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A Revolting Remedy: A Word About C. diff and Experimental Treatments

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A Word About C. diff and Experimental Treatments

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Imagine yourself in a battle against a video game boss; when all strategies of attack fail, what do you do? Resort to desperate measures or use a new, unconventional plan? This is the situation I imagined as my class was presented a superbug boss: *Clostridium difficile* (*C. diff*). When this superbug resists all intensities of antibiotic treatments, there is only one other option to treat it, but it is unconventional and many find it disgusting: the Fecal Microbiota Transplant (FMT). Despite its squeamish name, this procedure can be an effective life-saver, and is classified as an "experimental" treatment, which is normally not covered by healthcare providers. The "experimental" classification, which lowers treatment numbers despite the transplant's effectiveness, raises questions as to why FMT is not prescribed as "standard" procedure. Because FMT has yet to achieve solid support in journals for its mechanisms and safety, it's defined as an experimental treatment; however, it should not be relegated to a last-resort treatment — access to FMT should be increased due to its efficacy, low cost relative to other therapies, and sound regulations.

C. diff is a species of spore-forming, gram-positive bacteria, and one of the most common healthcare-associated infections in the U.S. According to the Centers for Disease Control, in 2011, *C. diff* caused almost half a million infections across the U.S. About 29,000 of those infected died within 30 days of the initial diagnosis. The bacteria is commonplace in soil, feces, and can also live in animals. However, detection may be difficult in humans because the presence of *C. diff* is subdued by the overwhelming number of bacteria in the human microbiome.

The standard course of action for a bacterial infection is antibiotics, but *C. diff* has evolved a resistance to basic treatments. Symptoms of infection usually appear after taking antibiotics as a treatment for a separate condition. This is because antibiotics target bacterial components like cell walls, and can kill numerous other beneficial bacteria with similar cell wall characteristics, lowering the overall bacteria number in the microbiome. This allows *C. diff* to spread, infecting its target with symptoms of severe diarrhea, stomach pain, nausea, high fever, and blood or pus in stool.

This initial antibiotic procedure is usually followed up with a regimen of stronger antibiotics, such as vancomycin. However, these stronger antibiotics are generally not effective due to the evolved resistance to such treatments. *C. diff* also forms spores, which allow it to stay dormant for long periods and makes treatment more difficult. When all antibiotic treatments fail, more drastic measures are planned such as surgeries or last-resort measures such as FMT. The FMT process works by taking the stool of an uninfected subject, liquefying it with added saline, and inserting a feeding tube or enema into the patient to transplant the fecal bacteria. This treatment is incredibly effective with success rates reported around 90%. If the efficacy is so high, why is the procedure only used as a last resort? The answer is that there are many hurdles that need to be cleared before FMT becomes "standardized."

First, the procedure needs to be researched to understand its effects on the human body. FMT's effects on the microbiome are not fully understood due to a deficit of research on the topic. The literature only reports the positive impacts of FMT, which Dr. Andrew Webb of Fraser Health claims is not enough to support FMT as a rescue option. He adds, "There's a rather long list of nasty infections that can be transmitted from bodily fluids." The concern that FMT increases the risk of spreading other diseases is valid, which is why the procedure is now screened more regularly for diseases like HIV,

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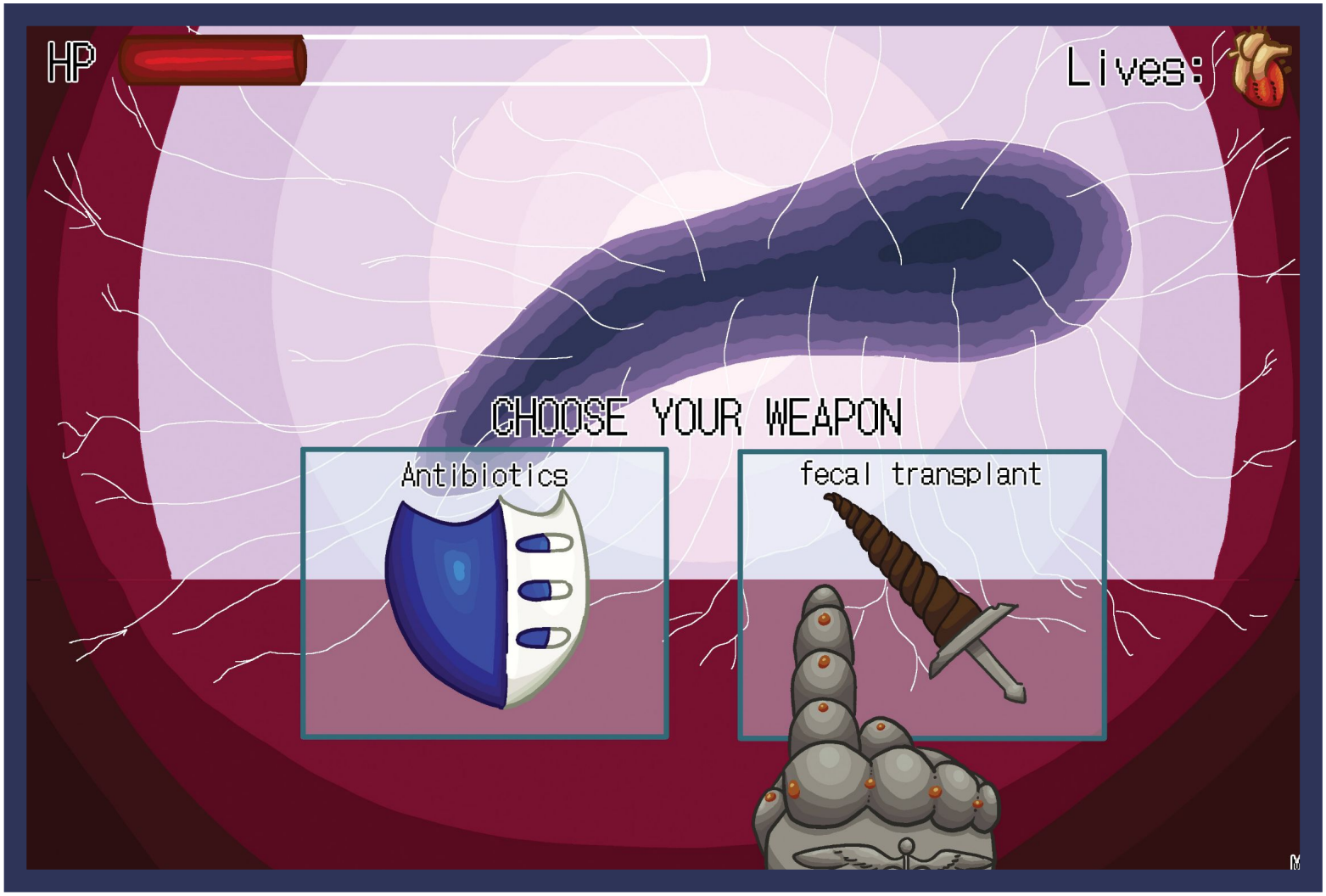
Giardia, and Hepatitis. Also, the cause of FMT's high efficacy is still unknown. A 2013 meta-analysis in the journal Nature demonstrates the potential for FMT as a treatment for C. diff but recognizes that more studies on its safety are needed. A 2016 meta-analysis in Alimentary Pharmacology and Therapeutics came to a similar conclusion but noted that further studies are needed to assess long-term side effects.

