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Lilly, you've heard of the gut microbiome, you may have even heard of the skin microbiome, but how much do you know about the vaginal microbiome? We know that the microbes that live within us are important for our health and an imbalance can contribute towards disease. Well, this is no different for vaginal health. You're listening to *microbe talk* the podcast by the microbiology society today, we'll be talking to Wilhelmina Houston, a molecular microbiologist specializing in sexually transmitted infections, to learn more about what a healthy vaginal microbiome looks like, how it can impact sexual health and how research is looking into more effective future treatments. Could you introduce yourself and your work?

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Sure can. Hi, Lilly. My name is Willa. I'm a professor of microbiology at the University of Melbourne in Melbourne, Australia, and I am fascinated by sexually transmitted infections in women's health.

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Perfect. And how did you get into this field of research?

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I love that question. I got into the field not originally planning that this was where my career would take me. I've had a really fun time, though, becoming a microbiologist. So my career, I thought when I was in high school was that I thought I would be in go into medicine and study to be a doctor, and I went to university to study a Bachelor of Science, and during that bachelor's experience, I really got fascinated by microbiology, and I didn't sit the entrance exam for medicine. Instead, I did an honors research project in the field of microbiology, and I still enjoyed research and really loved microbiology, so I stayed to do my PhD, and the rest is history. I've stayed in the field ever since.

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That's amazing, great to have your expertise on to talk about the vaginal microbiome for maybe some people that don't know you know how it relates to health and disease. Maybe we should start with what a healthy microbiome looks like. What? What species are included, what, and why do we need them?

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Well, first of all, I'm sure your your audience, will understand that the microbiome in the human body is a really important part of what we now think of as our whole organism. Every part of our body there's microbes living there, in the skin, on the skin, in our mouth

and, of course, in the vagina. Many people are well aware of the importance of the microbiome in the gut, but now they're becoming more aware of the importance of the vaginal microbiome in the vaginal space in the vagina, the microbiome is actually really intrinsically linked to the biology of that tissue. So we actually it changes during the hormonal changes of our life. Our diet can have an impact on the vaginal microbiome, and it is really important to maintain the tissues and protect the tissue and the space from pathogens as well. So we know that a healthy microbiome matters. We know we need to have that little ecosystem of microbes there. But we also know that the microbes have a whole range of ways that they protect our cells and make that a healthy environment. It's things like acidity, which is actually generated by the microbes. What that looks like, typically, is lactobacillus dominant, which means most of the microbes there are lactobacillus, and there's plenty of them. In some women, you can have an absence of lactobacillus, or very few, and a whole range of other organisms there instead. And for some women, they may have no symptoms, and they may, in fact, feel perfectly healthy, and they may remain very healthy, but there is a subset of those women who seem to be at slightly higher risk of developing things like bacterial vaginosis, or indeed sexually transmitted infections and more severe, severe outcomes. So we do know that a healthy lactobacillus, dominant, and certain types of lactobacillus, such as lactobacillus, crisp artists even better, and plenty of it, is what makes the the niche, the the most protective environment for for women's health.

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Would you mind explaining how, how they protect? Do they produce something that is able to fight back against pathogens.

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They do so. Lactobacillus crispatus is one of the best of the lactose for a healthy vagina, they produce a specific type of lactic acid, which works really well to create a more acidic niche environment, but also seems to cross talk to our own cells and make ourselves go into a nice, healthy defensive mode as well. But they make a raft of other things. So it's not just about the type of lactic acid they make. They also make what we call is a bacterial cidal toxin. So it's a back it's called a bacteriocin, and it's a molecule that they shoot out, but they're protected. From that actually kills off other bacteria, and it largely targets the bad bacteria for one of a better word. So they, they they deliberately target other bacteria. They create the environment more acidic to make the other harder for the other bacteria to grow there. They do a whole range of other things as well. They they grow really well in the space. So they kind of crowd out or compete physically for space with the other organisms. So it's actually multi factors. There's a range of really clever things that particularly lactobacillus, crisp barbus, although some of the other lactose do some of these things, but not as well, to make that healthy environmental space in the in the vagina.

