



Transcript of “Les Dethlefsen: Fecal Transplant, Hacking the Microbiota & How to Recover Gut Health - #240”

Bulletproof Radio podcast #240

Warning and Disclaimer

© The Bulletproof Executive 2013



The statements in this report have not been evaluated by the FDA (U.S. Food & Drug Administration).

Information provided here and products sold on bulletproofexec.com and/or upgradedself.com and/or betterbabybook.com are not intended to diagnose, treat, cure, or prevent any disease.

The information provided by these sites and/or by this report is not a substitute for a face-to-face consultation with your physician, and should not be construed as medical advice of any sort. It is a list of resources for further self-research and work with your physician.

We certify that at least one statement on the above-mentioned web sites and/or in this report is wrong. By using any of this information, or reading it, you are accepting responsibility for your own health and health decisions and expressly release The Bulletproof Executive and its employees, partners, and vendors from from any and all liability whatsoever, including that arising from negligence.

Do not run with scissors. Hot drinks may be hot and burn you.

If you do not agree to the above conditions, please do not read further and delete this document.

Dave: Hey, everybody. It's Dave Asprey with Bulletproof Radio. Today's cool fact of the day is that scientists just found a bacteria that's the first ever that can infect an organization just by touching it rather than by basically reacting to the organism's chemical signals which is what most bacteria do.

Because this bacteria has the ability to infect only through contact, the *Pseudomonas aeruginosa* and this is a word I have not yet learned how to speak, *aeruginosa*. I could tell that today's guest is going to fix that for me. I can infect humans, plants and animals and surfaces, making them way more diverse than normal other bacteria. Since they don't respond well to antibiotics, it's a little more dangerous as well.

Seems like every time we look at bacteria, we're finding something new and interesting, which is why today's guests Les Dethlefsen is on the show because he's a staff scientist at the Relman Lab at Stanford University and has been for more than a decade with a PhD in microbiology and ecology and evolutionary biology which is kind of cool. You've heard from people like Emily Deans who are evolutionary biologists but tying this back into microbiology as well. Way cool because this is the stuff you don't see easily but evolution happens a lot faster with these little bugs in your gut. That's why Les is on the show. Les, welcome to the show.

Les: Thanks, Dave. I'm glad to be here.

Dave: Tell me how to say *Pseudomonas aeruginosa*.

Les: *Aeruginosa*.

Dave: See? I knew I said it wrong.

Les: Yeah, which is a well-known bug but I wasn't familiar with whatever research you've just mentioned from the contact inhibition. It's an interesting bug in that it's evolved to live both in the environment and it causes infections. It can infect plants or mammals. Not that many bugs are that versatile so scientists are interested in studying it, find out how it pulls off so many different evolutionary roles.

Dave: I certainly don't want it to infect me unless maybe if it's in my gut. Who knows?

You're doing some stuff that got my attention because you're doing a study or you're looking at 100 people looking at sampling them every weekly or daily to know what happens when they change their food or when they eat antibiotics and things like that. That's fascinating work. As far as I know, that's never been done before, has it?

Les: Thanks. I certainly think it's fascinating, too. It's related to work that's been done before but I think we're blazing new territory in terms of the scale at which we're working because you know, there's been huge explosion of interest in the last 5 years let's say about the microbes, mostly bacteria but other microbes also that live in us and on us and contribute to our health.

The very first studies, just like the first explorers to go to a new continent, they lay out the landmarks. "Okay. Where is the coastline? Where are the big mountains? Where do the rivers go?" The first attempt is a survey. We've got a lot of that done. Certainly for people who live in the developed world with their scientists, we've got a good sense of what bacteria, what microbes live where hidden on their bodies. We still don't know for people that live in other places, indigenous people around the world. They may have a lot more, different things going on than we know about but we're now moving on beyond the first exploration just to say, "Okay, what are the microbes there? What are the plants and animals in the new continent?"

Now, we're at the stage of saying, "Okay, how do they relate to each other? How do they change over time? How do they respond when the environment changes?" A storm comes through, which of the trees that tend to get uprooted or the ones that tend to persist? When there's been a landslide, which of the first things to come back? Those are the kind of questions we need to ask about our microbiota. What comes back quickly after a prodibation. What takes a long time? Which microbes sometimes will take advantage of an opportunity to get abundant when they aren't usually abundant and when they get abundant, they can cause problems. We need to understand the dynamics to really know the system.

Dave: How long have you been working in this field because it's a highly unusual field in that it's become popular for a little while but 10 years ago, not a lot of people were paying that much attention to what grows in the gut.

Les: Yeah. It's crazy. My own career is a little bit of a microcosm of how the whole field has gone. When I was getting my PhD, I thought I'd be studying, say, marine microbiology or somewhere I was going to look at the way microbes interact with each other out in the environment somewhere. I was aware that, gosh, the human body might be a really cool environment. It probably has a lot to do with our health and medical issues. I never thought I'd go in that direction myself but my fascination was really just how do microbes evolve which, like you said, they do very quickly to solve their current ecological problems, how do we interact with other living things, how do we get the resources we need? It's really a series of accidents, the direction I wanted to go fell through.

In short notice, I came to Relman Lab out after my PhD at Michigan State, knowing I was going to study the human microbiota which I found exciting but I knew very little really, ironically about the human body, human physiology. I'm not trained clinically. I'm not an MD. For me, the human body is an environment for the microbes. Of course, I've learned a lot more about human physiology and human health issues. From the

microbial perspective, they sometimes care about our health because if there's bugs that are living in us and we are their environment, just like we care about our planet Earth environment, they want to care about the health of their planet Les or planet Dave that they live on.

There's other times that the microbes may have an advantage to say, "You know, I don't care if I make Dave sick because I'm going to reproduce 1,000,000,000 times and going to go jump on the next guy." For me, I bring this ecological questions and evolutionary understanding to how the microbes interact with us but it is directly related to are they keeping us healthy or did they have an advantage in making us sick.

Dave: I've gotten to the point, having spent at least \$50,000 on probiotics. I've taken pig whipworm eggs to see if they would do anything. I don't trust those little bastards. They do not have my best interest at heart except to the extent they want to make sure that they have a walking support system but the things I want and the things they want often times don't have anything to do with each other. Am I a bit paranoid or what?

