

Real-world Applications of Microbiome in Bladder Cancer. What should patients know?

Dr. Laura Bukavina, MD, MPH



Stephanie Chisolm:

I really appreciate it, Laura. This was wonderful. So in your opinion, what percentage of urologists or even medical oncologists are tuned into this or are beginning to pay attention to the microbiome?

Dr. Laura Bukavina:

I would have to say probably very low. I think most likely patients are bringing up to oncologists as well as surgical oncologists. And I think they're learning because patients are asking questions, but it's not as mainstream as people think. I think over the last five years with some of the melanoma trials, that started to highlight the efficacy of this. People are paying more attention.

Stephanie Chisolm:

Sure. Well, we have some really good questions that have come in already. Some we'll summarize. "Should bladder cancer patients try to minimize their use of antibiotics?" If you're trying to keep a nice colony growing and you get something else, should you take antibiotics or try to minimize that use?

Dr. Laura Bukavina:

That's a tough question because we usually give antibiotics for a reason, right? So what I can tell you is based on patients who are undergoing immunotherapy, there's no prospective data, but if you look at data afterwards, which is called retrospective data, if you look at the patients who were receiving immunotherapy and receive antibiotics within three months of receiving their immunotherapy, those patients typically have a lower response to immunotherapy. Now, that's not to say that the reason why they receive antibiotics potentially maybe they were in the hospital, maybe they were sicker, is the reason why they couldn't get the immunotherapy that they needed.

However, we should minimize antibiotics to only what's necessary and really very specific. So instead of being an antibiotic that kills everything, really asking the question, "Can I just take antibiotic that's specific to my bacteria?" And at the same time, while you're taking antibiotics to make sure to ask your physician if you should be taking pre and probiotics at the same time?

Stephanie Chisolm:

Right. Yeah. Okay. That's a great question and thank you for answering it. I appreciate it. "Is there research on whether a high-fiber diet improves BCG responsiveness?"

Dr. Laura Bukavina:

There is no research on BCG and fiber diet, unfortunately.

Stephanie Chisolm:

Okay. I'll probably say this wrong, Casei, C-A-S-E-I is not on the list of beneficial probiotics. Can you explain that one?

Dr. Laura Bukavina:

So Lactobacillus Casei is one of the beneficial probiotics. Again, I only mentioned the few that are listed, but Lactobacillus species is wide and it is one of the beneficial ones.

Stephanie Chisolm:

Okay, thank you. So it was on there.

Dr. Laura Bukavina:

Yes.

Stephanie Chisolm:

Okay doke. "Are you familiar with Visbiome and if so, do you recommend it prior to a radical cystectomy?"

Dr. Laura Bukavina:

I am familiar with Visbiome and I have a lot of patients that take it before and after cystectomy, and I can only tell you what the patients tell me, but they tell me that they feel much better and they have less infections when they have their conduits. So I am not a salesperson for Visbiome or any probiotic or prebiotic company, but at least in my experience they do use it.

Stephanie Chisolm:

Okay. You did a lot of work with Dr. Phil Abbosh when you were at Fox Chase Cancer Center, and I know he's looked at a lot of things, the urine, there's a question about, "Do the organisms and probiotics make it into the urine?"

Dr. Laura Bukavina:

So there's this concept what's called translocation, which is some bacteria are able to cross the colon and then enter into circulation without making you sick. So not as if you have bacteria and then end up in different organs. So if you think about melanoma, the studies that I talked about, those mice are given gut bacteria, probiotics, and then all of a sudden they get a better response in their melanoma. And yes, some of the concept is it's based on their immune response. They're able to really target their immune

response, but we know that those bacteria that translocate from the gut then go to a lymph node, and then inside the lymph node they're able to increase the response of your own immune system to cancer.

Stephanie Chisolm:

Great. Are there dangers of prebiotics?

Dr. Laura Bukavina:

When you look at prebiotics studies, the most common adverse events is bloating, gas, and diarrhea. So those are the most dangerous. In probiotics, there's some documented case reports of people getting sepsis. Those are typically highly immunosuppressed patients, otherwise there's very minimal side effects to pre or probiotics.

Stephanie Chisolm:

Another question, sort of two parts. "What's the proposed mechanism that probiotics could impact bladder cancer and is it from direct contact with the bacteria on the bladder cancer cells?"

Dr. Laura Bukavina:

So both ways. So if we look at LGG, which is that Lactobacillus that I studied, there's two ways. One is the LGG is actually able to penetrate the cancer cells and kill them directly. The other is that the bacteria is able to increase the local tumor, what we call microenvironment, by increasing the T-cells actually coming in and killing the cancer cells themselves. So both ways.

