So you have to take antibiotics. How do you repair your microbiome?

If your answer was "probiotics"...think again.

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If there's one message that I hope has come through loud and clear from this blog so far, it's:

Don't take antibiotics unless you absolutely have to.

And when I say "absolutely have to", I don't mean for things like "my throat's been sore for a whole four days" or "I ate some buffalo chicken pizza that sat out all night, and now I've got diarrhea". These are things that can typically be managed by rest, good nutritious food, tea, and time. For minor GI emergencies, I keep a bottle of a Japanese medication called seirogan in the apothecary, which is plenty effective for things like traveler's diarrhea. [1]

But say you get an STD. It happens to the best of us. (Some would say *only* the best of us.) You probably shouldn't try to manage syphilis by eating right and taking supplements, unless you want your face and brain to slowly dissolve over the next ten years.

But, as longtime readers already know, taking antibiotics impairs your ability to excrete dietary heavy metals like mercury. It's associated with an increased risk of getting multiple sclerosis, probably Parkinson's, and likely a whole host other diseases. These facts are especially concerning when you've got something like Lyme on your hands, which can take weeks or months of heavy-duty antibiotics to clear.

If you take a week-long course of antibiotics **and all goes well**, your microbiome can return mostly to normal within a month. But **whether or not all goes well** depends largely on what you do during the week you're on antibiotics and the weeks that follow. How outcomes vary with diet, lifestyle, drug, and supplement use is an enormously important question, and it's one that hasn't gotten nearly as much attention as it deserves.

Playing Russian Roulette With Your Meta-Genome

For instance: Recently, we talked about the role of bacteria in reducing blood cholesterol levels, by trapping it in the gut as *coprostanol*. I linked a study where they gave 51 people antibiotics for a week, to see how it impacted fecal coprostanol production.

In most of the subjects, the antibiotics knocked down the rate of cholesterol→coprostanol conversion while they were on the drug, and for a short while after. But by five weeks later, most of their microbiomes had recovered: on average,

there was no statistically significant difference from before the antibiotics for the group as a whole.

But the problem with averages, especially when you're looking at large numbers of people, is that they necessarily annihilate the individual's experience. The *average person* will suffer next to no ill effects from lightning strikes in their lifetime, but this doesn't change the fact that—if you're the one guy in a million who gets hit—it really, *really* sucks.

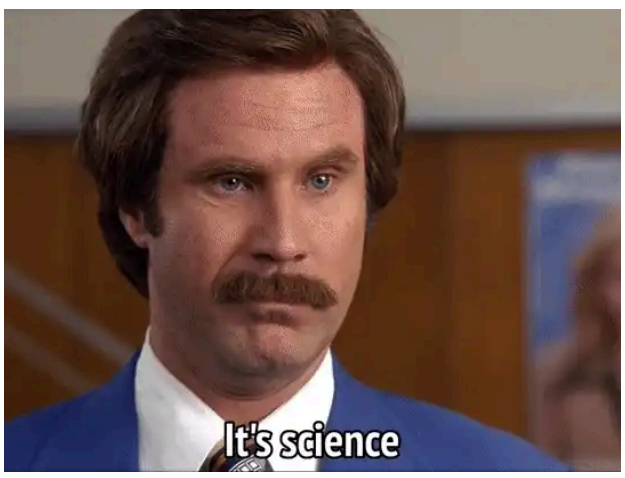
And in that study, the odds were a lot higher than one in a million: 6 of the 51 people saw their fecal coprostanol levels drop to zero…and stay there, even five weeks after they were done with the antibiotics, when everyone else's microbiomes had recovered. Whatever species *had* been there in their guts, helping reduce their cholesterol levels, had apparently gone extinct, or been so crowded out by non-cholesterol-reducers as to make no difference.

What determines who ends up among those unlucky 6? Part of it comes down to chance—maybe some of your "good guys" happen to be resistant to the antibiotic you took—but my guess is that a lot more of it has to do with things like diet and lifestyle.

So, if you've got to roll those dice and take a Z-pack, what can you do to make sure you're **not** one of the unlucky few who ends up with a neurodegenerative disease or high blood cholesterol as a result?

Not probiotics.

Naturally, a lot of people—including many doctors—assume that probiotics are a good place to start. After all, it's right there in the name. Probiotics, that's the opposite of antibiotics. So they cancel out, right?



Unfortunately, wrong.

