Macular Chats

TRANSCRIPT

Explaining the Results from the AREDS2 Study

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Featuring: Emily Chew, MD

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

MICHAEL BUCKLEY: Hello, I'm Michael Buckley with the BrightFocus Foundation. Welcome to today's BrightFocus Chat, "AMD: The Latest Results from the AREDS2 Study." If this is your first time joining us, welcome. I'll briefly tell you about BrightFocus Foundation and what we'll do today. BrightFocus is funding some of the top scientists all around the world to find better treatments, and hopefully cures, for macular degeneration, glaucoma, and Alzheimer's. We share this information with families that are impacted by these diseases to help you better manage these diseases. We have a number of free publications, including free materials on our website, BrightFocus.org. Today's BrightFocus Chat is another way of giving you the latest news from the world of science.

Let me tell you about today's Chat. One of the areas we get the most questions about here at BrightFocus when it comes to AMD is vitamins and nutritional supplements, specifically, the AREDS for AMD. We have a lot of questions about that, so today we are talking to the best source in the world on this. Her name is Dr. Emily Chew. She's one of the top vision scientists at the National Institutes of Health. She's with the National Eye Institute, and she has done research over the years about vitamins and nutritional supplements, particularly AREDS, so we're very fortunate to have the opportunity to have Dr. Chew with us.

She is a winner of the Helen Keller Prize for Vision Research, which a lot of people think of as the Nobel Prize for vision science, and BrightFocus is fortunate to partner with Dr. Chew and her colleagues at the National Eye Institute to try to better educate the American public about vision health—particularly macular degeneration from glaucoma. So, Dr. Chew, thank you very much for returning to the BrightFocus Chat.

DR. EMILY CHEW: Well, thank you very much for having me. It's always fun to be here and to share our knowledge and to talk to our patients, who are a big part of our focus, as well.

MICHAEL BUCKLEY: I want to start by saying: How did you end up doing this? Why did you become a vision scientist?

DR. EMILY CHEW: Well, we rely on mentors, and mentoring is very important for us, and as a young medical student, I met a mentor who was interested in doing research; her name is Dr. Brenda Gallie—at that time at the University of Toronto—and she works on retinal blastoma, which is an eye tumor in children. I wanted to be a pediatrician when I first went to med school and ended up doing ophthalmology because of her, and she impressed upon me that doing research, she can help thousands of people at once and really be very fulfilling, and I … throughout my training, I went to places where there was very active research. I was at Johns Hopkins for my fellowship, and during those days, macular degeneration was just beginning to have a lot of research, and people were very interested, and it was such excitement. All the faculty, all the trainees, were really super-excited, and I learned a lot about clinical trials, which are so important. So, that's the reason I ended up doing research, and then I went back to the National Eye Institute. I've been there ever since, and I've really had a wonderful time. We've been given a lot of opportunities to work for the American public, especially for patients with vision loss and macular degeneration.

MICHAEL BUCKLEY: Yes, it really cuts to the core of people's quality of life, so we really appreciate all the work that the National Eye Institute is doing. Today's discussion – the connection between diet and nutrition and vision health, is really interesting because, to me, the average person, when they think about the impact of diet on their health, they think about it in so-called, I'll say, traditional ways, like, "Can I still fit into these clothes? What am I going to look like?" But I don't think people automatically make the connection between diet and vision health. So what is the connection? How does someone's diet impact the quality of their eyes?

DR. EMILY CHEW: Well, I think diet is important for life. We're actually realizing that more and more. At NIH, we've put a lot more resources on studying nutrition. Nutrition is the basis for many chronic conditions. Well, look at diabetes. People … the rate of diabetes has increased because you're not fitting into your clothes like you should be. People are gaining weight—there's overall an increase in overweight or obesity that has increased chronic conditions, such as diabetes. In macular degeneration, one of the risk factors is what we call body mass index—so, the heavier you are, the more likely that you are to have one of the risk factors—that isn't the only one, but certainly it plays

a role.

