Mycobiome, Yourcobiome

Morel Dilemma Episode 9 Script. Written and copyright Elizabeth S Gall 2017.

Izzie: Hey guys, this episode is about the microscopic critters that inhabit the human body, and about some normal functions and diseases of the body, including the gut, mouth, lungs, and female reproductive system. If you're squeamish, eating lunch, or listening with someone sensitive to those topics, this episode might not be for you.

[Music begins]

Izzie: Welcome to Morel Dilemma: an exploration of why some mushrooms are so highly sought, some are so heavily cultivated, and some are so very dangerous. I'm your host, Izzie Gall. And to the fungi living on every surface of my body: hello, I am your host as well. Today, we'll be diving into the most intimate fungi around: the human mycobiome.

[Music ends]

Izzie: The *micro*biome is the collection of bacteria that live in and on the human body, outnumbering the human cells. They are largely beneficial, and when they aren't beneficial, they're mostly commensal - basically, they don't bother us at all. The human microbiome has been extensively studied; while the word only entered everyday life in 2000, the earliest usage I've found is from 1894. (Thanks, Google Books!) As a result of this long history, we know that the bacterial microbiome plays a role in almost all of human function - from physiology to immune system function and even neurological development! But what about the *myco*biome?

The mycobiome is the community of fungi that live in and on us. It's much less studied; the term was only coined in 2010. Before that, people did not think about fungi as anything less than signs of illness. There was actually a flare-up of mycophobia in the 1980s because new DNA analysis techniques revealed a lot of fungi in people's mouths and feces, and these were interpreted as infections that needed to be stopped. In fact, this frame of mind still isn't gone - researching this episode, I came across a study from 2014 that only considers mycobiome fungi as factors in disease or potential pathogens. But we are starting to understand that like bacteria, fungi have important roles in human metabolism and immune function, and even help the microbiome do its job.

All the same, research on the mycobiome is seriously lagging. PubMed, the online library for the National Center for Biotechnology Information, is often used as a yardstick to see how much research attention different topics are receiving. On Dec 20, 2016, I searched PubMed for papers about the human microbiome, and found 12,379. By contrast, my search on the human *myco*biome only had *forty-one* hits. For

the most part, mycobiome research still focuses on disease states - that is, what a person's fungal communities look like when they aren't at their best. This can make it hard to understand what fungal community represents the disease state, as opposed to what's ordinarily around in someone healthy. Because that's where the funding comes from, the best thing for healthy-state mycobiome research might actually be discovering more illnesses that involve fungi. That's why a new study might temporarily worsen the mycobiome's reputation while improving our understanding of it.

[Musical tone]

Izzie: Crohn's disease is one of those conditions that's either completely invisible to you or rules your life. A form of irritable bowel disease, Crohn's is an inflammatory disorder that affects the gastrointestinal tract and can lead to abdominal cramping, persistent diarrhea, bleeding, and irregular bowel movements, not to mention loss of appetite, weight loss, and general fatigue. It's a chronic illness that gets progressively worse and can sometimes lead to life-threatening complications.

Though it was first described in 1932, there is no cure for Crohn's disease, and the base cause is unknown. It's generally hypothesized that some of the bacteria that inhabit the healthy human gut are mistakenly targeted by the immune system, leading to inflammation. Because the bacteria belong in the gut, they don't go away, and the inflammation only gets worse. Since the cause is not known, there are no real treatments. Instead, there are several recognized ways to manage the symptoms and put the Crohn's into "remission". One common method is to give the patient immunosuppressants, which obviously isn't a great long-term solution because it makes the patient very susceptible to new infections. Another method is to surgically remove the inflamed parts of the intestine, which is obviously an even *worse* long-term solution, especially because the swelling can spread to new areas, and there's only so much intestine you can remove!

Crohn's disease is estimated to affect 700,000 Americans, but is prevalent in other developed countries and is becoming increasingly common. It runs in families - five to 20% of Crohn's sufferers have a parent, child, or sibling who also suffers from the disease. Basically, it's a huge problem, and people have been trying for a very long time to figure out what causes it and how it can be cured. Well, as with the lichen mystery from Season 1, this is a mystery that's been at least partially solved by finding a fungus in a three-part interaction. Funny how that worked out.

