BrightFocus® Chats

AMD: Your Questions Answered
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Transcript of Teleconference with Dr. David S. Liao, Retina-Vitreous Associates Medical Group

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

MICHAEL BUCKLEY: Hello, I'm Michael Buckley with the BrightFocus Foundation, and welcome to today's BrightFocus Chat, "AMD: Your Questions Answered." BrightFocus funds scientific research around the world to find better treatments—and ultimately cures—for macular degeneration, glaucoma, and Alzheimer's. Through our website, www.BrightFocus.org, and a wide range of print materials, we share the latest news from the world of science and best practices in medicine with families that are impacted by these diseases, and that's why we have today's Chat. It's a fantastic opportunity for us to hear from one of the leading researchers in the field of macular degeneration. So, today we'll be joined by Dr. Joshua Dunaief at the University of Pennsylvania in Philadelphia. He conducts research on macular degeneration, some of which has been made possible by donors to BrightFocus' Macular Degeneration Research Program. He also sees patients in the University of Pennsylvania's Medical Center. And if his name is familiar, we've been

really fortunate to talk with him on previous BrightFocus Chats, and he's written a number of expert articles for our website. With that, Dr. Dunaief from the University of Pennsylvania, thanks so much for being with us.

DR. JOSHUA DUNAIEF: Thank you, Michael. It's great to be back with you.

MICHAEL BUCKLEY: You're one of the top researchers in the field of macular degeneration. Is there anything new and exciting in the field of vision health that you'd like to share with our audience today?

DR. JOSHUA DUNAIEF: There are several things that I'm excited about. In the area of dry macular degeneration, there's an advanced form called geographic atrophy, and there are a couple of drugs that are now in Phase 3 clinical trials that are looking promising. These are from companies called Apellis and Iveric, and what these drugs do is they target inflammation, specifically something called the complement cascade. And the complement cascade has been implicated in macular degeneration for years by genetic studies, and these drugs look like they can slow the progression of geographic atrophy in Phase 2 trials. So, now they're in Phase 3 trials with larger numbers of patients, and I'm hopeful that they will prove safe and effective and useful for patients with geographic atrophy. Now, these drugs are injected into the eye, kind of like the drugs that are used for wet macular degeneration. People are typically more familiar with those. Do you want me to talk about the drugs for wet macular degeneration?

MICHAEL BUCKLEY: That would be great.

DR. JOSHUA DUNAIEF: The drugs that have been available for a few years now all target a protein called VEGF. VEGF is kind of like a fertilizer for blood vessels that causes them to grow like weeds. The blood vessels grow too much, and they leak and they bleed and cause some loss of central vision. So, these drugs all target this VEGF. The drugs are called Avastin®, Lucentis®, Eylea®, and a new one called Beovu®, and they can actually improve vision by decreasing the amount of blood vessel growth and leakage. So, they're very exciting, but they do need to be injected into the eye once a month or every other month, or in some cases even a little bit less frequently than that. They're good, but it's, of course,

annoying for patients to have to come into the office so frequently, and sometimes it can be scary to get these injections. So, patients have asked me for years, "When are we going to get a drug that lasts longer?" And there are a couple of advances on that front. One is called the PDS implant—Port Delivery System—and what that is, is it's implanted into the ... near the front of the eye, and it can be filled with Lucentis. And the Lucentis is released slowly over time so that the port may only need to be refilled every 6 months or perhaps even less frequently. So, that could really help reduce the frequency of visits and the frequency of injections. And another thing that's being tried is gene therapy for wet macular degeneration, where drugs can be delivered once by gene therapy and then constantly release the drug that inhibits VEGF. And the companies that are working on that are REGENXBIO and Adverum, and they're both in clinical trials now. So, I'm hopeful that these things are going to become available. The PDS implant—Port Delivery System—is going to be reviewed by the FDA in October, so it could actually be available to patients pretty soon.

MICHAEL BUCKLEY: It's a really exciting time in the field of vision science. We get questions. Some people wondered: Do you think there'll be an ability to ever prevent AMD? Do you think that science will be able to prevent it from happening in the first place?