Stephanie Chisolm:

"From all the commercial brands that you've considered, which ones do you recommend?" You don't have to answer this because that's a tricky question because there could be so many, so we can go ahead and skip that.

Dr. Laura Bukavina:

Yeah.

Stephanie Chisolm:

All right, let's skip that one. I don't want to put you on the spot. I think you covered most... Let's see, "Treated with BCG. Every time I get a cysto, I get an antibiotic." Okay, somebody's being treated with BCG. I think that's what it is. Is it counterproductive to get an antibiotic when they're being treated with BCG?

Dr. Laura Bukavina:

So I suspect you're getting probably the cystoscopy antibiotic, which is that Keflex. So as long as you're not getting, like we talked about, very broad spectrum antibiotic, it's not counterproductive. Now, if you're getting an antibiotic that kills a lot of gut bacteria, that could be considered counterproductive.

Stephanie Chisolm:

Great. Is there anything that you recommend that people can take to lower the possibility of getting a urinary tract infection that seems to be a common side effect from bladder cancer treatments in some way?

Dr. Laura Bukavina:

Yeah, that's a good question. So if you look at studies in Norwegian, I think some are Norwegian countries and UTIs overall, they don't do a lot of probiotics, but what they do is what we call natural probiotics, which is fermented foods, so fermented vegetables, fermented cheese and fermented milk. And those patients had a much lower risk of cancer and urinary tract infection. Again, this probably is because of the whole pre as well as the Lactobacillus component. So if you like fermented vegetables or pickled vegetables or fermented milk, I think that's what you can potentially extrapolate the data from.

Stephanie Chisolm:

Okay. All right. So everybody can go out and get some fermented...

Dr. Laura Bukavina:

Pickles.

Stephanie Chisolm:

For dinner, some pickles and some kimchi or something along those lines. Okay, sauerkraut. You mentioned resetting the microbiomes similar to a colonoscopy prep. What if you have a healthy microbiome and have to have a colonoscopy? How harmful is that and how long does it take to restore your microbiome?

Dr. Laura Bukavina:

That's a tough question because when you have a colonoscopy prep, depending on the prep, sometimes they give you this low-dose antibiotic in addition to MiraLax. MiraLax alone should not affect it because it doesn't get rid of all of your microbiome and it will auto-populate. However, we know that every time you have any sort of prep and you take your sample of gut before and after, it's going to be very different. It might be similar in the number of bacteria, but the total percentages are going to change. So the short answer is yes, you're going to change it every time with colonoscopy prep, but is it going to be bad? Not necessarily.

Stephanie Chisolm:

And it looks like we have one more question. You are on top of this... There's two more questions, on top of this in terms of getting through all of these questions. You mentioned clearing the microbiome prior to using probiotics. Is that something that somebody should try to do on their own and how would they do it? Or is it something that should only be done under the supervision of a physician?

Dr. Laura Bukavina:

Currently, that this is only done under a clinical trial setting and under supervision of a physician who's able to monitor because there's a risk of dehydration, there's a risk of bowel perforation. So this

shouldn't be done at home with some MiraLax and coalesce. This should only be done within the setting of a clinical trial.

Stephanie Chisolm:

Good advice. Is there any value in rotating the type of pre and probiotics that one is taking every few months just so you get a different supply, a different set of organisms that are growing and is there value in that?

Dr. Laura Bukavina:

Unfortunately, there's no studies looking at the value of switching pre, before and after. And if you look at a lot of these probiotics and the prebiotics, they're essentially the same. Majority of them are focused on either Lactobacillus or Bifidobacterium. There's very few variation. So I think switching from one to another, if I had to sort of think about it, it probably doesn't make much difference. I think it's the quality of your probiotic that matters more than the brand.

Stephanie Chisolm:

So again, looking at the back of the labels, you identified all of the criteria that would identify a high-quality probiotic. So it's really on the patients to really start looking at all of those, if they're looking at over the counter. Do doctors often recommend sort of specialty probiotics where they're not available at say Costco or something like that, where you can pick up a big bottle of probiotics? Do they sometimes recommend something else?

Dr. Laura Bukavina:

So sometimes what I have seen in practice is that probiotics are digested too early. So when I had that slide about small intestine and your large intestine, what you really want to target is probiotics within your colon. And if you swallow a probiotic, it really gets degraded in your small intestine in your stomach, so it might not actually ever make it to your colon. So some of the new formulations actually have what's called the double capsule, meaning they have almost like a delayed capsule response that the top of the capsule gets digested in the stomach and in the small intestine and the inside where all of the probiotics actually are makes it all the way to the colon.