In September of 2016, Dr Horeau and other researchers published a study of the gut microbes in families where some members suffer from Crohn's and others do not. By comparing the microbes between the ill and healthy family members, the researchers could confidently identify more factors of the disease. They found that it's not just the bacteria in the gut that the immune system mistakenly attacks; it's a mat of microbial goo that two bacteria and one fungus make together.

Sometimes, when bacteria and/or fungi are living together, the enzymes and other materials they secrete turn into a physical and chemical structure that protects them. This structure is called a biofilm, and it's generally a good thing for microbes. It keeps them safe from environmental dangers, like dehydration or, say, their host's immune system. In individuals with Crohn's disease, the biofilm is mistaken for a disease-causing infection, but the biofilm protects itself and its member microbes from attack. The immune system keeps trying to defend the body from something that isn't really a problem, and a chronic disease develops.

The bacteria contributing the biofilm, were already known to be elevated in Crohn's patients over healthy individuals. The newly discovered member is a yeast, *Candida tropicalis*. Though it's not fun from a medical standpoint, the interaction is pretty neat from a biological perspective: the *Candida* interacts with each bacterium in a way that makes the three-part biofilm thicker and more resilient than the biofilm any of the microbes makes individually, *or* in pairs.

While knowing about the biofilm might help researchers develop new treatments for people living with Crohn's disease, it doesn't get us any closer to understanding why the immune system attacks the biofilm in the first place. This study isn't going to cure Crohn's. But it does demonstrate, once again, that fungi hiding in plain sight might be important parts of problems we're trying to solve or understand. With that in mind, the rest of this episode is devoted to what we currently know about our intimate fungal friends. We'll start with the practical differences between the microbiome and the mycobiome, and talk briefly about the role of antibiotics in maintaining or breaking the balance. Then we're off on a full tour of the body and the fungi that live with us when we're healthy - and take advantage of us when we're not.

[Musical tone]

Izzie: Because of handwashing campaigns, you probably know that bacteria and fungi are living on every surface of the environment, and we're constantly exposed to them. It makes a lot of sense that microbes might get onto our skin. But how do they get inside of us?

It's generally theorized that a baby's first exposure to the microbes that will colonize its body is when it travels through the vaginal canal during birth. In 2007, a study of 10 healthy, vaginally delivered babies found that the fungal sequences present in the mother's vagina are also usually found in the baby's first feces. A study on mice in 2008 found that babies born by C section also had some of the mother's microbiotic bacteria in their first stool. Within days of birth, the human gut microbiome already outnumbers the baby's cells, and by the time the infant is one year old, their gut microbiome looks very much like an adult's.

If fungi and bacteria are both present from the time of birth, and they're both microscopic, you might think it should be just as easy to study both of them, and the

lag in mycobiome research is only due to mycophobia. In fact, our mycobiome is much harder to study than our bacteria. For one thing, fungi make up less than 0.1% of our overall microbiome. Bacterial biomass is 1000 times greater than fungal mass in our bodies, so even when fungi are isolated, it can be hard to know if we're getting all the members of the community. That makes it super hard to study how the fungi interact with each other, with bacteria, and with our cells.

Another issue is that fungal cell walls contain chitin, the same thing bug exoskeletons are made of. Those tough walls have to break if scientists want to get at the DNA that tell them what species are present. Because they're so tough, any method scientists use to crack open fungi are also going to break open any human cells in the mix, contaminating the fungal samples and making them harder to identify. Scientists can use specific primers that exclude human DNA, but as we know, restricting your library can make you miss something important. Add that to the fact that fungal libraries are generally smaller than bacterial libraries: GreenGenes, the most up-to-date reference library for species identification, has 203,000 bacterial genomes but fewer than 65,000 fungal genomes available.