DR. JOSHUA DUNAIEF: I hope so. I mean, what we understand about AMD is that it's caused by aging. It's very uncommon in people under 55 and quite common in people over 80; about 25 percent of people over 80 have some form of macular degeneration. So, "What causes the aging?" becomes the question, and one of the leading theories on this is that free radical damage—oxidative damage—gradually damages molecules, like proteins and fats and DNA, and the accumulation of this damage contributes to aging and age-related disease. Another thing that contributes to age-related disease is inflammation, which is when the immune system, rather than attacking viruses or bacteria, actually attacks our cells, and the inflammation definitely plays a role in macular degeneration. So, to prevent macular degeneration I think what we need to do is reduce oxidative damage and reduce inflammation, and one way to do this is diet.

It's been shown over the past decade that people who eat certain diets that reduce oxidative damage and inflammation have a decreased risk of macular degeneration. So, these diets include fruits and vegetables—especially green leafy ones, but all kinds of fruits and vegetables—and also fatty fish twice a week. There's something about the fatty fish that is protective—possibly the fish oil, although supplements of fish oil have been tested, and they are not helpful. So, you have to have the whole fish to have the protection, not just a pill with fish oil. Also, this diet reduces inflammation. I've done some studies with my brother who practices internal medicine—integrative medicine—looking at patients in his practice who go on a whole-food, plant-based diet, and they have lower levels of inflammation in their blood; quite quickly they can reduce the amount of inflammation. So, I think with diet you can go a long way toward preventing macular degeneration. Things that are unhealthy for macular degeneration, shown in epidemiological studies, are certain fats and sugar—refined simple sugar, red meat, and also smoking—it increases the risk of macular degeneration, probably because it causes oxidative stress, free-radical damage.

There is something new that I'm actually quite excited about now in terms of a therapeutic: it's deuterium. So, deuterium is a nonradioactive isotope that can affect how molecules behave, and deuterium has been added to vitamin A by a company called Alkeus to prevent the buildup of a toxic product of vitamin A that is very likely to play a role in Stargardt disease—which is a hereditary form of macular disease—and also in macular degeneration. So, Alkeus is conducting a Phase 3 trial—advanced trial now—with geographic atrophy and also a trial for Stargardt. There's also another company that has put deuterium on fish oil—docosahexaenoic acid, DHA, which is an omega-3 fatty acid. It's a company called Retrotope, and this altered form of DHA is harder to oxidize; it doesn't develop oxidative damage as easily as the native form of DHA. And research in my lab with mice that we use to test potential drugs for macular degeneration suggests that it's very promising and suggests that this could be very effective. So, I'm hopeful that Retrotope will be able to move forward with clinical trials soon.

MICHAEL BUCKLEY: Dr. Dunaief, we have a question that came in.

Listeners are kind of curious. Who gets AMD? Is it more likely to be women or men? Or does race and ethnicity vary? Are Americans more or less likely to get AMD than other countries? Our listeners are kind of curious about: Are there differences?

DR. JOSHUA DUNAIEF: AMD means age-related macular degeneration, and so as people age, they are much more likely to get it for reasons I mentioned before. Among the different races, Caucasians are at the highest risk, and behind them are Hispanic, and the least vulnerable are Black. And among the different countries, it seems to hit the more developed countries most severely, and I suspect that may have to do with the Western diet, which tends to be high in fat and sugar and refined foods and lower in those whole-food, plant-based products that are protective.

MICHAEL BUCKLEY: I think you've done a great job of showing the impact of diet on vision health. And you're right, people in America and other places don't always have the best diet. We have a question. Someone is wondering: Can a doctor predict kind of the extent or the timeline or the pacing of how someone might lose vision to macular degeneration?

