



# **C. Difficile colitis and Fecal Transplant**

**Presented By:  
Mohammed Mazumder M.D.  
Licking Memorial Health Systems**



# Objectives

- Current Management as per Infectious Disease Society of America(IDSA) AND Society for Healthcare Epidemiology of America(SHEA)
- Preventive strategies
- True/false questions for audience
- Describe fecal microbiota transplantation(FMT)
- Case history-recurrent C. difficile infection(CDI)



# Clostridium Difficile Infection(CDI)

- CDI is one of the most commonly recognized cause of infectious diarrhea in healthcare settings
- Close to 500,000 infections annually in US
- 15,000-30,000 deaths
- Inpatient cost 4.8 billions
- Incidence was highest in age>65, greater in female in Whites( population based surveillance system in 2011)



# Preferred population for *C. difficile* testing

- Patients with unexplained and new-onset  $\geq 3$  unformed stools in 24 hours are the preferred target population for testing for CDI.
- Ribotype 027 associated with severe disease
- Diagnosis of CDI
  - Several test methods
  - In LMH-molecular test: DNA(PCR)
    - EnzymeImmunoAssay (EIA): TOXIN. False neg can be issue. Use clinical judgement .
- DO NOT perform repeat testing within 7 days during the same episode of diarrhea and do not test stool from asymptomatic patients



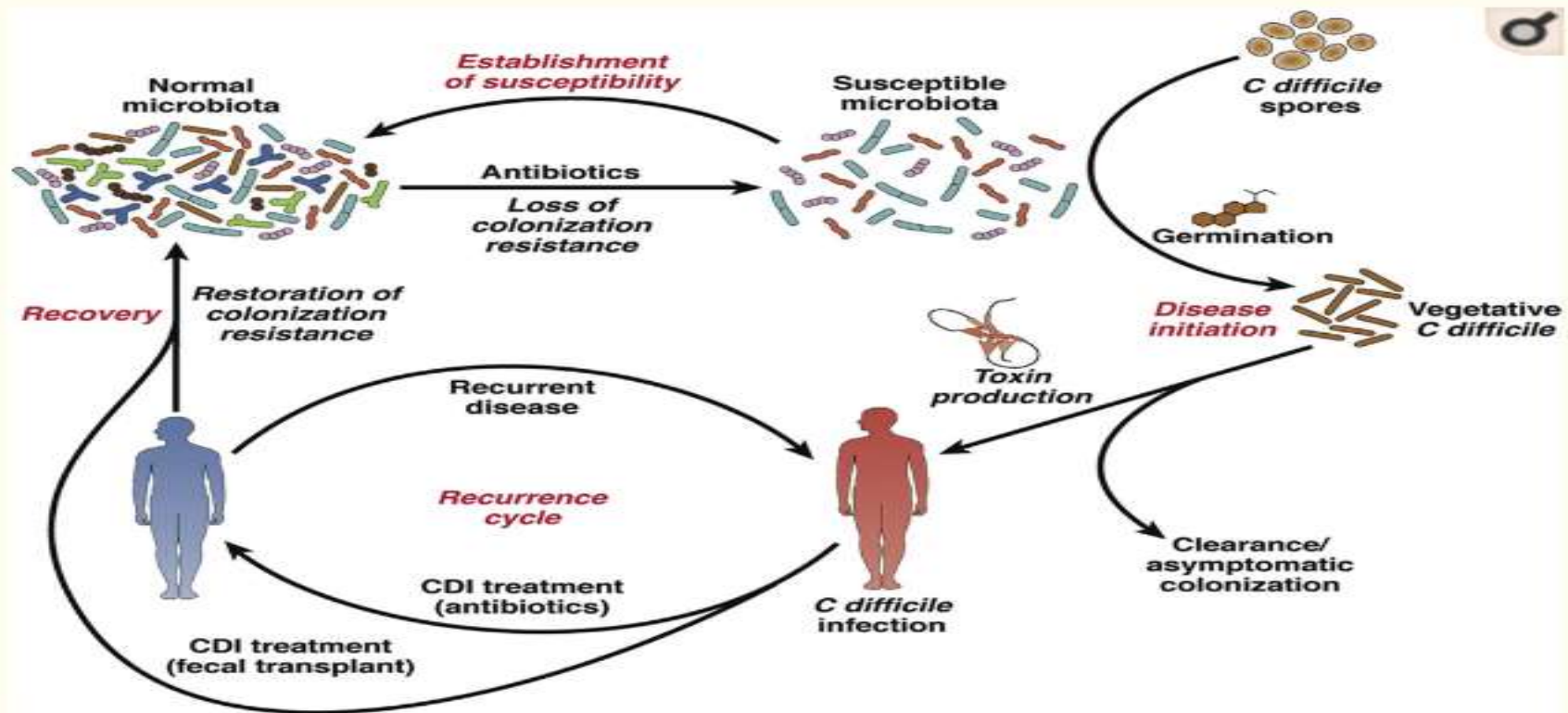
**Table 3. Summary of Available Tests for *Clostridium difficile* Infection, in Decreasing Order of Sensitivity**

