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# Treating Clostridium difficile Infection with Fecal Microbiota Transplantation

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## Abstract

*Clostridium difficile* infection is increasing in incidence, severity, and mortality. Treatment options are limited and appear to be losing efficacy. Recurrent disease is especially challenging; extended treatment with oral vancomycin is becoming increasingly common but is expensive. Fecal microbiota transplantation (FMT) is safe, inexpensive, and effective; according to case and small series reports, about 90% of patients are cured. We discuss the rationale, methods, and use of FMT.

### Keywords

*Clostridium difficile*; transplantation; microbiota; fecal enema; recurrent infection; diarrhea

## Background

Over the last 15 years, *Clostridium difficile* infection (CDI) has become epidemic and continues to gain momentum with greater incidence, morbidity, and mortality than in decades past. In the United States, the National Hospital Discharge Survey, revealed doubling of CDI diagnoses from 31/100,000 in 1996 to 61/100,000 in 2003.[1] This rise has been accompanied by increasing rates of colectomy and mortality over the same time period.[2] In 2010, the yearly incidence of CDI was estimated at 500,000 with mortality at 15,000 – 20,000[3-5] and the cost of managing CDI estimated to be at least $1 billion per year in the U.S. alone.[6] One major reason for this growing problem is the emergence of newer, more virulent and more antibiotic-resistant strains including North American pulsed-field gel electrophoresis type 1, restriction endonuclease analysis group BI, and PCR ribotype 027 (NAP1/BI/027) among others.[7, 8] Although acquisition of CDI still occurs most commonly in health care facilities, it is increasingly recognized that CDI can also be acquired in the community by young, healthy individuals without prior exposure to antibiotics or hospitals. Furthermore, patients at greater risk are no longer just the elderly, but also patients with inflammatory bowel disease, compromised immune systems, and peripartum women.[5, 8]

As the *C. difficile* epidemic continues to grow, the numbers of failed treatments and patients who experience relapses or recurrences also are increasing. Metronidazole and vancomycin are the first-line agents for *C. difficile* treatment; however, recent data suggest that metronidazole is losing its efficacy, and expert opinion is shifting towards the use of vancomycin as first-line therapy.[9] Furthermore, the rates of recurrent and severe CDI continue to increase despite the efficacy of these agents. Recurrent CDI has been documented to occur in as many as 15-30% of patients after an initial bout of CDI and up to 65% of patients who experience one recurrence will have subsequent recurrences after antibiotic therapy is stopped.[10, 11] Recurrent CDI can turn into a chronic, recalcitrant disease in which repeated bouts of infection can continue for years leading to persistent use of antibiotics, repeated hospitalizations, and even death.

The basic pathophysiology of recurrent CDI is not completely understood. Antibiotics suppress and disrupt the distal bowel microbial communities that normally keep expansion of *C. difficile* populations in check. Because *C. difficile* spores are largely resistant to antibiotics, they can germinate back into vegetative forms after antibiotic treatment has been discontinued. If residual normal intestinal microbiota cannot restrain the infection, *C. difficile* bacteria proliferate and once again produce toxins that cause destruction of colonic

epithelial cells and return of inflammation with resultant disease symptoms. While spores are thought to play a role in the pathophysiology of recurrent CDI, some patients may become reinfected with different strains. In one series of patients with recurrent CDI, molecular analysis showed that 6 of 18 (33%) had a new strain.[12]

Different treatment options exist for recurrent CDI, most of which focus on further antibiotic management. Tapered and/or pulsed courses of vancomycin therapy are favored over a traditional 10-14 day course of therapy. Patients from the placebo arm of two studies evaluating a probiotic adjunct to standard antibiotics for recurrent CDI were analyzed for recurrence rates. The overall recurrence rate was 44.8%. However, those who had a tapering course of vancomycin had a recurrence rate of 31%; those who received pulsed dosing of vancomycin had an even lower recurrence rate of 14%.[11] While vancomycin regimens are widely used and effective in many patients, the use of antibiotics represents a double-edged sword by suppressing both the pathogen as well as the protective microbiota. Indeed, the repeated and chronic use of antibiotics to treat recurrent infection has an adverse effect on the intestinal flora. Vancomycin is a broad-spectrum antimicrobial agent with activity against almost all Gram-positive aerobic and anaerobic organisms and thus may ultimately increase susceptibility to CDI by maintaining a persistently altered state of bowel flora.

