CV, et al. CID 2013

Why So Much Confusion?

- No true reference method
- Negative experience with toxin assays
- Lab studies without clinical correlation
- Belief that all toxin - /NAAT + or TC + = CDI

C. difficile diagnostic testing impacts all aspects of care



Overdiagnosis

- 70 yo F w/metastatic RCC
- Multiple episodes of PCR + CDI x 2 yrs
- 12-15 nonbloody, watery BMs/day
- WBC 13.7
- P.O. vanc and metronidazole
- No change>6 days

Matta, Greenberg, & Singh JAMA Intern Med 2015

Over Diagnosis Case

- Prior treatment minimal effect on diarrhea
- Colonoscopy negative for pseudomembranes & nondiagnostic
- Diarrhea began with axitinib
  - Comon adverse effect
- D/C axitinib dramatic improvement in 3 days
- Medication induced diarrhea with C. diff colonization

Consequences of Overdiagnosis

- Antibiotic dysbiosis, > MDROs
- Misdiagnosis delays
- Penalties for excess CDI cases

- Important for clinicians to use clinical judgement

Diagnostic Stewardship

Institution	Intervention	Strength	Effect
UVA (2018)	CPOE discourage repeats, testing w/o indication	++	↓41% tests
UC Irvine (2018)	CPOE criteria, approval, monitoring, feedback, enforcement	++++	↓56% tests
Penn (2017)	CPOE order set to stop laxatives, no hard stop	+	NS
Royal Victoria Hospital, UK (2016)	Physical ordering checklist	+	↓17% tests
Christiana Hospital (2017)	CPOE laxative alert + lab approval	+++	↓30% tests
Children's Mercy (2016)	CPOE age, megacolon; lab reject formed samples	+	No sustained
USC (2018)	Education + lab reject formed or delayed samples	++	↓43% tests
Stanford (2017)	Lab enforced testing criteria (>3 stl, no laxatives)	++	↓31% tests

Adapted from Madden et al. *Diagnosis* 2018

Infection Prevention and Control

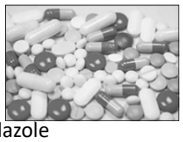
- Private room with dedicated toilet
- Cohort only with CDI
- Contact precautions (gowns and gloves)
- If hyper-endemic soap and water, not alcohol products
- Clean surfaces with sporicidal agent
- Minimize frequency & duration & number of antimicrobial agents
- Avoid use of fluoroquinolones, clindamycin and cephalosporins

Study of Cleaning Procedures

- After appropriate decontamination, spores persist
  - Hospital surfaces including stainless steel and vinyl
  - Surgical gowns
- Spores more resistant
- Sporicidal agents

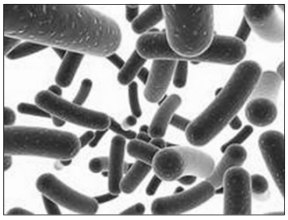
- *Dyer C, et al "Biocide Resistance and Transmission of Clostridium difficile Spores Spiked onto Clinical Surfaces from an American Health Care Facility" Appl Environ Microbiol 2019; 85(17): e01090-19.*

IDSA Recommended Treatment



- D/C inciting antimicrobial agents
- Oral vancomycin or fidaxomicin over metronidazole
- If fulminant--subtotal colectomy with preservation of the rectum OR Diverting loop ileostomy with colonic lavage and vancomycin flushes
- Recurrence—vancomycin with tapered & pulse regimen OR 10 days fidaxomicin
- Multiple (2) recurrences--FMT

Probiotics



- Literature—mixed reviews
- Probably will not hurt
- Some evidence may worsen
- IDSA—not enough evidence

Fecal Microbial Transplantation (FMT)

- ~85% cure rate in recurrent (80-91%)
- Minimal adverse reactions
- Mechanism of action
  - Establishes newly enriched microbiota
  - Indirectly inhibits *C. difficile* by competing for resources
  - Directly inhibits by producing bacteriocins
- Problems
  - Lack of standardization
  - Uncharacterized viruses and bacteria