Test	Sensitivity	Specificity	Substance Detected
Toxigenic culture	High	Low <sup>a</sup>	<i>Clostridium difficile</i> vegetative cells or spores
Nucleic acid amplification tests	High	Low/moderate	<i>C. difficile</i> nucleic acid (toxin genes)
Glutamate dehydrogenase	High	Low <sup>a</sup>	<i>C. difficile</i> common antigen
Cell culture cytotoxicity neutralization assay	High	High	Free toxins
Toxin A and B enzyme immunoassays	Low	Moderate	Free toxins

<sup>a</sup>Must be combined with a toxin test.



# Pathogenesis of CDI



[Open in a separate window](#)

**Fig. 1**

Pathogenesis of *Clostridium difficile* infection (CDI). This figure shows how a healthy gut microbiota (upper left corner) is altered by antibiotics to a susceptible state in which either asymptomatic colonization or symptomatic CDI can occur. Some patients do not have recovery of the microbiome back to a healthy state and experience recurrent CDI. Fecal microbiota transplantation can help restore the microbiome to a state resistant to CDI. (Adapted from Britton RA, Young VB. Role of the intestinal microbiota in resistance to colonization by *Clostridium difficile*. *Gastroenterology* 2014;146(6):1547–53; with permission.)



# Recommendations for the Treatment of initial CDI in Adults

Clinical Definition	Supportive Clinical Data	Recommended Treatment <sup>a</sup>	Strength of Recommendation, Quality of Evidence
Initial episode, non-severe	Leukocytosis with a white blood cell count of $\leq 15,000$ cells/mL and a serum creatinine level $< 1.5$ mg/dL	<ul style="list-style-type: none"> <li>• VAN 125 mg given 4 times daily for 10 days; OR</li> <li>• FDX 200 mg given twice daily for 10 days</li> <li>• Alternate if above agents are unavailable: metronidazole, 500 mg 3 times per day by mouth for 10 days</li> </ul>	Strong/High Strong/High Weak/High
Initial episode, severe <sup>b</sup>	Leukocytosis with a white blood cell count of $\geq 15,000$ cells/mL or a serum creatinine level $> 1.5$ mg/dL	<ul style="list-style-type: none"> <li>• VAN, 125 mg 4 times per day by mouth for 10 days; OR</li> <li>• FDX 200 mg given twice daily for 10 days</li> </ul>	Strong/High Strong/High
Initial episode, fulminant	Hypotension or shock, ileus, megacolon	<ul style="list-style-type: none"> <li>• VAN, 500 mg 4 times per day by mouth or by nasogastric tube. If ileus, consider adding rectal instillation of VAN. Intravenously administered metronidazole (500 mg every 8 hours) should be administered together with oral or rectal VAN, particularly if ileus is present.</li> </ul>	Strong/Moderate (oral VAN); Weak/Low (rectal VAN); Strong/Moderate (intravenous metronidazole)



