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### The Experts Weigh in: Is Bacterial Vaginosis an STI?

Announcer Open:

Welcome to ReachMD. This is a special edition of "What's New in Bacterial Vaginosis," supported by Lupin Pharmaceuticals, Inc.

Dr. Caudle:

This is ReachMD and I'm your host, Dr. Jennifer Caudle. In this episode we'll take on an open question in women's health that's drawn no shortage of debate. Is bacterial vaginosis a sexually transmitted infection? Taking the position that BV is a sexually transmitted infection will be Dr. Caroline Mitchell, Assistant Professor of Obstetrics and Gynecology and Reproductive Biology at Harvard Medical School and Massachusetts General Hospital. Her colleague, and temporary opponent taking the position against, will be Dr. Jeanne Marrazzo, Director of the Division of Infectious Diseases and endowed professor in Infectious Diseases at the University of Alabama at Birmingham School of Medicine. Doctors and debaters, welcome to you both.

Dr. Mitchell:

Thanks so much for having us.

Dr. Marrazzo:

Thanks, Jennifer, nice to be here.

Dr. Caudle:

Well, we're happy that you're here. So, Dr. Mitchell, we're going to start with you, and let's start with the perspective of BV being sexually transmitted. From a general level just to set the stage, what supports this assertion?

Dr. Mitchell:

So there are several pieces of data that support the idea that bacterial vaginosis is a sexually transmitted infection. First, women who have never been sexually active in any way, no genital contact with fingers, mouth, or penis are very unlikely to get BV. Women with more partners who have more sex are much more likely to get BV. Women with female partners who have a symptomatic partner or partner with bacterial vaginosis are more likely to get BV. And circumcising the male partner, decreases the risk of bacterial vaginosis in the female partner significantly. All of those epidemiologic pieces of data really suggest that there is a transmissible agent that's passing between partners to cause bacterial vaginosis.

Dr. Caudle:

Okay, thank you. Now, Dr. Marrazzo, having heard these points in favor, what are some of the basic concepts that call this idea into question?

Dr. Marrazzo:

Yeah. I think those are excellent points that Dr. Mitchell raises. I think the challenge that has raised skepticism about the simplistic hypothesis that BV is a sexually transmitted infection is that there really has been no success in identifying what I think of as the elusive male factor in provoking this infection or this condition in women. We really haven't been able to identify a single transmissible ideologic agent, and that really has been the biggest challenge I think to determining if BV is a classical sexually transmitted condition. And whether you want to postulate that it is a group of organisms is a different question, but I think that gets us into a whole different discussion. The second line of evidence that people often raise to refute the idea that BV is sexually transmitted is that when men or male partners of women with BV have been treated with antibiotics that we know are effective against BV pathogens like gardnerella vaginalis. That has not shown to be effective in helping women experience fewer episodes of recurrent BV or clear their BV faster. As I'm sure Dr. Mitchell will point out, those studies are not definitive so there are a lot of holes that can be poked in them, but it does give

one pause because you would think that sort of trying to sterilize the male genital tract from these punitively responsible organisms should actually have some effect, and we really haven't seen that.

Dr. Caudle:

Let's move a little bit further into sexual partners and multiple sexual partners, which, Dr. Mitchell, I know that you mentioned in the beginning. So, you had mentioned, and we know that new sexual partners or multiple sexual partners can contribute to a greater risk of developing BV similar to contracting other sexually transmitted infections. The question, though, is is this proof of concept or is this coincidental?

Dr. Mitchell:

That's a very tricky question to answer because I think the answer is neither. It is not proof of concept by the traditional Koch's postulates, which is sort of the Bible for most infectious disease folks, where we need to find an organism that's present all the time, that can be isolated and grown, we can demonstrate that giving this organism to a healthy person causes the disease and then get it back from that person. We can't do that in bacterial vaginosis, but there's a really lovely article in science in 2016, that suggested a new era of Koch's postulates for an age where we understand that the microbial community on our bodies is very complex, and it may no longer be a one-to-one relationship with transmission of a disease. So the fact that the epidemiology looks just like an STI, the fact that if you use condoms, you decrease your risk of recurrent bacterial vaginosis; the fact that women who share sex toys with each other are more likely to transmit BV; the fact that female partners, and my esteemed opponent has done a lot of this research, that female partners are more likely to have BV if their partner has BV. I think all of those really point to it being a sexually transmitted infection and we have just not yet been smart enough to figure out what's the transmissible thing.