Les: You might be appropriately paranoid. It's certainly the case as in a lot of relationships. You can't just assume that the other person in the relationship, the other side of the relationship, they have your interests at heart. They have their own interests. That's just a fundamental realization. We have to get away from this mythical state that, "Oh, there was some point in the past, this Garden of Eden thing where everybody wanted everybody else to get along and if everybody worked together, all would be perfect." No.

There've been pathogens and disease for as long as there's been living things. There's been some critters try to eat other critters. If it's a big critter eating another critter, you say it's a predator but if it's a bunch of little critters eating you from the inside, we call it a pathogen. That's all natural but it doesn't mean that I want to have it happen to me.

The trick is, I think with a lot of relationships, there are times when you can set up a situation where your interests and the interests of these other living things actually coincide. It turns out that the evolution of multicellular creatures, plants and animals both but I'll talk mostly about animals. The evolution of animals with the associated microbiota actually is 1 of those cases where you can expect there to be a convergence of interest. The reason for that, this is directly tying into my ecological and evolutionary training and background, if the microbes are specialized to live on and in people, they want people to be a habitat, they could get to that habitat by spreading quickly between a bunch of people but for most of human evolutionary history, there weren't a lot of people living close by each other. It was a small tribal group, kin group, several dozen families, a 100 people, 1,000 people maybe that would interact over a year.

A pathogen that spread very easily would very quickly infect those 1,000 people. If they all died, the pathogen would die. The pathogen would maybe benefit from turning down it's virulence so it didn't kill people so quickly but even then, it spreads to all 1,000 people. What does it do next? Its best strategy is to make sure that 1,000 group tribe not only continues to survive but has lots of offspring, has lots of healthy kids. If the evolutionary fate of us and our microbes are closely intertwined, we want to keep them going because they help us with nutrition, with fighting off the pathogens we do encounter and the microbes that depend on us want to keep us healthy and fit.

One of the keys here is that our offspring, the things that we want. We want to have a long, happy life, lots of kids that those have to be the habitat for the microbes that live in us. The microbes have to count on saying, "Well, if I keep my host healthy and fit, there'll be offspring for me to get passed to." It's that transmission across generations that will give the microbes an incentive to say, "We want to keep people healthy and strong." It's the transmission horizontally from person to the next person to the next person that lets a microbes say, "I don't care how healthy my host is because I'm just going to jump ship to somebody else."

That's where it's appropriate to be skeptical. If you get a bug that isn't committed to your evolutionary future, it's going to be happy to make your life miserable if it gets an advantage that way. You want to be living with bugs that are committed to you so you can commit to them, say, "All right. I'm going to keep you healthy. I'm going to eat things that are going to keep those gut microbes there." It's going to provide the signaling, the immune regulation, all the other things in exchange for having the chance to spread through your family and your kin.

Dave: That sounds like a little wedding ring would be in order.

Les: Yeah. It'd be hard to make as many of them as you might need. There's more microbial cells in your gut than there are stars in the galaxy.

Dave: Bacteria fingers are in short supply anyway so,

Les: Yeah.

Dave: ... it's the wrong form factor.

I read about something in the Bulletproof Diet. I had a weird experience. I was looking at what happens when you try to gain weight on a high fat, low carb diet. I'm in ketosis so I ate stupid amounts of calories, up to 4,500 calories a day. I quit exercising. I slept 5 hours or less a night. I ate lots and lots of coffee with butter and this Brain Octane Oil which is caprylic acid which is essentially an antimicrobial. I did this and I lost weight over the course of almost 2 years. I actually grew a 6 pack which violates all the laws of thermodynamics, which actually not thermodynamic systems, oops.

Anyhow, all this happened. When I searched for reasons that this may have happened, there's 6 or 8 of them I read about in the book but the 1 that caught my interest the most was about the gut biome. I wanted to ask your opinion on this theory so that we can throw it out as a bad theory or we can maybe say that there's some merit to further research.

What I found was a mouse study that looked at the effect of coffee plus a high saturated fat diet. I had no idea some researchers in China basically did this. What they were testing was the suppressive effect of fat on bacteria. Fat kills bacteria. They don't like it. They don't feed off it very well, at least most of them don't. They're looking at the proliferative effect of polyphenols from coffee, that it feeds the Bacteroidetes family. The fat suppresses the Firmicutes family.

The theory that I brought forth in the book is that the Firmicutes family which includes Lactobacillus and things like that. That's for people listening. I'm guessing you know these families way better than I do. This family makes something called fasting-induced adipose factor which means that when they're getting extra sugar, they send a signal to the body that's normally done by the liver. They copy the liver signal and say, "Store extra fat," because I want to make sure that my host doesn't starve to death. I'll make him extra obese just in case I need it.

Then, if the bacteria has no fuel, it uses the same hormone and says, "All right. Now, it's time to burn extra fat to make sure the host stays alive." They're amplifying my liver's ability to make my energy regulation work. By smacking all bacteria down with fat and then feeding the ones that don't have fasting-induced adipose factor, the ones associated with being lean instead of obese, that this could be 1 of the reasons that Bulletproof Coffee had this effect on me. Am I totally out in left field or is this a reasonable theory? I'm really curious.

Les: I have to say, it's absolutely not the grounds. That cited evens doesn't exist to say, "Yes, this is what's happening," but it's not crazy either. It's not impossible this is happening. There are some pieces of this that actually are known to happen. We know that the microbes in our gut influence our hormonal regulation. I could be wrong but I don't think the microbes are actually making the FIAF hormone. I think they influence the amount of that hormone that's made by our own body. I could be wrong.

Dave: Yeah. I'll check that 1 out. I could be wrong, too.

Les: It is the case. The reason I'm saying that I don't think the bacteria are making it is not because bacteria can't make things like that. There are plenty of chemical compounds that if our bodies made them, the human physiology would say, "Oh, that's a hormone. Look at how it signals. Look at how it has dedicated receptors to make it." The only reason that it's not called a hormone is it's made by a bacterium instead of a mammalian cell. It's not like there's anything that's too chemically complex or anything like that. The bacteria can make whatever they want. I'm not aware specifically that the FIAF hormone has been shown to be made by bacteria but it is absolutely clear that bacteria in our gut can send signals to our cells that make our cells produce either more or less FIAF in different circumstances.