Fecal Transplants May Transmit Deadly Drug-Resistant Infections

- 2 patients FMT – 1 died
- Extended spectrum beta-lactamase producing *E. coli* (ESBL)
- Same donor—not tested for MDROs
- New regs—test for ESBL, CRE, VRE, MRSA

https://www.fda.gov/news-events/fda-brief/fda-brief-fda-warns-about-potential-risk-serious-infections-caused-multi-drug-resistant-organisms

Eligible Patients

- Clinical symptoms and positive microbial tests
- Recurrent CDI following adequate treatment (10 days of vancomycin, metronidazole, fidaxomicin
- First recurrence—retreat with fidaxomicin unless severe
- 3 liquid stools per day for 2 days or 6 per 48 hours with 8 weeks of treatment and positive test for CDI
  - Free toxin by EIA

FMT Support in Literature

- By Jan 2018 4 RTC
- Van Nood et al halted early superior effectiveness of FMT
- Kelly et al 90.9% effectiveness vs. 62.5% placebo
- Kassam Z, Lee CH, Yuan Y, Hunt RH. Fecal microbiota transplantation for Clostridium difficile infection: systematic review and meta-analysis. *Am J Gastroenterol*. 2013;108:8–500.
- Moayyedi P, Yuan Y, Baharith H, Ford AC. Faecal microbiota transplantation for Clostridium difficile-associated diarrhoea: a systematic review of randomised controlled trials. *Med J Aust*. 2017;207:72–166.

Literature in Support of FMT

- Cammarota G, Ianiro G, Gasbarrini A. Fecal microbiota transplantation for the treatment of Clostridium difficile infection: a systematic review. J Clin Gastroenterol 2014;48:693-702.
- Kelly CR, Khoruts A, Staley C, et al. Effect of fecal microbiota transplantation on recurrence in multiply recurrent Clostridium difficile infection: a randomized trial. Ann Intern Med 2016;165:609-16
- van Nood E, Vrieze A, Nieuwdorp M, et al. Duodenal infusion of donor feces for recurrent Clostridium difficile. N Engl J Med 2013;368:407-15. 19.
- Youngster I, Sauk J, Pindar C, et al. Fecal microbiota transplant for relapsing Clostridium difficile infection using a frozen inoculum from unrelated donors: a randomized, open-label, controlled pilot study. Clin Infect Dis 2014;58:1515-22.

History of FMT

- 4th century China, during the Jin dynasty
- 1958 in journal *Surgery*
- 1983

FMT Delivery

- Upper GI via nasogastric tube, endoscopy
- Lower GI via colonoscopy or enema—right colon or terminal ileum
- Capsules –nasogastric release & targeted colonic release (no bowel prep)
- Lower GI colonoscopy better
- Phloral® coating for capsule release in colon
- Comparison of upper vs lower capsules
  - Both safe, well-tolerated, no bowel prep, preferred by patients, same engraftment as colonoscopy

Digestive Diseases and Science. (2019). 64:1672-8

FDA Regulations

- 2016 second draft guidelines on buying samples unless clinical trial (IND)
- Not finalized today—"Enforcement discretion"
- Suggested Track 1--Regulated as "practice of medicine" suggested (state reg only)
- Suggested Track 2—Regulate stool banks: submit safety data & outcomes to FDA
- Informed consent—FMT to treat CDI investigational (other diseases must file IND)

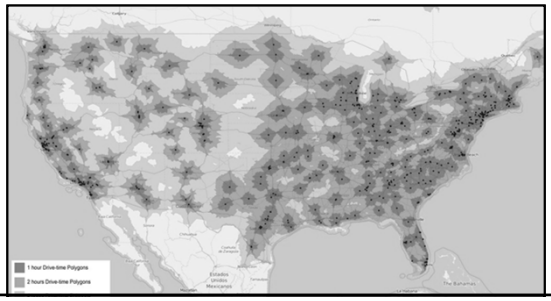
FDA Regulation of FMT

- Prevailing FDA guidance allows physicians to perform FMT using OpenBiome material to treat C. difficile infection not responsive to standard therapy without filing an IND
- Physicians who intend to use FMT to treat CDI not responsive to standard therapy must obtain adequate informed consent from the patient or a power of attorney for the use of FMT products.
- FDA does not require donors to be "known" to either the patient or physician
- FDA does not restrict the use of FMT to any particular route of administration (e.g., colonoscopy, naso-enteric delivery, oral capsule).
- Treatment of indications other than C. difficile infection not responsive to standard therapy must be done as part of an IND application to the FDA

