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# Same poop, different gut

For physicians and researchers alike, fecal transplants present an opportunity to gain insight into disease

Most people might find the idea of having another person's feces injected into their intestine hard to stomach, but for those with intractable gastrointestinal problems, another person's bodily waste is all that's standing between a lifetime of severe illness and a full recovery.

This therapy—known as fecal transplants, bacteriotherapy, or human probiotic infusions—has taken to the limelight in recent years, not only because its gross factor makes for great headlines, but in great part because of the growing epidemic of a particularly toxic strain of *Clostridium difficile* that has been plaguing hospitals across the U.S. for the past decade and affecting more than a quarter of a million Americans per year. By producing sturdy spores that can linger in the intestinal tract even after repeated antibiotic treatment, *C. difficile* can continually give rise to new toxin-producing colonies that wreak havoc on the colon.

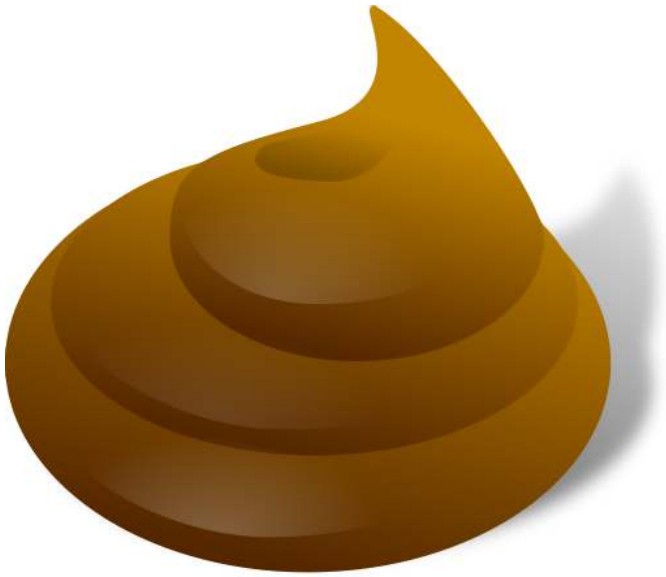

*Image: siteflight via stock.xchng*

But these colonies prove no match for fecal transplants, which boast a cure rate of up to 95 percent. At the heart of these transplants are the trillions of microbes that inhabit the gut and have a profound impact on the host's biology—for better or worse. As Australian gastroenterologist, Thomas Borody, jokingly puts it, "we are 10 percent human, 90 percent poo."

Borody did his first fecal transplant back in the mid 1980s, when he was confronted with one of the most difficult cases he had seen at the time: a woman who had vacationed at Fiji and had developed an incurable colitis through an unknown pathogen. While searching the literature for alternative treatments, he stumbled upon a paper published in 1958 in the journal *Surgery* that described four cases in which a similar condition was cured by infusing the inflamed guts of the patients with fecal samples from healthy donors. "So I looked at the method and I kind of made up the rest of it," Borody said.

He collected stool from the woman's brother, and after screening it for known pathogens, he stuck it in a blender, added some brine, and filtered it to get rid of any undigested material. The stool, now turned into slush, was administered to the patient—who had her gastrointestinal tract previously flushed—via two enemas over the course of two days. The results were nothing short of surprising, Borody said. Within days her colitis was gone, never to return.

The procedure, which has deep roots in veterinary science, has been tried and tested in animals for centuries. Farmers handling livestock have long realized, for example, that indigestion following a change in diet in grazing animals, such as cows, can be treated by feeding the sick cow rumen fluid that

has been sucked out of a healthy cow's stomach. Currently, while most fecal transplants in the U.S. are performed exclusively to treat *C. difficile*, a growing list of doctors, such as Lawrence Brandt, chief of Gastroenterology at Montefiore Medical Center in New York, are beginning to expand to other gut disorders such as inflammatory bowel diseases. Because stool is not yet a marketable biologic product, the procedure is not federally regulated. Brandt, and to his knowledge, most other gastroenterologists in the U.S., do not charge patients for the fecal transplants, but only for the single colonoscopic injection by which he administers the stool.

