Tracey ([00:01](https://www.rev.com/transcript-editor/Edit?token=gbqunFeJ1eIWtTKOcP1aJdTQfcuOgLNmSzyX09kP8GX-rG0g1ELgIT_pp3M9iaOXz_0G2dWf_XjASuIWfA8HdcwCWnU&loadFrom=DocumentDeeplink&ts=1.04)):

Hello, and welcome to NC State's Audio Abstract. I'm your host, Tracey Peake. C. diff is a nasty little microbe. It can set up shop in your gut and cause painful sometimes fatal infections. It's also notoriously hard to get rid of once it gains a foothold. Casey Theriot is an Associate Professor of Infectious Disease. She's here to talk about how C. diff does what it does and what researchers are doing to stop it. Welcome, Casey.

Casey ([00:27](https://www.rev.com/transcript-editor/Edit?token=i00-V3qGX6DajgdnYM3juPYXui8t1ORAabR1vwh9s-GqvmTKJyzvBG_PzaQtf2jG8p5WCjZZ8hbs2DISMyg7pfA6WP4&loadFrom=DocumentDeeplink&ts=27.95)):

Thank you for having me, Tracy. It's great to be here.

Tracey ([00:30](https://www.rev.com/transcript-editor/Edit?token=Qt6TITFHP97XqbBScUyg2gklJt_Xsg7-wTeRibMOd21gzjuQwmm-m4uOYX6e-sefRanl6tQJWH-9I5sNW-GcsmyiAVw&loadFrom=DocumentDeeplink&ts=30.47)):

I am glad you could come. Let's start by talking a little bit about the gut microbiome and how important it is to your overall health and wellbeing. Some people even refer to it as the second brain. And what does that mean? Why is a healthy gut vital to your health?

Casey ([00:48](https://www.rev.com/transcript-editor/Edit?token=FJrs9WBub_aOubOyEaAdMG3stF21cLqPGwg138R0184EZdSxnjj7Yit_XNEKG6ZvGDs-CY6TxO307u04eN6n6229p14&loadFrom=DocumentDeeplink&ts=48.62)):

Yeah. Great question. So we get this question quite a bit. The gut microbiome is very important to human health, as it provides many functions to the host or the humans, and also other mammals. The gut microbiome is the compilation of bacteria and their collective genomes or genes that reside in the GI tract. It makes up over 70% of the total microbiome in and on the body, which houses a substantial amount of diverse bacteria that can perform many different functions. The gut microbiota is really important for aiding and digestion of food. So I would say that that's actually super important for human health because you need food digested to get nutrients. It also is important for priming the host immune response. Also, very important for wording off infectious agents. And it also provides something which my lab really works on called colonization resistance, which is the ability to provide resistance to colonization of incoming pathogens.

Casey ([01:56](https://www.rev.com/transcript-editor/Edit?token=EQgzzRi123zXyhYkcQoKvFPvj6jrdyJA9ysO9ti2elDOe0-mHHCLg-XGcDLVt9SRdEuDzJDb2hFuLyFMsvoP_OXpZh4&loadFrom=DocumentDeeplink&ts=116.29)):

And one of these pathogens is actually Clostridium difficile. So let me give you an example of what that looks like. So normally we have a healthy, stable gut microbiota, bacteria producing certain metabolites, everything working pretty well. And then a lot of times that you take an antibiotic and you take an antibiotic for bacterial infection, so a good reason, it will alter the community or the bacteria that are present. And what this does is it lowers colonization resistance to where a pathogen like C. diff can actually then colonize and take a foothold in the gut. And so this is really the focus of my research, trying to figure out how the microbiota provides colonization resistance in that healthy, stable state and how the antibiotic will alter that. And in the future, what we're trying to do is figure out how we can restore the colonization resistance after insult from an antibiotic.

Casey ([02:59](https://www.rev.com/transcript-editor/Edit?token=4vxytnqA_rZRzKtgbTdV5Ni2AV6ir264kWOXslXjNFl-ldRHlSIlZvi0dISPBdeQcvlTrTcijs2jCvg18f9SNlLyDRA&loadFrom=DocumentDeeplink&ts=179.93)):

Now, the other question you asked is about the brain or the second brain, why it's called that, the enteric nervous system can be called the bodies second brain. There are hundreds of millions of neurons connecting the brain to the nervous system in the gut. And it's part of the nervous system that really is tasked with controlling the gastrointestinal system. And we have many different bacteria that are present that are producing certain small molecules, small molecules, such as hormones, serotonin, and all of these can actually be taken through enterohepatic circulation and brought to many different organs in the body, including actually going back to the brain. So the gut, especially healthy gut and its products, the bacteria, what it's making, the crosstalk between the gut and epithelium is really connected to many other parts of the body and many other parts of the organs, many other organs. And that is why it is really important to overall health of a human.