Are there gut microbes that are able to influence our hormone that specifically influence our metabolism, the degree to which we pack the calories into stored fat or burn the calories to have a higher body temperature and higher resting metabolism rate and more ability to exercise. Yes, there are absolutely gut microbes that influence that process.

Are there things we can do in our diet that change the proportion of gut microbes? Yes. We know that for a fact. Is it possible that changing our diet will influence our metabolism in addition to any direct effects because of the indirect effects, the diet changes the microbes, the microbes change our hormonal regulation, yes. Not only is that possible, we know it happens but we don't have all the details worked out to say, "Here's the roles that these bacteria play. Here's the role that those bacteria play. Here's the specific diet that has this effect or that effect." We don't have those mechanisms at all worked out. It's going to be a very complicated story to tell that may well be different for you and for me and quite possibly for somebody who grew up in a different part of the world and has a very different composition of the microbiota but there is absolutely a story to be told here but it's not credibly going to be as simple as what you've laid out. I know you didn't think that was really truly the only story to be told there, either.

- Dave: It was 1 of 8 hypotheses. I just looked in my Mendeley because I do research and stuff reasonably well. You're correct. It is a suppressive effect on FIAF. It's not that they make it. Thanks for having your science down. If we understand, this is a really complex system. That's inconvenient because we'd like to be able to basically say that we're all robots. If you just change the battery, everything happens. That just simply is a bad model.
- Les: We know that because we all go to the doctor. A hundred people with the same condition or apparently the same condition go to the doctor. They all get the same prescription. It works for some of them. It doesn't work for some of them. It works for some of them but has bad side effects. Some of them ... We know that people are different, our physiology is different. The same treatment doesn't always do the same thing.
- Dave: I'm 1 of those challenging cases where I've always gone in with ... "Oh, I have a dozen symptoms and there's weird stuff going on." I've actually did a documentary about the root cause of that which was not bacteria, it was fungal for me. One of the effects of that fungal mycotoxin including antibiotics have on bacteria is they radically change what the bacteria do, even the shape and form of bacteria. What happens when someone takes antibiotics? What's the reaction in the gut microbiology, knowing that different antibiotics do different things but walk people listening through what happens then.
- Les: Let me be right out there saying the shortest honest answer to that question is we don't know. We do know some things but we have to acknowledge we really don't understand in detail all the effects. That's part of why we're doing exactly the study we're doing is that we'd like to not just do what the scientists were doing decades ago when they were focused on, "Hey, somebody's got an infection. Here's a compound that looks like it kills that bacterium in a Petri dish. Let's make him swallow it, see what happens." The infectious disease doctors looked at what they cared about which is the patient health and the progress of the infection.

We have some sense. It's not my area of expertise. We have some sense of what the antibiotics do to the microbes that were trying to control or eliminate and how they work, at what concentration they work, how resistance develops. That area is somewhat well understood but what has not been studied nearly as much is this topics that's been important only in the last few years of saying, "Wow, there's a bunch of microbes we depend on for health. How are they affected by antibiotics?"

The things we do know: Pretty much any bacteria or any antibiotics you care to name, it will effect some bacteria in our gut or any complex community. It will leave other bacteria relatively untouched. Some antibiotics will take out a lot of microbes and leave only a few untouched. Others will have the opposite effect. They'll be more narrow spectrum. This is even before we develop this so-called acquired antibiotics resistance. Just intrinsically, some microbes are just by the way they make a living, they aren't affected by certain antibiotics.

Beyond that initial, either bugs are susceptible or not, even the microbes that get damaged or killed by antibiotics initially can acquire, they can evolve the resistance. Which microbes are effective or not are a moving target.

Picture you've got a very complicated ecosystem with a lot of interacting organisms, the Amazon rainforest example. You went in and just took 20% of all the species present, some plant, some animals, some fungi. Just different sorts of critters and just dramatically changed them, made some of the extinct, made some of them half as abundant as they used to be. It's going to have ripple effects through all the other microbes, even these other living creatures that weren't affected like the example of a tree in the rain forest that you didn't effect in this experiment but it's pollinated by a organism that is affected. That organism that seems to be resistant to the antibiotic still may get damaged because it relies on an organism that was damaged by the antibiotic.

Once you have changes in the community, some of them are direct changes because certain microbes get wiped out. Others are indirect changes, it now changes the chemical environment of the gut. That causes further changes. You know what's most remarkable to me after looking at the antibiotics effects for a while, it's not what a dramatic effect the antibiotics have. It's how resilient our communities are. It's astounding that we can swallow these drugs and mostly, bounce back with no side effects. There are definitely some cases where there are side effects, sometimes some serious ones. Some of them are directly from the antibiotics. Some of them are due to the change in composition but most of the time for most people, we can take antibiotics and our microbial communities are resilient, they come back to mostly where they were before. We go on more or less in a healthy state.

It's a shame that that happens because what it means is we've gotten way too used to prescribing antibiotics unnecessarily. The more subtle damage that occurs is not something we're picking up on. Now, we're realizing, "Okay, it did seem like things mostly bounce back." You ask someone, "What's your health today? You had to take antibiotics 2 months ago. How you feeling today?" "Great." The antibiotics didn't have that effect but maybe 10 years from now, you're 5 or 10 pounds heavier than you would have been otherwise. You'll never know it was because of the antibiotics but it turns out, it did have an effect on your health that was more subtle, more long term. If the antibiotics were so poisonous so quickly, we'd never use them, then we'd never be facing the more long term problems that I think we are facing.

Dave: It's also true that a lot of people don't really have a good radar. How am I feeling today versus 2 days ago? Our memory of how we're feeling is not quantitative unless you sit down and you say, "On a scale of 1 to 10, I'm feeling like 9 today," then you can see patterns. "Oh, wow, maybe I did not have ... My sleep was down for the month after I took my antibiotics but it's just not visible to normal people who aren't doing quantified self kind of stuff.