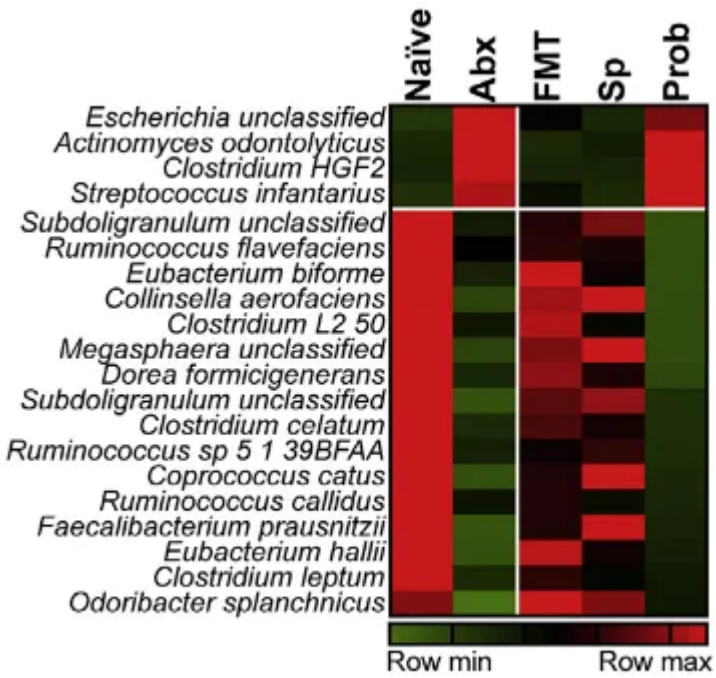
There's *no* good evidence that probiotics can protect the microbiome from the damage of antibiotics,[2] or help it recover afterward. In fact, most of the data we have suggests that probiotics make this damage *worse*.

It's only within the last decade or so that people have started questioning this seemingly common-sense assumption, and it wasn't until about 2018 that a study came out which really tore into it using molecular and genetic techniques. In it, researchers looked at the structure of people's microbiomes before and right after a week-long course of antibiotics—and then regularly over the next few months, to chart how the intestinal bacterial community recovered.

The study sorted participants into three groups:

- One got antibiotics alone.
- One got antibiotics followed by a month of daily dosing with a standard *Lactobacillus*, *Bifidobacterium,* and *Streptococcus* probiotic.
- The third group got antibiotics followed by "autologous FMT", meaning they had a sample of their own stool frozen before they took the antibiotics, which was then used to recolonize their gut with their own flora afterward.

In both humans and mice, the results were clear: after antibiotics, you're **likely better off doing nothing than taking probiotics**.



Here, "Sp" means "spontaneous"—as in, letting the microbiome recover on its own after antibiotics. The takeaway is that probiotics increased levels of *Escherichia* and *A. odontolyticus* (both of which you typically want as little of as possible) while decreasing abundance of key players in the gut ecosystem like *F. prausnitzii* and *Odoribacter*.

The "autologous FMT" was heads and shoulders above the rest: in that group, the microbiome returned pretty much to normal within a day after the procedure. [3] In the "spontaneous" recovery group, which got antibiotics alone, it took about 21 days after going off antibiotics before a person's microbiome was no longer significantly different from the baseline.

The probiotics group **never returned to baseline, even after six months**, when the study's designated followup period ended. Keep in mind, they only got probiotics for the first month after antibiotics—but that was enough to alter their GI ecosystem semi-permanently.

A little learning is a dangerous thing

Maybe you've heard that most probiotics don't "engraft": they don't colonize the gut and hang around to eat your food and reproduce, the way your indigenous bacteria do. This is why you need to keep taking them if you want whatever benefits they're supposed to offer. Under ordinary circumstances, this is correct.

But a big part of the reason for this is *niche competition*. A lot of the bacteria in your average probiotic are isolates from yogurt, which means they've been bred for billions of bacterial generations to be good at making yogurt—*not* at surviving in a human

body or helping us function, except to the extent that it's useful to be able to turn milk sugars into protein.

These strains are like Yorkshire terriers: if you release them into the wild, they're not going to survive very long. They'll have a hard time competing with the local foxes and hawks, and might even end up as hawk food. But if you killed off 95% of the animals in the forest, and *then* released your terriers—well, you'd have a good shot at establishing the most ridiculous population of feral dogs the world has ever seen.

