



SciCafe: The Power of Poop — Video Transcript

ARI GRINSPAN (Gastroenterologist):

Happy New Year. Thank you to the wonderful folks here at the American Museum of Natural History to invite me to talk about my passion: shit. My mother's very proud.

These floating things that you're seeing here are bacteria. Bacteria have a really bad reputation. So a hundred years ago, if you lived anywhere in the world, you were going to die most likely by one of these bacteria: an infection. Whether it was pneumonia, whether it was the flu, whether it was tuberculosis or another infection of the gut, like some sort of dysentery, an infection was going to get you. Now, 2018, an infection is not even in the top 10 reasons why we die. Other things get us: cancers, heart disease, strokes. But the idea of a bacteria still sits inside of us as, ooh, we should kill that. We don't want that to be in our system. Take that antibiotic.

Well, turns out that's one of the worst things you can do for yourself, because these bacteria are vital for our health. We grew up with these bacteria. We evolved with these bacteria. They help us and we help them. It's a very symbiotic relationship. So my microbiome... And let me preface that. What is the microbiome? Microbiome is a complex connection, interaction, structure of these bacteria within a habitat. And I will be focusing on the gut microbiome; the collection of these bacteria; the proteins that they produce; the DNA that they have and how that interacts with us, and it is so incredibly important for our survival.

So my microbiome is very different than yours and different from the person next to you; different from a person in China or rural India or in Westchester. Our microbiome began at birth. So when you were in utero, there was no bacteria in you. The first contact you had with bacteria was with how were you delivered? Were you a C-section baby, or did you come down the birth canal? That will determine what the first bacteria you have, and there are very clear differences. You can tell, just in the microbiome, you can separate C-section babies from vaginal delivery babies, and that can last for a long period of time.

Up until the age of three, your microbiome can change depending on what you eat: were you breast-fed, were you a bottle baby, did you get an antibiotic for an ear infection? That will dramatically alter your microbiome. And then at the age of three, things sort of stabilize for a long, long period of time. Now, don't get me wrong. If you go to Mexico City, if you go to some place and you come back with a little Montezuma Revenge, your microbiome will be different for a period of time, but then it usually comes back to its homeostasis.

Because your bacteria are a community, and they like to support one another. They support you by helping you digest certain foods. They support you by telling you, ooh, there's a bad bug, here. This doesn't belong in our community, and you can prevent it from causing a problem. So they protect us, and we protect these bacteria. We feed them every day multiple times a day, and they love it. And we give them a habitat to live in that's protected from the bomb cyclone that's coming tomorrow.

I am—well, I think I am—an average human being. I have about a trillion cells, human cells that make up me. But in my gut, I have 10 trillion bacteria who are not all bad. So I am 10% human and 90% bacteria. It gets a little bit more complicated, because the blueprint of human life is DNA. So if you take the DNA that is within me and look at it, you'll find that 1% of the DNA in me is human, and 99% is bacteria. This relationship is incredibly important, and we're just beginning to investigate it. For a long period of time we ignored it, because we didn't really know that it even existed. Oh, but it exists, and it's incredibly, incredibly important. Because when things go awry in the microbiome, it can affect you and it can cause problems.

I'm going to talk about the posterchild for how to look at the microbiome. It's an infection called *C. diff* that Susan mentioned to you just a moment ago. It is a very bad bug. This is the human colon. This is, actually, this is a beautiful-looking human colon. I mean, I would eat off this colon. No, too much. Too much. This is a beautiful colon. It is healthy, it is vibrant, and there are trillions of bacteria that you cannot see floating around and [attached] sort of to the lining. *C. diff*, when it gets inside of the colon, causes that. Yeah. That is a sick colon. In fact, I don't even want to look at it. It's pretty gross.

So how does *C. diff* even get there? So you have 10 trillion bacteria, and the most important thing about this 10 trillion is that it's diverse. You've got bacteria coming from different species, different phylum, different everything, and they all come together as one unit, and that unit is there to protect you. The problem happens when you get an antibiotic to treat a pneumonia or a urinary tract infection, or maybe your doctor gave you a CPAP for that sniffle that you got.

Okay, if it's a pneumonia or if it's a urinary tract infection, that bacteria that's causing it is causing you harm, so the antibiotic is appropriate. Get rid of the infection, and you'll get better. But it doesn't just kill the bad bacteria. It kills a lot of the microbiome in your gut, and you get a contraction of this rich, diverse microbiome. You could lose the diversity. You lose the richness, and then you become susceptible to certain things. In this case, *C. diff*.

Now, the problem with *C. diff* is I can treat it with antibiotics, I can control it, but your microbiome is still so not where it should be. It's contracted. So if I get rid of the infection and your microbiome is still in this low state, the *C. diff* comes right back, and it comes back again and again and again, and it's a classic story. We call it recurrent *C. diff*. It causes 30,000 deaths per year just in this country. It costs \$4 billion in extra healthcare costs to take care of patients who have recurrent *C. diff*. It's a bad bug. It's an expensive bug.

