

Macular



Chats

How Diet and Nutrition Impact Macular Degeneration

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Transcript of Teleconference with Dr. Sheldon Rowan, Assistant Professor of Ophthalmology, Tufts University School of Medicine

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Please note: This Chat has been edited for clarity and brevity.

DR. DIANE BOVENKAMP: Hello and welcome. My name is Dr. Diane Bovenkamp, Vice President of Scientific Affairs at BrightFocus Foundation. I'm pleased to be your host for today's Macular Chat, "How Diet and Nutrition Impact Macular Degeneration." This Chat is brought to you today by BrightFocus Foundation. Macular Degeneration Research is one of our programs at BrightFocus. And we fund exceptional scientific research worldwide to defeat Alzheimer's disease, macular degeneration, and glaucoma, and we provide expert information on these heartbreaking diseases. You can find much more information on our website at www.BrightFocus.org. I am extremely pleased to introduce today's guest speaker. Dr. Sheldon Rowan is an assistant professor of ophthalmology at Tufts University School of Medicine in Boston, Massachusetts, and is a scientist on the Nutrition and Vision Research Team at the Jean Mayer USDA Human Nutrition Research Center on Aging, located at Tufts, as well. Dr. Rowan is also a Chair of the Division of Biochemical and Molecular Nutrition and an assistant professor of nutrition at the Friedman

School of Nutrition Science and Policy at Tufts University. Dr. Rowan, thank you so much for joining us today.

DR. SHELDON ROWAN: I'm really happy to do this, and especially, to talk about this topic that I'm very passionate about.

DR. DIANE BOVENKAMP: Very passionate about, and you are definitely one of the world experts, so I think that all the listeners are in for a treat today.

DR. SHELDON ROWAN: Oh, thank you.

DR. DIANE BOVENKAMP: So, I think, talking about diet and lifestyle—and I want to explain, when I say diet, I don't mean a restrictive diet, Jenny Craig or whatever, something like that. We're just talking about a diet, the food that you eat every day as part of a healthy lifestyle. So, there are many types of diets that people can adapt into their lifestyle, including vegetarian, carnivorous, Western, Mediterranean, lactose-free, gluten-free, keto, and the list goes on and on and on. Is there any one diet or a couple of diets that might be better than others, especially as it relates to risk for or prevention of macular degeneration?

DR. SHELDON ROWAN: Yeah, this is a great way to start. Obviously, we think about people's diets as being fundamentally linked to their overall health. And one of the things that we've come to do is we've kind of started to study diets in terms of patterns of foods that people eat together. And this allows us to do a more defined research approach toward diets and the risk for certain diseases. So, yes, we do know that some dietary patterns are protective of macular degeneration, and some dietary patterns probably increase your risk for macular degeneration. So, the patterns that we know the most about, which is partly just because we've done the most research on, are the Mediterranean diet patterns. And that would be consistent with an American diet, that would be one that adheres to what the FDA and USDA have defined as a healthy eating index, as well. So, we have pretty good data that those diets are protective against macular degeneration. We also have good data that the typical Western dietary pattern—this isn't necessarily one that you're going to want to read about in the textbook to stick to, it's the one that we often

end up eating anyway, kind of like our baseline diet—is probably not particularly good for macular degeneration. It increases your risk. And then, there's all kinds of variations on these dietary patterns. And so, a vegetarian diet would probably be protective. It would probably look more like a Mediterranean diet than a Western diet, but it depends on what you choose to eat. You can have an unhealthy vegetarian diet; you can have a very healthy vegetarian diet.

And then some of the other diets that are becoming popular, especially ones that get promoted in the media, we don't know for sure if they are or not going to be associated with risk protection from macular degeneration, but there's some that I would be maybe a little nervous about. So, you mentioned the carnivorous diet. I'd be concerned about the diet that have too much red meat, especially if you're not eating other lean meats or fish as your main protein sources. I might be nervous about certain gluten-free diets if you're eating too much processed foods and not eating enough whole-grain foods, for example. But definitely the ones that we know have the most data about being protective are things like the Mediterranean diet.

DR. DIANE BOVENKAMP: Can you just quickly mention, for those who might not know, what typically is a Mediterranean diet?

DR. SHELDON ROWAN: Yeah, the Mediterranean diet, which doesn't bear 100% to what's eaten nowadays in most of the Mediterranean, but it's like the more ancient diet there, is one that has a high intake of whole grains—so unprocessed carbohydrates, for example. It would have a fairly low amount of red meat, but you might see a lot of the protein in the source of fish, lean poultry, shellfish, things like that. The Mediterranean diet is also associated with a higher intake of nuts. Nuts are absolutely fantastic. Olive oil would be another aspect of the Mediterranean diet that I don't think has to be stuck to in every healthy dietary pattern, but they definitely have higher intake of olive oil in those diets and not too much consumption of sweets and desserts and baked goods and things like that. So, a really healthy pattern with a lot of fruits and vegetables, whole grains, and lean protein sources, and also occasional intake of alcohol, which we can talk about later. But, for example, red wine, a

serving a day would be very typical of the Mediterranean dietary pattern.