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And what can determine, you know, what bacteria might be dominant for you?

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Really great question, and we don't really know. So we have monitored we, and when I say we, I'm talking about globally. The scientific community has monitored women over time. We know that the microbiome is very, very dynamic in the vagina. It changes. We do know that hormones make a difference. We think that diet makes a difference, but it hasn't been robustly studied. Behaviors like dou Shing or any kind of behaviors that interfere with the vaginal microbiome don't necessarily have a positive outcome to change the structure of the microbiome.

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That's really interesting. And yeah, the reason I reached out to you was because of a recent paper that you published about the relation between the vaginal microbiome and a disorder called celvic inflammatory disease. So that's, I suppose, one of the ways that it can interlink with health. Would you mind explaining a bit more about your research?

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Our most recent research, we monitored women who presented at family planning clinics with really severe pelvic pain. And when we when the clinicians investigated further, they diagnosed some of these women with a condition called pelvic inflammatory disease. Now this is when there's really severe inflammation, lots of pain. There's a number of ways that we categorize and diagnose, and it's problematic because a high proportion of those women, maybe 20 or 30% will go on to develop a tubal factor in fertility or other severe sequelae like chronic pelvic pain that they can't resolve. So pelvic inflammatory disease is related to inflammation, and it's related, we believe, to infection. But we've known for many years that it's not just sexually transmitted infection. We have these women who present with what we call idiopathic so no known pathogen is present in the women in the study, we they were very kind and generous provide us with the opportunity for the clinicians to collect samples from the vagina and the cervix, and we analyzed those samples to look at what the composition of the microbiome was in those women presented with pelvic inflammatory disease. And what we our aim was, was to understand what the microbiota is there in the presence of pelvic inflammatory disease compared to women who are healthy, and also to deep sequence that microbiome to really try to explore if there's any unknown pathogens that might be contributing to the development of pelvic inflammatory disease, or perhaps a combination of microbiota that we would often see there and a pathogen that might be the factor. So those were the kinds of questions we were asking in our study. We sequenced, did a lot of analysis, and we were able to identify that there

was not one pathogen or one organism associated with pelvic inflammatory disease, whether there was a sexually transmitted infection or not, or no known factor. But most interestingly, the absence of or a low absolute abundance or low real measures of lactobacillus. CRISPR does was the most strongly associated microorganism with pelvic inflammatory disease, and we're familiar with lactobacillus Chris bartus, because we know that that's one of the most protective organisms. So the one consistency was that it was really the one significant consistency for these women with pelvic inflammatory disease was an absence or a very low level of lactobacillus, again, supporting that pelvic inflammatory disease is a microbial condition. But there's not just one player who might be causing it that's

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so fascinating. And through this result, is there something in that that you think will lead to a treatment? Or how do you envision kind of the next steps to getting towards helping women that have PID?

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Really like that question, and that's what our ultimate aim is. Is, how can we improve things for women who have PID? And on that finding that a lot of lactobacillus, and particularly lactobacillus crisp artists, was most beneficial to show women who did not have PID there's a couple of answers we have in mind for what the future might be. First of all, clinically evidence based probiotic therapies based on lactobacillus deliberately made for the vagina, could be a really important intervention for women who are at risk of developing pelvic inflammatory disease. So. In our study, we saw that women who had a recent past history of taking antibiotics were also more likely to be in the pelvic inflammatory disease group than the control. So potentially taking antibiotics for any reason can impact your natural microbiome. So maybe women, particularly those also exposed to sexually transmitted infections or engaging in high risk, higher risk behaviors like more sex, which is associated with pelvic inflammatory disease, may benefit from future clinically proven microbiotic interventions like a probiotic. So that's one option. The other option is probably to just be aware, in a precision medicine kind of context, that women who are at risk for pelvic inflammatory disease, and that's young, quite sexually active individuals, should be carefully monitored by their clinicians when they present with symptoms. We want to intervene early in pelvic inflammatory disease to stop that risk, and so in the absence of clinically evidence based probiotic formulations, in the meantime, being really careful about monitoring women at risk. Those women who've recently had antibiotics or had a sexually transmitted infection exposure, are the ones that we want to make sure don't go on and develop is that the same

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risk comes with treating these diseases with antibiotics as there is in the gut microbiome. I know that some people take antibiotics and it kind of kills off beneficial bacteria there, and that can have more complications, is that something that can happen with the vaginal microbiome.