So then there is something called... So if the antibiotics don't work, what can we do? Well that's where fecal transplant comes to be. Fecal transplant is the idea is, okay, I'm going to take somebody else's healthy microbiome, and I'm going to transfer it to the patient with the low microbiome—with the no diversity, the lack of richness—and I'm going to expand their microbiome. And hopefully that will cure the infection. It turns out it does it so remarkably well that it blows everybody's mind. Antibiotics work for this recurrent *C. diff* infection maybe 30 to 50 percent of the time. A fecal transplant cures it more than 90% of the time. We don't see these dramatic differences in modern medicine: 90-plus percent versus 30 to 50 percent for standard of care. This is dramatic. But it's a little icky.

So when I first starting doing this, five, six years ago and patients would come to my office for *C. diff* and I'd be like, "You need a fecal transplant," and they're like, "You want to do what? You're going to put what in my butt?" And I said, "No, no, no."

So I don't use shades of brown when I'm talking about this. I use shades of green. It's life. It's wonderful. Look at that lawn. You could eat off that lawn. Okay. Imagine that healthy lawn as your microbiome. Every blade of grass is a healthy microbe. It's beautiful. Well, something happened to you. You got an antibiotic. You had a contraction, a decrease in your microbiome; less diverse, less rich. Then you get these dandelions. You got *C. diff*. Now, I don't know how many of us actually have lawns, being in New York, but if you did have a lawn, you would try to kill that dandelion with weed killer. You spray the weed killer at it, but the dandelions keep coming back. You throw the antibiotics at the *C. diff*, but the *C. diff* keeps coming back. So the idea behind a fecal transplant is we need to re-sod your soil. We need to repopulate your gut. Re-poop-ulate your gut. I wish I coined that term. I didn't, dammit. Re-poop-ulate your gut to bring it back to health, and that's the idea behind a fecal transplant.

Now, there's nothing new here. Fecal transplant is an old therapy. It was first done in fourth-century China. The Chinese physicians would use a fecal slurry, give to patients to treat anything from diarrhea, constipation, abdominal pain, and my favorite, nausea and vomiting, and they actually had success.

Now, it lost favor for a long period of time, and then it showed up in the English literature in 1958, where a professor in Denver used it to treat patients who had this in their colon. Now, he didn't know it was *C. diff*. He just saw this, the patients weren't getting better with antibiotics, and so he looked in where most doctors look about how to treat things we don't know: in the veterinary literature. Nobody actually does that. But he did, and he found that horses who had dysentery and similar findings, if you feed them healthy horse manure, they get better. So he took the spouses of these patients, and he gave them fecal enemas from the spouse, and all four of those patients got better. It made a small splash in 1958 and then lost favor, because people were like, that's ridiculous.

And in the '80s and '90s and even the early 2000s, it remained on the fringes of medicine until the landmark paper in The New England Journal of Medicine showed that fecal transplant: 90% cure rate, and standard of care of antibiotics: 30% cure rate. Again, you don't see these kind of

things in modern medicine. And then all of the sudden like, whoa, whoa, whoa. Yeah, fecal transplant, of course. Of course. We've known it all along. Now, it took a long time for people to really get on board with this.

Now, is that what we're doing, here? So how does this whole process work? Is it just me re-poop-ulating the gut with healthy bacteria? So this is what our patient with *C. diff* looks like before their transplant. This is their bacteria. This is what we call microbiota disarray. And this is the donor. This healthy swab of orange is healthy bacteroides; these wonderful, healthy bacteria that we all consider to be a normal part of our gut. And so we give this to the patient, and this is what the patient looks like two weeks later: remarkably similar to the donor. If you look at that patient a month after their transplant, they look like this. So not like the donor, they share some similarities, but the patient is healthy. No *C. diff*. Feeling great. Playing tennis.

What we don't know is, is this what the patient looked like before *C. diff*, or is this their new normal? We don't have that information. How much of this donor stool, these donor microbes, how many of them stayed in the patient? We don't have that information. And then it begs the question, well, who's going to be your donor? So I get that question all the time. Okay, I want to do a fecal transplant, they sign up, okay, okay, great. Wait, whose shit are you going to use? And then I say, well, whose shit do you trust?

So we used to ask the patients, all right, do you got a brother or sister or mother, a spouse, family friend, the guy at your office who goes to the bathroom like clockwork every day? Like who do you want to use? So they'd have to give me a donor, I'd have to screen them, make sure that they were safe, so similar to as if you were going to be a blood donor, and then some. I had to make sure that they are healthy, they don't have diabetes. They can't be too big, they can't be too small. It's gotta be Goldilocks poop, or something like that.

They'd come, they'd have to produce the sample—the drug—on the day of the procedure. Now, you've heard of stage fright. Imagine me [unintelligible] like, hey, I got things to do, man. You gotta... That gets a little problematic. Well then they'd have to produce it, I then take it across the street, and make what we call the dirtiest martini. And then I bring it back, I do a colonoscopy to administer the drug; the fecal slurry. Because the problem is in the colon, I want to deliver it exactly there.