DR. JOSHUA DUNAIEF: Yes. So, the eye is kind of a window to what's going on in the rest of the body. We can use drops to dilate the pupil and then look into the eye at the retina—in the back of the eye, which is the light-sensitive part—and that's where macular degeneration is happening. And we can actually see with our instruments some changes that indicate the risk for vision loss from macular degeneration. The major one is called drusen. Drusen is a German word that means "pebble," and it represents little accumulations of material in the retina that shouldn't be there. They look like little white spots, and the more numerous and the larger these spots, the greater the risk of vision loss. We can also see some changes in pigmentation that can help us to predict ...also, if somebody has had advanced macular degeneration develop in one eye, then they're more likely to have it occur in the second eye, as well. So, yeah, absolutely. We can give a pretty good idea to patients as to what their risk is over time.

MICHAEL BUCKLEY: There are a few questions where people

are wondering: In between their appointments or their treatments with their eye care professional, are there signs—sort of warning signs—that they should be on the lookout for that their macular degeneration could be getting worse?

DR. JOSHUA DUNAIEF: Absolutely. Yeah, any changes in central vision would be concerning. So, greying out of the central part of the vision or waviness of lines that should look straight, like on a page of lined paper or the edge of a door frame looking wavy. Ophthalmologists will give macular degeneration patients something called an Amsler grid, which is a piece of graph paper, essentially, and instruct them to close one eye at a time and then look at the dot in the center of the grid, and if there are any missing or wavy lines that are different from the way they looked at the last visit to the ophthalmologist, then you should contact your ophthalmologist. And it is important to look at this one eye at a time because if you have both eyes open, and one eye has a change—progression of macular degeneration—the better eye can compensate for that, and it won't become obvious to you that macular degeneration has progressed. You really have to cover one eye at a time and test each eye independently.

MICHAEL BUCKLEY: Dr. Dunaief, a few minutes ago you did a great job kind of giving an overview of the different injections—anti-VEGF injections—that are out there. We have a few callers wondering: Do those injections ... can they lose their effectiveness over time?

DR. JOSHUA DUNAIEF: The biggest reason for the decreased effectiveness over time is less-frequent injection. Some patients really need to have an injection every month in order to maintain their best vision, but it's difficult for people to come in every month and get that injection. So, there tends to be a decrease in frequency even when there really shouldn't be, and that's the major problem. Some people are more fortunate in that they really don't need an injection every month; they can make do with one every 6 weeks or every 2 months or sometimes even less frequently and still maintain vision. So, that's the main reason that people would lose vision even though they're still getting the injections; it's just that they're just not able

to come and get them as frequently as their doctor would recommend.

MICHAEL BUCKLEY: Makes a lot of sense. We've got two questions that are related to ... one type of medical condition is related to another, and the first is cataracts. A couple of listeners are wondering: Do cataracts cause AMD? Does AMD cause cataracts? And if somebody needs surgery to remove cataracts, does that have any good or bad impact on macular degeneration?

DR. JOSHUA DUNAIEF: Good question, Michael, and one that patients frequently ask. So, cataracts are a clouding of the lens in the front part of the eye, and macular degeneration affects the retina in the back of the eye—these two structures are separated from each other and independent from each other. If somebody has enough clouding in the lens that it's blocking light from getting into the eye and reaching the retina, then typically the cataract lens should be removed, and a clear plastic lens is inserted in its place. Now, the fact that the cataract is there doesn't really indicate anything about the macular degeneration. The procedure to remove the cataract is generally very safe and effective, and it does not increase the risk of macular degeneration. The one big question that comes up is—for somebody with macular degeneration—they'll ask, "If I had my cataract removed, will my vision get better?" And that can be tricky to answer in someone with macular degeneration who has both some clouding of the lens and also some damage to the retina. Typically, what we'll do is we'll use a special device to shine an eye chart through the cloudy lens at the retina so that we can assess the function of the retina if the cataract were to be removed. The device is called a PAM, or a potential acuity meter. But to reassure, again, cataract surgery does not increase the risk of macular degeneration.

MICHAEL BUCKLEY: And now another question along that same line of two different eye conditions and wondering if there is a connection. We have a question about dry eye. And so, wondering is dry eye ... it sounds a lot like dry AMD. Are there connections between dry eye and macular degeneration and vice versa?