DR. DIANE BOVENKAMP: Yeah, I'd love to get to that, especially since I've heard nowadays that the amount for men and women for alcohol might be different. But before we get to that, one of the things that you spoke of was the whole grain in the Mediterranean diet. And then you were mentioning to try and cut back on the sugar and the simple carbohydrates. Is part of that—being a biochemist, trying to relate it to the disease process itself—is this because sugar might be causing inflammation and that inflammation has been shown to increase risk, especially if you are vulnerable genetically or otherwise?

DR. SHELDON ROWAN: Yeah, that's definitely a part of it. So, we know that sugar intake is pretty much bad for you across the board. So, like you mentioned, it's linked to increased inflammation. One of the things that having a diet high in sugar will do is it will cause a greater insulin release after you eat those foods, which has its own consequences on fat metabolism, for example. And so, there's a lot of different pathways downstream of sugar metabolism that could end up being bad for you and bad for your eyes. One of the things that I work on in my research is looking at what we call glycemic index, which has to do with how quickly different carbohydrates get broken down into sugar. And so, for example, one of the things we found is that eating a diet high in very processed grains—so for example, corn starch, foods like Doritos or corn flakes with very processed grains—it gets really rapidly broken down into sugar, which can have the same effect as if you drank a can of Coke or a sugar-sweetened beverage. So, the kinds of grains and carbohydrates that we eat could have a really important impact. And that works on the level of the gut, it works on the level of metabolism, and it could also work directly in the eye.

DR. DIANE BOVENKAMP: I think we were going to talk about this later, but is this what you're referring to as ultra-processed foods? Might as well talk about it.

DR. SHELDON ROWAN: Yeah, ultra-processed foods. And we can get back into it, but yeah, definitely a lot of ultra-processed foods would have high amounts of either added sugar or very processed grains.

So, those would be some of the components that we would consider ultra-processed foods. And there's other things about ultra-processed foods—for example, food additives, things like emulsifiers—the way that it's described to you is if you look at the list of ingredients and you don't understand what they are, if they don't sound like things that would be in your kitchen cabinets, then there's a chance the food you're eating would be considered ultra-processed. We don't always know if it's those other food additives, like the added sugar and added salt, that make them bad. We just know that we eat more of them and they lead to bad health consequences.

DR. DIANE BOVENKAMP: That is so interesting, how health science has been trying to make things easier for us to eat and/or have a better storage life, but it's probably not good for our health, or at least researchers are trying to determine if that's so. So, that's so interesting. So, I think one of the next questions on my list was ... okay, so thank you for saying that healthy vegetarian and Mediterranean diets are probably better than others, especially as it relates to macular degeneration. But how does this diet impact our risk of either developing AMD or, if you have AMD, progressing to later stages?

DR. SHELDON ROWAN: Yeah, that's a great question. So, there there's two different aspects: One of them is how does it affect onset of AMD, and the other is progression of AMD. So, for example, does eating that healthy diet prevent you from ever getting AMD, or is it that it would help prevent your AMD from advancing from being early or intermediate form to a progressive form? And we've looked at those kinds of questions and been doing epidemiological research. And so, what we know is this. For example, the Mediterranean diet seems to work really well at preventing progression of macular degeneration, especially the dry forms of macular degeneration. There's also data that it can protect progression of the wet forms of macular degeneration. We don't know as much about whether it can prevent the development of the disease at the very beginning. There was some data that suggested that, yes, eating a Mediterranean diet helps prevent development of macular degeneration. But when they actually looked at the data carefully—and this is the challenge in doing nutritional research—the same kinds of people that might want to eat a healthy

diet are also likely to think about, "Oh, maybe we should exercise more. Maybe we want to make healthy lifestyle changes." It's hard to disentangle those things. So, when they tried to do it, they actually found that it was exercise that seemed to be more protective against early forms of macular degeneration. So, there's both the question about is this preventing the disease or preventing the disease from progressing. And in terms of how it does that, I would say that's still an open question. That's one of the reasons why we spend a lot of effort trying to understand how the disease progresses, how the disease initiates, so that we can get an idea for how diet might impact that. And then, we could think about, with that understanding, can we design new treatments or get better at doing it?

DR. DIANE BOVENKAMP: Great. That's really good to know. And it's very interesting about how, yeah, it's really hard for scientists to break down, if there are these, quote, "confounding factors" of obesity or guides and diets. And then, people have different underlying genetic risks that we don't even know what all of the risk genes are, so that's why it's very important to support scientists like yourself to try and figure this out. And then another player, and this is really the more I learn about this, the more I'm just fascinated, is, maybe people have heard the term microbiome or gut microbiome. And before we talk more about that, can you just define what is a microbiome?