I also believe like you that this is a major problem. I'm interested because I took the antibiotics for 15 years, just about every month because I had chronic sinus infections and strep throat that wouldn't just go away. I'd take it, it would die down. It would come again and again and again. I think I've done a pretty good job of rebuilding my gut biome as far as things go, like I have a better functioning gut now than I have throughout my life. I still have a few food allergies left over but how do you go about rebuilding this? Okay, now you've taken out this 20% of the species in the Amazon. Now, you want to fix it. What do you do?

Les: Yeah. That's a very important question as you know. I'm sure all of your listeners realize, too, because most of us don't have the luxury of saying, "Wow! I'm lucky, I never had any of that happen to me. I'm lucky I've always had a healthy diet and I've never had antibiotics." We aren't that lucky so what are actions we can take now that will give our microbes the best shot at being their best community to help us be healthy? I'll be surprised if in a couple of decades, we aren't the state of saying, "Oh, here's a list of microbes or more importantly microbial functions that everybody needs. Let's see what you got. Here are specifically what we would need to add to bring you back into balance." We don't have the knowledge today to do that.

Many of us in the field think we're going in the right direction. We're going to get there but for now, we can't offer a prescription. I'm sure some of the probiotics that are out there, they have demonstrated beneficial effects in some context. It doesn't mean that those are the only good bugs or that you need always those bugs. It doesn't mean that if you have those good bugs there aren't other good bugs that you can't buy that you also need.

For me, the probiotic approach is not the first thing I think of. I think of providing the environment that the bugs need. Think of it like the garden. If I've got the best seeds in the world that I don't have well-prepared soil, I don't provide the sunlight, the water, the conditions that are going to let those seeds grow, it doesn't matter how much money I

spend on seeds or how many seeds I put there but if I really pay attention to what the environment is that these living things need, I'm able to get some probably good results without even all that much invested in seeds themselves because the plants can grow from a few seeds and provide a flourishing community.

I focus on what food am I feeding to the gut microbes and the probiotics, that'd be a fine thing. Some probiotic supplements I'm sure are helpful. I prefer to get my bacteria food just from eating a diverse diet myself. All the probiotics we can get pretty much are plant-derived complex polysaccharides. I'm just going to eat a wide diversity of plants, some fresh, some in raw, some cooked because different compounds are either damaged or brought out by the cooking process. Just a wide diversity of different stuff because most of those microbes that have evolved with us for countless generations would have evolved with us at a time when people were eating a diverse plant-based diet. I'm not saying that meat is necessarily bad. I think a meat only diet or very high meat diet probably isn't the way to go.

Dave: Yup. Agree.

Les: I do think that the absence of diversity in our diet is probably a bigger problem than the presence of any 1 single component. I tend not to be fanatic about, "Oh, my god. That's toxic! You can't ever eat that because it'll kill you." It's more if you're focused too much on any 1 thing, if your diet is too much for too long just 1 subset, you may wind up with a lot of microbes that are part of a healthy community but usually aren't so dominant. In balance of what would otherwise be healthy microbes can also be a problem.

A diverse range in diet that supports a diverse community of microbes, that's what I can control. I can't control necessarily because I can't buy in a probiotics supplement, I can't control the 1,000 different species of microbes that are in there. I have to hope that they've either persisted, even just a few of them survived and they'll come back when I provide the right diet or there'll be these chance, rare events where I'll pick up something, horizontal transfer of some microbial strain that I need but I

don't have right now because I either didn't get it from my family or I got it wiped out from antibiotics but I happen to hang out with people who have a healthy lifestyle. I just so happen to pick it up from them somehow. If I've got the healthy environment for the microbes, they're going to probably find a way to get there. Then, they can flourish.

Dave: If you put on your evolutionary biologist hat and you go back to the idea of hunter gatherers. I've seen the advice. They eat a lot of varieties of food but I'm thinking back to our cavemen. There's meat and the fermentable collagen in meat which is a major source of food for bacteria. That's the meat fiber that bacteria can eat.

Then, there's also the vegetables in season but the variety of those isn't that big. It varies seasonally but what we're doing today is, "Oh, I had Thai and then I had Indian and then I had pizza and then I had ..." It seems like that is a wide variety of foods but the gut biome must be like bouncing all over the place because you know, I can't digest any of those well because it takes time for the microbiome to adjust to the types of food that are in the environment around us. At least that's my question. Doesn't it?

Les: It's a good question. What's the diversity that matters to the gut microbes? You're absolutely right. We think about our hunter gatherer ancestors. We absolutely shouldn't think of what is the diet they had as if they ate the same thing every day. Absolutely their diet was highly variable. There were times when they were hungry for long stretches of time and they were going to be eating anything they could find. They're breaking the new buds off of the end of twigs and chewing on them. Very low quality food, like pandas that have to eat pounds and pounds and pounds of bamboo because it's digesting so poorly.

We pretty much know that current hunter gatherer societies of which there is very, very few but our ancestors, they would have periods of time when they'd be eating that low quality food. They'd have a kill and they'd be gorging on meat for some period of time. The Hadza in Tanzania that have been studied a lot recently. When they can find honey, they wind up being most of their calories for some stretch of

time. Then, at other periods of the year, during the dry season, there's lots of animals gathering around watering holes. They've gotten more meat. During the wet season, the animals are dispersed. When they can't do anything better, they can always dig up tubers but that's the lowest priority food for them is this hard starchy woody things they can chew on and get some benefit from.

Over the course of a year or several years perhaps, they've got a wide variety of stuff but on a day-to-day basis, they may be gorging on their favorite food when it's available and being forced to eat a lot of some boring, monotonous, not very appealing food when nothing else is available. What do we see? Like you said, I can go out and go Thai, go Mexican. Do a home-cooked meal, all within the same week but if the ingredients are similar. It's broccoli and the Thai food. When I make pizza at home, I put broccoli on that. It might be the same relatively limited set of ingredients that are used to prepare what looks like, in a culinary sense, the spices and the way things are prepared, really looks like and tastes like different cuisines but the chemical composition of that food to our microbes may not look that diverse at all.