Scientists can try to work around the problems of contamination or low sequence abundance by using culture-based methods. See, to sequence the DNA of a cellular soup, you don't need them to actually *grow*. But if you try growing the microbes instead, you can use something called selective media to grow only fungi, excluding bacteria and human cells. This can be a good way to find out about fungi that grow in very low abundance and can't be found with mass sequencing methods. The best thing is to combine culturing and culture-free methods, because each of them catches different species. In the study that coined the term "mycobiome", researchers found 101 fungal species in subjects' mouths, fewer than 70 of which could be cultured. A different study on the gut mycobiome found 37 species by sequencing, but two were grown in culture that the culture-independent method hadn't revealed. Those hard-to-detect species often have an effect far exceeding what you would expect for microbes of such low abundance.

[Musical tone]

Izzie: The last thing we need to talk about before diving into the wacky world of which fungi are crawling all over which parts of you *right now* is antibiotics. First things first: antibiotics don't work on fungi. Antibiotics are antibacterial agents. This also means they don't work on viruses, so if anyone tries to tell you to take antibiotics for a cold or other viral infection, don't do it. It won't help and it will actually probably only make your health worse.

Why? Because antibiotics don't target just problematic bacteria like the ones that cause Strep throat or whooping cough. Antibiotics are general medications that target *all bacteria.* And with the bacterial cells outnumbering your human cells by the time you're two weeks old, helping with things like immune and neurological

development, you might imagine that killing all your bacteria at once is a pretty bad plan. Ideally, antibiotics kill whatever gnarly bacteria are causing you distress. But what are they doing to all the good and useful bacteria in your body?

[Musical tone]

Izzie: The effect of a course of antibiotics depends on many factors - the specific antibiotic, what bacteria you're trying to eradicate, how long you take the medication, how long the medication stays in your body, etc. But all antibiotics seriously decrease the overall density and diversity of your microbiome. Once the helpful bacteria are killed by antibiotics, your risk of getting a new illness actually increases. Sometimes, bacteria and fungi that are perfectly safe inside you in small populations overgrow in the clean post-antibiotic landscape, which can lead to problems.

Another issue arises from antibiotic resistance. This doesn't mean that you yourself become resistant to antibiotics, but that the bacteria inside you do. Because of natural variation, it is likely that some of the bacteria in your gut, helpful or harmful, will be able to survive some antibiotic treatment of certain types. When the non-resistant ones get killed off, the resistant ones remain. This can reduce the efficacy of new antibiotic treatments, and the effects can stack until bacteria are resistant to multiple antibiotics. In some studies, resistant bacteria have been found in the guts of people who haven't taken antibiotics in four years. One study of two unrelated, healthy individuals who had not taken antibiotics in one year found that they had gut bacteria resistant to 13 antibiotics. Some of these might not even be antibiotics the subjects took for their own infections, but might have been ingested in food, which is why people are so concerned about antibiotic use on food animals like cows.

[Musical tone]

Izzie: Why am I discussing antibiotics in a fungus podcast, if they don't kill fungi? Well, for one thing, antibiotics are increasingly prevalent and I think it is important to be aware that they aren't a side-effect-free cure-all. But also, remember how microbes that are fine in small amounts become problematic when their populations overgrow? Fungi do this a lot. Antibiotic usage has a big effect on how many fungi of various types are in your body. Also recall the breakthrough in Crohn's disease from the top of the episode: fungi interact with the bacteria in your body in important ways, for better or for worse. Altering your bacterial population also influences how your fungi work.

And your fungi work very, very hard.

[Intermission music]

Izzie: Now it's finally time to talk about the human mycobiome in detail! I'll let you know how much research has been devoted to bacteria or fungi in each part of the human body, as of my PubMed search on December 20, 2016. Then I'll tell you about what fungi live in that area when we're healthy, and when we aren't. While there's less research

on the mycobiome than the microbiome, I still wasn't able to read ALL the research out there. I only read 14 academic papers and a few more academic paper summaries and also some articles. The point is, this will be a pretty good summary of current research, but does not encompass all human knowledge of the mycobiome, limited though that knowledge may be. Also: I am not a doctor, and none of the stuff in this episode should be used to diagnose or treat any condition.