DR. SHELDON ROWAN: Yeah, the microbiome is a collection of all of the living space within a given part of the body. So, when we talk about the gut microbiome, we're specifically talking about all the different organisms that reside within the gut. And it's mostly us, but we have a lot of other inhabitants that go along with our guts. What most people have studied, including myself, tend to be gut bacteria. There are trillions of gut bacteria that live within our gut, and they have really important roles in controlling our health and controlling risk for disease, as well. But we shouldn't forget that the gut microbiome includes everything, so it includes fungi and includes viruses. Some of those viruses infect bacteria, so you can imagine how complex this ecosystem with our gut is. There's even other single-celled organisms that are sometimes normal inhabitants of our gut, and some people have them, and other people don't. So, the gut microbiome is this complex ecosystem, but it's all within us. And of

course, we have other microbiomes. We have a skin microbiome, we have a nasal microbiome, we have an oral microbiome. But because the food is going right into the gastrointestinal system, that's why we tend to think about more how diet can impact the gut microbiome.

DR. DIANE BOVENKAMP: That's just fascinating that we're not alone. We always have all of our little microbial buddies living inside us. That's a little creepy when you think about it.

DR. SHELDON ROWAN: I know. For them, we're like the universe.

DR. DIANE BOVENKAMP: Oh my gosh, we could get a little too existential here, but are there good or bad microbes? Bad in the sense of I've done a little bit of reading where maybe there's a microbiome that could break down carbs into more sugar. So, maybe that makes that one person who has a certain profile of microbiomes gain more weight than someone else who has a quote "good" microbiome profile, and they eat the same thing. Just to explain, are there good or bad, or is it just a neutral whatever mixture?

DR. SHELDON ROWAN: Yeah, that's a great question. There are definitely good microbes, and good microbes are found in most people, and we know about their normal functions. And there's bad microbes that may be associated with infection. The way that I like to think about it is not so much like good and bad bacteria, but I like to think about: What are our normal inhabitants? And obviously, that's going to change a little bit depending on all kinds of conditions. But there's bacteria that are just usual inhabitants for each given person, and the term that we use for those are commensals. So, these are our normal microbiota, the bacteria, for example. And that might include ones that are normally associated with being good and being bad, but when they're all in balance and in the numbers, it's completely fine. The problem is when certain bacteria expand too much or go from being maybe 0.1 percent to 10 percent or 50 percent. When things get out of balance, that's when you have a problem. And the gut microbiome, when it gets out of balance, there's a term we call that. It's called dysbiosis, and that's when we're no longer in balance. And some of those may be bad bacteria that get out of control, but they're normally tightly controlled, and have a risk for causing

problems. And those problems could be infection or inflammation or things that we don't even understand yet. And so, it's helpful to think about the normal, balanced microbiome and then this unbalanced, dysbiosis microbiome. And a lot of work in chronic disease, especially in areas like diabetes and cardiometabolic disease, has focused on what happens to individuals that have evidence of dysbiosis. And there's even some evidence that dysbiosis may be connected with macular degeneration. It's still an open question. We tend to not be very good at even knowing how to define dysbiosis. There's disagreements in the literature. There's certainly no single standard. But that's the notion I like to think of: Are bacteria being kept in check and normal, or are they out of control?

DR. DIANE BOVENKAMP: I like this. We're learning a lot of new words today, so commensal means it's a normal profile, a normal fingerprint, right?

DR. SHELDON ROWAN: It's the normal inhabitants of our gut. Yeah.

DR. DIANE BOVENKAMP: Dysbiosis is: Something caused it to go all out of whack, and maybe one or more that do more harm are going up. So, are there certain foods that cause it to go into dysbiosis? Is there something that we can do, I guess is what I'm asking, to prevent that from going out of whack?

DR. SHELDON ROWAN: Yeah, I definitely think that the diets that we eat could be connected to that. The easiest way to think about our gut bacteria going out of whack is, say you go to another country where the water supply isn't sanitized to the same degree we're used to. This happens, what is it, traveler's diarrhea, right? You drink water from another place, and then all of a sudden you've introduced some new bacteria or other organisms into your gut, and everything goes out of whack, and you end up with diarrhea for 3 days. That's classic dysbiosis. And there are ways to deal with that. It will often self-correct itself. One of the amazing things about our gut microbiome is its resilience. It will tend to get itself back in balance, even without us needing to do too much. But there are things that can make the gut microbiome continually stay out of balance. And so, if all of a sudden you've introduced some new foods into your diet

that are just delicious for some of those bad microbiota that are already getting out of control, that could exacerbate a condition of dysbiosis. So, we tend to usually get back in balance, but some people can't, so they have this chronic dysbiosis.

DR. DIANE BOVENKAMP: So, it's almost like the ultra-processed, Twinkie-loving microbiota that go crazy.

DR. SHELDON ROWAN: Yeah.

DR. DIANE BOVENKAMP: So when you just think about this for the normal person sitting here, we do, "the ankle bone is connected to the knee bone is connected to the hip bone." But this is just crazy. The gut is connected to the eye, if you just sit back and think about it, so how do the microbes in our gut affect macular degeneration development?