And I think we are now understanding that that's where it has to happen. And the previous formulation, really just put everything together. It gets digested in your stomach, it never makes it to your colon.

Stephanie Chisolm:

Right. And if any of them happen to make it all the way through to the colon, yay. That was a good thing. So there's no guarantee though. Okay. Do any foods like cranberry juice, green tea help to modulate the organisms in the bladder in a beneficial way?

Dr. Laura Bukavina:

Yeah. So cranberry is one of those prebiotics that we talked about, but you have to be careful with cranberry juice because it's usually high in sugar. So if you are getting cranberry juice from your grocery store, you're probably going to turn the bottle around and see there's 40 grams of sugar, and that's probably more hurtful than helpful. The real cranberry juice without any sugar is a prebiotic and it does help.

Stephanie Chisolm:

Okay. Somebody said they're not clear whether you're recommending taking a pre or probiotic?

Dr. Laura Bukavina:

Both.

Stephanie Chisolm:

Both. Okay, great. And then the last question maybe, "My doctor probably using the right kind of antibiotic for my cysto, could you re-say what that right kind of antibiotic is?" I think somebody just wants to double-check.

Dr. Laura Bukavina:

Double check. So typically for cystoscopy, your doctor will use what we call a narrow spectrum antibiotic, and that means that it doesn't kill all types of bacteria, but just aimed at the ones that are in the urine and around the skin. And that's usually things what we call Cephalosporins or Keflex. But again, this is highly dependent in each patient's situation. So this is Brian. Brian, if you've had infections before, and for example, you've had bacteria that are very resistant to that specific antibiotic, your doctor might be using something different.

Stephanie Chisolm:

Should you take those during a meal or before the meal? Would it make a difference?

Dr. Laura Bukavina:

You should take it before the meal or two hours after the meal because of the digestive juices and the bile that's in your gut.

Stephanie Chisolm:

Good to know. One more question. "Is kombucha fermented and if so, is it recommended?"

Dr. Laura Bukavina:

If you look at kombucha, if you actually turn the bottle around, what you're going to find is LGG.

Stephanie Chisolm:

Okay. So let's see. "So take pre and pro, even though they're so small in dosage versus what's recommended."

Dr. Laura Bukavina:

I think what you're trying to say, Kelly, is that I pointed out all the problems with the prebiotic, how they're not... But you can find ones that are higher when you might have to take a couple. In addition, don't forget that you're also eating vegetables, so you are getting the necessary prebiotics from your vegetables. This is a supplement, meaning you don't need to supplement all five grams with prebiotic. You just need to understand that in addition to your healthy diet, high in vegetables, you also can supplement with prebiotics.

Stephanie Chisolm:

So there was a question about the CFUs lumping them together because they can't be divided. You mentioned that the number of billions of CFUs alone might not actually mean that much. Is that what you were indicating there? So that's something on the label. We think you're trusting it and you think you're getting the right thing, but you don't know.

Dr. Laura Bukavina:

You don't know because it's lumped. So you're getting a little bit of the good thing and a lot of the other thing that's cheaper for them to make. So I generally don't like the probiotics that list 80 different types of bacteria and then lump them. I prefer the ones that have one or two listed and then they give you the breakdown. The minimal, the minimal should be 10 to the six. We know this that it should be the minimal that's necessary. If it's more, it might not give you the better effect. However, there's a minimal concentration that's been studied and that's 10 to the six.

Stephanie Chisolm:

Best to take them once or twice a day or at every meal, if you're looking at pre and probiotics?

Dr. Laura Bukavina:

It's dose-dependent. So if you think you're getting the necessary prebiotics with your diet and you need to take two or three pills, it's better to split them up, but they don't give you the side effects of bloating and indigestion. If you're not getting it and then you need to take more, then you might have to lump two at a time. However, it's very difficult for anyone to start taking three pills three times a day together in addition to all the other medications that they have to take. So I wouldn't concentrate so much on how many times you have to take it. I would concentrate on your diet and small amount of supplementation.

Stephanie Chisolm:

Okay. You didn't talk about vitamin C, but one of the participants, urologist suggested taking 500 milligrams of vitamin C twice a day to help prevent UTIs. Is that a good thing? It's not exactly what you were talking about.

Dr. Laura Bukavina:

Vitamin C, 500 milligrams is fine. If you do too much, vitamin C can actually cause kidney stones, so you have to be careful with that. Vitamin C improves your immune response and your immune system, which is why you have all that marketing towards vitamin C when you get sick. However, you have to be careful not taking too much of it because then you'll end up with kidney stone.

Stephanie Chisolm:

Okay. Thank you. Well, this has been phenomenal. I learned something. I think the participants have learned something. And thank you again for joining us, everyone

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