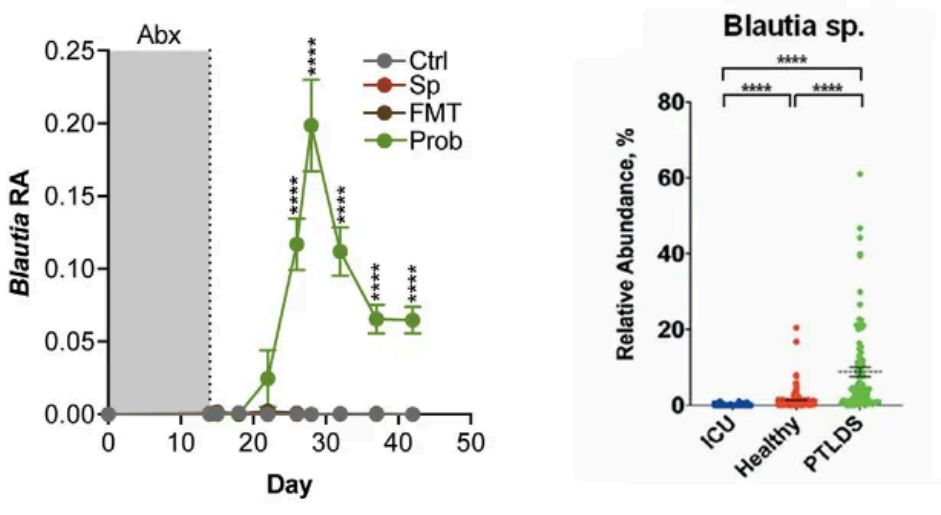
My point is: clearing out the microbiome before starting a probiotic regimen *does* improve the probiotics' ability to colonize the GI tract, by eliminating that niche competition. As a result, in that study, it didn't matter that participants stopped taking the probiotic after one month; the bacteria in it had taken root in the gut, and prevented the health-critical species like *Faecalibacterium* from returning even months later.

This is a bad thing, the same way that having a colony of brewer's yeast set up shop in your GI tract [4] is less like "free beer" and more like "perpetual hangover any time you eat a carbohydrate, and also cirrhosis". It's a little like wishing on a monkey's paw for free yogurt, only to find that everything you eat is turning into some form of yogurt once it gets into your intestines, and it's really hard to live on yogurt alone.

It's a perfect example of why the microbiome is powerful magic. It's largely autonomous and self-perpetuating, which is why it's so promising: the ability to chronically alter someone's biology with a one-time intervention lets us start talking about *cures* for conditions that, thus far, we've struggled even to *treat*.

But it's important to remember that right now, we're all just Mickey Mouse cracking open the sorcerer's spellbook, and nobody really knows what they're doing. Just because something is on the market doesn't mean it's universally safe, especially in combination with drugs like antibiotics. I'm not trying to fearmonger here, just to point out that you should think carefully before swallowing a living thing—because it's pressing a button that you might not be able to un-press.

One more point of interest before we leave this study and get on to what ***to*** do, rather than what ***not*** to do. In that study, the probiotics generally suppressed a lot of important species, but there were a few kinds of bacteria that thrived in the environment created by the probiotics, both in mice and in humans. One of them is *Blautia*—which was roughly 1000x as abundant after the antibiotic/probiotic regimen compared to control mice. This is intriguing, because a drastically elevated abundance of *Blautia* is one of the key signatures of "Post-Treatment Lyme Disease Syndrome", or PTLDS.



Left: Probiotics after antibiotics in mice caused *Blautia* to take over the gut in a really startling way, making up a full 20% of the animals' fecal microbiome at its peak. Typical levels are on the order of 1%. Right: *Blautia* abundance is also abnormally high in PTLDS as compared to healthy controls or patients in the ICU who had received antibiotics.

PTLDS (and "chronic Lyme" more generally) deserve their own post—but the gist is that many people who get Lyme disease, then get proper treatment, still feel like shit months or even years later, despite the absence of detectable Lyme bacteria in their bloodstream. This has left a lot of patients convinced that No, the doctors just haven't looked hard enough, and the *Borrelia* is still there, just hiding somehow. I'm all for believing patients' lived experiences, but it seems likely to me that a lot of these people's suffering is the result of collateral damage to the microbiome caused by the months-long course of antibiotics used to *treat* the Lyme. Since only a fraction of Lyme patients go on to develop PTLDS, maybe there's some lifestyle or dietary factor that predisposes a person to it. Seeing this study, I have to wonder if it might be probiotics.