Alternative antibiotics are being investigated but their efficacy in patients with recurrent disease is unknown.[13] Fidaxomicin had a lower rate of recurrences compared to vancomycin in two studies but its role in the therapy of recurrent CDI has not been established. *C. difficile* toxin-binding resins are not curative and are best used as adjunctive agents to vancomycin.

The only currently available immunologic approach to treat CDI is administration of pooled intravenous immunoglobulin (IVIG). However, the role for this therapy in CDI remains unclear as the results of studies, all retrospective so far, have been equivocal at best.[14]

An alternative approach to treatment of recalcitrant CDI is to restore the damaged microbial intestinal communities. The efficacy of the probiotic *Saccharomyces boulardii* as an adjunct to antibiotics has been tested in two trials. While it did not decrease recurrence rates in those with their first episode of CDI (19% compared to 24% with placebo), it did decrease the frequency of relapses in those with recurrent CDI (34.6% vs 64.7% with placebo)[10]. However, a second trial showed *S. boulardii* had efficacy only in the subset of patients who were given high-dose vancomycin (2 g/day) (16.7% compared to 50% with placebo). No significant benefit was seen in those given metronidazole or lower-dose vancomycin[15]. Although the probiotic *Lactobacillus* GG showed promise in case reports, recurrence rates were worse than placebo (37.5% vs 14.3% with placebo)[16]. A controlled, albeit underpowered, trial of *Lactobacillus plantarun* 299v as an adjunct to metronidazole in 11 patients with recurrent CDI, the probiotic arm had a lower recurrence rate (36%) compared to placebo (66%)[17]. The data to date indicate that probiotics may have a role in treatment, but their efficacy is less than ideal.

In contrast, fecal transplantation, also known as Fecal Bacteriotherapy, is proving to be an effective alternative intervention. Case reports and small case series to date suggest that recurrent CDI can be cured with a single treatment. The material is readily available and very inexpensive. Because the exact agent or combination of agents which may affect the cure is unknown, the terms “fecal transplantation” and “Fecal Bacteriotherapy” will henceforth be replaced with a new term: “Fecal Microbiota Transplantation (FMT).” The rationale behind FMT is simple: antibiotics and other factors disrupt the normal balance of colonic flora and reduce “colonization resistance,” allowing pathogenic *C. difficile* strains to grow, leading to the typical clinical presentations of diarrhea and pseudomembranous

colitis; by reintroducing normal flora via donor feces, the imbalance can be corrected, the cycle interrupted, and normal bowel function re-established.

The idea of FMT has parallels in the veterinary world, where the practice of transfaunation has been used for centuries to treat ruminants with severe ruminal acidosis and other gastrointestinal disorders and for the treatment of equine diarrhea.[18] In humans, the first use of FMT dates back at least to a 1958 case series of four patients with pseudomembranous enterocolitis.[19] Of note, three of four patients reported in the 1958 series were in a critical state when fecal enemas were administered, and in all patients symptoms resolved within hours of FMT. The first documented case of confirmed CDI treated with FMT was reported in 1983 by Schwan *et al.*: a 65-year-old woman who had “prompt and complete normalization of bowel function”.[20] At follow-up nine months later, the patient remained asymptomatic. Up until 1989, retention enemas had been the most common technique for FMT. However, alternative methods subsequently included fecal infusion via duodenal tube in 1991, rectal tube in 1994, and colonoscopy in 1998. FMT for recurrent CDI has been reported to be successful whether given via colonoscopy[21,22,23], nasogastric tube[24,25], or enemas administered at home[26]. No clear superiority of one method over another has yet been demonstrated. However, of the approximately 200 cases reported, regardless of route, a mean success rate of 96% has been achieved.[27]

It is now well appreciated that intestinal microbiota constitute a microbial organ that is integral to overall host physiology, including pivotal roles in metabolism and immune system function.[28] So far, recurrent CDI appears to represent the clearest known example of near complete disruption of the intestinal microbiota resulting in gastrointestinal dysfunction. Until recently, the intestinal microbiota has been generally inaccessible to scientific study because most of its constituents could not be easily cultured in the laboratory. In part this is because individual microorganisms are highly specialized and exist in structured community networks that become disrupted in attempts at single cell cloning.