Tracey ([05:30](https://www.rev.com/transcript-editor/Edit?token=4eu6hAEYmD31B_EAj4D9b8bz43yw-hkOGcXSNg-MyRyZmEOgGD96_eMStBsvVc3zIvcdY3n4feftDizQ3PZkrHiMys8&loadFrom=DocumentDeeplink&ts=330.47)):

So let's get to C. diff specifically, what is this bacteria and how do people most commonly get an infection with C. diff?

Casey ([05:44](https://www.rev.com/transcript-editor/Edit?token=0nbpBnodxJVLAg80kLkbQfEuhEVdcxKsMF9D8M6KXVozI8b4zCsm9HUaG1xZE9ttLt9sIKFLYYES8G7yKpWbK2TIruI&loadFrom=DocumentDeeplink&ts=344.58)):

The most common way that they'll get an infection is nosocomial. So it's hospital acquired, but we'll back up and talk a little bit about what it is first, and then we'll go into how people will get it. Because people in the community are now getting it too. It's not just a nosocomial or hospital acquired infection anymore. So C. diff is a gram-positive anaerobic bacterium. Anaerobic again means it has to grow in the presence of no oxygen. So it's also really hard to grow in the lab. You have to grow it in anaerobic chambers that have a head space with no oxygen present in it. So it is really hard to work with difficile difficult, gives it it's nice name. It's also a spore forming organism, which is really important for potentially how it transmits in a hospital or in the environment.

Casey ([06:36](https://www.rev.com/transcript-editor/Edit?token=YHSww8Dj9M371SIAkG-g1gt8dH6f-knXdrvhjTulmYwFKt4wi9KyhQTZgJKdt7y83vVmsDkCEzuPTBdwN_jBIlx1IIA&loadFrom=DocumentDeeplink&ts=396.23)):

And so the spore form of the bacterium is really a dormant state and it's hard to kill. So it's dormant, it's resistant to denaturation. So if you're actually cleaning your hands and you have spores on them with ethanol, it's not going to kill the spore. It needs 30 minutes of contact time with bleach submerged in it to actually kill the spore. And this is important because I think this is a really big part of how it's being transmitted in the hospital potentially or in hospital sometimes and even in the environment, where if you have somebody who's shedding C. diff or has CDI C. difficile infection, these spores are shed through the feces and then you can pick them up on your hands, you can ingest them. If you're not washing your hands properly, that's how it will go through, the life cycle, go back into your body and you'll ingest it. And then the life cycle starts all over again in the gut.

Casey ([07:38](https://www.rev.com/transcript-editor/Edit?token=yztIiiwoK3Z_FfqKdlAkTsL0EcLEI7syaXMOf4txYGiwfhpF3u8mnt5MRgF3nI9V9pbuobKHeK1jrYYgJLzc0T0LtGc&loadFrom=DocumentDeeplink&ts=458.99)):

So if somebody is on antibiotics, they're more susceptible to C. difficile infection because of the reasons I already explained, they have an altered gut community, gut microbiota. They are more susceptible to getting C. diff, colonizing and causing infection. And usually that's in a hospital. So again, it's a nosocomial infection. And then in hospitals, people are shedding more of the spores. And so it starts the whole process over again. And again, the major risks of C. diff or C. difficile infection, antibiotic usage, for the reasons I talked about, alters gut microbiome makes it more susceptible to colonization if you're elderly. And then also if you're in for GI surgeries or GI procedures. There's 500,000 cases of C. difficile infection per year in the US, and about 29,000 deaths per year, based on what the CDCs estimate is. So it is still a very significant problem, even in the times of COVID as well.

Tracey ([08:45](https://www.rev.com/transcript-editor/Edit?token=1ILhw2wssdnUh6feAguk_FJSEkdIrxmiO36BZr79H9xLM2ARV4lIibhq3O4-x5OWKuxQDsJu0FD-N-HmtI0dZU858SA&loadFrom=DocumentDeeplink&ts=525.31)):

Yeah. That's not a good ratio. Let's talk a little bit about its actual life cycle. So we know the spores are out in the world, they're out there. And if you ingest one, what does it do once it's actually in your body?