[Musical tone]

Izzie: Let's start with our very biggest organ, the skin. The outer surface of our bodies gets the most exposure to new bacteria, fungi, and viruses. PubMed has 551 papers on the skin microbiome, and only seven on the skin mycobiome. Generally, bacterial populations are similar if they live in similar environments on the skin - for example, dry locations like the elbow or the shin will have similar bacterial populations, which will be distinct from the populations in oily areas like the face. On the other hand, fungal populations are grouped by location, so the elbow and shin populations will be distinct. Skin microbes are sampled with either swabs, which don't break the surface of the skin, or scrapes, which pull off some outer skin cells but don't draw blood. The skin is the least fungally diverse region of the human body, and is overwhelmingly dominated by a fungal genus called *Malassezia*. (A genus is a group of closely related species.)

Malassezia species grow by eating lipids, or fats, off the host. First discovered on human skin 100 years ago, they are the dominant fungi on almost every human skin site that's been studied, and are also abundant on the skin of every other warm blooded animal ever tested. Not only that, *Malassezia* fungi also live in the deep sea, in hydrothermal vents, and on lobster larvae, corals and sponges. An imbalance or overgrowth of *Malassezia* is associated with dry-skin conditions like dandruff, dermatitis, and eczema. Imbalance of other fungi can cause problems like athlete's foot. Fun fact: the most abundant fungal species in the outer ear canal and on the sole of the foot is *Malassezia slooffiae*, which is amusing to spell and even more fun to say. "Sloofiae."

[Musical tone]

Izzie: Up next on our tour is the mouth, the body's major "port of entry". The mouth has a lot of little pockets that make different localized environments, and each micro-environment has a different microbial community. The mouth is actually one of the most microbially diverse areas of the body. Searching for the human oral microbiome on PubMed will return 1834 hits, while the oral mycobiome only gets twelve. Oral communities are tested with cheek or gum swabs, or with the classic rinse and spit method.

Strangely, for a long time the only research on the oral mycobiome was related to the symptoms of individuals with HIV-AIDS or other immunocompromising conditions,

so it took a long time for scientists to learn the baseline of a healthy mouth mycobiome. Recently some studies have investigated how the fungal community looks in healthy individuals, and there is a lot of individual variation. In 2010, a study led by Dr. Ghannoum found a total of 101 culturable fungal species in the oral cavities of 20 participants, though one person has from 9 to 23 species. Various studies have found 74 culturable and 11 non-culturable fungal genuses, or genera, in the oral mycobiome, though any one person has only about 15 genera, and 39 genera were only found in one subject. To put this in perspective, a healthy adult's mouth may have species from 50 to 100 bacterial genera.

Abundance in human populations doesn't necessarily imply abundance in the human mouth. While 75% of the participants in Dr. Ghannoum's study had yeasts from the genus *Candida*, a 2014 study led by Dr. Dupuy found that one person's oral fungi may only be 9.5% *Candida*. Similarly, the genus *Cladosporium* appears in 65% of Dr. Ghannoum's subjects, but makes up only 3% of an individual's oral mycobiome. There are also species from these studies that don't overlap, including almost one third of the fungi isolated from Dr. Dupuy's subjects. Even more mysterious, every subject's mycobiome, in both studies, was half composed of unclassified fungi that were not possible to cultivate! So there's still a long way this research needs to go.

When the oral mycobiome goes out of whack, the fungi can contribute to gingivitis, serious gum infections, and oral candidiasis - which basically means "a lot of *Candida* fungus in your mouth". Remember that *Candida* fungus is supposed to comprise about 9.5% of your oral mycobiome; this is another example of disease that happens when your fungi get overgrown. In 2014, a study led by Dr. Mukherjee found that while oral bacterial genera are similar between HIV-infected and uninfected subjects, the fungal genera are significantly different. In fact, oral candidiasis is the most common complication of HIV infection, which is why there was so much early research on the oral mycobiome of HIV patients. HIV and other immunocompromising diseases, including cancer, can lead to imbalance in the microbial community as surely as antibiotics do, causing fungi that are perfectly safe in low abundance to overgrow and cause issues. Other oral infections caused by such fungal overgrowth include the genera *Aspergillus, Cryptococcus*, *Fusarium*, and *Alternaria*.