# Recommendations for the Treatment of recurrence CDI in Adults

First recurrence	...	• VAN 125 mg given 4 times daily for 10 days if metronidazole was used for the initial episode, OR	Weak/Low
		• Use a prolonged tapered and pulsed VAN regimen if a standard regimen was used for the initial episode (eg, 125 mg 4 times per day for 10–14 days, 2 times per day for a week, once per day for a week, and then every 2 or 3 days for 2–8 weeks), OR	Weak/Low
		• FDX 200 mg given twice daily for 10 days if VAN was used for the initial episode	Weak/Moderate
Second or subsequent recurrence	...	• VAN in a tapered and pulsed regimen, OR	Weak/Low
		• VAN, 125 mg 4 times per day by mouth for 10 days followed by rifaximin 400 mg 3 times daily for 20 days, OR	Weak/Low
		• FDX 200 mg given twice daily for 10 days, OR	Weak/Low
		• Fecal microbiota transplantation <sup>5</sup>	Strong/Moderate





# Routes of Transmission

- The hands of healthcare personnel, transiently contaminated with *C. difficile* spores
- Environmental contamination
- Asymptomatic carriers



# Risk Factors for Disease

- Advanced age
- Duration of hospitalization
- Antibiotic exposure

Antimicrobial agents that may induce *Clostridioides* (formerly *Clostridium*) *difficile* diarrhea and colitis

Frequently associated	Occasionally associated	Rarely associated
Fluoroquinolones	Macrolides	Aminoglycosides
Clindamycin	Trimethoprim-sulfamethoxazole	Tetracyclines
Cephalosporins (broad spectrum)		Metronidazole
Penicillins (broad spectrum)		Vancomycin



# Risk Factors for Disease

- Cancer chemotherapy
- HIV
- Gastrointestinal surgery/tube feeding
- Vitamin D deficiency
- Inflammatory bowel disease(particularly UC)
- ?PPI



# Ancillary Treatment Strategies

- Discontinue unnecessary PPI. Instead H2 blocker if needed
- Discontinue inciting antibiotics agent(s) as soon as possible due to risk of CDI.
- Treat empirically if delay in lab confirmation



# Alternative Therapies

- Alternative antibiotics
- Intravenous immunoglobulin
- Probiotics: Several probiotics including *Saccharomyces boulardii* and *Lactobacillus* species have shown promise for the prevention of CDI recurrence. However, as yet, none has demonstrated significant and reproducible efficacy in controlled clinical trials.



# Monoclonal Antibody

Monoclonal antibodies – Adjunctive therapy against *C. difficile* toxin may reduce the recurrence rate of *C. difficile* infection ([Bezlotoxumab](#) -a monoclonal antibody that binds to *C. difficile* toxin B) received US Food and Drug Administration (FDA) approval in 2016