What TO Do

Think of this as a chance to reboot your gut microbiome.

Ordinarily, your large intestine is like a battlefield, where every square inch of territory is occupied by the biofilm of some species, friend or foe. And it's trench warfare. With the right foods, it's possible to tip the scales in favor of the good guys, but for them to gain ground in a way that leads to lasting improvements in health, they've got to claw that terrain from someone else and become well-established enough that they don't lose it again next time you do a late-night Taco Bell binge. This is part of why it takes weeks or months of adherence to a healthy diet before you see benefits in chronic disease. Still, there are good things about this arrangement: it's why a fast-growing pathogen can't just waltz in and rout the allied forces.

But by wiping the battlefield nearly clean, antibiotics amplify the impact of your dietary choices. A typical course of antibiotics is unlikely to eliminate *all* of any given species—but reducing the total number makes it a mad dash for the remaining bugs to grow back and claim the land that's been wiped clean. Whatever bacteria get fed first have a huge advantage in that race.

So this is when it really counts. Eat right. No alcohol, no soda, no processed foods. Simple sugars feed fungi, which are already at an advantage because most antibiotics don't target them. Eat organic, and cook for yourself as much as possible, creating as

diverse and nutritious of a diet as you can. I've recently seen someone recommending "eat twenty different plant products every week", and while this is a lot for most of us to manage habitually, it's certainly doable for a week or two—especially when your long-term health hangs in the balance.

Eat whole grains, and fish, and nuts. Eat natto (see this post); it suppresses fungi like *Candida*, and contains a unique polysaccharide called levan that selectively feeds *Bacteroides* and *Lachnospiraceae*. Eat apples like it's your job. Beans are a good source of unique fibers, but fresh vegetables are really critical; get whole broccoli heads at the store, and **slice the stems into the steamer along with the tops**; these "woody" bits contain lignin, another unique plant polysaccharide that's not found in the soft leafy parts. A lot of the as-yet-uncultivated gut microbes that are protective against depression and mental illness are closely related to bacteria that require lignin for growth.

Get watermelon, and dark chocolate, and berries—the cheesy advice about "eat the rainbow" applies: most biological pigments are polyphenol-based, which provides selective food for SCFA-producing symbionts like *Bacteroides.* Tea and coffee are good, as are herbal teas like ginger; there's a reason these things have been major components of herbal medicine for millennia.

The same goes for herbs and spices; a lot of these have selective antimicrobial properties, which is part of why they smell good to humans. You don't need to go overboard, though; I've seen people mess themselves up by taking oregano oil at concentrations that are fully bacteriostatic in the lab, and this is another case of "a little learning is a dangerous thing". The antimicrobial activity of a lot of natural compounds varies by species, so the point is not to kill all the bad bacteria, but to infuse your food with chemicals that slow the growth of pathogens without impairing the symbionts. (A good rule of thumb is: if it tastes gross, it's too much.) This is also why taking things like garlic pills is a mug's game—it should be incorporated into the matrix of the food to be effective, or at the very least taken with the food so it has a chance to mix in the stomach.

So make some mashed potatoes for the good starch, load 'em up with fresh garlic herb butter, and throw some cream cheese in for the milk oligosaccharides and lactic acid. (Animal fats feed unique sub-groups of *Bacteroides* and *Prevotella*, and these are both associated with better weight control and metabolism.)

While you're *on* antibiotics, some recommend a diet low in non-absorable carbohydrates. This is probably sound advice, because by this point we've all got some antibiotic-resistant organisms living in our guts, so pouring too much "bug food" into the ecosystem while it's being periodically blasted with azithromycin is a recipe for trouble. Here, as always, listen to your body: if fruits and veggies are going right through you while you're on antibiotics, don't try to "power through"; opt for things that don't require much microbial action to ready them for absorption by the body, like rice and eggs. Kitchari, an Indian blend of rice, yellow mung beans, and spices, is one of the easiest things on Earth to digest, and is often given to weaning children as their first solid food. It's a little bland and gruel-y, but it's a complete protein and I suspect

the spices do a good job of keeping the calories from falling into the wrong hands—turmeric is a solid antifungal.