Casey ([09:03](https://www.rev.com/transcript-editor/Edit?token=rxkdlLQExy8yHWGk0yShixZESGWdkt_5ePYMmfepJnmACAvQkAII7Gi8vZ0ybRXXzzqivASNe3oTI5eMEiCYzgSzck4&loadFrom=DocumentDeeplink&ts=543.18)):

So usually, in order for you to have infection, you would need to have the susceptibility or the loss of colonization resistance. So normally, like let's say you're a person that is not treated with the antibiotics, you have a normal, healthy gut microbiota, the spore is going to come into your body. It's going to make its way down to your small intestine and the spores going to germinate. And so what that means is it goes out from the dormant state to this vegetative state where it can then grow if it finds the right nutrients in the right niche. So in the small intestine, we have many bile acids. These are small molecules that are really important for host physiology. They're also altered by a lot of gut microbes that are present. And so some of these bile acids are beautiful germinant for C. difficile spores, but a normal person and a healthy person without antibiotic, the spore will turn into a vegetative cell.

Casey ([10:00](https://www.rev.com/transcript-editor/Edit?token=qmvgAkTacUcPSSDvtaDuJelDgvSUf8WMC1uFzIFjh9qk2QervDvf3OO0E-7vU0Yb4B3ERxshhCOp4dluFQ1hz4iSxp4&loadFrom=DocumentDeeplink&ts=600.56)):

It'll make its way to the colon and it can potentially be out competed by the normal gut microbiota that's there. So it'll pretty much keep it in check and or they're small molecules, other bile acids called secondary bile acids in the large bowel, the colon that can actually inhibit C. diff growth. So this is the mechanism we think is happening in a normal, healthy person, when they ingest C. diff. Okay. So what happens if you're susceptible to C. diff or you've been on an antibiotic recently, and then you ingest the spore, it's a bit different. So the spore will germinate in the small intestine still, but as it makes its way to the colon or the large bowel, it then can grow because it has one, nutrients and it has decreased competition. It has really no other competitors or other gut microbiota to compete with it because it's been wiped away with the antibiotic.

Casey ([10:57](https://www.rev.com/transcript-editor/Edit?token=WFAxKo3DD-u-qkA9tFFzwNEksnW-WbnnmyIWikqccrbWUt93cBYeKUXL-0c_xKJtuBg_hcweHoySyHIENM3YKzG05Mk&loadFrom=DocumentDeeplink&ts=657.33)):

Okay. So now it has this niche and it also has no inhibitory products because the products that were being made by or secondary bile acids are made by a lot of those bacteria that were there before the antibiotic. So it pretty much has a beautiful niche to grow. So it grows to high level cell density, and then it produces toxin. And the toxin is actually what mediates disease, that causes severe inflammation, can cause colitis, causes diarrhea. And there's a range of clinical disease that can happen from very mild diarrhea, can be asymptomatic, can be mild diarrhea, can be Clostridium colitis, and it can be more severe where you can actually have significant colitis or death.

Tracey ([11:47](https://www.rev.com/transcript-editor/Edit?token=jcOLA__HqvbWRDWHaPu2YJlMcQMN_SNZv8R-Ra8VdRzbUk6On8tpKAy7IjCg1BMYFPSZfES422vPm4eysPfXZS-CTcU&loadFrom=DocumentDeeplink&ts=707.73)):

It almost seems as though it's a self perpetuating cycle with antibiotics you have to take antibiotics to fight it because it's a bacteria, but the more antibiotics you take, it clears out all of the other normal bacteria.

Casey ([12:05](https://www.rev.com/transcript-editor/Edit?token=4oNEph-pwbr4MeVv2P-_KKeMBeeMmP68Ekxl2jc0fsw1cfpEI3SI9SFVllWHTi3KX2B48LjBmvX46WgLlhVURKrv8nc&loadFrom=DocumentDeeplink&ts=725.23)):

I think that is actually the major problem. And so why is it hard to get rid of, this is probably the number one reason why it's really hard to get rid of. You have severe C. difficile infection. You got it potentially because you were on an antibiotic and you altered the microbiota. You had a loss of colonization resistance and you were exposed to spores somewhere, because you have to have the exposure as well. Then you get C. difficile infection, you're going to be put on vancomycin most probably, vancomycin or fidaxomicin. So other broad spectrum to narrow spectrum fidaxomicin is not as broad as a vancomycin, but vancomycin will then alter the microbiota further. And so in 70% of people or patients, it will clear the infection. So C. difficile infection will be cleared.