DR. SHELDON ROWAN: Yeah. Isn't that an interesting question? Yeah. So, the gut–retina access is something that was described maybe 7 or 8 years ago, and it was built on some of the research I did—and some of my colleagues—with this understanding that there seems to be a direct relationship between the microbiome and eye health. And it's really interesting to think about what connects us to the eye. So, we have some ideas about how the microbiome is connected to other parts of the body. So, for example, the gut–brain axis is one that people have been really interested in and studied for quite some time. And there's direct connections between the brain and the gut. There's some nerves—for example, one called the vagal nerve that directly connects between the brain and the gut. But for the gut and the eye, we don't have any direct connection between them, so we have to think about what is the microbiome doing to our whole body, and then how is that affecting the eye. The way that I think that's probably going to be happening is through our immune system, because our immune system is everywhere, and it's, really, constantly being instructed and reprogrammed in the gut. So, I think there's a very good chance that the immune system is a connector between the gut and the eye. And obviously, we know a lot about how the immune system also affects macular degeneration. But there could be pathways we haven't discovered yet, and I think it's really worth trying to discover all the different pathways that can go between the gut and the

eye.

DR. DIANE BOVENKAMP: Okay. So, yeah, that's really fascinating. So, how will I know that there are problems with my gut microbiome, right? Are there symptoms that I should look out for?

DR. SHELDON ROWAN: Yeah. So, the strongest link ... there was a really interesting paper that was just published on this, actually, trying to figure out what physiological changes are most connected with a big change in our gut microbiome. And it really does have to do with changes in our bowel movements. That's probably the easiest way to know if something is off. So, I think most people have a fairly wide range of what's normal for them. But obviously, when you get into something that's really abnormal—like severe diarrhea, severe constipation—those are things that we know are linked to changes in the gut microbiome. There could be changes in the gut microbiome that you just don't have any way to really know that something's gone amiss. But that's the one that I think most people notice, and that seems to be best connected in terms of asking people, "What are your symptoms? Why did you go to a doctor?" and then looking at what could be changed in your microbiome. So, that's what people should be on the lookout for.

DR. DIANE BOVENKAMP: So then, if I go to a doctor, do they do a test? Are there FDA-approved tests to check the quote "health" of my gut microbes?

DR. SHELDON ROWAN: I don't think there is. And part of the challenge is, we don't have a great reference for what your gut microbiome should be. And I think that's partly because people have different gut microbiomes from each other, and each one of those is a version of what was good for you. So, there isn't a single way for us to know if we could do this test on your gut microbiome, whether it's healthy and in balance or not. I think we have a good sense for, on a whole population, like if we look at like a million people and we measure their gut microbiomes, we can see a lot in common and different trends that would lead us to say, "Okay, these are normal healthy microbiomes." But for an individual to go and get your microbiome tested and be like, "This is bad,." that's going to be fairly hard to say, so I don't think that there are doctors that would do that test.

One question would be: Should you go yourself and find a commercial place that does microbiome analysis? And you could try that, but we're not ready for that to be part of our standard medical practice. And then, there's another consideration—what's that, Diane?

DR. DIANE BOVENKAMP: I was just saying, it could be a waste of money, right?

DR. SHELDON ROWAN: I totally think it could be. And so, it's not a particularly regulated industry because a lot of these microbiome companies aren't trying to make actual health claims, so it's a little bit of a Wild West out there. There's definitely players in there that want to get you thinking about it and want to get you concerned about your gut microbiome, and maybe for good reasons. But what we're seeing is that different people have tried sending the exact same samples to three different companies, and they get three different results from those companies because there isn't any standardization of the methods that they use or the way they analyze the data. And so, who's right and who's wrong? That troubles me a little bit. I don't think we're ready for people doing more personalized microbiome analysis. But it's not to say that this won't happen down the road.

DR. DIANE BOVENKAMP: Yeah, and that's what I was going to say. We'll invite you back in another 2 years and we can maybe talk about them.

DR. SHELDON ROWAN: You could be like, "Everything you said was wrong. How come?"

DR. DIANE BOVENKAMP: No, no, no.

DR. SHELDON ROWAN: Yeah, I think a doctor, if they're concerned, there is standard microbiology where they'll look for known pathogens, and they'll look for things, like if you have diarrhea, they'll check for a bacterium called *Clostridium difficile*, for example. And that's part of a standard medical microbiology. And if you do, you should definitely go to your doctor and find out if there's something wrong.

DR. DIANE BOVENKAMP: Okay. And so, I find it very consoling that you

say that for the most part, the microbiome self-corrects, but are there certain foods that one can eat to, quote, encourage a good microbiome? I've seen some people claim that you eat fermented foods like kimchi or yogurt or high-fiber foods to help that out.