OpenBiome Fecal Bank

- 1st and largest in U.S.
- Non-profit
- 968 partner providers/1200+ healthcare facilities
- 8-week follow-up—no side effects linked
- Registered with FDA voluntarily
- Collaborates with Finch Therapeutics to develop CP101, a freeze-dried oral FMT capsule
- Practitioners responsible for evaluating safety and quality

98% of US Population with 2 Hours



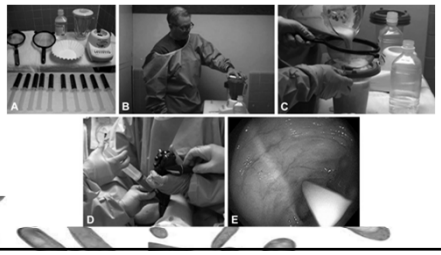
Established Stool Banks Outside of U.S.

- Netherlands Donor Feces Bank—Leiden U
- Birmingham, UK
- Portsmouth, UK
- Saint-Antoine Hospital Paris, France
- University Hospital, Cologne, Germany
- Hospital Ramón y Cajal, Madrid, Spain
- Medical University Graz, Austria
- Asia Microbiota Bank, Hong Kong

Clinical Microbiology and Infection Volume 23, Issue 12, December 2017, Pages 924-930

Stool Bank

- Unregulated
- 30,000 frozen doses sent



Donor Exclusion Criteria

- Age <18 or ≥50
- BMI <18.5 or >25
- High risk fecal- and or blood-transmittable diseases
- Recent antibiotic use (<6 months)
- GI complaints: diarrhea, obstipation, or irritable bowel-like symptoms
- Recent travel to endemic areas of GI diseases
- 1st degree relative with a GI malignancy <60 years, substantial comorbidity, various medications, autism, neurological disease

Laboratory Testing of Donating Stool

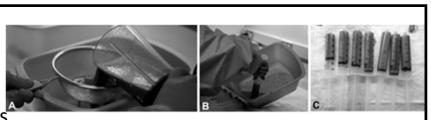
- Serum IgM and IgG
  - Hepatitis A, B, C, E
  - HIV
  - Syphilis
  - CMV
  - EBV
  - *Strongyloides*
- Parasites OCP
- Stool PCR
  - *C. difficile*
  - *H. pylori*
  - *Salmonella, Shigella, Campylobacter, Y. enterocolitica & pseudotuberculosis, Aeromonas, Pleisiomonas, Shiga toxin producing E. coli*
  - Viruses
  - Parasites
- MDROs

Donor Questionnaire

- Stool frequency/pattern
- General health
- Use of antibiotics
- Travel history
- Sexual behavior

Video of procedure (~11 minutes)
https://www.videogie.org/cms/attachment/a729ee8a-2fbb-4ece-9a1a-8d22009f7030/mmc1.mp4

FMT Processing



- Time: within 6 hours
- Prevent environmental contamination
- 60 grams (decreased cure rate if <50 g)
- Homogenized with saline by mortar and pestle or blender
- Metal sieve to remove food fragments
- Centrifugation 15 min. 6000g
- Cryoprotectant (glycerol) 10% in 200 mL
- Freeze at -80°C for 5-6 months to 2 yrs

FMT Procedure

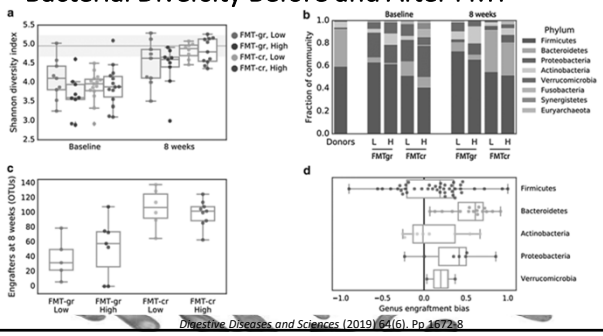
- Transport on dry ice
- Thaw 4°C overnight or 5 hours room temp
- Kept 3 hours room temp and 6 hrs refrigerated
- Treat patient with vancomycin until 1 day before procedure
- Infusion through gastric or duodenal tube or enema (repeated)
- No antimicrobials for at least 1 month

