Microbiome and Non-traditional Therapies for *C. difficile* Infection
A Primer for Healthcare Professionals

The Microbiome is Essential for Human Health
The human microbiome is comprised of more than 100 trillion microbial cells and over 1,000 known bacterial species, including the predominant phyla Bacteroidetes, Firmicutes, Proteobacteria, and Actinobacteria. Given the critical functions of commensal microbiota, healthcare professionals can care for a patient's microbiome by trying to preserve the diversity and abundance of microorganisms.

**Microbial abundance varies by body site**

<table>
<thead>
<tr>
<th>Body Site</th>
<th>Abundance</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI tract</td>
<td>30%</td>
</tr>
<tr>
<td>Mouth</td>
<td>26%</td>
</tr>
<tr>
<td>Skin</td>
<td>21%</td>
</tr>
<tr>
<td>Airways</td>
<td>14%</td>
</tr>
<tr>
<td>GU tract</td>
<td>9%</td>
</tr>
</tbody>
</table>

**Gut microbiota promote and preserve health**
- Metabolizes drugs
- Modulates immune response
- Protects against injury
- Regulates hormones
- Resists pathogens

**Dysbiosis May Result in Reduced Microbiome Functional Capacity**
Dysbiosis is defined as a significant change in the microbiome structure or function and is associated with more than two dozen health conditions, including infection, inflammatory bowel disease, obesity, diabetes, cancer, cardiovascular disease, & immunosuppression.

**Microbiome in Homeostasis**
- Characteristics associated with reduced diversity include antibiotics, gastric acid suppressants, older age, and chronic disease

**Microbiome in Dysbiosis**
- Reduced microbial diversity, loss of beneficial microbes, and expansion of pathogenic microbes occurs with dysbiosis

**Clostridioides difficile and the Human Microbiome**
- Suitable environment for pathogen colonization
- Restored defense against pathogen colonization
- Treatment (antibiotics)
- C. difficile infection (CDI)
- Treatment (fecal microbiota transplant)
- Clostridioides difficile: An Urgent Public Health Threat
  - 500 thousand Americans infected annually
  - 1 in 4 patients experience CDI recurrence
  - 9% mortality in hospitalized patients
  - $5 billion annual healthcare costs

**Microbiome-Targeted Interventions**
Prescribers can positively impact the microbiome through evidence-based interventions including:
- **Antibiotic Stewardship**
  - Avoid unnecessary antimicrobials
  - Preserve narrow-spectrum antibiotics for the shortest possible duration when indicated
  - Practice diagnostic stewardship
- **Diet and Prebiotics**
  - Plant-based, Mediterranean diets increase bacterial diversity
  - Prebiotics (substrates used by microbiota) may promote beneficial microbes
- **Fecal Microbiota Transplant (FMT)**
  - Transfer of healthy donor feces into GI tract
  - Effectively restores microbiome diversity
  - Recommended after three episodes of CDI
  - Currently being studied for cancer and IBD
- **Probiotics**
  - Live organisms intended to promote health
  - Safe for most patients
  - Not recommended to treat CDI
  - Discrepancies in dose and organisms studied

**FMT Preparation and Process**
1. **HEALTHY DONOR STOOL SAMPLE**
   Donor samples are screened for general health and pathogens
2. **SAMPLE PROCESSING**
   Preparation and filtration leave a healthy microbiome
3. **SAMPLE FORMULATION**
   Pill and liquid formulations available for transplantation
4. **TRANSPLANT**
   Administered via nasogastric, oral, enema, or colonoscopy

References: