Fecal microbiota transplantation (FMT) for treatment of recurrent *Clostridium difficile* infections using recipient-directed donors sero-matched for latent viruses: the University of Pittsburgh Medical Center (UPMC) experience

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**ABSTRACT**

Background: Fecal microbiota transplantation (FMT) is effective for recurrent *C. difficile* infections (rCDI), but donor-derived infections remain a concern. We report the success rates and seroprevalence of herpesviruses (HSV, EBV, CMV, and JC virus) and human polyoma virus (HPV) among FMT recipients who are seronegative for HSV, EBV, CMV, and JC virus.

Methods: All patients undergoing FMT for rCDI at UPMC were included. Donors were selected by recipients and donors were matched for latent viruses. Blood was collected from donors within 30 days before FMT. Donors were seronegative for herpesviruses, leading to an endoscopist to use only HSV, EBV, CMV, and JC virus donors.

Results: Of 129 patients enrolled, 125 (97%) were successfully colonized with donor microbiota, and 11/12 (92%) by nasoduodenal (ND) tube, 6/7 (86%) by saliva, 5/5 (100%) by urine, and 6/7 (86%) by stool. Of the 11/12 (92%) successes by ND tube, 4/7 (57%) were from donors with HSV1/2, 3/7 (43%) with CMV, 6/7 (86%) with EBV, 5/7 (71%) with JC virus, and 5/7 (71%) with HPV. Of the 6/7 (86%) by saliva, 4/7 (57%) were donors with HSV1/2, 2/7 (29%) with CMV, and 1/7 (14%) with EBV. 7/14 (50%) were seropositive and 6/14 (43%) seronegative for CMV and HSV1/2.

Conclusions: FMT for rCDI using HSV1/2, EBV, CMV, and JC virus seronegative donors results in successful colonization with donor microbiota for 97% of patients. A donor-derived infection was not observed in the study.

**METHODS**

### Donors

- Able to provide informed consent
- 18 years of age
- No use of antibiotics ≥90 days prior to FMT

### Recipients

- ≥3 documented CDI episodes OR severe CDI
- ≥18 years of age
- No travel outside US/Canada in 12 months from FMT

### Shedding of human herpes and polyoma viruses

- EBV 1/9 (11)
- CMV 3/14 (21)
- HSV1 seronegative 13/14 (93)
- HSV2 seronegative 17/19 (89)
- JC virus seronegative 6/19 (32)

### Use of FMT

- ND tube: 14 donors with 11/12 (92%) successes by ND tube, 6/7 (86%) by saliva, 5/5 (100%) by urine, and 6/7 (86%) by stool.
- Saliva: 4/7 (57%) were donors with HSV1/2, 3/7 (43%) with CMV, 6/7 (86%) with EBV, 5/7 (71%) with JC virus, and 5/7 (71%) with HPV.
- Urine: 7/14 (50%) were seropositive and 6/14 (43%) seronegative for CMV and HSV1/2.

### FMT preparation

- Dedicated laboratory / safety cabinet (no other material handled)
- Personnel in PPE
- Donor provides 25-150g sample in labeled container
- Dose used within 8 hours of defecation
- Steam sterilization of all items in sterilization cabinet (no other material handled)
- Loaded into 60 ml saliva transplanter

### FMT routes

- ND tube
- Saliva
- Urine
- Stool

### Post-FMT testing:

- Bloodborne pathogens
- Polymicrobial pathogens
- Stool cultures
- VRE/MRSA
- EBV, HSV 1-2, CMV, JC virus

### Fecal microbiota transplantation endpoint:

- Any diarrhea by 2 weeks
- C difficile testing after FMT

### Outcomes for FMT recipients and donors at UPMC December 2014-May 2016

<table>
<thead>
<tr>
<th>Patients (n=19)</th>
<th>Donors (n=14)</th>
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<tbody>
<tr>
<td>Female gender</td>
<td>11/19 (58)</td>
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<tr>
<td>Median age</td>
<td>68</td>
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<tr>
<td>Mean age</td>
<td>62</td>
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<tr>
<td>Age range</td>
<td>25-85</td>
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### Characteristics of FMT recipients and donors at UPMC December 2014-May 2016

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n/N (%)</th>
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<tbody>
<tr>
<td>EBV seronegative</td>
<td>1/9 (11)</td>
</tr>
<tr>
<td>CMV seronegative</td>
<td>10/19 (53)</td>
</tr>
<tr>
<td>HSV1 seronegative</td>
<td>12/14 (86)</td>
</tr>
<tr>
<td>HSV2 seronegative</td>
<td>17/19 (89)</td>
</tr>
<tr>
<td>JC virus seronegative</td>
<td>6/19 (32)</td>
</tr>
</tbody>
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### Abbreviations

- CDI
- FMT
- rCDI
- rCDI-therapy
- MTX
- SCF
- HSV
- EBV
- CMV
- JC virus
- GHV

### Conclusions

- FMT recipients may be at risk for donor-derived FMT infections
- Avoiding EBV, CMV, HSV, and JC virus donors is logistically feasible but may extend wait time for FMT
- Continued antibiotic use for non-CDI indications may predispose to FMT failure
- Volunteer frozen stool banks may shorten time to FMT with an improved safety margin by closing the serologic window period

### REFERENCES