Dr. Caudle:

And, Dr. Marrazzo, any rebuttals here or anything to add?

Dr. Marrazzo:

Not so much a rebuttal, I actually agree with everything Dr. Mitchell is saying, and I think in some way this leads into a question we might be discussing next or very soon, and that's, I actually think the problem, part of the problem with here, is how we're asking the question and how we're measuring the association. So everybody knows that asking somebody how many partners they've had in their lifetime or in the last year or whether you've had a new partner in the last say two weeks, one week, six months, whatever, they're all very crude measures of the actual per behavior exposure of potentially transmitted bacteria. So, I mean, nothing is more complicated or less reducible than sexual behavior, and yet we continue to use the very crude measures of sexual activity and even "risky sexual activity." So, as Caroline pointed out, this idea of looking at sexual behaviors that might be extremely efficient at transmitting vaginal fluid, which you would expect to have the highest concentrations of these bacteria, yeah, maybe that actually is a very good way to inoculate someone with these bacteria in a quantity that's enough to shift the balance of what's going on in the vaginal environment. So, I think it's not so much a rebuttal, I think it's more just that I don't think we're asking the questions in as sophisticated a way as we should be to really get at some of the answers.

Dr. Caudle:

Normally in defining a sexually transmitted infection, we can identify a specific pathogen or pathogens responsible. Can you talk a little bit about why it's particularly challenging in this particular situation?

Dr. Marrazzo:

Sure, this sort of definition, fundamental definition, of BV is that it is what's called a dysbiosis and a dysbiosis is a deviation from the optimal community organism for a given environment. We've known for a long time that the best reproductive health outcomes, the lowest risk of reproductive tract infections come when you have a vaginal environment that's dominated by *Lactobacillus crispatus*. So that is the sort of anti-pathogen in this scenario of BV. On the other end of the spectrum, when you have the dysbiosis of the BV, it's more defined by the absence of that *Lactobacillus* species or related species and a proliferation of an often complex group of anaerobes. And that is not easy to define as a pathogenic consortium, I guess is the easiest way to say it. So, then when you go to say okay, are people transmitting that community or that consortium, are you getting that from the male foreskin area in an uncircumcised man? Are you getting it from another woman who maybe has BV? That's quite possible, but to zero in or hone in on the components of that transmitted community that we think are the triggers or whatever the precipitant is is very difficult. I think the best hypothesis for that would be oh, maybe there is a virus or we call them bacteriophages that is specific for the *Lactobacillus* species. And if that's true, and it's a theory that many people have brought up to explain BV, that would explain a lot of this because it's a little bit like the Wizard of Oz behind the curtain of what we're seeing in BV.

Dr. Caudle:

Dr. Mitchell, what are your thoughts about this, any additions?

Dr. Mitchell:

So, I would absolutely agree with everything Dr. Marazzo said, and I would just add that one of the challenges for this field in determining what are the pathogens of interest is the fact that there is no animal model. The human vagina is unique. We are the only species with this Lactobacillus dominance, and so we can't use mice the way the folks who study gut pathogens do, there's not a model system in which we can test out some of these pathogens to see which ones might cause BV. And so that is one of the huge challenges in this area that has, I think, really held us back.

Dr. Caudle:

So, moving on, we've talked about different variations and ways to think about this and some potential causations and why it's difficult to figure out what the pathogen is, but, you know, I'm really interested in whether we have a clear cause-and-effect relationship here, you know, is BV caused by sex? What are your thoughts, Dr. Mitchell?

Dr. Mitchell:

So, I'm going to answer that yes and, to say yes, BV is in many cases caused by sex. And even though I can't demonstrate the pathogen, I think for some patients it is so clear, but if you look at things like Zika virus; Zika virus can be transmitted sexually and it can be transmitted other ways. And so I think it's possible that bacterial vaginosis is both a sexually transmitted infection and a dysbiosis that can be caused by other things potentially. And that's sort of a slippery answer, but it is what clinically, and my experience really seems to be true.

Dr. Caudle:

Dr. Marazzo, what do you think about this?

Dr. Marazzo:

Yeah. I absolutely agree with Caroline. I think it's a nuanced answer not a slippery answer, and I would just point out that all clinicians who care for women with BV, and I hate to be too absolute, but I'm fairly confident in saying this. Most of us anyone have seen women who can very clearly associate their BV recurrence with resumption of sex with a specific male partner. And, you know, we haven't gotten to the point where we've been able to isolate those couples and say, "She didn't have this consortium of bacterial in her vagina before they had sex, and she got it back after he reappeared in the picture." That would be pretty powerful, and I do think that's the case for some women, but clearly not all.