Casey ([13:08](https://www.rev.com/transcript-editor/Edit?token=XDBoK2eE2IBqPaw4udzt9Niifdh8CT-uX17hiYTaT7p56iGRQ35yXM7gM2YF0QBTGUckhmov5uYiZbfrCrei1-DUk7A&loadFrom=DocumentDeeplink&ts=788.21)):

The issue is in 30%, you have something called recurrent or relapse of C.difficile infection. This is a significant problem. And so these are patients that are put on vancomycin, it'll look like it's cleared, symptoms will go away and then there'll be taken off vancomycin and within days to weeks, it comes back again. They will be put on vancomycin again, they will take and it'll clear, there'll be taken off, it comes back again. So this can go up to six plus relapses. And so these people fall into a different class of group where they really need a fecal microbiota transplant. So an FMT is what it's called, it's called a fecal microbiota transplant. And basically, it's what it sounds like, where you're looking for a healthy donor stool. So you're looking for healthy stool and healthy stool you have many different bacteria, and you're hoping that it has a normal gut microbiota or fecal microbiota present.

Casey ([14:22](https://www.rev.com/transcript-editor/Edit?token=pVelttKvW03RPNFPPHUguQ9OB4tF4Oh7yvtpxvtDpNitD6GIznFjNFB1wxYWcQ6ntioIptEmezFHzrNBPIQT9R6do6s&loadFrom=DocumentDeeplink&ts=862)):

And then the healthy microbiota stool or sample is infused via colonoscopy into a recipient or a person or a patient that has recurrent C. difficile infection. And that has an 80 to 90% efficacy of working, where within days the person or patient with recurrent CDI feels a hundred percent better and symptoms clear. So is a very important tool or therapeutic. The problem is we don't know the long-term consequences of infusing healthy stool into another person. And so if you think about what's in stool, if you think about what's in the gut, as far as the bacteria, their genes, their products, and it's person to person, we don't know what the long-term consequences of infusing that into another person. But for C. diff infection, for currency diff infection, it works beautifully. It's being used now at many hospitals around the country. And this is probably what most people would do if they have recurrent C. difficile infection.

Tracey ([15:42](https://www.rev.com/transcript-editor/Edit?token=gzJobKjTIrsBIJE5fJ864LTiRN4DBtyQoZOCdl7txQhidp7NlOpZQh_x4_MceBzLmYEKJ2UXelZNCD13RYnnMiPCDkc&loadFrom=DocumentDeeplink&ts=942.25)):

I mean, it seems like I was just reading about it not too terribly long ago as an experimental, this new treatment. So how long have folks been actually using this as a therapeutic? Do you know?

Casey ([15:56](https://www.rev.com/transcript-editor/Edit?token=_SoWaWeuED-nmxS8b3nFO-haLW0MKSbfpA7DapbX4U7ghTpRcUxoeKbZF3eWdWJMLLte40XdplmUBOEuQICghOg-F94&loadFrom=DocumentDeeplink&ts=956.12)):

So historically, it was introduced in the 1950s, in Colorado as an approach. And again, but since like, I'd say recently in the last 10 years, it started off at FDA as an investigational new drug where hospitals could apply for an investigational new drug and they could use it. And it was different then where, and this was at Michigan when I was at University of Michigan Medical School in 2010, where you'd have to enroll patients and they'd have recurrent C. difficile infection and they'd have to actually find their own donor. So they have to find a donor, someone they live with, someone they knew, someone they knew that wasn't on antibiotics, hadn't been in the hospital for the last six months. And we had to collect that person's stool and bring it in the same day as the person's colonoscopy. So it was a bit different, again, all the stool is tested and that's a really important point, which I'll get to in a minute.