There's also the question of whether feces is a classified as a drug or tissue in the FMT procedure. The FDA defines a drug in many ways, one of which applies to FMT: "a substance intended for use as a component of a medicine but not a device or a component, part or accessory of a device." On the other hand, tissue products are defined as, "human cells or tissue intended for implantation, transplantation, infusion, or transfer into a human recipient is regulated as a human cell, tissue, and cellular and tissue-based product". Much of the research that supports manufacturing FMT as a pill suggests feces is a drug, and even the FDA states that FMT is a drug — a "live biotherapeutic product." Despite the FDA's definition, feces is treated more like tissue in stool banks, which have developed due to the rise in popularity of FMT as a treatment.

Stool banks function much like sperm (semen) banks, where individuals donate stool to be used for FMTs. In the FMT



procedure, feces should be regulated as tissue because it contains human microbiota that will be infused into an infected patient. Stool banks are important because accessibility to donated fecal matter is an issue to those infected with *C. diff*, and stool banks attempt to increase accessibility for patients by providing larger amounts of feces from donors. Critics to the rise of stool banks question how they will be regulated considering feces as a drug. However, given that feces bears more semblance to a tissue in FMT, it necessitates more screenings and regulations. Science News writer Bethany Brookshire, Ph.D. in physiology and pharmacology from Wake Forest University School of Medicine, states that FMT is cheaper than other contingency plans for infected patients, and accessibility is a problem due to the FDA's indecision on making FMT a tissue. She argues that a lack of regulation of stool banks will not help FMT in the long term if fecal matter operates like tissue but is not regulated as such. Since accessibility is also a concern, she believes that FMT's status as an investigational procedure limits its access to patients.

This affects the accessibility to those suffering with *C. diff* due to a lack of FDA oversight. Investigational treatments are, per the FDA, "a mechanism for providing eligible subjects with investigational drugs for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments." These treatments are usually expensive and directly charged by a pharmaceutical company because they are still under investigation. Though FMT is actually cheaper than other last-ditch measures to combat *C. diff.*, issues of cost are still prevalent but to a lesser extent than most other life-saving measures. This raises the question as to the pragmatism of spending money on antibiotics with increasing potency. This is because they are inconsistent in treatment, instead of attempting FMT sooner. The issues of FDA approval, regulation as a drug or tissue, and lack of research limit the treatment's reach to infectees. Despite this, it is possible to increase access to FMT through distinction in FMT treatments (such as a drug developed from feces to the traditional transplant via enema, where it operates like tissue).

FMT's status as an 'investigational treatment' limits its ability to aid those infected with *C. diff*. As this superbug is resistant to most antibiotics, FMT offers a potent albeit not widely-known treatment. While classifying it as 'investigational' is valid, it does not mean it should be treated as an exclusive last resort. FMT is a cheaper and more effective alternative to other contingency measures against *C. diff*. To increase access to FMT, the FDA needs to regulate FMT as a drug and as tissue if the source is from stool banks, but it also needs to regulate stool banks. As for research, it is unknown how FMT is effective, but meta-analyses conclude promisingly for the treatment. Further research is being done to develop the drug as a pill and to understand its effects. Time will tell if FMT is deemed "safe" by the FDA and researchers, but for now, FMT should be given increased access to patients with *C. diff* through stool banks or pills. • • •