[Musical tone]

Izzie: Working our way down the body, our next stop is the lungs. If you've ever lived through flu season, been on a plane, ridden public transit, or gone to a conference, you know that microbes are in the air, in every breath you breathe. For a long time - until the year 2000, actually - doctors were still operating under the assumption that healthy lungs are sterile lungs, and no microbes make it past the trachea. By contrast, some studies in 2016 investigated the inter-kingdom relationships between lung microbes. We now know that microbes thrive all the way into the lower respiratory tract. PubMed has 356 articles regarding the human lung microbiome, but only four for the

mycobiome. Still, based on those four studies, it seems that respiratory fungi are present in both healthy and diseased individuals, with fungal diversity highest, and overall fungal abundance lowest, in healthy people.

The microbes of the lung are usually sampled in a way that is called "induced sputum" and sounds pretty uncomfortable: the subject is asked to intentionally inhale some saline, and then they cough it back up. Sampling can also occur in an even less pleasant way called bronchoalveolar lavage. In this method, doctors send a small tube into the lungs via the nose or mouth, squirt some saline into a small portion of the lungs, and then suck it back up into the tube for analysis. Besides being uncomfortable, lung sampling of either type has a scientific flaw: because the sputum and tube both have to pass through the mouth or upper respiratory tract, the sample could become contaminated. Researchers could find a fungus that actually lives in the mouth, for example, and think that it's actually from the lungs. The best way to correct for this is to also sample the mouth alone, to establish a baseline community.

Like the oral mycobiome, lung fungi are highly variable between individuals - one study I read found that the so-called private species, which are found in only one subject, can outnumber the shared species, which are found in multiple subjects. The study was quick to point out that the high number of private species in the lung could be due to misidentification or sampling error - for example, when the lung sample traveled through the highly diverse oral mycobiome.

Overall, the most common fungal genus in the healthy lung seems to be *Aspergillus*, which you may remember from our tour of the mouth - but that finding probably isn't due to contamination. A 2012 study led by Dr. Charlson found that samples of bronchoalveolar lavage are more similar to oral washes from the same person than they are to the lavage of other people, indicating that the lung mycobiome arises from the oral mycobiome.

Lung diseases from the mycobiome crop up because the cell walls of fungi can contain molecules that activate immune cells, leading to inflammation that can cause lung disease or make existing lung disease worse. As in the mouth, decreased fungal diversity is associated with illness, including asthma, lung transplant complicatons, and cystic fibrosis, a genetic disease that involves the progressive buildup of mucus in the lower lungs.

Scientists are beginning to see low fungal diversity as a cause of poor respiratory function, rather than just a symptom of it. Lung disease may be influenced by the loss of some species that are normally present in small amounts but are disproportionately important to the lung biome. The fungal community is thought to shift after a person takes immunosuppressants or antibiotics, such as those administered after a lung transplant. As in the mouth, illnesses may also be caused by overgrowth of a fungus that is normally kept in check by the diversity of the community. This is why diseased individuals usually have lower fungal diversity but

higher fungal abundance. The most common fungal genus in the diseased lung is *Candida*, which you'll also recall from the mouth, as well as from the Crohn's study at the top of the episode.

Some of the fungal spores found in people's lungs have included macrofungi - the fungi that can make mushrooms. These spores are inhaled from the environment, but the fungi don't live in your lungs, and you cannot have mushrooms grow in your lungs. However, people who work extensively with basidiomycetes, like button and oyster mushrooms, can develop pulmonary issues known as Mushroom Worker's Lung. The condition was initially reported in the 1950s, but become increasingly common as the specialty mushroom industry expanded. Essentially, a large volume of spores gets into the lungs and the immune system reacts, leading to respiratory distress of varying degrees. Some time away from the factory is usually all that is required for full recovery. The most common type of Mushroom Worker's Lung actually comes from the compost made for button mushroom production, as single-celled fungi fly around on drafts of warm air radiating from the hot compost.