Casey ([16:58](https://www.rev.com/transcript-editor/Edit?token=FwXd1PI-Xai0e5hrzeDmbM1CaajD3XTide9YSy9WpfH9gep81e9XUoY52l8E8BnOJAUzHVUFxrRJB3HLd67Ts4PEyMs&loadFrom=DocumentDeeplink&ts=1018.94)):

So since then, it's really evolved. And there were stool bank, a stool bank called OpenBiome, which is now, I think, turned into Finch Therapeutics in Boston, where they would pay young people, healthy people for stool, and it was a stool bank. And then that stool bank was sending samples, frozen to all the hospitals that had these programs. One is UNC Hospital that I've been working with over the last five years. And then they would use that stool as the donor healthy stool to infuse into these recipients. Now, what happened recently in the last two years, that stool is always tested. So it's tested for infectious diseases, viruses.

Casey ([17:52](https://www.rev.com/transcript-editor/Edit?token=_8-qxjwhVp9N8ANoOs3SjmjigWQNiBu9tHArbmYdebs2yAZRdFYToTUXVv4J_3ZKSwJ5UsmNEu1BIJJ8QYP024ezT70&loadFrom=DocumentDeeplink&ts=1072.97)):

What happened recently is that there were a couple of patients, I think one that passed away because the donor stool had a bacteria in it that was resistant. It was inner bacteria say resistant to many different antibiotics and it was transplanted into the recipient and that person passed away. And so now in the last couple of years, they've been evaluating how they actually test the stool. And since the age of COVID, COVID can be in stool as well. I think they had to halt things for a little while and actually evaluate how they're testing and evaluating the safety and efficacy of the donor stool. And I think it's back on track now. So the stool will be COVID tested as well.

Tracey ([18:39](https://www.rev.com/transcript-editor/Edit?token=v7sAE2SLF6E9dnOd4o9cEi5PJ2Sfs_NJbiQEGRDGJoKGOcwXIs59cXrM3z76UwNIzqxThBm52af_k4WNO8wFE6ycVNA&loadFrom=DocumentDeeplink&ts=1119.26)):

It's amazing that we can do that.

Casey ([18:50](https://www.rev.com/transcript-editor/Edit?token=HfTa_h2oYZMua0bZ31cUsVaacTFhpI1ekpy_ymZ4D7QN2goYooLjjFtuWmiRfJPeEe_eOBulvuXJt3AYOxS66uCo4C8&loadFrom=DocumentDeeplink&ts=1130.12)):

There's new approaches for this too, where if people need an FMT in the future, especially like, let's say they're going on chemotherapy. I think Sloan Kettering is doing this. They'll, before the person goes on chemotherapy, which again, they're going to be severely immunocompromised after the chemotherapy process, they might have to have an FMT. They're having them store their stool before they go on chemotherapy. So the patient will come in, they'll collect their stool, they'll freeze it and store it for later, just in case they need it down the road.

Casey ([19:41](https://www.rev.com/transcript-editor/Edit?token=mwLqTP_2UaoNgSU9JSdGPWFHVUCqOdqGCvStYQ8u1nVabWORdKahNFiohJba3gQu6FMvnKPqEf4K9fEk3IpgMnnPF0s&loadFrom=DocumentDeeplink&ts=1181.44)):

So again, we don't, we would not know the downstream consequences of this. And so there's a real push, which we'll talk about, I think soon, to really harness some of the bacterial and the bacterial products in FMT to make a product or a therapeutic that we actually know what's in it versus taking stool from somebody and infusing it into another person. So it's actually like, how can we figure out how the FMT is working? What's the mechanism of actually how it works and cures and clear C. difficile infection in patients, can we then figure that out and actually make a targeted therapeutic?

Tracey ([20:25](https://www.rev.com/transcript-editor/Edit?token=qMqCvorp9bAqxmuRP7N8xX14DYsYa6HMZLcJUoAykFvwqnJfBq297aKAP42rNlQmFwCiH9oidYFD7OlSEoMkDTnUhU4&loadFrom=DocumentDeeplink&ts=1225.35)):

That'd be neat. So it would be almost like you would have a universal type O fecal donor kind of thing. Almost like blood types. If you came in something like that, where they could look at what your microbiome looks like, and then maybe find a donor match that fits.