DR. SHELDON ROWAN: We can definitely affect our microbiomes with what we eat. So, you mentioned one of the ways that we can do that is by eating probiotic-containing foods, fermented foods, and we know pretty clearly that eating those foods changes your microbiome. Not a ton, but, for example, the bacteria, or sometimes the fungi that you would eat in the fermented food, because they've been selected for in that whole process, they often can go and enter into our gut and colonize it and stay there, and we can measure that. Whether that leads to a long-term healthy change or not, I would say the evidence is less clear. But what we do know is that a lot of times, people that eat those fermented foods tend to have fairly healthy profiles. So, there's a good chance those are positive impacts on your gut microbiome. One of the caveats if you do want to try to take on a new fermented food, say you really discover that you love kombucha and you think microorganisms coming from kombucha are great for you. One of the caveats is you have to keep taking it. You have to keep eating it. It's not like you take kombucha and you've changed your gut microbiome forever. It's a very short effect, so you may have to have it several times a week to get a potential benefit. We also know that there's some foods that maybe encourage the growth of bacteria that you might not want to have. So, for example, certain kinds of bacteria really thrive in eating products from red meat, and you may just find, "Okay, I don't feel so great after having a lot of red meats." And it's possible that you're encouraging the growth of some bacteria that have made you feel that way, so obviously, if you cut that out, you're going to not encourage the growth of those bacteria. Whereas we can always encourage the growth of a really diverse set of bacteria by eating high-fiber-containing fruits and vegetables, and this is where nuts are also really positive, legumes—those kinds of foods that have a lot of different kinds of fibers will almost always increase the diversity of bacteria in our guts and promote ones that tend to be more health-promoting.

DR. DIANE BOVENKAMP: What if I have something balanced? What if

I have red meat with legumes and high fiber? Does that counteract the effects of red meat, or is that not known?

DR. SHELDON ROWAN: It definitely could. It could promote the growth of both of them at the same time. But there's always the possibility that the ones that you're encouraging to grow with those plant fibers are going to occupy spaces that prevent the ones that are associated with red meat from growing in there. So, the bacteria are all in competition with each other. And so, you can sometimes change the balance by eating multiple kinds of foods that encourage their growth. This is one of the challenges in doing nutrition research is that with every food we eat, we're not having something because of that. And so, it's really always hard to know whether it's the positive effect of one food or the positive effective of removal of a different food from your diet. These are great questions. There's so much research in this area, and we need this research. We just don't know enough yet.

DR. DIANE BOVENKAMP: Okay, so what about another question? What about wholesale maybe killing off certain populations, and does this put you at risk for AMD? So, does having huge amounts of alcohol when you have it, does that kill off some of the good microbiome? Or maybe if you have a course of antibiotics where it might kill it off?

DR. SHELDON ROWAN: Yeah, those are two separate questions and both interesting ones. Let's do the antibiotics first, because if there's anything I know we can take that's going to kill off those bacteria, it's antibiotics. So, without question, most oral antibiotics that we take are going to affect your gut microbiome. And they're probably not going to affect it in a positive way. They often lead to loss of diversity. We lose a lot of our different kinds of bacteria after a course of antibiotics. And people feel that some people get really bad GI problems from antibiotics. But we know from a lot of data that antibiotics will kill off your gut microbiome, including the ones you're trying to get rid of and the ones you want to keep. So, antibiotics are a special consideration. Alcohol is a little different. Alcohol probably has some effect on the gut microbiome, but it doesn't kill it off. If anything, there's some microbiota that would be happy to use your alcohol as a food source, so I wouldn't worry about alcohol killing

off the microbiota. It's definitely going to work in a different way than antibiotics, but that's not to say that it has no impact on the microbiome either.

DR. DIANE BOVENKAMP: Yeah, because you did mention that part of the Mediterranean diet that some amount of red wine, which is alcohol, is good. So, is there just a certain amount of alcohol, I guess? And I guess then you could maybe move into are there any foods ... what's the general healthy lifestyle that what's good for your heart and your gut is good for your eye's kind of diet?

DR. SHELDON ROWAN: Yeah, alcohol is such an interesting one because I think the more we're learning about alcohol intake, especially for cardiovascular disease, my feeling is that we're all moving towards a no alcohol guideline. I think right now the guidelines call that one serving a day for women, two servings a day for men, is probably safe. And I think that's already been cut down. So, the evidence for cardiovascular disease we have thought that there was maybe a possibility at some point that alcohol could be a little protective in very small amounts. I think that was in line with what we know about the Mediterranean diet. But right now, at least for your heart, it doesn't seem that alcohol has any particular positive effect. But what's good for your heart is usually good for your eye, but not always. So, when it comes to data about macular degeneration, there's still enough data that suggests that maybe one serving of alcohol could be okay. It might be a little protective, and it's unlikely to be harmful, so there may be a slightly different effect of the alcohol on the eye versus the rest of the heart. Or it's always possible that people that have alcohol in a lot of moderation are already thinking about a healthy lifestyle, right? And so, maybe they're also doing some extra exercise, and maybe that's where the benefit comes from. But I don't think we have a clear answer about alcohol. My guess is that it's probably not going to end up being very positive for macular degeneration, but it may not be bad for macular degeneration. And that's probably going to be similar to what we know about how it affects the gut microbiome. The other thing about the Mediterranean diet is most of the alcohol intake tends to come in with wine, especially red wine, and red wine is just so rich in other nutrients, things like phytochemicals. We've studied one of them, called

resveratrol, for a really long time. So, we know there's all of these other positive impacts of consuming red wine, and maybe those are the ones that are associated with the protective effect on macular degeneration. And it's not the alcohol, it's the other nutrients that are associated with wine intake. These are open questions, I would say.