DR. JOSHUA DUNAIEF: It does sound like dry AMD, but they are not related. Dry eye affects the very surface of the eye, the tear film. If

the ... the tear film is needed to nourish the front part of the eye—the cornea—and if there's not enough tear film, then the cornea becomes very irritated, sticky, and painful. Sometimes patients can even get a reflex flood of tears when the eye really dries out a lot, but it's not related to macular degeneration. And for patients who have dry eye, what we would recommend is artificial tear drops, and those do not ... so, those wet the front of the eye, but they do not increase the risk of wet macular degeneration because the tear drops don't get into the retina.

MICHAEL BUCKLEY: We received a question—someone is asking about CBD oils—something we've been hearing about in a number of settings lately. Is that something that is possible for use in macular degeneration?

DR. JOSHUA DUNAIEF: There's really no evidence that it's helpful at this point, so I wouldn't recommend it for macular degeneration.

MICHAEL BUCKLEY: Earlier we were talking about the impact of diet and nutrition. And some of our listeners that were with us last month ... we had Dr. Emily Chew from the National Institutes of Health on, talking about the AREDS formula. But I was wondering, Dr. Dunaief, if you could just kind of quick ... you know, for those who weren't on last month's Chat, could you just briefly explain what the AREDS formula is and who should be ... you know, who that would help?

DR. JOSHUA DUNAIEF: The Age-Related Eye Disease Study, or AREDS, was conducted by the NIH by Dr. Emily Chew and others there, as well as Centers around the country, and what they showed is that certain antioxidant vitamins can decrease the risk of macular degeneration progression. And there was an initial study, AREDS1, and then a follow-up study, AREDS2, that modified the formulation a little bit to see if it was just as good. And the formulation that they came upon with AREDS2 involves antioxidants called lutein and zeaxanthin—which go to the retina when you eat them—also vitamin C, vitamin E, and the minerals zinc and copper. And these vitamins are available over the counter. The formula that was used in the study will be labeled AREDS2 formula, and the brand that I like is called PreserVision® by Bausch + Lomb, because that one was actually tested to ... significantly tested to see if it contains the ingredients it says it contains, and in fact, it does, and that's a concern because the vitamin

market is not regulated, unlike the drug market, so vitamins may not actually have what they say they have on the package. Also, let me just say at this point that I am not supported in any way by any of the products that I have mentioned today.

MICHAEL BUCKLEY: I appreciate that. Thanks.

DR. JOSHUA DUNAIEF: No conflict of interest.

MICHAEL BUCKLEY: That aisle in the pharmacy and the supermarket, I've always found it overwhelming and a little expensive, so I appreciate the tips on this. We had another question about kind of in the diet and nutrition realm: carbs. We've heard a lot over the last couple of years about carbs, what's good for you, bad for you, which carbs are ... is there a connection between carbohydrate intake and vision health?

DR. JOSHUA DUNAIEF: There's evidence simple sugars are bad for macular degeneration [inaudible] eye disease. And when I say simple sugars, I mean anything that contains added sugar, fructose, sucrose, and also products that release sugars rapidly, like bread, pasta, baked goods, things made from whole ... from white flour; these actually release the carbs rapidly. There are other products that contain carbohydrates that are released much more slowly, like fruits. Fruits typically release their carbs more slowly and contain complex carbohydrates. Beans have fiber, which is broken down much more slowly. So, it's the non-refined whole foods that are generally safe when it comes to carbohydrates, and the refined packaged products that have the added sugar—the soft drinks that have the sugar—that is ... it's harmful. It causes stress and inflammation and weight gain and fluctuations in blood sugar levels that make it feel like [inaudible]. So, I really recommend trying to stay away from those sugars.

MICHAEL BUCKLEY: In the couple minutes that we have remaining, there's a couple of questions sort of about daily life with vision loss. From your experience seeing patients in the clinic, do you have any advice for caregivers, whether that's someone that might be in the same area as the patient or caregivers that are, you know, family members that are longer distance? From what you've seen, in your perspective, any advice for families on caregiving?