Chang *et al.* constructed 16S rRNA-encoding gene clone libraries from the fecal material of four patients with first-time CDI and three patients with recurrent CDI, performed phylogenetic analyses and compared them with normal control samples.[29] They found the microbiomes of patients with an initial episode of CDI were largely intact at the phylum level, i.e., the majority of sequences belonged to *Bacteroidetes* and *Firmicutes*, the two dominant bacterial phyla in the colon. However, major reduction and even disappearance of *Bacteroidetes* was noted in patients with recurrent CDI and accompanied by markedly increased proportions in other phyla that normally are only minor constituents of fecal microbiota. Khoruts, *et al.* compared the microbiota of a patient with recurrent CDI before and after FMT using terminal-restriction fragment length polymorphism and 16S rRNA gene sequencing approaches.[30] Before transplantation, the patient's microbiota were deficient in members of *Bacteroidetes*. Instead they were composed of atypical bacterial populations such as *Veillonella, Clostridium, Lactobacillus, Streptococcus*, and unclassified bacteria similar to *Erysipelothrix*. Two weeks after infusion of donor fecal suspension into the patient, the bacterial composition of her feces changed to closely resemble that of the donor with dominance of *Bacteroidaceae* including *B. vulgatus*. Thirty-three days after the procedure, the patient's flora still was predominantly composed of multiple *Bacteroides* species, highlighting the durability of engrafted donor bacteria administered via FMT.

In summary, CDI exists today in epidemic proportions and continues to increase steadily along with rising rates of complications, including recurrent disease and death. Recurrent disease can become an especially difficult clinical challenge, particularly in older patients who need additional antibiotics for other indications, those with additional co-morbidities, and patients presenting with severe disease. Although vancomycin is the only drug that is

approved by the FDA to treat CDI, it is clearly insufficient for many patients with recurrent disease. This predicament has forced a number of alternative therapies to be tried and to be developed. However, none has yet proved to be highly effective, safe, and inexpensive. In contrast, with a cumulative reported cure rate of >90%, negligible rate of significant adverse effects, and response of hours to days, FMT appears to fit these criteria. Furthermore, FMT is the only therapy that restores the phylogenetic richness of the recipient's intestinal microbiota without prolonging the perturbation of the normal microbiotic composition. Additional data are needed to assess the efficacy of FMT; however, given the encouraging data to date and pending additional research data on the intestinal microbiome and metagenome, it appears to be an effective option for the treatment of refractory CDI. Therefore, we offer the following guidelines for its use.

## I. Indications

### Primary indications

1. Recurrent or relapsing CDI.
    a. At least three episodes of mild-to-moderate CDI and failure of a 6-8 week taper with vancomycin with or without an alternative antibiotic (e.g., rifaximin, nitazoxanide).
    b. At least two episodes of severe CDI resulting in hospitalization and associated with significant morbidity.
2. Moderate CDI not responding to standard therapy (vancomycin) for at least a week.
3. Severe (and perhaps even fulminant *C. difficile* colitis) with no response to standard therapy after 48 hours.

In all cases, primary consideration must be given to the severity and pace of the patient's CDI when deciding whether early use of FMT is appropriate to prevent further clinical deterioration.

## II. Donor Selection

### A. Choice of donor

At this time, little or no data are available to suggest that any factors other than specific exclusion criteria based on medical history and laboratory testing would endorse a particular donor to be optimal. There may be certain advantages and disadvantages, however, which can be considered. Intimate contacts (e.g., spouse, significant other) have the advantage of sharing infectious risk factors, which minimizes the risk of transmitting an infectious agent. Despite the possibility that an intimate contact may have a higher chance of being a *C. difficile* carrier, limited experience has suggested that transplant of *C. difficile*-containing stool from a carrier into a recipient with recurrent CDI does not necessarily adversely affect success of the procedure. Maternal-line first-degree relatives may have a theoretical advantage of sharing the greatest number of microbial species in their intestinal microbiota with the recipient. Therefore, it is conceivable that adaptive immune elements in the mucosal immune system (e.g., antigen-specific antibody) may be more tolerant of microbiota derived from such donors. However, material from alternative donors has been equally effective in curing CDI. Similarly, it is possible to speculate that men might make preferred donors over women as women may harbor microbiota that are more apt to result in IBS. Finally, there are certain advantages in using unrelated, healthy, but rigorously screened donors. Availability of this large donor source can facilitate execution of FMT. Furthermore, as intestinal microbiota have recently been theorized to be potentially involved

in pathogenesis of a number of systemic diseases, healthy volunteer donor sources may have advantages, especially for young patients.