Would you like to see it? [Guard] your loins. Again, sick *C. diff* colon. What you're going to see is a fecal transplant in action. So it's moving because the patient is breathing—that's good—and here it is. Boom. That's the money shot. Too much? Too much. So this is wonderful. This is happy. This patient was in the hospital three times over six months with *C. diff*. Went to hospital to hospital, got multiple courses of antibiotics before coming to Mount Sinai. A young woman with ovarian cancer, she couldn't function for the past six months prior to this. And this is what she looked like a month later. She walked out of the hospital. She was an avid tennis player, she was able to play tennis, and she is picture perfect health. Pretty remarkable.

But the whole process is pretty cumbersome. We don't like to screen donors over and over again, so we don't do that anymore. I import my poop. You've heard of blood banks, you've heard of sperm banks, but have you heard of stool banks? They exist, and they do all the things for me. They screen the donors, they make sure that they're healthy, they make sure that there's no diseases, they process the stool, they put it into a nice little canister, they freeze it for me—I don't know if you know this, but fresh poop is just as good as frozen poop—they ship it to me via UPS. What can brown do for you? And I have a treasure trove in a freezer in my unit that I can use when it is required. So they always ask me, "So, wait, wait, wait. Where is this bank?" And I tell them, "It's in Boston, and they usually screen Harvard and MIT students, so it's smart shit. You're welcome."

But again, this whole thing is cumbersome. I still have to do a colonoscopy, it's invasive, there's anesthesia, you have to take a bowel prep, and people with *C. diff*, they don't want to take anything that's going to give them more issues.

So the future of this is the crap-sule. It shouldn't be brown. We should probably fix that. But this is developed. We have this. It's not quite ready for primetime, because there's a lot of technology that goes into delivering this product. First of all, you don't want it to release too soon. That would be a bad burp, oof. Again, I crossed a line. Too much, okay. But I don't know what I'm supposed to put in it. Do I put the entire microbiome like I do via colonoscopy, or do I just take sections of the microbiome; some of the species; some of the bacteria? And that's what we're trying to figure out.

For *C. diff*, this bad infection, fecal transplant is a homerun. It's rare in medicine that you find something for such a bad disease that just knocks it out of the park, and fecal transplant does that. And so if fecal transplant can be so remarkably effective for *C. diff*, where we think that the issue is with the microbiome being... we just need to restore the microbiome, can we take that to other disease processes?

Now, there have been a number of diseases that have been associated with changes in the microbiome. But association does not mean causation. And I don't know if that change in the microbiome may have led to the disease state or if the disease state led to the changes in the microbiome. You name a disease, and there's somebody who can show that there's changes in the microbiome. Notably autism, multiple sclerosis, heart disease, diabetes, obesity, liver disease, inflammatory bowel disease—which is what I focus on—including Crohn's disease, ulcerative colitis, and a number of other conditions.

But again, I don't know—and nobody knows—is if the microbiome led to that problem. *C. diff* is easy. It's a bug. The infection. Get rid of the bug, you've cured the disease. But all the things I just mentioned to you, there's no single infection, single bug that causes these diseases. It's multifactorial. Maybe the microbiome has a role. Maybe. But there's genetics, there's the environment, there's your immune system—whether it's overactive or underactive—among other things. So it gets all very complicated. So while the association may be there, I don't know

if we can be—and I doubt—that we're going to have a homerun by changing the microbiome to affect the other disease process that I just mentioned.

But with the research by investigating the microbiome, and we're at this explosion of research that's going on, maybe we won't find a new therapy for some of these conditions, but maybe we can prognosticate. Maybe we can identify people who are going to be susceptible to certain diseases later in life and potentially enact prevention strategies to prevent that disease from coming on later. That would be a wonderful outcome from all of this.

The microbiome is incredible, and there are so many secrets that we have yet to uncover. There's all this crosstalk between the bacteria that are floating in our gut and in lining of the intestine. Now, we don't have Rosetta Stone yet. I don't know what they're talking about. We're trying to figure that out. And maybe what we can do is, once we figure out the conversation, maybe there will be ways that we can manipulate the microbiome to change the conversation; to change maybe some of the outcomes of certain diseases. That would be another wonderful outcome.

I'm going to leave you with three things before I stop the talk. Number one, don't do this at home, okay? Don't treat your headache, don't treat your hangnail, don't treat your abdominal discomfort with a fecal transplant. Leave that to the professionals. I need the business. I'm kidding.

Fiber. Fiber is your friend. If you want to promote a healthy microbiome, if you want to augment your microbiome for a health purpose, fiber is your friend. Don't go to the local drugstore and buy all of the probiotics off the shelf, okay? That's not going to do it. Fiber is your friend.

And number three, as my father always says, wear your seatbelt. Thank you very much.