DR. JOSHUA DUNAIEF: That's an important issue. People who've lost their central vision really need assistance, and it's very difficult for people to lose the ability to drive and with that dependence. So, I think they need to understand that people with macular degeneration are going through some difficulties because they have lost this that we all value so much. Things that can really help patients who've lost a lot of central vision include visiting an optometrist who is a low vision specialist and getting lights and devices to use the vision that they still have or an assist from an occupational therapist who specializes in low vision who can help with the house—like the lighting, marking things with special tape in the kitchen or edges of stairs—to make it safer and easier to cope with the loss of the central vision.

MICHAEL BUCKLEY: Those are great tips, and I think that there are things that a lot of us can do to help friends and family that are impacted by low vision. Dr. Dunaief, you've been, as always, a great resource on so many topics. I'm just wondering, you know, as we conclude today's conversation, do you have sort of big picture advice that you'd want to give to patients and families? You know, sort of a common concern that you hear and how you address that? Just kind of concluding remarks.

DR. JOSHUA DUNAIEF: Thanks Michael. One major concern I've heard patients ask is, "Am I going to go blind from this disease?" And the answer is hardly ever do patients lose all of their vision from macular degeneration. In the worst case, the vast majority of patients lose their central vision but keep their peripheral vision, which is harder to use. It takes some time to learn to use it, but it's still very valuable. Also, a lot of patients who are diagnosed with early macular degeneration are asymptomatic or barely symptomatic, and they have just a few of those white spots in the retina that can be seen by an ophthalmologist—the drusen—and those patients have a good chance of not losing their central vision at any point in their life, especially if they do things to live a healthy lifestyle: Don't smoke; get some exercise; and eat a healthy diet rich in fruits and vegetables, and fatty fish twice a week, and not packaged foods that are high in sugar or fat. Sunglasses, when you're out in bright light, are also recommended to protect against potential damaging effects of bright light. And then, I just want to share my optimism about all the

new treatments that are coming through the pipeline that I mentioned. I mean, there's a number that are looking promising, and there are a lot of people working on this. There are researchers, there are pharmaceutical companies that are constantly trying to develop better treatments. So, I think the future is bright, and I'm grateful to the BrightFocus Foundation for providing information; the opportunity to reach all of you with the information; and also grant funding to all the researchers who are working on this disease, especially early career researchers who are trying to get launched and can find it hard to get grant funding. And it's really critical for them to get some funding to … and develop a research … help them develop a research program that has the potential to develop new treatments for AMD.

MICHAEL BUCKLEY: That's great. I appreciate that. And you know, kind of what I've taken away from this conversation—kind of two-fold. One, that there's some really exciting science going on around in this country and in labs around the world, and secondly, you gave us a number of very specific things that we can do in our daily lives to either prevent or better manage macular degeneration. So, on behalf of everybody at BrightFocus and in our audience today, I just really want to say thank you for the work you do in the lab and also with your patients, and I think today's been really helpful. Dr. Dunaief, thank you so much for joining us again, and I hope we can do another BrightFocus Chat in the future.

DR. JOSHUA DUNAIEF: My pleasure, Michael. Be well, and to all the listeners out there, best of health to you.

MICHAEL BUCKLEY: Thanks. Take care.

Useful Resources and Key Terms

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- BrightFocus Foundation Live Chats and Chat Archive
- Clinical Trials: Your Questions Answered
- Healthy Living and Macular Degeneration: Tips to Protect Your Sight
- How Low Vision Services Can Help You
- Macular Degeneration: Essential Facts
- Research funded by BrightFocus Foundation
- Safety and the Older Driver
- The Top Five Questions to Ask Your Eye Doctor
- Treatments for Age-Related Macular Degeneration
- Understanding Your Disease: Quick Facts About Age-Related Macular Degeneration (AMD)

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E-mail: 2020@nei.nih.gov
Phone: 301-496-5248
Mail: National Eye Institute
Information Office
31 Center Drive MSC 2510