It is the case that all the different meat sources we get, the chemical difference between, say, beef versus pork isn't that big. By the time you get fish and chicken, you're getting a bit bigger diversity but the diversity that's found in the chemical composition of the plants we eat is just simply greater than the chemical diversity of the meats we eat. To get a diverse range of things in our diet, it's a better, truer and easier advice to follow to say, "You can get that diversity by eating a lot of different types of plants and nuts and whatnot rather than thinking I can really try to get all these exotic meats and rattlesnake and buffalo and whatnot.

Dave: Yeah. Doesn't work very well.

Les: It's not going to be that different anyway but I'm not saying that it's not worthwhile to have different sources of animal protein as well, dairy and eggs and different types of meat but the things that most of our gut

microbes are most are going to have evolved to be using for their food sources either complex polysaccharides and plants that our bodies don't digest and so they make it through the stomach and small intestine, get to the large intestine where the microbes get to ferment them.

Dave: That, I would say, extremely well documented, like we were meant to grind up plants in our gut. Then, my nutritional recommendations are eat a plate full of vegetables, moderate amount of very high-quality antibiotics free grass fed animal protein and put lots of fat on there. The fat may be bad for the gut biome depending on what you're trying to do with it but it sure does make it's brain work better. There's certainly debate about that.

Les: I actually wanted to jump back in there. You mentioned at the beginning how fat having this antimicrobial effect. It's not that simple. There are definitely some microbes that get knocked down when people are eating a high fat diet. There's other microbes that thrive on that. I don't think it's accurate to have a blanket statement about antimicrobial effects on ...

Dave: I was talking specifically about caprylic acid as more of broad spectrum just the C8 MCT. Correct me if that's wrong too.

Les: I don't know. I'm not familiar about the MCT story in terms of how it will act on microbes. I would almost bet, though, if people have looked and said, "It has antimicrobial effects in a broad way," that was probably work that was done in pure cultures in the lab,

Dave: Probably.

Les: ... and does not imply that that same phenomena might be but it's not a guarantee that the same thing is going to happen in the gut. As I understand it, a lot of those triglycerides, especially the medium chain ones are going to be absorbed mostly higher up in the GI tract. There might be a whole lot of them that wind up making, even If we're eating a lot of them, we may not get to the large intestine where most of the

microbial fermentation is happening. Those bugs down there may not care much 1 way or the other if you're eating a lot of it.

If it's good for your brain, don't avoid it just because it's going to hurt your gut microbes. They'll probably be just fine.

Dave: That's a really interesting perspective. I haven't thought of it. Now, let's switch gears to talking about fat a little bit, not just eating it but obesity. Let's talk about gut bacteria and obesity. What do they have to do with the calories you eat, like just give me your understanding of this from your interesting perspective.

Les: As you well know, the sort of thing we were taught growing up is that, okay, this is really just an arithmetic problem. This is the number of calories you burn based on your activity. This is some number for the calories you eat that we can measure by burning food in a sensitive way to measure how much heat it gives off. It's just an arithmetic problem. If the calories that you eat subtracted by the calories you burn off by exercise is a positive number, you're going to gain weight. Over a lifetime, you get fat.

That's not wrong. It just doesn't provide nearly the level of detail that we need because it turns out that the amount of calories actually extracted from the food isn't just the same number for you and for me. You can eat the same diet I do but the calories on the plus side that you extract may be very different than the calories I extract. A big part of that difference, not all of it probably but a big part of it is what are the gut microbes we have. Some of us will have gut microbes that are really, really good at getting more energy out of food or we may have, this is not very well documented but I think many of the researchers in the field, including myself, think it's likely that different people may have gut microbes that are more specialized.

I may have a gut microbe biome that's really good at the kind of degrading the plant polysaccharides from the brassica family because I eat a lot of them in the Allium, the onions and stuff. That's a big part of

my diet. Somebody who's eating different stuff, if we did eat the same meal that's rich in broccolis and cabbages and onions, maybe my microbes do a great job of extracting those calories and the other people does a poor job but we switched to eating a meal that is more like the other person's typical diet, their microbes do a good job of getting their calories out and mine done.

We can't just say blanket, Person A always gets more calories from their diet than person B. It may well be dependent on who is eating what diet, how many calories we get. We know for sure the number of calories we get from food varies from person to person, even if the food is the constant.

Then, the other piece of it is our body's tendency to take calories and either burn them by having a high metabolic, a resting metabolic rate, even independent of how we chose to exercise, just our body temperature, our base limit metabolic rate is influenced by hormonal system, our hormonal system is influenced by our gut microbes. That's another way that our gut microbes change not the plus side of how many calories we extract but the negative side, how many calories we burn or conversely, store as fat cells.

It's still an arithmetic problem, if the calories we're gaining are greater than the calories we're burning, we are going to ... That energy has to go somewhere but how much we do each of those 2 things is dependent on a lot of aspects. What exactly we're eating, how do our gut microbes interact with that, how our human physiology may be different and interact with that.

Dave: It's safe to assume that I have the bacon digesting biome and we're good to go.

Les: You probably have a gut microbe that's really good at tolerating the bacon, whether there's much bacon left by the time they see it. Maybe it's all taken care of and absorbed into your body by the time it gets to the end of the small intestine.

- Dave: I've been tested for having high levels of bacon receptor hormones so perfect, yeah.
Okay. That's a great overview of bacteria and how they effect that equation because there's so many variables for calories in, calories up that I, as a former 300 pound guy, I could have rolled my eyes when people say, "Oh, it's simple. Eat less." I started becoming a biohacker when I noticed that I ate less than all of my thin friends and that I worked out more than all of them. I was still fat and I was doing it consistently and I just realized, "Wait. There must be other variables." I didn't at the time think about gut bacteria but obviously now, knowing what you just talked about, I would have been ...
- Les: Let me add 1 other thing. I didn't bring this up here but this is maybe 1 of the keys, maybe the most important key underlying a lot of these phenomenon. When our bodies are feeling under attack, it changes our physiology. Think of it, the simplest thing you can imagine. If it's a life or death situation, you're there, the hunter gatherer tribe and it's like, "I'm going to get either fight off the Saber-tooth or I'm it's meal." Your body's priorities is delivering energy for you to fight back, run away, do something. If your body's fighting against pathogens or an infection, it's a higher priority for your body to take care of that. Anything long term is less important because if you don't live long enough, long term doesn't matter.
- When our bodies have an inflammatory condition going on, somehow we're reaction as if there's some pathogen to fight off, something that we need to be doing. Our bodies devotion of resources to the regular ongoing maintenance function goes way down because the priority's okay, fight off the immediate threat. There are bacteria that can establish reasonably high populations in our gut that are really good at signaling our bodies to be inflamed. Chronic low-grade inflation can be exactly what happens from a certain composition of the gut microbes biota.