## B. Donor Exclusion Criteria

Although the following represent absolute or relative contraindications to FMT, it is critically important to give primary consideration to the severity of the patient's illness. That is, mutual agreement to proceed with FMT between donor and recipient may trump the risk of transmitting an infectious disease if a risk-free alternative donor cannot be found in a timely fashion or the condition of the potential recipient is so precarious that time is a critical factor in predicting mortality from CDI. At the same time, the physician performing FMT has to assume responsibility to independently evaluate the donor for potential risk and does not need to abide by recipient-donor agreement if the risk is felt to be unreasonably high. The primary purpose of questioning the donor is to ensure that the donor is in good health, the donation process is safe for the donor, and that any risk factors for diseases transmissible by stool can be identified. The donor interview is especially important to identify risks for diseases and conditions for which there are no laboratory tests, for which tests are not sensitive enough to detect infectious disease agents, and for which tests are unable to identify early stage or window-period infections.

### 1. Absolute

**a. Risk of infectious agent:** Consider using AABB Donor History Questionnaire: http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/BloodDonorScreening/UCM213552.pdf

- Known HIV, Hepatitis B or C infections
- Known exposure to HIV or viral hepatitis (within the previous 12 months.)
- High-risk sexual behaviors (examples: sexual contact with anyone with HIV/AIDS or hepatitis, men who have sex with men, sex for drugs or money)
- Use of illicit drugs
- Tattoo or body piercing within 6 months
- Incarceration or history of incarceration
- Known current communicable disease (e.g., upper respiratory tract infection)
- Risk factors for variant Creutzfeldt-Jakob disease
- Travel (within the last 6 months) to areas of the world where diarrheal illnesses are endemic or risk of traveler's diarrhea is high

### b. Gastrointestinal co-morbidities

- History of inflammatory bowel disease
- History of irritable bowel syndrome, idiopathic chronic constipation, or chronic diarrhea
- History of gastrointestinal malignancy or known polyposis

### c. Factors that can or do affect the composition of the intestinal microbiota

- Antibiotics within the preceding 3 months
- Major immunosuppressive medications, e.g., calcineurin inhibitors, exogenous glucocorticoids, biologic agents, etc.

- Systemic anti-neoplastic agents

#### d. Additional recipient-specific considerations

- Recent ingestion of a potential allergen (e.g., nuts) where recipient has a known allergy to this (these) agent(s).

#### 2. Relative exclusion criteria that may be appropriate to consider

**a.** History of major gastrointestinal surgery (e.g., gastric bypass)

**b.** Metabolic syndrome

**c.** Systemic autoimmunity, e.g., multiple sclerosis, connective tissue disease

**d.** Atopic diseases including asthma and eczema, eosinophilic disorders of the gastrointestinal tract

**e.** Chronic pain syndromes, e.g., chronic fatigue syndrome, fibromyalgia

### C. Donor Testing

Donor screening and testing for relevant communicable diseases should be performed. However, as before, it is critically important to give prime consideration to the patient's illness when weighing the delays inherent in waiting for the results of stool testing.

Consider using FDA guidelines for donors of human cells, tissues, and cellular and tissue-based products (HCT/Ps): http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/ucm073964.htm

The FDA recommends donor screening and testing for relevant communicable diseases for donors of human cells, tissues, and cellular and tissue-based products (HCT/Ps). A communicable disease agent or disease is relevant if:

- it is one for which there may be a risk of transmission by stool either to the patient or to those people who may handle or otherwise come in contact with the stool; and
- it could be fatal or life-threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of body function or permanent damage to a body structure; and
- it is one for which appropriate screening measures have been developed and/or an appropriate screening test for donor specimens has been licensed, approved, or cleared for such use by FDA and is available.

The tests listed below, the respective CPT codes, and fee schedules are listed in Table 1.