If inhaling a lot of fungal spores leads to pulmonary distress, you might imagine that trying to get high by inhaling a lot of spores would be a Bad Idea, not to mention ineffective. Strangely enough, people have actually tried it, and guess what? It was a Bad Idea. I wish I were making this up. In April of 1994, several teenagers in Wisconsin were having a party with no illegal drugs, and I guess they wanted to compensate. Several teens deliberately inhaled the spores of puffball mushrooms, and within 12 hours had developed nausea and vomiting. Within a week, eight of them had developed cough, fatigue, shortness of breath, muscle aches, and fevers up to 103 degrees. These are the kids who went to see doctors, and they're the reason we know about the party.

Five of the teenagers had to be hospitalized, and *Lycoperdon* puffball spores were found in their lungs, surrounded by inflammation. When the spores were isolated from lung biopsies and put on culturing plates, they didn't grow. To reiterate: mushrooms can't grow in lungs. All of the teenagers fully recovered after less than a month of treatment with antifungal agents and corticosteroids, anti inflammatory drugs commonly used to treat bronchitis.

So remember, kids: Just say "No" to inhaling a lot of puffball spores for no reason.

[Musical Tone]

Izzie: Our next stop is the one that's gotten the most microbial attention: the gut. This is the site of the greatest quantity and diversity of the human microbiome, with more than 1 trillion organisms present. Recall that by the age of two weeks, a human baby's cells are outnumbered by the cells in its gut. An adult human's cells are outnumbered 10 to 1 by the cells in the gastrointestinal tract!

Microbial density increases moving from the stomach to the colon. The stomach contains fewer than 100 microbial cells per milliliter, while in the colon the density might be up to one *trillion* cells per mil' [milliliter]. Sampling is usually done by taking fecal samples, as they are noninvasive. It's hard to know the living locations of the microbes when they are isolated this way, but this type of sample does give a good "snapshot" of the microbially dense colon.

Ninety-nine percent of the genes isolated from the gut microbiome are bacterial, which can make it very hard indeed to find the fungi. In PubMed, the human microbiome has 2,676 studies, while the mycobiome has only fourteen. While the gut mycobiome was first studied in the 1900s a 50-year gap in gut mycobiome studies between 1917 and 1969 means the fungal players are still pretty mysterious.

Here's what we do know: Seventy percent of the healthy adults studied have detectable fungi in all sections of their gastrointestinal tracts. While gut bacteria are comprised of 500-1000 species, only about 270 distinct fungal species have been found in the gut, and most of them only appear in one study. More than half of those species come from one 2013 study. The research, led by a Dr. Hoffman, studied 98 healthy people and found 184 fungal species, covering 66 genera. Not all of these species necessarily live in the gut - as with spores in the lungs, some of them are taken in from the environment. These include the yeasts present in bread and beer, *Saccharomyces cerevisiae*, which is the second-most abundant fungus in the human gut. Overall, the genus *Saccharomyces* was found in 89% of Dr. Hoffman's subjects. Fifty-seven percent of subjects had *Candida* species, which we also saw in the mouth and lung, and 42% had *Cladosporium* fungi, which you may also recall from the mouth. *Malassezia*, the prolific skin fungus, is also common in the gut.

The different fungal species in the gut interact with each other, and with bacteria, to help us digest various compounds that we humans couldn't digest otherwise. Bacterial-fungal interactions are also important for gastrointestinal health and the health of the host, as we saw in the Crohn's study from last year. For a more positive example, *Saccharomyces boulardii* stimulates other microbes to produce compounds that are toxic to *Clostridium difficile*, a bacterium that causes diarrhea. Some *Candida* yeasts express toxins that prevent invasive or pathogenic fungi from invading the gut. Finally, the presence of certain yeasts can promote good bacteria, keeping the host healthy.