Now, your body's in the state of saying, "I don't really need to put much energy into maintaining a healthy state," because it's a priority to fight off the invaders. I may not be able to gather food for a while. I'm going to be sick. I'm going to be laid up here, said the priority here will be to conserve calories as much as possible so try to not burn things. If you've got a bit of excess, put it in the fat cells now.

It does turn out that a typical Western, developed-world diet tends to promote bacteria that promote low grade inflammation. The low grade inflammation may be a major source of the obesity as well as other chronic diseases, heart disease, cancer, autoimmune diseases may all be linked into this. I don't want to sound as if, "Oh, my god! It's the 1 thing that everybody knows is the true source of all of our problems." It's not going to be that simple but chronic low-grade inflammation is definitely not a good thing. It's far more abundant in the population of this country and the developed world than it should be. Our diet that influences our gut microbiota may be a big piece of that.

Dave: It's pretty safe to say that chronic, low grade inflammation from any source is a risk factor and you want to get rid of that. Of course, the bacterial source would be 1 but there's lifestyle and diet and so many things can drive it.

Les: Pollution.

Dave: Yeah, pollution, mercury. Anything that drives it up, we got to do something about it.

Now, here's a question related to that. We talked about eating but the Bulletproof diet, specifically for the gut biome as well as some ecological reasons, I recommend flat-out grass fed meat or no meat. Simply don't eat meat that's been fed grain because most of that stuff has been fed grain also has problems with the bacterial composition of its gut. It has inflammatory fatty acids in it but also, you don't want low-grade antibiotics messing with your gut. I really just don't eat industrial meat because I like what's going on in my gut right now and I don't want to

change it. How important is this mass use of antibiotics in our livestock to the work we're doing and just, are you worried about that.

Les: If I put on my strict scientist, evidence-based cap and say, "All right. You know, what's been clearly demonstrated to be the case," I have to say and it sounds like something that would come from the Department of Agriculture, the FDA and say, "Well, there's not documented proof that the exposure that humans have to low concentration of antibiotics due to industrial agriculture has any measurable health effect. It's not been documented." Okay. That's a true statement.

However, what do I suspect might be going on? Food producers for 50, 60 years have known, "Hey, when we give these low doses of antibiotics to our food animals, not stuff that's concentrated enough to treat an infection but just low grades, they put on weight faster. Gosh! As a farmer, I can make more money. I don't need to spend as much on buying food if I put low doses of antibiotics in the feed that I am providing and my animals put on weight faster. I can sell them for money, I can sell them faster."

If the animal producers have known for decades that regular exposure to low doses of antibiotics promotes weight gain, it seems like the likeliest hypothesis, animals are all really pretty closely related, especially mammalian physiology doesn't vary all that much across all different types of animals there are. It may not be proven but the best guess would be people aren't going to be any different, that exposure to low doses of antibiotics over an extended period of time may very well promote weight gain.

If you didn't know the answer, if you didn't have proof, that would be the way to bet. That's what I think. Yet, for reasons that I probably don't need to go into here, our government regulatory scheme does not chose to take that approach to say, "All right, the sensible bet would be that these things are contributing to obesity." I'm sure you're well aware of what the reasons our government doesn't quickly take steps like that.

Dave: Okay, because we don't pay them enough taxes, obviously.

Les: Yeah. There are some people paying money in the system here in places but we don't need to go into that.

Dave: Exactly. There's another thing that I haven't heard addressed. It's something that I think of great importance and I'd like you to steer me back from that if I'm wrong so I'm open minded about this. Pharmacists started spraying glyphosate or Roundup on things like wheat. It's sprayed on the crop right before harvest because it stresses the plant which causes the plant to basically put more energy into protecting the seeds for the next generation because the plant is getting desiccated, it's dried out. This increases the amount of glyphosate that is left in the food. This is allegedly not harmful to people because it only activates bacterial pathways that humans don't have but we have bacteria in our gut. We're eating this constant low dose Roundup. Have you or has anyone done research into what that does to the gut biome?

Les: I have not, no. Honestly, I am not aware of anybody who has looked at that specifically. There certainly are a lot of people who have looked at in general sense what our risks do to ... So, the low doses of exposure, whether it's to Roundup or other herbicides and pesticides, what's the exposure risk to typical people that are eating the food they get at the grocery store or to processed food that they buy restaurant meals. It's a hard question to address. I think it probably is fair to say what risks there are are probably not huge. It's not the sort of thing that 5% of people are dropping dead within 10 years. That's the kind of effect that would be big enough that people would have noticed and paid attention.

That the studies that have been done a lot, have been looking for the general connections, say, "Is there a relationship between exposure to low doses of these chemicals and overall human health," I'm not aware of anybody who has specifically said is there some element of that risk that is due to changes in the gut microbiome or not? My guess is that the intuition of most scientists would be the concentrations of those chemicals are at low enough concentration, even if you're never eating

any organic food, you're always just buying the typical standard produce at a regular grocery store. You still probably don't have a high enough concentration of those things in your gut that you would predict there to be a strong effect. Not to say there may not be some effects. I certainly wouldn't say that the effects are likely to be good. If there are effects, they're probably not beneficial.

I do have a lot of concerns about this sort of industrial agriculture. My greater concerns about the effects close to those farms and fields, what's the damage we're doing to the people who have to work in those fields, people who live in those communities, to the people who live next to the chemical plants that are making those things, what's the effect on the broader ecology around these systems? I don't think that that model of applying toxins to the environment is a viable strategy really almost ever in a long term thing.