#### 1. Stool testing

**a.** *Clostridium difficile* toxin B by PCR; if unavailable, then evaluation for toxins A and B by EIA.

**b.** Routine bacterial culture for enteric pathogens

**c.** Fecal *Giardia* antigen

**d.** Fecal *Cryptosporidium* antigen

**e.** Acid-fast stain for *Cyclospora, Isospora* and, if antigen testing unavailable, *Cryptosporidium*

**f.** Ova and parasites

**g.** *Helicobacter pylori* fecal antigen (for upper GI routes of FMT administration)

#### 2. Serologic testing (unless otherwise stated, all tests should be performed using FDA-approved test methods)

**a.** HIV, type 1 and 2

**b.** HAV IgM

**c.** HBsAg, anti-HBc (both IgG and IgM), and anti-HBs.

**d.** HCV Ab

**e.** RPR and FTA-ABS

**Confirmatory tests:** Confirmatory tests will be performed when a positive or reactive screening test result is received for such purposes as donor counseling or investigating discordant test results.

Serologic testing of the recipient for these agents is optional.

### Donor eligibility determination and testing when stool donors are sexually intimate partners of the patient

There are situations in which determination of donor eligibility, donor screening and testing are not required (for example; reproductive cells or tissue donated by a sexually intimate partner of the recipient for reproductive use). Theoretically, sexually intimate contacts would have previously shared bodily fluids and exposure to relevant communicable diseases. Stool donation by an intimate partner for purposes of FMT should not significantly increase risk for the patient. In this circumstance, the physician performing FMT might consider an abbreviated version of the above testing. This could be very important in situations where FMT must be performed expeditiously (such as severe/fulminant *C. difficile* infection) and there is insufficient time to await test results.

## III. Recipient Exclusion Criteria

Many patients have significant comorbidities that should be considered before performing FMT; however, it is extremely rare for these to result in exclusion.

### A. Considerations for increased risk of adverse events should be given to

1. Patients on major immunosuppressive agents including high dose corticosteroids, calcineurin inhibitors, mTOR inhibitors, lymphocyte depleting biologic agents, anti-TNF agents, and others; chemotherapeutic anti-neoplastic agents.
2. Patients with decompensated liver cirrhosis, advanced HIV/AIDS, recent bone marrow transplant, or other cause of severe immunodeficiency.

## IV. Protocol for performing FMT

### A. Donor preparation

1. Consider the use of a gentle osmotic laxative the night before procedure.
2. Avoidance of any foods to which recipient may be allergic for 5 days prior to the procedure.

3. Instructions to notify the practitioner if any symptoms of infection (fevers, diarrhea, vomiting) which occur between screening and time of donation

### B. Recipient preparation

1. Large volume bowel prep regardless of route of FMT. The severity of the patient's illness may limit the ability to perform this step.
2. Loperamide (if giving FMT via enema or colonoscopy) is optional. Though described in some protocols to aid in the retention of transplanted material, others have performed FMT without it with similar rates of success.
3. If FMT is to be delivered by NGT, then a PPI should be given to the recipient the evening before and the morning of the procedure.

## V. Preparation of stool

### A. Stool handling/storage

1. Use as soon as possible after passage, but certainly within 24 hours and preferably within 6 hours. Stool should be kept in an airtight container and may be chilled but should not be frozen.
2. Use of a hood if possible (stool is a Level 2 biohazard).
3. Universal precautions. Those involved with mixing and/or handling the fecal transfusion material should wear a fluid-resistant gown, gloves, and mask with goggles or eye shield.

### B. FMT preparation

1. Although the choice of diluents may differ among practitioners, the use of either preservative-free normal saline for intravenous injection or 4% milk is preferred to dilute the stool sample.
2. For best results, a conventional household blender (dedicated to this purpose) should be used. The stool should be homogenized, adding more diluent as necessary, until it reaches a liquid slurry consistency.
3. The stool should be filtered to remove as much particulate matter as possible. This can be accomplished using a number of methods (e.g., gauze pads, urine stone strainers).
4. The finished stool slurry should be used immediately.
5. The ideal volume for instillation has not been established. However, smaller volumes (e.g., 25-50 mL) should be used for delivery from above; larger volumes (e.g., 250-500 mL) should be used for delivery from below.