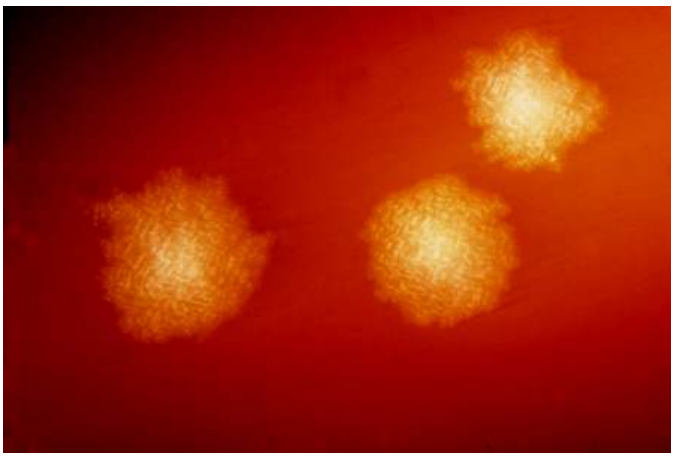

*Image: Wikimedia commons, Clostridium difficile colonies*

"It is currently considered a last resort," he said. But he hopes that will soon change. "It's relatively simple, relatively inexpensive, and it's very rapid in its actions." But there is still much to be learned about how these transplants actually work, stressed John Rawls, a microbiologist at the University of North Carolina. Rawls is one of a handful of researchers who performs gut microbiota transplants across species in order to understand in molecular detail how organisms shape the microbes in their guts and how gut microbes affect the physiology of their host.

In a study that made the cover of *Cell* in 2006, Rawls—under the tutelage of Jeffrey Gordon at Washington University in St. Louis—colonized the guts of mice that had been raised completely sterile, with the gut microbiotas of zebrafish (and vice versa) and found that the composition of the communities changed considerably when they changed homes.

Gordon has also developed a "humanized" mouse model by feeding germ-free mice human feces in order to probe the relationship between obesity, diet, and the gut microbiota. He's found, among other things, that germ-free mice gain more body fat when fed microbiota from obese mice than microbiota obtained from lean mice.

"It is tempting to think that if you wanted to treat human obesity, that you could do fecal transplants with the microbiota from lean individuals," Rawls said. But it may be somewhat premature to proceed, he cautioned—"if we don't understand the rules that govern the establishment and maintenance of those microbial communities in the gut, the effects of other people's transplants could potentially be short-lived or even deleterious."

At the European Association for the Study of Diabetes Meeting in Amsterdam last September, Dutch researchers presented the first controlled clinical trial that tested whether the treatment helps with metabolic syndrome, a catch-all disorder that has a high risk of developing into diabetes. They found that 18 obese patients with metabolic syndrome responded better to insulin and had lower triglycerides after they were infused with stool obtained from lean, healthy donors. The human subjects did not experience any change in weight, however, and the improvements in insulin and triglicerides eventually reverted.

As for Borody—who has himself performed over 1,500 human fecal transplants since the first colitis case—he believes the resurgence of interest presents a unique opportunity to gain further insight into the mechanisms of a bevy of diseases. As director of the Centre for Digestive Diseases in New South Wales, Borody oversees five to six fecal transplants a week, most of which are for patients with irritable bowel syndrome. But occasionally, he treats patients that, in addition to bowel complaints, also have seemingly non-gut related conditions such as chronic fatigue syndrome, acne, and multiple sclerosis. And he's getting some early evidence that, in some cases, the transplant can reverse the symptoms of those accompanying conditions as well.

He recently received funding to carry out a clinical trial using anti-*C. difficile* antibiotics to treat 18 cases of Parkinson's—an idea that occurred to him after observing that patients with chronic constipation and Parkinson's who received fecal transplants experienced a marked decrease in their neurological symptoms. Nonetheless, he remains cautious about overstating the procedure's power. If anything, "this method has opened the door to a better understanding of a multitude of diseases," Borody said.

**P.J. Turnbaugh, et al., "The effect of diet on the human gut microbiome: a metagenomic analysis in humanized gnotobiotic mice,"** ***Science Translational Medicine*****, 1(6):6ra14, 2009. T.J. Borody, et al., "Bacteriotherapy using fecal flora: toying with human motions,"** ***J Clin Gastroenterol*****, 38: 475-83, 2004.**