I'm not saying it shouldn't be used sometimes. I got pneumonia myself a number of years back but I was delighted to go to my doctor and get a prescription for a selective toxin. I wanted to swallow those pills that had a poison for certain microbes. Man, I was delighted to take those but I did take probiotics at the same time. That is 1 of the situations where I do take probiotics is if I need to take antibiotics. It doesn't replace everything that's probably getting disrupted but it tides the system over perhaps that there's a little bit of a protective buffer to let the natural community come back but it'd be good if we didn't rely, if we didn't build entire systems of how our society works around the assumption that we need to be applying toxins to broad swathes of the ecological community, rather that's the ecological community of the Midwest or in our gut.

Dave: That's very well said. Now, there's another up-and-coming technology for addressing broad swathes of stuff in the gut. Something that I first read about and considered back when I was really working on my gut and that's fecal transplants. This is the idea of taking poop from someone who's got a healthy digestion and introducing it into someone who doesn't have healthy digestion. Yeah, you introduce it the way

you're probably imagining or the FDA has this thing where they put it into capsules you can swallow as well and see if they can market that as a drug. I want to see what they're going to name that drug because it's going to be hilarious.

Les: Re-poop-ulate.

Dave: Nice!

Les: It's a Canadian group that actually got, it's not ...

Dave: No way. Really? Is that what they're called.

Les: Yeah.

Dave: Is that what they're called?

Les: It has been done to just take the native stool and put it in a capsule and have people swallow it but there's a Canadian group that, to get away a little from that ick factor, have got a defined community of 30 different microbes that are gut microbes that they grow in pure culture and mix and put into a swallowable capsule. They've shown some good results for that. It may be a substitute fecal transplant in a pill rather than an enema of the original, native material put in a blender.

Anyway, you're right. It's an area with a lot of interest. If there's a problem with the composition of the gut microbiota, well, let's get a healthy community and put it in there.

Dave: It gets a bit awkward, too, if you think about that. You go to Facebook. "Hey, I'm looking for someone's really healthy poop," like the whole donor screening thing is really weird but I did have the advice from actually a couple experts in the field who said that your best bet is if you have a child who's never taken antibiotics, they probably have a good biome so use that and I've never done that. My gut is actually functioning so well now that I'm really happy and I don't want to mess

with it. If I take antibiotics, who knows what I'll do but I'm not planning to do that either unless like you, there's a really good reason. What's your take on this? Is this a fad or is this something that's going to be continued to be researched and studied and should people who are really sick really consider it because the harm isn't that big?

Les: It's definitely not a fad in the sense that it's a life saving treatment for some people. The condition for which it receives the most attention and the 1 condition for which the FDA has said, "Yeah, you can go ahead and do this. We could regulate it but we're choosing not to." The condition is chronic infection with *Clostridium difficile*. Disease used to be sometimes called pseudomembranous colitis but this is a single microbe that produces a toxin or 2 toxins actually. If it gets into high abundance in somebody's gut and starts producing the toxin, it's a life-threatening illness. Even if it doesn't kill somebody, the majority of people who die from *C. difficile* are elderly, frail individuals who wound up taking a lot of antibiotics and perturbing their gut microbiota and the *C. difficile* got established.

There's an increasing number of people that are younger and not say, in hospitals and nursing homes that are getting this. They may not be killed by it but It really is incredibly destructive with their quality of life. Many, we're talking about perhaps dozens of bowel movements, bloody diarrhea a day. It's hard to have much of a life if that's what you're facing. In some cases, not always but in some cases, a single fecal transplant within a day, it's over. It's a miracle cure. The people who have had that or who want access to that treatment, it doesn't become so gross to think about what the treatment is if you're already dealing with dozens of bloody bowel movements a day. They're the ones who went to the FDA and say, "How dare you regulate this. If you try to stop our ability to get this by going to our GI docs, there's plenty of instructions online. We're going to be doing this at home ourselves. What do you want? You want a doctor to get involved and screen for pathogens or you just want me to do it with my spouse's poop?"

That's why the FDA backed off. That's why this treatment's not going away. It's not a fad. It really is an amazing medical advance which by the way is not really that new. Chinese have known about it since the fourth century AD but using it for a lot of other conditions, there's obviously a lot of interest to say, "Well, not just for this 1 fairly narrow condition of *C. difficile* which is as much as that's increasing epidemic, there's still nowhere near the number of people with that problem as there are people who maybe are obese and think, "Gosh. Can't I just change my gut microbiome?" People with autoimmune diseases, people who have Crohn's disease or ulcerative colitis, there's a lot of hope and expectation that, "Wow, maybe this is going to be the ticket."

The evidence that's been collected so far and it hasn't been a lot of evidence. For ulcerative colitis, it seems like fecal transplants can be helpful. They're not a miracle cure. They're not going to have the cure rate they have for *C. difficile*. That's not surprising because ulcerative colitis is a much more complicated disease. It's a vicious cycle interaction between gut microbes and the body's own immune system. There's far more moving pieces rather than just 1 microbe producing 1 toxin. It's not surprising that it helps but it's not surprising that it doesn't cure it. Other conditions may be even more complicated.

I think in a way the fecal transplant as a tool is really going to be a stand in, once we know enough perhaps in a decade or a couple of decades, we might be able to be much more intelligent about saying, "Hey, let's get a read on what your gut microbe is given that you're a patient with ulcerative colitis, let's look at the functions that are there, let's go to our shelf of 1,000 different probiotics with defined functional contributions and select which 8 of them you need but the next person comes in, even with ulcerative colitis will have a different set of microbes that they need. Somebody else comes in with an autoimmune disease. They're going to get a different set of microbes. It won't be 1 size ... Well, let's just put somebody's healthy community in there because something in there is probably what you need.

In the meantime, until they get to that point, fecal transplants are not 0 risk. They're not terribly high risk but certainly not 0 risk when you think about the transmission of hepatitis or HIV with blood transfusions. It shouldn't be taken lightly. "Oh, yeah. Just a casual thing. I'll just pop down to the local spa for my weekly fecal transplant." Yeah. People shouldn't be taking it lightly. On the other hand, to my mind, it's not nearly as scary as, say, multiple courses of potent antibiotics that were the only treatment we used to have for *C. difficile*.

Dave: That attitude of, "I'm going to do it at home without help if you don't make it legal," that's 1 of the reasons I'm a fan of biohacking, this idea that we have control of our own bodies. If someone wants to regulate technologies that you can buy online for \$100, good luck regulating that. Just like you've succeeded in regulating marijuana.