Unlike most areas of the body, where disease correlates with lower microbial diversity, in the gut a diseased biome is a more diverse biome. In a pattern that should feel familiar by now, other illness in the body permits the growth of fungi that can't usually colonize the gastrointestinal tract, or are usually present in the GI tract in low numbers. *Candida albicans*, the most prevalent fungus in the gut, can take advantage of an immunosuppressed host to spread throughout the body and cause problems. *Aspergillus* is a genus of filamentous fungi that is very common in the environment,

and the genus is the main source of gut infection in immunocompromised people. The guts of obese people have increased abundance of certain ascomycete fungi compared with non-obese subjects, but nobody is sure if that's a cause or a symptom. Also, studies go back and forth on whether the gut microbiome has a role in obesity, so take the sensationalist news stories with a grain of salt.

[Musical tone]

Izzie: Now at last we arrive at the mycobiome studies that only apply to half the population. The vaginal mycobiome is the least studied of all the areas we've explored this episode, with only three articles on PubMed. The vaginal microbiome, however, has 557 - more PubMed hits than either the skin or the lungs. A lot of that focus is because, well, the vagina is where most babies come from, so it's a good place to look if you're trying to figure out where the microbiome originates, or, you know, how to make sure a baby is healthy. Remember from the top of the episode that the yeasts present in a mother's vagina are generally also found in the baby's first feces. Many bacteria in the vagina apparently also colonize the emerging infant.

Few microbiome studies focus on the healthy vaginas of non-pregnant women, but we are fortunate today because fully a third of the published studies on the vaginal mycobiome - that is, one study - looked at just those vaginas. In 2013, a study led by a Dr. Drell surveyed the vaginal mycobiome of 294 Estonian women of reproductive age. Thirty-four percent of the total fungi found were *Candida* species, while 37% were *Saccharomyces.* I think it's fair to assume that unlike in the gut, these *Saccharomyces* don't come from bread. Many of the fungi Dr. Drell found could not be classified any further than the kingdom - fungi - which further demonstrates that fungal genome libraries are still very limited.

The pH of the vagina is very important to vaginal health. pH is a measure of acidity, where a lower pH value corresponds to a more acidic environment. Interestingly, vaginal pH is correlated with certain bacteria, but does not correlate with any fungi. The healthy vagina has a pH value of about 4.5, which is also the resting pH of the stomach. The low pH is partially due to the presence of *Lactobacillus* bacteria, and it keeps the fungal population in the vagina relatively low.

An unhealthy vaginal mycobiome usually results when something, like antibiotic use or an illness, causes a decrease in *Lactobacillus* bacteria and an increase in pH. Then, say it with me: fungi that are safe in small numbers overgrow and cause problems. The most common issue with the vaginal mycobiome is a yeast infection, which is exactly what it sounds like. *Lactobacillus* goes down, leading to an increase in good old *Candida* yeasts. A yeast infection is not a sexually transmitted infection, and women who aren't sexually active can get them. In fact, 75% of women are expected to have at least one yeast infection in their lifetimes, and some have two or more. Generally, yeast infections are mildly unpleasant but easily resolved with over-the-counter medication or ointment. However, some women can have stubborn or very

frequent yeast infections. Women who suffer four or more per year may need to work out a maintenance plan with a doctor, usually involving stronger ointments or oral medications, and behavioral changes like avoiding hot tubs and - to bring this episode full circle - unnecessary antibiotics.

[Music]

Izzie: So there you have it: the mycobiome in a nutshell. If this crash course intrigued you, consider going on PubMed and seeking out the topic that most interested you. If the papers seem daunting, feel free to send me an email and I'll be happy to help you out, or write a blog post explaining the tougher parts of the paper for all to enjoy. Remember, I may not be a doctor, but I am a biology person, and I did read a lot of papers preparing for this episode. Maybe you'll find something I didn't, and we'll both learn something new about the miraculous microbes that live within us!

[Music]

Izzie: "Morel Dilemma" is written and produced by me, Izzie Gall. Thanks to Meg France for inspiring this episode by asking about fungi that live on people. Our theme song is "Fungi Among I", composed and performed by John Bradley.

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Resources

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