DR. DIANE BOVENKAMP: So, I think I want to skip to, because you talked about supplements and other key macronutrients influencing microbiome, what's the role of vitamins and minerals and other supplements, especially since we know there's the AREDS2 recommendations for people who have intermediate dry to take this to try and prevent going to wet AMD? There have been 15 or 20 years now they've been doing follow up, and 35 percent of people or whatever prevent the moving through. So does that affect the microbiome? Are the microbiome affected by the AREDS2 vitamins and supplements?

DR. SHELDON ROWAN: It's such an interesting question. So, AREDS and AREDS2, it's definitely held up over the test of time. And just to remind people, if they've forgotten, that it contains vitamin A, vitamin E, zinc, lutein, and zeaxanthin, so a combination of some vitamins and other minerals that people might have thought were largely like antioxidants. Something to consider about AREDS2 is that those levels of those vitamins and minerals are higher than we could possibly get in our diets. So, we're kind of taking them at levels maybe tenfold higher than what you could eat in your diet. So, we don't really think that they're necessarily working the same way that having a healthy diet might work. And then there's a question of: Do they affect the microbiome? And I think the answer is probably. They probably do. I was trying to look into whether we have any really good research about AREDS on the microbiome. And I think people have identified that as an area of interest, and they're doing the studies, but I don't think we have the results yet. So, there's a good chance that it does affect the microbiome. Whether the protection is through that effect on the microbiome is also an open question. And then, you also have to ask yourself: How does the microbiome affect how those vitamins work?

DR. DIANE BOVENKAMP: Oh.

DR. SHELDON ROWAN: I know, right? Nothing is ever as simple as you

think. So, the microbiome affects the bioavailability of vitamins in our body. If you think about fat-soluble vitamins, they end up going into the intestine, and then they have to go and get taken up by, usually, part of our fat metabolism systems, and those are highly impacted by the gut microbiome. So, I think it's probably unlikely that AREDS work through the gut microbiome, but it probably impacts the gut microbiome in a way that could affect how it interacts with other aspects of our diet. These are really great questions.

DR. DIANE BOVENKAMP: I think you just blew my mind. So, these little passengers in our in our body could be affecting us more than we think.

DR. SHELDON ROWAN: Definitely. And again, we talked a little bit about antibiotics, but a lot of the medications that we take probably affect our microbiome, too. In some cases, we know that the microbiome affects how we respond to different medications. So, this is just the beginning of a giant area of specialization.

DR. DIANE BOVENKAMP: That's very interesting. Do you think that how we process and the bioavailability of drugs, vitamins, and supplements, just maybe with the alcohol, are sex-based differences? Have people done research on that yet, or is that still in its infancy?

DR. SHELDON ROWAN: I think that's still in its infancy. But what we do have are we have some great projects ongoing looking at really large populations. So, the NIH has this project called the All of Us Research Program, and they're recruiting hundreds of thousands of individuals across really diverse racial backgrounds, and men and women, and are trying to get at some of these questions. So, they're looking at the microbiome in a lot of these studies and trying to get answers to these. But yeah, it's going to take some pretty extensive research to come up with all of the answers.

DR. DIANE BOVENKAMP: Yeah. Thank you so much for mentioning the other obvious potential difference, which is the ethnic and racial difference. But then again, how do you separate the potential cultural differences in diet versus your genetic makeup, right? So, those are probably things that are being studied in that.

DR. SHELDON ROWAN: Yeah. One thing I will mention in terms of thinking about genetics, because, obviously, we know that genetics have a role in risk for macular degeneration, maybe accounting for about 50 percent of the risk. And people were really interested in knowing whether their actual genetics affects how the diet works on you. So, for example, does a Mediterranean diet only protect you if you didn't have genetic risk for disease? And some of those studies have been explored, and I think it's worth mentioning that the protective effect of the Mediterranean diet definitely works in individuals that have genetic risks for macular degeneration. So, no one should ever think that genetics are destiny—the role for a diet, environment, and lifestyle are really independent and can enhance what we know about our genetic risks for macular degeneration.

DR. DIANE BOVENKAMP: That's a really empowering statement right there. No matter where you are in your current life situation, there's always something that you can do to change your situation, and it's never too late. I really like that.

DR. SHELDON ROWAN: Yeah. And again, I think this also speaks to the fact that we know that the Mediterranean diet protects against progression of macular degeneration. So, it's never, "Oh, you should have done that when you were 40 years old, and you'd be fine." It's like, do it now. Wherever you are in the disease process, know there's something that you can do, and it's something that you can modify. So, yeah, we have a little more control over our destiny than we think.