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There are a number of more recent studies emerging to suggest that that might be a risk, firstly, that it might kill off the good microbes in the vaginal microbiome space. Even antibiotics taken for any reason orally could have an impact on the vaginal microbiome, but there's also evidence that there's some of the players that we might not want to keep in the vaginal microbiome, as much as some of the other ones seem to acquire resistance. So women who've had antibiotic exposure in the past, they seemed, in another study, not ours, they seemed to find that there was more evidence of resistance being acquired in the vaginal microbiome. So there's a number of risks from antibiotics. We absolutely need to take antibiotics when we need them, not just when we have a cold, but when they're needed, but we also just need to be aware of the risks associated with those and hopefully in the future, new interventions such as probiotics will help us to mitigate those risks.

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Yeah, of course. And I guess that's kind of the opposite in terms of probiotics, kind of introducing more healthy bacteria. And I guess a lot of people will know that word. You know you can buy them at the shop, and people take them to improve their gut health. But could you explain more about how that works for the vaginal microbiome, like, if it's still taken orally, I guess, but made up, perhaps, of different species.

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There is actually been a number of clinical studies to explore vaginal probiotics. And yes, people have looked at whether you can take them orally and they end up in the vagina. There are vaginally administered probiotics in what we call pessaries, or gels, different formulations that people have also tried, but the evidence is quite mixed, and there's nothing super convincing yet, but it's a really difficult field to work in, because the vaginal microbiome changes really quickly, already naturally. Because some of those studies were on conditions that are already very difficult to treat, like bacterial vaginosis, recurs a lot, but also the formulations and the type of lactobacillus in some of those studies were not the ones that we already know naturally occur in the vagina. They were probiotics formulated for other environments, like the gut in some studies. So yes, I believe there will be great vaginal probiotic interventions in the future, but the clinical evidence for the ones that are out there at the moment are mixed, and the ones off the shelf often have very little clinical evidence of their impact at the moment. So there's many that you can buy. You can see them. Some industries are trying to do good

clinical studies on them, but we need to know a lot more about the effect of them before they proceed. Typically, in most countries, they are required to show no harm before they go on the market, particularly if it's something that women are encouraged to administer directly to the vagina. But showing no harm is not the same as showing a clinical positive benefit. So unfortunately, apart from being as healthy as you can, maintaining overall a healthy body, reducing your risk factors, there isn't any great probiotics that I'd be prepared to say you should go out and try.

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Is that where your work will be going next as well? Absolutely.

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So we're really interested in working with partners to explore and provide an evidence based framework to look at interventions in sexually transmitted infections, women at risk of PID women at risk of bacterial vaginosis, and really see if there is a way, with a lot of evidence, that we can vary and change that vaginal microbiome in a way that provides continued benefit. We're really optimistic that that will be possible in the future, and super excited to be involved in those kinds of studies in the future.

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Amazing and. I have one final question for you, which is just kind of a roundup question. What's one thing you hope people kind of take away from this discussion, perhaps if they've never even heard of the vaginal microbiome, or perhaps even if they have

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one thing to take away from the discussion. I like that question. Look, I think I would say that there has been a massive ground or massive gains in understanding the vaginal microbiome by researchers all around the world, and we know that it's an incredibly important part of our body's well being, but there's a lot more to do yet to understand it and to also figure out how we can intervene in a beneficial way. But I would say that it's natural part of our body, and it's important that, along with all the other parts of the body that we want to understand, we just continue to explore the microbiome as one part of the body, the immune system, our tissues, they're all important components, our genotypes. So it's great to be involved in studies like this, of people who participate and researchers who participate, because that's the only way we'll continue to understand is to look at all of those

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factors you've been listening to microbe talk. Thank you again to our guest, Wilhelmina Houston, for sharing her time and expertise. If you enjoyed this episode, give us a like,

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