Assume vaccine in future



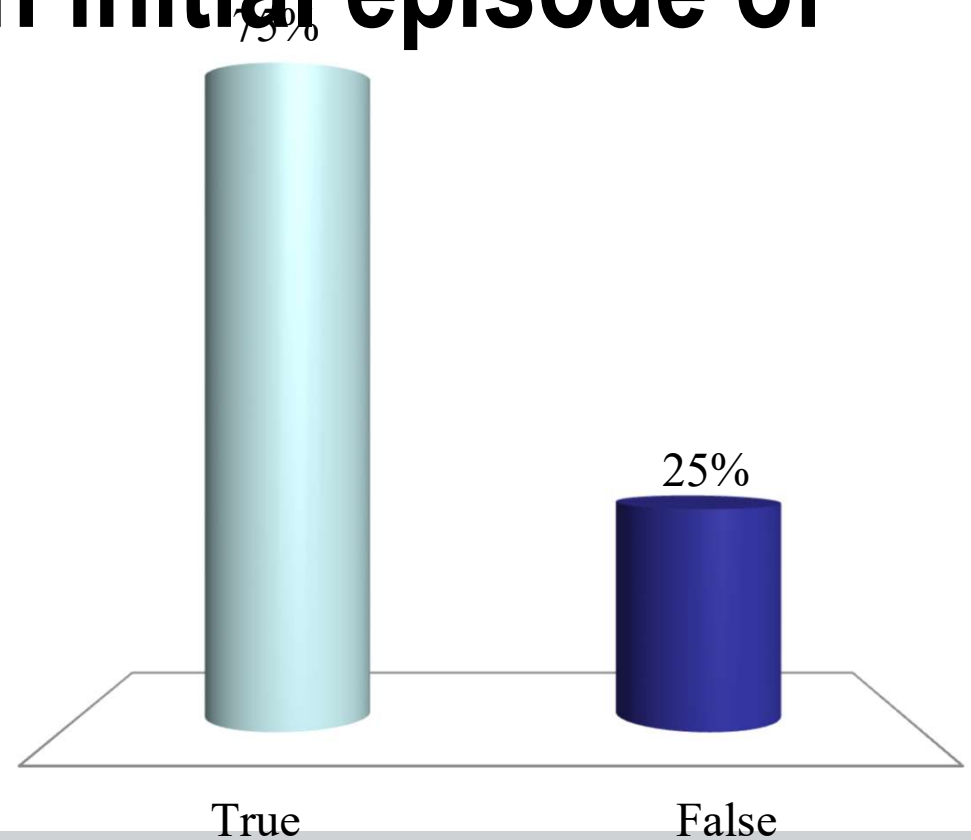
# True or False Questions

*Use your voting boxes to select the correct answer.*



**Metronidazole is recommended over either vancomycin or fidaxomicin for an initial episode of CDI. False**

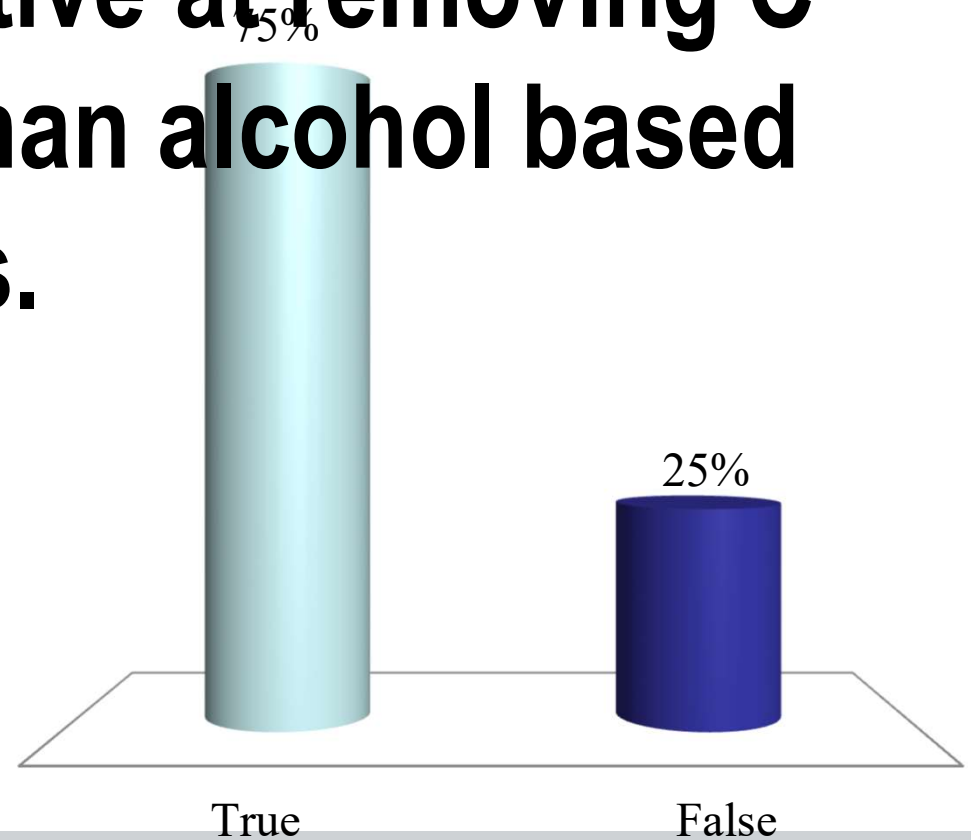
- A. True
- B. False





**Handwashing with soap and water,  
or with an antimicrobial soap and  
water-more effective at removing C  
Difficile spores than alcohol based  
hygiene products.**

- A. True
- B. False



**Healthcare personnel must use glove and gowns on entry to a room of a patient with CDI.**

A. **True**

B. False



# CDI prevention and control

- Hand hygiene
  - Healthcare personnel must use gloves and gowns
  - Hand wash with soap & water . *C. difficile* spores are highly resistant to killing by alcohol
- Private room with a dedicated toilet to decrease transmission to other patients.
  - CDI patients with stool incontinence should be prioritized for placement in private rooms
- Isolation of patients with CDI or suspected CDI



# CDI prevention and control

- Antibiotic Stewardship

- Minimize the frequency and duration of high-risk antibiotic therapy and the number of antibiotic agents prescribed, to reduce CDI risk

- Restriction of fluoroquinolones, clindamycin, and cephalosporins

- Environmental disinfection

- Continue contact precautions for at least 48 hours after diarrhea has resolved