DR. DIANE BOVENKAMP: What about other things that we can control, sleep and exercise? And actually, I'm going to throw in something like calorie restriction or intermittent fasting that I've heard about. Is that something that could affect the microbiome and, hence, the AMD risk?

DR. SHELDON ROWAN: Yeah, all of those are great things to discuss. So, let's start with lifestyle, and then we can get to intermittent fasting, because I don't want to neglect to talk about what we know about exercise and what we know about sleep, because I think all of those things are pillars of a healthy lifestyle, and all of them can enhance each other. So, exercise we definitely know can help protect against macular degeneration in some context. It looks like ... this is interesting. It looks

like exercise is more linked to prevention of early forms of macular degeneration, and then the data about progression is a little more ambiguous. So, exercise can go together, and it has so many positive effects, not just on our metabolism, but it has effects on our brain, so, obviously, it's going to have effects on our eyes, as well. Sleep is an interesting question. I think there's no question that sleep is going to be connected to your risk for macular degeneration, but it may not be because of direct effects of sleep. We know, for example, that people that are chronically under slept are at higher risk for chronic disease. They're also at higher risk for eating unhealthy diets. And so, if you're only sleeping for 4 hours a night or if you're up half the night, there's a good chance that you may start snacking at some point. So, those are ways that sometimes aspects of our lifestyle get connected to each other, so sleep and diet are really tightly connected. We know that shift workers, for example, people that have to work at night and then try to sleep during the day, also that's associated with negative health outcomes.

And that could also be connected with what time in the day they eat food, which connects to our normal circadian rhythms. These are all emerging areas of study. I'm excited about all of them because they're all interconnected. People that tend to get better sleep or that tend to exercise more often are going to find ways to also eat a healthier diet, so it's a nightmare for the epidemiologists doing their research, but it's great in terms of how we react to these lifestyle changes. And then, intermittent fasting is interesting. I think the idea of intermittent fasting is that you restrict when you eat foods to only a certain window of time in the day. And we know from studies of our circadian rhythms that we process carbohydrates more effectively in the morning and in the afternoon than at night. And so, the idea is if you eat most of your food calories, and especially your carbohydrates, at those times where we process the food better, you're going to have better metabolic health. And there's a little bit of truth to that. I think the studies have borne that out, but it also turns out that we eat fewer calories when we restrict the window of time that we eat. And it's probably because a lot of people get a third of their calories in the evening through having snacks. So, if you stick to intermittent fasting, you're probably not going to be snacking at night. That's going to be better for your metabolism. You're going to eat fewer

calories. You're also probably going to have a higher quality of sleep. You see how all of these things become interconnected.

DR. DIANE BOVENKAMP: Yeah. Thank you so much because I do not want to do fasting. I'll just not snack at night.

DR. SHELDON ROWAN: I don't either, but I was thinking about lifestyle a little bit, and one of the things I realized is that you don't have to change everything at once to make positive impacts across the board. So, you can really tackle this one part of your lifestyle at a time. And if you feel like, "I can control my eating best," do that, and the other things will come along with it. If you're like, "I can add more exercise in my life," then do that, and other good things will come from it. Because sometimes the advice all just seems so daunting, like if you do A, B, C, D, and E, it's impossible. How can I possibly find enough hours in the day to do it? So, don't. Just do one of them, and then go from there.

DR. DIANE BOVENKAMP: Yeah, baby steps.

DR. SHELDON ROWAN: Exactly.

DR. DIANE BOVENKAMP: So, I think one of the things before we go on to maybe your final word or summary or maybe something that maybe I've missed asking that you think is important, the last question I'll have before we go to that is, is there any current research in your lab, others, and/or clinical trials going on studying the role of diet and nutrition on macular degeneration that maybe our listeners can follow over the next year or two until we can bring you back?

DR. SHELDON ROWAN: Yeah, there are some studies, and I'm really excited that these have happened because, again, it's an area where we've identified the need for 20 years in doing these kinds of studies, and they're so hard to get going. So, ones that I'll mention that I know about—there may be some I don't know about—but there's a study in Europe called the AMD BITE study, and that's looking at what happens when you think about looking at people's risk for macular degeneration based on, say, their genetics and their age and their biological data, and then adding in lifestyle interventions and coaching, and especially trying to look at

encouraging people to have a more Mediterranean diet approach. And so, that study is ongoing in Europe.

And there's a study I know about in Australia, where they're trying a randomized clinical trial where they're having some people do telephone-directed coaching. So, it's a noninvasive kind of intervention. You just call people on the phone and try to encourage them to eat a healthier diet, again trying to increase how close their diet is to the Mediterranean diet compared to people that don't get that kind of coaching. And they're trying to look at the first step is just to even see if we can effectively change people's diets, and then we can really see if we're preventing, say, progression of macular degeneration.