Les: Yeah, that worked out really well.

Dave: Alcohol before that, right? These are technologies for being more human or for saving a life. They deserve study and they deserve caution and they don't deserve to be hidden because someone didn't say it was okay.

Les: Yeah, I agree. I feel bad when, like I did a Reddit Ask Me Anything. People were sending in questions where it was obvious they had a disease or they had a loved one with this disease. It was all heart wrenching was the scientists to say, "You know, we don't know enough to help yet. We think this is an area where we know enough to make a big difference but we can't yet give you an answer that's going to help you in your condition." I really feel for people who say, "You know, I'm going to just try that fecal transplant at home." I don't want us to sound as if I'm not telling people, "Okay, that's dumb. Don't ever do that." I want to respect people's choices. I don't want people to take it lightly and think that, "Okay, this has just got to be something that's healthy and harmless," because it's a fad. Be a little more cautious with that.

It is the case, it's simply the case that humans, as all other mammals, evolved with a huge concentration of tremendous diversity of microbes

in our gut. It's not all that strange to introduce complex community of microbes back in there so that the idea that fecal transplant, it doesn't strike me as crazy or gross. Fairly, the Chinese physicians from the fourth century who are doing this stuff, they must have thought it had some beneficial effects.

Dave: Compared to the taste of a lot of those Chinese teas, it's probably easy to work with. That's just me.

We're coming up on the end of the show. There's a question that I've asked every guest on the show since I think episode 77 when I forgot.

Les: Don't forget.

Dave: All right. I'm not forgetting this time. It's given all this stuff that you know. Just about the microbiome, just your whole life path, if someone came to you and said, "Look, tomorrow, I want to perform better at everything I do at life, what are the 3 most important things I should know about or the 3 most important things I should do?"

Les: It's interesting. I am going to get an answer that goes well beyond my scientific training specifically but to my life. It is something I'm going to speak to very much on the basis of my personal experience. I would say that the 1 single most important thing is going to be the attitude you bring to having a compassionate view towards yourself and the others in your life and to all living beings. Even if people are sick with an illness that cannot be cured, they can have happy and productive lives for as long as their life lasts which is really all any of us can ask that in addition to that attitude and approach that's a mental, spiritual, emotional thing, healthy diet and lifestyle in terms of sleeping, exercise, something that bridges all these is being part of a community of people that you love and are loved by that you belong to, that there's meaningful relationships there. The quality of that life and lifestyle, the diet that you eat and the attitude you have, that defines a good life, I think. You can simply look at what studies have been done and who's happy and why or what are changes people can make that reliably lead from unhappy states to happiness. They get tied up with that. The little

details of this minor aspect of diet versus that are probably not the whole story. The big picture of these items. Pay attention to that first.

Dave: That's a great answer and thank you. I've heard some of those before but your answer on compassion was very well stated. Thanks.

Les: It's a pleasure to talk to you.

Dave: It's a really fun interview and thanks for going deep and still making it so people can understand what we're talking about. Have an awesome day but first, I want you to tell people where they can find out more about your research. Your name is Les Dethlefsen which is hard to spell. It was going to be in the show notes but do you have a faculty page or a blog? How do people get a hold of you?

Les: There is a website that we're using to recruit first. You mentioned that we're doing this study with 100 people. We haven't got the last few people recruited so if people want to be part of our study, they should come to this website, even if you don't want to be part of the study, the website has a lot of microbe-related information links to both popular articles and scientific articles and places you can email a question. It'll get to me or the other people working on the study.

I'll give you the shortened URL. bit.bo/microbes. That'll take you to a website that will tell you a lot more and let you get in touch with me. If people want to be part of a study that over many months involves contributing stool and urine samples for us to examine. One of the benefits of being involved is that you get to learn about your own microbiota. We will share the data we learn about from your samples, we'll share that data with you. Hopefully, we'll progress in our understanding of how people's lifestyle affects the microbiota and how the microbiota affects their health.

Dave: Right. I think you just filled up your study because the Bulletproof community has no problem with weighing our poop and other things

like that. In fact, at the first ever Bulletproof biohacking conference, I believe we sold out uBiome.

Les: Awesome! Yes.

Dave: This is an audience who's going to pay attention and wants that quest for knowledge. I would be shocked if people didn't go to bit.do/micorbiome to fill out ...

Les: Slash microbes.

Dave: Oh, sorry. Slash microbes. I spelled it wrong. Bit.do/microbes and that'll be in the show notes. I fully support that. I'm not going to sign up myself because I travel so frequently that I'm not carrying buckets of poop around with me on airplanes. The TSA doesn't like that but otherwise, I'm eager for that knowledge myself. Just thanks for the work you're doing, keep it up and I really want to see the results of this study.

Les: Thanks, Dave. We will be publishing. Maybe have another interview when I've got some study results. I'd be happy to come back and share with your listeners how we're moving the science forward.

Dave: The second you know when the release date is, let me know. I'd be happy to have you on the show. It'd be really cool to hear what you learned.

Les: Thanks, Dave.

Dave: Bye.

Les: Bye-bye.

Featured

[Sign up for Les Dethlefsen's experiment](#)

Resources

[Pseudomonas aeruginosa](#)

[Microbiota](#)

[Trichuris trichiura \(pig whipworm eggs\)](#)

[Polyphenols](#)

[DD-transpeptidase \(Bacterial DD\)](#)

[Firmicutes](#)

[Fasting-induced adipose factor \(FIAF\)](#)

[Mycotoxin](#)

[Quantified Self](#)

[Probiotics](#)

[Hadza, Tanzania](#)

[Polysaccharides](#)

[Caprylic acid](#)

[Chronic low-grade inflammation](#)

[Glyphosate \(Roundup\)](#)

[Fecal Transplant](#)

[Clostridium difficile \(pseudomembranous colitis\)](#)

[Ulcerative colitis](#)

[ubiome](#)



Bulletproof

[Brain Octane Oil](#)

[MCT Oil](#)

[Bulletproof Coffee Shop](#)

[Bulletproof Conference](#)

[Moldy Movie](#)

[Bulletproof Diet Book](#)

[Free Bulletproof Diet Roadmap](#)