- Prolong contact precautions until discharge if CDI rates remain high despite implementation of standard infection control measures against CDI



# CDI prevention and control

- Encourage patients to wash hands and shower to reduce the burden of spores on the skin
- Use disposable patient equipment when possible . Reusable equipment to be cleaned thoroughly and disinfected, preferentially with a sporicidal disinfectant.
- May consider Terminal room cleaning with a sporicidal agent , daily cleaning with a sporicidal agent



# Proton Pump Inhibitor(PPI) restriction in controlling CDI rates?

There is an epidemiologic association between PPI use and CDI.

Unnecessary PPIs should always be risk for CDI or recurrent CDI.

Will require further causal proof.

Need stewardship activities to discontinue unnecessary PPIs .



# Case study

- 86 year old male with a history of hypertension, cardiomyopathy, sick sinus syndrome s/p Pacemaker placement, hyperlipidemia and A. fib admitted April 9, 2019 with abdominal pain and diarrhea. Diagnosed with recurrent Clostridium Difficile.
- Previous Testing: Positive C. difficile→
  - November 11<sup>th</sup>, December 21<sup>st</sup>, January 7<sup>th</sup>, January 26<sup>th</sup>, March 13<sup>th</sup>, March 16<sup>th</sup>, April 9<sup>th</sup>.
  - Prior failed treatments: Vancomycin & Difcid
- Prior Admissions November 2018 x 2, February 2019, March 2019 and April 2019→ GI consulted on all admissions