Adverse Event with FMT Capsules	N = 51
Any	45%
Treatment-emergent AE	43%
Treatment-emergent related to drug study	31%
Serious (Acerbation of COPD)	1
Serious related to drug study	0
Serious leading to death	0

Most common: bloating, flatulence, abdominal pain, constipation

Digestive Diseases and Sciences (2019) 64(6). Pp 1672-8

Bacterial Diversity Before and After FMT



Digestive Diseases and Sciences (2019) 64(6). Pp 1672-8

Business Plan: Break-Even for The Netherlands

- 100 patients yearly—899 Euros
- 400 patients yearly—785 Euros
- Recruitment, screening, selection of donors
- Periodic rescreening
- Assessment of patients' eligibility
- Post treatment monitoring
- Laboratory testing, personnel, storage, 10% retreatment

Do-It-Yourself

- 10,000/year
- Blogs and social media
- "PowerofPoop" connects to potential donors--$30--$200
- Mix stool with saline
- Squirt into rectum w/enema bottle or bag
- No gelatin capsules!
- Not available or unaffordable

Bezotoxamab and Actoxumab

- Monoclonal antibody binds to & neutralize CDI toxins
- Bezotoxamab—toxin B
- Actoxumab—toxin A
- Very expensive
- Bezlotoxumab associated with substantially lower rate of recurrent infection

Ribaxamase Reduces C. Diff Infection After IV Beta-Lactam Therapy

- Beta-lactamase
- Oral drug degrades antibiotics in upper GI
- Less disturbance of gut microbiome
- Doesn't affect pharmakinetics of antibiotic
- Decreased risk of VRE but not ESBLs

Lancet Infect Dis 2019; published online March 15. http://dx.doi.org/10.1016/S1473-3099(18)30731-X.

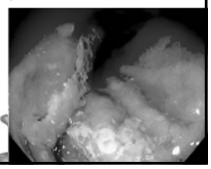
Case Report

- 54-y-o white female BMI of 40, hypertension, heart failure, anxiety disorder
- Small bowel obstruction Nov 2016 with 1 dose of cefazolin (2000 mg)
- 5 days post discharge: nausea, vomiting, abdominal pain, intermittent diarrhea
- Colonic wall thickening on CT and PCR positive for CDI toxins
- 14 days of metronidazole IV
- Exploratory laparotomy for recurrent small bowel obstruction and partial resection

Anaerobe. Vol 55 February 2019, Pages 112-116

Case Report cont.

- 10-day post-op metronidazole & ciprofloxacin
- 3 week checkup—severe watery diarrhea (20), hypotension and fever
- Positive CDT PCR—second episode
- Treated with metronidazole and oral vancomycin and fidaxomicin
- Recurred few weeks later with positive CDI
- Colonoscopy with FMT to cecum
- Pseudomembranous ulceration



Case Report cont.

- FMT failed do to loss during diarrhea
- 3 weeks later, second FMT performed
- Patient improved for 3 weeks and CDT undetectable
- Recurrence of diarrhea and positive CDT
- 3rd FMT and infusion of Bezlotoxumab infused
- Cure with a side effect of fever

IBD and CDI

- IBD patients: > antimicrobials, exposure to healthcare & immunosuppressive drugs
- Independently higher risk for CDI
- Less diverse gut microbiome in IBD and obesity
- Loss of resistance to CDI colonization

FMT for IBD

- No difference at 12 wks 221 FMT recipients and 236 placebo
- Responders had higher B to F ratio (*Prevotella spp.*)
- Not recommended treatment

The Lancet Gastroenterology & Hepatology
Source Reference: *Aroniadis, OC, et al "Faecal microbiota transplantation for diarrhoea-predominant irritable bowel syndrome: a double-blind, randomised, placebo-controlled trial" Lancet Gastroenterol Hepatol 2019; DOI: 10.1016/S2468-1253(19)30198-0L.*

Conclusions

- CDI serious ongoing problem for patients and providers
- FMT effective if carefully carried out but not without risk
- Antimicrobial stewardship necessary