Casey ([20:44](https://www.rev.com/transcript-editor/Edit?token=LNEuiKRceLJfg_z3JgOQpAgsOiVtEB1fTc9yWpvvcgFi0f9wrGQ3UZQuAun8UVr4_2HBHnSPyCb_j82ABaKSH4B-ah8&loadFrom=DocumentDeeplink&ts=1244.03)):

Yeah. No, that's definitely something else that people I think are looking into. And I think that's going to be really challenging just because everyone's different, it's so variable. So I think when you're trying to figure, and again, my lab is trying to figure this out too. We're trying to figure out how the FMT is actually working, the mechanism behind it, because if it's potentially just a certain group of bacteria that are driving this process, or they're producing a micro, a metabolite, a small molecule that is then killing C. diff off or it's also potentially altering the immune response and kicking it into high gear, can we then just harness that? Can we then just focus on that bacterium itself or a couple of those bacteria, or can we actually focus on the metabolite itself or the small molecule and actually just use that alone? So there are many researchers, there are many companies out there trying to figure this out and that have been trying to figure this out, I'd say for the past like 15, 20 years.

Tracey ([21:53](https://www.rev.com/transcript-editor/Edit?token=T373_eMLaTp7h8piuDHRAzH0oBsjeKlKLXAwiAB7txZnj2iKsErRqV2uYFkGmnOGvqnK0R_rFVaqgcVTBPbFX7ZG3-w&loadFrom=DocumentDeeplink&ts=1313.76)):

It would be great. If you could just somehow put all that in a pill, you take a magic pill, suddenly your gut microbiome is all better. So that leads into the promising strategies for treatment. So you're looking at specific bacteria or metabolites, you're looking at donor banks and things like that. Absent that and just massive doses of antibiotics, is there anything else folks are looking at or is it specifically we're going to use the antibiotics and then we're going to try to figure out a way to help people rebuild a healthy gut so that they can fight off C. diff themselves or keep it under control?

Casey ([22:41](https://www.rev.com/transcript-editor/Edit?token=IYOX9_EokLCAkndQJ6qcPsIwHzjw5gVsxwhWJRSIPo4XT-0VR9vCwTu4WCgfxSNioaJXP05XgYfaOY_8GPpDwbkI_6w&loadFrom=DocumentDeeplink&ts=1361.64)):

Yeah. There's many different approaches I think that are going on now and I'll touch on a couple, but this nowhere near is going to touch on exactly everything that's going on right now. But I think there's some really exciting therapeutics in a range of phase one, two, three clinical trials that are ongoing. So one thing is that there are new antibiotics that are being made, not many. So antibiotic discovery is really on the decline, but fidaxomicin was one example that's already been approved for the use of recurrent C. difficile infection. And the idea there is it's more narrow spectrum. So if you're looking for a new antibiotic, you really want to try to target C. diff alone and you don't want to target anything else in the gut microbiota, other commensals, other things that are going to be coming back to where they're going to be important for restoring colonization resistance.

Casey ([23:41](https://www.rev.com/transcript-editor/Edit?token=mca_WthG-4xlJlgrtZ9zKmgAISB8J0PuQX2mUFQ4hwY1IWZGH2uwk9TzszR3-uizdpjRFxIKlZocSYXnPLKqEuLEJ_4&loadFrom=DocumentDeeplink&ts=1421.46)):

So fidaxomicin is one example. It does target C. diff. It does not target or effect the other clostridia in the gut or the other anaerobes that could be important. So that's an example of, I think, a success. The other approaches are a bit different. So the other approaches are not on a targeted, precise antibiotic per se, but they're actually trying to give back different bacteria. And so these are called LBPs or live bio therapeutic products.

Casey ([24:47](https://www.rev.com/transcript-editor/Edit?token=ld0mWM7z1QFSUl0AuPcx07o3c6x_nJvKa7Qku_eXKRlZev9EybEfCKB-QW_JpyS4-gIAVrYXimFl5K21cWfmYBz7nw8&loadFrom=DocumentDeeplink&ts=1487.47)):

And it's a biological product that contains live organisms such as bacteria, is applicable to the prevention treatment or cure of a disease. And it is not a vaccine. So this is actually important moving forward because LBPs, there are multiple in processes of clinical trials. So some of these would be taking stool from a donor and actually processing it further to where you maybe have a hundred different bacteria that fall out of that. And then, or you have a consortium where you only have eight to 12 bacteria that you think is actually going to be able to treat, prevent, or cure C. difficile infection. So there are some really exciting clinical trials of a very broad range going from taking many different bacteria that you've enriched from a stool sample to taking just a consortium of eight to 12 bacteria. And you're seeing an effect of both.