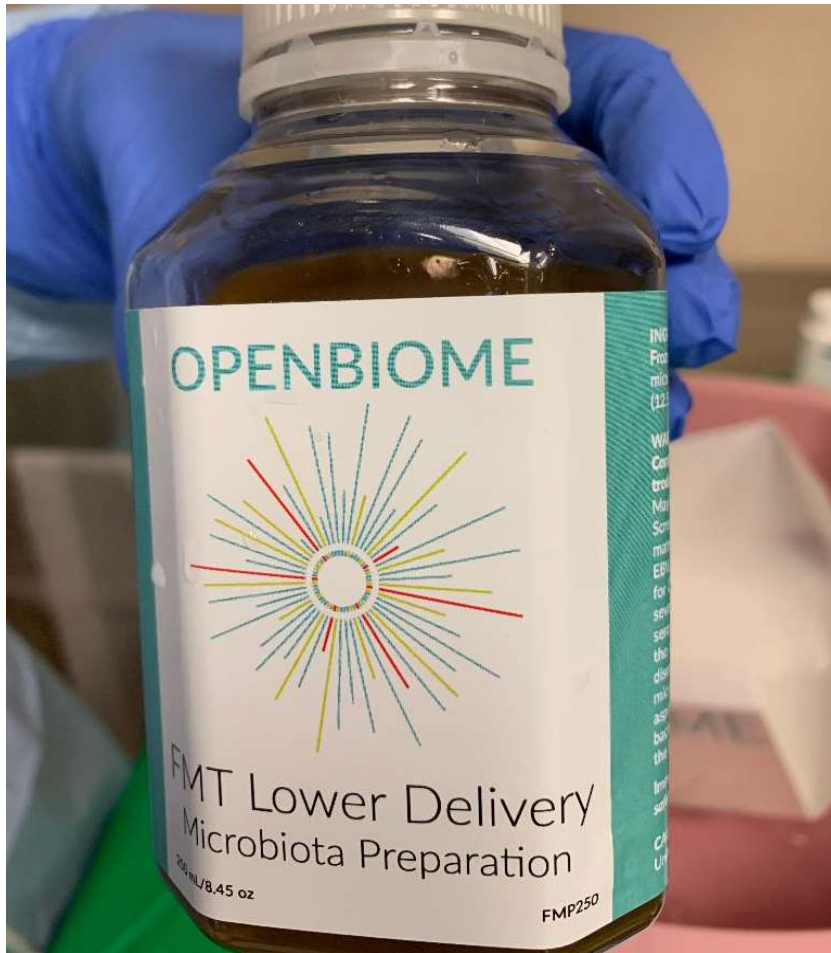
# Fecal Microbiota Transplantation(FMT)

- Multidisciplinary approach -  
PMD/Hospitalist/Gastroenterologist/ID specialist.  
Consultation by ID specialist is recommended for  
inpatient FMT candidates
- Alternative treatment option
- Registration with Donor organization(OPENBIOME)
- FMT is a process of transplanting fecal bacteria from  
a healthy individual into a recipient for the purpose of  
restoring healthy colonic microflora





# Fecal Microbiota Transplantation(FMT)



# Fecal Transplant

- Stop taking antibiotics for *C. diff.* 48 hours before procedure

clean the bathroom or bathrooms prior to fecal microbiota transplant (FMT).

- Success rates of FMT have been high: 77%-94% with administration via small bowel, 82%-100% via colonoscopy
- 2 out of 10 people treated with FMT require more than one treatment.



- **Instructions for Cleaning the Bathroom Prior to FMT**

- **Offer these instructions to the family member, friend or cleaning service who has agreed to clean the bathroom. If you yourself are cleaning the bathroom, it is important to do so just before leaving for the procedure. Do not use the bathroom once cleaned in order to avoid recontamination.**
- **To thoroughly clean the bathroom, the following items are needed:**
  - **Bleach\***
  - **Water**
  - **Bucket**
  - **Measuring cup**
  - **Clean rags**
  - **Clean sponge**
  - **Trash bag**
  - **Rubber gloves**
- **\*It is very important that bleach such as Clorox™ is used for cleaning – do not use a different cleaning agent.**
- **For protection, wear rubber gloves throughout the process.**
- **Prepare the cleaning solution in the bucket by mixing 1 cup of bleach with 9 cups of water.**
- **Wipe away any visible stool with the clean rag, then throw the rag away.**
- **Wet the sponge in the cleaning solution – scrub all surfaces vigorously.**
- **Continue to wet the sponge as necessary while cleaning.**







**C. diff. can contaminate many surfaces in the bathroom, not just the toilet. When scrubbing down surfaces, include the following high-touch areas:**

**Toilet**

**Sink**

**Shower and bathtub**

**Faucet and taps**

**Once scrubbed, leave the bathroom and allow the cleaning solution to dry for 10 minutes before entering again.**

**Dispose of the gloves, sponges and rags in the trash bag.**

**Place the trash bag in an outside trash can. Wash your hands and arms up the elbows in a sink other than the one in the cleaned bathroom.**