And then, there's actually the third study I'll mention that I'm involved with, so I'm really excited about it, it's called GLOVE. We just have some money from the NIH to do the early trials, and this is going to be centered at UCLA and Stanford University. The idea is we're really trying to focus on not just doing a dietary change, but getting people to eat lower glycemic index diet. And one of the ways that we're going to test that out is by having people do continuous glucose monitoring, so do virtual dietary advice and then actually connect them to these continuous glucose monitors to see whether we can see changes in how their bodies response to glucose and food over time, and do these in patients with macular degeneration, where we could eventually determine if it affects their progression or not. There is research going on in this area. It's early, so no answers yet, but call me back in a few years and we'll see where they are.

DR. DIANE BOVENKAMP: Great. We will. And yeah, if you give us links to those trials, we can post them on our texts and everything, so people can follow it for themselves. So, yeah.

DR. SHELDON ROWAN: Yeah, definitely.

DR. DIANE BOVENKAMP: Yeah. So, before I do the closing remarks, I think we have a few minutes here. What is your final word or summary of what we can do to reduce our risk of age-related macular degeneration and have an overall healthy lifestyle? What do you think are the first steps that

we can do to empower?

DR. SHELDON ROWAN: It's funny. The first step is one that we haven't talked about yet, which is quit smoking. If anyone is still smoking, that's the first step. It should be. So, there's some basic things, so quit smoking. Whatever it takes to do, try to make that happen. See an ophthalmologist regularly. Get a dilated eye exam. I know it's a pain having to get the eye drops in and then your eyes get all sensitive to light and you need to wear sunglasses. It's really worth doing. People really neglect going to an ophthalmologist. So, those are always the first things that I would suggest people do. I know we haven't talked a ton about food supplements and nutrition supplements. I don't think people should worry too much about them. I think if you have a good diet and if you try to improve your diet by adding in, say, nuts or trying to add in legumes or eat some more high-fiber fruits and vegetables. I love avocado. Most people do. And it's a great way to get great fiber in your body. If you do those things, I don't think most people need any nutritional supplements. I doubt that there's harm from taking a daily multivitamin, but some people really are going and getting very specific kinds of nutrients that are being marketed to them, and I think we really don't have any data that speaks to doing that, including for your vision. So, don't worry so much about food supplements and nutritional supplements.

We talked a little bit about antibiotics. The one thing that I would not do is I wouldn't start taking commercial probiotics in conjunction with the regime of antibiotics. We have some data that says your body recovers the microbiome better when you don't take probiotics than when you do. And so, I kind of mentioned, too, that there's these industries doing microbiome analysis, and they're completely unregulated. And the probiotic industry is the same way. It's completely unregulated. They could say anything they wanted to. There's no regulation on it. There's no standards for it, and there's no strong evidence of benefits. Unless your doctor tells you to take it, I would generally tell people, probably, don't take probiotics. We just don't know enough about what they might do, and you can't always assume it's going to be a positive thing. But those are my take-home messages. Find foods you really like. I think a lot of people find the Mediterranean diet challenging. They're nervous

about making a change to their diets. No one should have to eat foods they don't like. If you're like, "Really, okay, I want to add in more green vegetables to my life, but I hate kale." Don't eat kale then. I think that's not the right approach, but maybe you could find something else, that cooked in a certain way you do like it, or maybe, "Okay, I don't like the kale that I buy in the supermarket, but I kind of like the kale Caesar salad that they have at Sweetgreen." Then go and eat that. I think food should always be enjoyable, and you should always find a way to eat foods that you like. I would say that's an important message. People really get overwhelmed by dietary advice. It doesn't have to be scary or hard.

DR. DIANE BOVENKAMP: Wow. You just changed my world right there with that. It's like, "Oh, we don't have to."

DR. SHELDON ROWAN: The goal should never be perfection, right?

DR. DIANE BOVENKAMP: Yeah, don't force yourself to do something that you don't have to, because there's always probably an alternative. And I guess you could always bring in a nutritionist or even talk with someone else who might be able to point you in the right direction.

DR. SHELDON ROWAN: Yeah, registered dietitians. This is their thing. They know this.

DR. DIANE BOVENKAMP: Thank you, Dr. Sheldon Rowan. So, thank you so much for sharing this information with us today about the gut microbiome and nutrition in general. To our listeners, I sincerely hope you found today's Chat helpful. Many thanks to our community of donors for making this possible. Our next Macular Chat will be on Wednesday, August 28, and I hope you can join us. Thank you so much, again, to our guest speaker and to our listeners for joining us today.

DR. SHELDON ROWAN: Thanks so much.

Useful Resources and Key Terms

To access the resources below, please contact BrightFocus Foundation: (800) 437-2423 or visit us at www.BrightFocus.org. Available resources include—

- [Macular Chats Archive](#)
- [Healthy Living and Macular Degeneration: Tips to Protect Your Sight](#)
- [Research funded by BrightFocus Foundation](#)
- [The Top Five Questions to Ask Your Eye Doctor](#)
- [Treatments for Macular Degeneration](#)
- [Understanding Macular Degeneration](#)
- [4 Nutrition Tips for Eye Health](#)
- [Lutein and Zeaxanthin for Protection Against Macular Degeneration](#)

Other resources mentioned during the Chat include—

- AMD BITE Study
- GLOVE Study