It might sound silly, but one other thing to keep in mind (whether or not you're on antibiotics): chew your food well, even if it's something soft like kitchari. Saliva and stomach acid are the key first steps in the digestive process, and if food isn't mashed to a homogeneous paste before you swallow it, they can't do their jobs. On that note: eating actual yogurt is probably fine—your stomach acid will take out most of the live cultures, preventing the engraftment effects we discussed earlier. Getting clever with things like enteric-coated capsules is where we start to run into trouble.

Yogurt may even be helpful for a recovering microbiome, because of the abundance of lactic acid in it. This can serve as a substrate for bacterial oxygen-reducing enzymes that maintain the anaerobic state necessary for a healthy gut. Opportunistic pathogens like *E. coli* and *Klebsiella* thrive in oxygen, because they can "breathe" it as part of their metabolism in much the same way our bodies do, whereas most gut symbionts can only get energy through anaerobic fermentation. Respiration yields about twenty times as much energy as fermentation per molecule of fuel, so keeping O2 levels down is a key part of how good bacteria level the playing field and prevent pathogens from growing out of control. When the microbiome is decimated by antibiotics, it can lead to a vicious cycle where O2 levels rise and prevent the symbiotic bacteria that would produce these oxygen-reducing enzymes from growing back. Succinic acid is another substrate that can power these oxygen-reducing enzymes. Although I don't know of many foods high in succinic acid, it's a popular dietary supplement in Russia that goes for about ten bucks on ebay. If any readers are looking to get experimental, I'd be very curious to see if those have any impact on gut health.

Caveats, and caveats to the caveats

Over the years, there have been dozens of trials on various probiotics as a preventative against some of the medical side effects of antibiotics, and—if you look at these studies all pooled together, the data suggests that probiotics can at least reduce the odds you'll get diarrhea by about 40%.

However, it's important to consider things like publication bias. Even if an intervention does nothing, one in twenty studies on it will end up finding a statistically significant ($p<0.05$) effect. So say you're a research clinician, and you test out a commercially available probiotic in a small but well-designed trial. It doesn't help your patients. You might publish that result, or you might just use it to inform your own practice—most scientific journals aren't really interested in negative results anyway. By the same token, if you work for a company that's making a probiotic, and you run a trial that fails, you *definitely* don't publish that.

This effect, applied over decades and worldwide, can seriously skew the literature so that meta-analysis reveals a fictional effect that's nearly impossible to control for. And when a bunch of the individual studies find no effect in preventing *C. diff* or other symptoms, I'd call that evidence mediocre at best.

It's also important to consider that the studies in that meta-analysis were just looking at likelihood of diarrhea, which is an endpoint that tells you next to nothing about the probiotics' effect on the diversity of the microbiome or its overall health. A

Saccharomyces probiotic might reduce the odds of diarrhea, but give one in twenty people a slow case of auto-brewery syndrome and we wouldn't know it from that kind of literature.

As usual, most of the advice we can derive from the latest literature seems to reduce to things we already knew about how to eat right. Still, in my experience the hard part isn't knowing what to do—it's finding the motivation to do it. If you're anything like me, any light we can shed on *why* to do the thing makes it a lot easier, so hopefully these words have been helpful in that regard. So cook yourself a good nutritious meal and turn down the beer when you go out to see some friends, knowing that you're making a good long-term investment in yourself and your health.

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1 It's also delightfully weird. The pills are squishy, black, and smell so strong of wood pitch that—even in a sealed glass bottle—it will make the room smell like a cheery campfire unless you keep it in a drawer.

2 Technically, this isn't entirely true: there are some probiotic strains currently on the market which have antibiotic-resistance genes that work by degrading the drugs. If you take one of these at the same time as your antibiotic, it might protect your microbiome from some of the damage of the antibiotic—by destroying the drug, making it as if you've just taken less of it. But in that case, it's not going to do any good against the pathogens you're taking it to treat…so why bother?

3 I've been told there's a company offering this as a service—where they'll prep your poop sample and store it in a -80°C freezer until you need it to reconstitute your microbiome—but I haven't looked into it, and I suspect it's criminally expensive.

4 Yes, you can end up making prison hooch in your GI tract; it's called auto-brewery syndrome. No, it's not fun. I can tell you from personal experience that being intoxicated all the time stops being enjoyable really quickly without the occasional break. (I never had auto-brewery syndrome or anything, I just went to Indiana University for undergrad. HOOsiers!)