Casey ([25:59](https://www.rev.com/transcript-editor/Edit?token=64P21f0lQk-E3HcIBPqYNLE40zR7FO0iW7QTW3Tsd5GAVidCp19WdlTM6S8gVU64B42qj_iUkNJOsCtcgd4lOsCRBmI&loadFrom=DocumentDeeplink&ts=1559.76)):

And then there's other things like monoclonal antibodies, which are very different. So Bezlotoxumab is a human monoclonal antibody where it binds to the toxin of C. diff. And so it's going to neutralize it. So that's very exciting as well. And then there are other therapies that people are looking at like phage therapies, where it's a bacteria phage, it's a virus that actually can target and kill a bacteria. So there are C. diff phage therapies. I think a lot of people are looking at as well.

Tracey ([26:37](https://www.rev.com/transcript-editor/Edit?token=7qQpbtIjW5KMb5iidmUD8B8QW8QUGGVCDTnFg2-7C0wcMNuBiOrHq9n3109_Gq_W9GDYL7EHSY1RjJpHGr50kJ1IGsU&loadFrom=DocumentDeeplink&ts=1597.85)):

Well, so we're not without strategy. We just see which one works best with the fewest side effects in the future.

Casey ([26:46](https://www.rev.com/transcript-editor/Edit?token=r3tqxl3zdtiGximtlFFI5alqd-ijtGZoZyJt1sygzRSPFkB0QmMt97jUvBLeVWTiAyZ6PjrnA7UHDHW2ri3LyWO_xXk&loadFrom=DocumentDeeplink&ts=1606.77)):

Yeah, I think it's just a matter of time now because a lot of these are in phase three clinical trials. And once the phase threes are done that usually, would go forward and be a potential treatment in the near future.

Tracey ([27:03](https://www.rev.com/transcript-editor/Edit?token=i9MfwzyJvj59W-XaQBApB19tGkdLKJRllXBAuObgXcHk5OMJl9JgsQDZOIS0fPhYUUG-1h-pu8IhdidmqPFEaAxd7gc&loadFrom=DocumentDeeplink&ts=1623.92)):

Well, the thing that interests me the most about this when I talked to you about your work is how studying something like C. diff is helping us learn more about just what your gut is doing for your body, not just processing your food, but all of the other things that it's involved with. And keeping you healthy and running and what all these little bacteria are doing and all of the bile acids and all of the secondary products they're making. But my question is what is the coolest thing like in your research and the work that you've done, what is the coolest thing that you've discovered either about C. diff or the gut microbiome, something that you were like, oh, that's so weird and interesting. I didn't know that was going on.

Casey ([27:48](https://www.rev.com/transcript-editor/Edit?token=xiuvsxE9-KAzffAkqbgFYRm0RvunjwxXWhyMLVQMdQkm5v2-ITLntG-Afx5uy34zHvJKWCC8LJiLf9vTHg-nN8Jx6Gc&loadFrom=DocumentDeeplink&ts=1668.23)):

Yeah. And there's actually a lot. So this area of study is fascinating and everyday you're learning new things and you're also learning how much more you have to learn. And so I'll be busy for the next 30 years doing research. So there's a couple of examples of this, which I can touch upon. So we just published a new paper in nature communications driven by my post-doc, former post-doc Dr. Joshua Fletcher, where he had a question, which was really cool. It was trying to figure out if the toxin in C. diff and the way the toxin causes inflammation actually gave C. diff an advantage or was a benefit to it moving forward. So most of my work has looked at how the antibiotics alone, how they alter up that niche, how they alter the gut microbiota, how that creates a foothold for C. diff. His question was different, it was more in when the disease is actually, or the toxin is actually causing inflammation, when you get symptoms and the disease is actually happening, is that giving C. diff an advantage? And what he showed was yes, it is.

Casey ([29:01](https://www.rev.com/transcript-editor/Edit?token=b13z2PS8M62EpblEA90dZ9ZcuUcTniC4BaGY3cau2QGbfwK3VkmjxSBPrkAQKtIFh8Wh8n5c4ZcuXlBhbRC8SObAHHc&loadFrom=DocumentDeeplink&ts=1741.25)):

So he showed that the toxin itself caused inflammation. It altered collagen in the gut, and the breakdown of collagen actually could give C. diff an actual nutrient or a source to actually to grow. And so that was really seminal work recently. And we're going to follow that up further to show if we can actually prevent that from happening once toxin is induced and once inflammation. The other thing that we found recently, which is super novel, and we really haven't talked about it, we haven't published it at all. Is we're working with a group from UC San Diego, Peter Dorrestein's lab. And we're also working with Erin Baker at NC State University College of Science, especially with a talented set of grad students and postdocs in my lab and their labs where they've discovered new bile acids.