Dr. Caudle:

So, moving forward along this theme, we'll start with Dr. Marazzo. We know that BV has been known to increase the risk of contracting other STIs such as chlamydia and gonorrhea. Do you think that this fact supports the case for BV being a sexually transmitted infection by proxy, or is this a false association?

Dr. Marazzo:

Yeah. That's a great question, and that gets into both biological and behavioral explanations and context. So, the challenge is that biologically, when you lose those Lactobacillus that I spoke about that characterize the healthy defended vaginal environment, you are more likely to get infected with chlamydia or gonorrhea if you are exposed to it. So those healthy Lactobacillus, i.e., the absence of BV, strongly protects against getting infected if you're exposed. On the other hand, we've already heard that disruption of the environment and perhaps BV in some women is associated with sexual exposure. So you've got this potential interaction between whatever is causing or whatever is promoting the BV and the fact that that's what's also going to get you exposed to the chlamydia. So, I think that that is probably a potentiating situation where if you don't have the Lactobacillus, you've got BV. Maybe that's related to the fact that you've been having a lot of unprotected sex or unprotected sex with a specific partner, then you get exposed to chlamydia and you're more likely to get it. I think that's kind of what we're talking about.

Dr. Caudle:

And, Dr. Mitchell, what are your thoughts about this, and what's your response to Dr. Marazzo's position and also the question?

Dr. Mitchell:

I would agree absolutely with what Dr. Marazzo said, and I would say also that for other sexually transmitted infections like HIV there have been some longitudinal studies showing very clearly that if you have this dysbiotic vaginal bacterial community, you are at increased risk for acquiring HIV suggesting, again, this biologic causation, this biologic susceptibility in women with BV, which is one reason we'd like to try and decrease the prevalence of BV for many women. But I also, as a marker of at risk sexual behavior, I think the correlation with BV and STIs is probably also partly that.

Dr. Caudle:

You two have been amazing guests, and before we close, I'd like to give you both an opportunity to give any final thoughts. Why don't

we start with you, Dr. Mitchell, any final thoughts on our debate and conversation today?

Dr. Mitchell:

Sure. Although I have come down very strongly that I think bacterial vaginosis is a sexually transmitted infection, I also want to caution listeners that if you are diagnosed with bacterial vaginosis, I don't think it necessarily means that your partner is being unfaithful because I think, as we talked about it, it may be an STI and something else. And it's possible that it can be an STI just because your partner's bacteria are not optimal for you. And so, although I do think it's transmitted sexually, I wouldn't put it in the same category as chlamydia, gonorrhea, herpes where you got it from your partner and your partner got it from someone else, and so you should be asking some questions. So I would just caution people that I do think it's sexually transmitted, but it's a little bit different than many of the classic STIs.

Dr. Caudle:

That's really interesting and I think it's a very helpful comment. And, Dr. Marrazzo, what are your thoughts? Any closing comments or anything you'd like to add?

Dr. Marrazzo:

Maybe one additional thing in addition to emphasizing what Caroline said I think that it is really important. We see a lot of women who deal with the consequences of being diagnosed with an STD, and it's not always, it's always challenging, but sometimes it's more than that. So we really do want to be careful how this is framed particularly when we're in a less than definitive data zone as we kind of like to say. The other thing I would add is that we see and have seen many women who have gone for a long time without an accurate diagnosis of their vaginal infection, and sometimes it's BV, but often it's not, and yet they've been treated over and over again for BV. They've been treated for trichomoniasis when they've had negative tests. They've been treated for yeast, and so I just would urge listeners and also providers to, you know, recognize that sometimes it can be challenging to make a specific diagnosis of vaginal infections and conditions, but there are ways to do it.

Dr. Caudle:

I think that's an excellent point as well, great clinical pearls from you both. This was an excellent conversation. I'd really like to thank you both, Dr. Caroline Mitchell and Dr. Jeanne Marrazzo, for joining us today.

Dr. Marrazzo:

It was a pleasure. Thanks for having us.

Dr. Mitchell:

Thanks so much.

Announcer Close:

This is ReachMD. The preceding program was supported by Lupin Pharmaceuticals, Inc. If you have missed any part of this discussion, or to find other episodes from "What's New in Bacterial Vaginosis," visit [ReachMD.com/NewinBV](https://ReachMD.com/NewinBV).