# FMT

- FMT should be considered for CDI patients meeting the following criteria:
  - a. Diarrhea at least for 2 consecutive days and positive stool for *C. difficile* toxin refractory to appropriate antimicrobial treatment
  - OR**
  - b. 2 or more episodes of severe CDI resulting in hospitalization and significant morbidities
  - OR**
  - c. Moderate to severe clinical worsening of first onset CDI refractory to standard therapy( oral vancomycin +/-IV metronidazole or fidaxomicin after 48 hours)



# FMT

Procedure for instillation as simple as colonoscopy

- Exclusion criteria:
  - a. Anatomic contraindications for procedure
  - b. Pregnancy
  - c. Toxic megacolon or ileus
- Use caution when considering FMT for patient with immunocompromise/complex comorbidities
- FMT appears to be less effective in patients with underlying IBD



TABLE 1

Screening tests for potentially transmissible infectious pathogens in donors and recipients undergoing fecal microbiota transplantation

Pathogen/Infection	Usual Tests	Recipient, Donor, or Both	Part of Routine or Extended Screening
Hepatitis A/B/C	Serum antibodies; serum PCR	Both	Routine
HIV	Third- or fourth-generation serum ELISA; serum RNA PCR if recent seroconversion possible	Both	Routine
Syphilis	Nontreponemal serum test followed by treponemal confirmatory test if positive (eg, serum RPR followed by TP-PA)	Both	Routine
Enteric bacterial pathogens ( <i>Salmonella</i> species, <i>E coli</i> , <i>Shigella</i> species, and others)	Routine stool culture	Donor	Routine
Enteric helminths and protozoa	Stool microscopy for ova and parasites; antigen ELISAs for <i>Giardia</i> and <i>Cryptosporidium</i> species	Donor	Routine
<i>Clostridium difficile</i>	Stool EIA for bacterial products and/or PCR	Donor	Routine
Epstein-Barr virus	Serum antibodies; PCR	Both	Extended (HSCT and SOT patients)
Cytomegalovirus	Serum antibodies; PCR	Both	Extended (HSCT and SOT patients)
Others ( <i>Helicobacter pylori</i> , HTLV, and many others)	Various tests	Usually donor only	Extended (research protocols)



# Recently FDA issues safety alert on fecal transplants after patient dies

- 2 adults with weakened immune systems who received investigational FMT developed invasive infections caused by extended-spectrum beta-lactamase(ESBL)-producing *Escherichia coli*
- Following transplant and the occurrence of the severe adverse events, the donor stool was tested and found to be positive for ESBL-producing *E. coli* identical to the organisms isolated from the two patients

**Our donor organization-Open biome wasn't involve with above occurrence**





## FMT continue....

- Colonoscopy is the route of FMT in LMH
  - bowel prep

Stop taking antibiotics for C. diff. 48 hours before procedure

- Administer 1-2 doses of loperamide prior to the procedure



# FMT

# continue....

- Post procedure care
- Lay on right side
- Retain contents(fecal microbiota) as long as possible:3-4 hours bedrest for out patients, 4-5 hours bedrest for inpatients
- No food for first 8 hours. Only water.
- Follow-up within 8 weeks



# First patient in LMH

- Our patient readmitted on 06/04/2019 with severe CDI( WBC 21.8, hypoalbuminemia, BM-7-8 times).  
No fever/hypertension
- Underwent FMT via colonoscopy on 6/4/2019, WBC decreased to 11, bowel frequency improve.  
However in 3 days, patient re experiences feature of severe CAD
- 2 out of 10 people treated with FMT require more than one treatment.



# Thanks

# Question?





# ISOLATION of Positive C Diff

- To remain in isolation until after the 10 days of antibiotic treatment and the patient is no longer having diarrhea.



Interpretation about C. difficile  
positivity  
Molecular-C. difficile DNA  
Serology



# Treating C. difficile-causing C. difficile colitis