Casey ([29:57](https://www.rev.com/transcript-editor/Edit?token=8MUNlSv6-QRt1SMRXQCoRWIHeI1f7KbgF99waDH2jfO4IbBUm6jpu86PSVdCELmLB9YRCok-3epH6PbOieC_eYqsC7A&loadFrom=DocumentDeeplink&ts=1797.11)):

So basically, we've known a lot about bile acid metabolism throughout the GI track. And a lot of the work has been seminal and really static though, in the last, I'd say 50 years about which bile acids are present and with new mass spectrometry, new ohmic platforms, they have discovered brand new novel bile acids, which we never knew about. And so what that's doing is that's opening up a whole new area of exploration with us, with C. diff, but not even with C diff, just understanding what bacteria in the gut are doing, which bile acids they're processing and how that's altering just the normal, healthy, stable microbiota and it's just really cool. And so again, it's another 30 years of work that we have on our hands, but the novel discovery of this is just so exciting.

Tracey ([30:58](https://www.rev.com/transcript-editor/Edit?token=c-U88cxR8YCELPG020PqAB6Y_ezzYKBs_jyP3EohwV5tJGcfboHynM1Scb47XMCMsldRORj2DAcMbJJVAhMp4MnkLUU&loadFrom=DocumentDeeplink&ts=1858.79)):

That is exciting. I mean, it's interesting to me that just trying to figure out how to stop people suffering from a bacterial infection can lead to entirely new discoveries and pathways for investigation. And you definitely picked the best field because you'll be busy forever and never run out of stuff to do.

Casey ([31:19](https://www.rev.com/transcript-editor/Edit?token=thFa7eyPOZS8cDsmHYoIh57hFdpEs2D9tUccy_SL0x6k2oILXRjeHvq7yIA6Mc1KBw_vDcohsSRhDb8dN_XFAlWJo6I&loadFrom=DocumentDeeplink&ts=1879.69)):

And I think a lot of people focus on C. diff too, because there is such a clear relationship with the alteration of the gut microbiota and how it actually can be colonized. I start with C. diff, but I'm also getting into looking at IBD, so other inflammatory disorders diseases, which are much more complicated or metabolic syndrome, obesity, diabetes. So there's a lot of other diseases and disorders that I would like to look at in the context of the GI track and the environment in the GI track. But with C. diff, it's just a very clear, clean relationship. And so I think we can learn a lot by studying it and how the gut environment is changing. Using many different omics platforms is what I do and many other people do. And it will then apply to potentially, or maybe set us down another path where we can then apply and look at other inflammatory diseases in the GI tract or metabolic syndrome or metabolic diseases as well.

Tracey ([32:31](https://www.rev.com/transcript-editor/Edit?token=mNCWgazwqfVXyaxRC__lGA055Pt0ONIe_lD3qLsFovKgGBTWvpHrQsvJ6fjyTpGir0ZDTyLA1zKUibFgU342WFlM0aU&loadFrom=DocumentDeeplink&ts=1951.57)):

Well, thank you so much for being here today, Casey. It has been super interesting.

Casey ([32:38](https://www.rev.com/transcript-editor/Edit?token=kFxNYBcXBsN4Z8z1jIu-UIlCsLJyueU_J3RfCh3O0uWi_oeVjjoIaBllhADL8sbrNnONZkClxlZdNX1BV3io4SpLG0E&loadFrom=DocumentDeeplink&ts=1958.12)):

Cool. Thank you so much having me, Tracy. I've enjoyed it.

Tracey ([32:41](https://www.rev.com/transcript-editor/Edit?token=2p2P-W2o5445q0qtkNdLaU_1TLuu3ex1rZOTqqHv0W_EfvdEb7EYsYC_zgdWrTBanQKn45tTxbASSs0ijuJ2YJ7thSY&loadFrom=DocumentDeeplink&ts=1961.46)):

We've been speaking today with Casey Theriault an Associate Professor of Infectious Disease here at NC State. This has been Audio Abstract. I'm your host, Tracey Peake. Thank you so much for listening.