## VII. Means of administering stool

There are many unanswered questions regarding the best route of administering the FMT and, indeed, the route may vary with the needs and status of the individual patient. Methods used to administer FMT have included fecal suspensions given via nasogastric and nasoduodenal tubes, through a colonoscope, or as a retention enema[27].

## VIII. Evaluation of success

A. Resolution of symptoms is the primary endpoint; absence of, relapse within 8 week of FMT is the secondary endpoint.

**B.** IDSA/SHEA guidelines do NOT recommend *C difficile* testing in patients who do not have symptoms, because patients can be colonized with *C difficile* and not develop disease.[31]

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## Abbreviations

| | |
|---|---|
| **AIDS** | Acquired Immunodeficiency Syndrome |
| **Anti-HBc** | Hepatitis B core antibody |
| **Anti-HBs** | Hepatitis B surface antibody |
| **CDI** | *Clostridium difficile* infection |

| | |
|---|---|
| **EIA** | Enzyme immunoassay |
| **FDA** | Food and Drug Administration |
| **FMT** | Fecal microbiota transplantation |
| **FTA-ABS** | Fluorescent treponemal antibody-absorbed |
| **GI** | Gastrointestinal |
| **HAV** | Hepatitis A virus |
| **HBsAg** | Hepatitis B surface antigen |
| **HCT/Ps** | Human cells, tissues, and cellular tissue-based products |
| **HCV Ab** | Hepatitis C virus antibody |
| **HIV** | Human Immunodeficiency Virus |
| **IBS** | Irritable bowel syndrome |
| **IDSA** | Infectious Diseases Society of America |
| **IFA** | Immune Fluorescence Antibody |
| **IgG** | Immunoglobulin G |
| **IgM** | Immunoglobulin M |
| **IVIG** | intravenous immunoglobulin |
| **mTOR** | mammalian target of rapamycin |
| **NGT** | nasogastric tube |
| **PCR** | polymerase chain reaction |
| **PPI** | proton pump inhibitor |
| **RPR** | rapid plasma reagin |
| **SHEA** | Society for Healthcare Epidemiology |
| **TNF** | Tumor Necrosis Factor |

## Table 1
## 2011 Clinical Diagnostic Laboratory Fee Schedule

| HCPC | Modifier | National Limit | Mid Point | Short Description |
|---|---|---|---|---|
| 86592 | | $6.01 | $8.12 | Syphilis test, non-treponemal, qualitative |
| 86593 | | $6.19 | $8.37 | Syphilis test, non-treponemal, quantitative |
| 86703 | | $19.30 | $26.08 | HIV-1/HIV-2 single assay |
| 86703 | QW | $19.30 | $26.08 | HIV-1/HIV-2 single assay |
| 86704 | | $16.96 | $22.92 | Hepatitis B core antibody, total |
| 86706 | | $15.12 | $20.43 | Hepatitis B surface antibody |
| 86708 | | $17.43 | $23.56 | Hepatitis A antibody, total |
| 86709 | | $15.84 | $21.41 | Hepatitis A antibody, IgM |
| 86780 | | $18.63 | $25.18 | Treponema pallidum |
| 86803 | | $20.08 | $27.14 | HCV antibody |
| 87045 | | $13.28 | $17.94 | Feces culture bacteria |
| 87046 | | $13.28 | $17.94 | Stool culture bacteria each |
| 87177 | | $12.52 | $16.92 | Ova and parasites smears |
| 87207 | | $8.44 | $11.40 | Smear special stain |
| 87209 | | $25.29 | $34.18 | Smear complex stain |
| 87272 | | $16.88 | $22.81 | *Cryptosporidium* antigen IFA |
| 87324 | | $16.88 | $22.81 | *Clostridium* antigen EIA |
| 87328 | | $16.88 | $22.81 | *Cryptosporidium* antigen EIA |
| 87329 | | $16.88 | $22.81 | *Giardia* antigen EIA |
| 87338 | | $20.24 | $20.24 | *H. pylori* stool antigen EIA |
| 87340 | | $14.53 | $19.64 | Hepatitis B surface antigen EIA |
| 87341 | | $14.53 | $19.64 | Hepatitis B surface antigen EIA |
| 87493 | | $49.39 | $66.74 | *C. difficile* amplified probe |
| 87803 | | $16.88 | $22.81 | *Clostridium toxin* A w/optic |

HCPC = Healthcare Common Procedure Code