So, in our studies, what we did was we started the Age-Related Eye Disease Study—the abbreviation is AREDS—starting in 1992. At that point, there was not a lot of information on the natural history of the condition. We didn't know who was all affected and how did it progress or what happens over time, and over that decade we studied patients; we learned a great deal. And one of the first things we did was to instigate a questionnaire. It's one of these things we ask you: What did you eat? It's daunting; you'll never know what you ate yesterday, let alone what you do … but it just gives you an idea of what the habits are, and we take people who don't eat certain things and people who eat lots of them—you get an idea of what that impact might be. And in doing so, we realized that patients who ate lots of fruits and vegetables—and this is from 1990 … I guess it was 1989, even before '92 when we started the study; there was a study called the … it's actually … it occurs every few years. It's called the National Health and Nutritional Examination Survey, or NHANES, where we actually ask patients—or not patients, but just the American public—what you eat, and they actually take blood levels to see what peoples' blood levels are of these nutrients, and they showed that people who ate a lot of fruits and vegetables had less macular degeneration. Well, that was even before we started our study.

And so, during our study, we have this questionnaire, and, of course, our study was looking at supplements, and supplements in the '90s were very important because the cancer field and the research in cardiovascular disease and heart disease pointed at the fact that people who have very high levels of certain vitamins in their blood were less affected by either cancer or heart disease. So, they said, "A-ha! That must be the problem, so let's put them on high doses of vitamins," and hence, we started doing that for macular degeneration, because that was what was being studied. And much to everyone's surprise, it didn't do anything for heart or cancer at all, but in macular degeneration, we found that a combination of vitamins—vitamin C; half a gram vitamin E for international units; beta carotene … 50 mg of beta carotene, which is a really high dose; coupled with copper; and zinc, which is sort of the key thing we're interested in, zinc is an important mineral—so, in doing so, we found that we can delay the progression of macular degeneration. If you already have macular degeneration, it's likely we can decrease the risk of going to the late form, which can cause vision loss, by about 25 percent over 5 years. So, it's really amazing that we were able to show that, because this is a very big public health problem. If we can reduce it by 25 percent, a lot of people can be affected by this. So, that was the reason we did that work. We also realized in the diet that there was a lot of other interesting aspects with this. Did you want me to go on talking a bit about the diet?

MICHAEL BUCKLEY: Yes, what did you find about the diet? Were there surprises or unexpected findings in your research?

DR. EMILY CHEW: Sure. So, in the first study in AREDS, we looked and found that lutein and zeaxanthin, which a lot of you have heard a lot about, are a type of a carotenoid or a type of a vitamin we eat, and it's important because it makes up a very special part in your eye, the macula. Macular degeneration occurs in the macula, and so those vitamins are really important. We also found that people eating fish had a lower rate of having macular degeneration, and what's in fish? We don't know. Is it the fish oils? So, based on that data, we actually did the second study for AREDS2, in which we gave fish oil and also lutein and zeaxanthin, and in that study we found that fish oil, unfortunately, made no difference. It wasn't harmful or beneficial, but what was important was actually that the lutein and zeaxanthin we added did have an incremental increase of beneficial effect.

So, the AREDS2, we actually have the lutein/zeaxanthin, and we wanted to look at that because beta carotene increases the risk of lung cancer in patients who are smokers. And so, for that reason, we were happy that lutein/zeaxanthin was good for the study, and we also found that people who were smokers or who were former smokers had an increased risk of lung cancer if given beta carotene. So, for those reasons, we now have the AREDS2 as our supplement, and it's important.

But in doing so, we also, as I mentioned, did the questionnaire on what you ate, and we were interested because there was a study done really in the more recent years. About 10 years ago, they started looking at what we call a Mediterranean diet. A Mediterranean diet is something that many of you are quite familiar with. You've probably heard a lot about this. It's really nine components of the diet—you're increasing your fruits and vegetables and legumes and nuts, more whole grains than anything else, and also low on red meat, and low and moderate intake of wine. And also, the study asked if the monounsaturated fatty acids, such as the olive oil, was preferred over the so-called saturated fats, and also taking fish and ... in fish and white meat and dairy. So, that's the diet that we looked at.

In looking at that questionnaire, we were able to calculate what each person would eat from the Mediterranean diet. Would you take a high Mediterranean diet? Would you take a moderate or not at all?

Because, like, small, medium, and large. If you take a large dose of Mediterranean diet, it was really helpful—so, patients who were already at risk for macular degeneration, if they were at very high adherence to the Mediterranean diet, they really had a very

much ... almost a 30 percent reduction in the risk of progressing to the late form. So, even though you have disease in the moderate form, if you have a good diet, you can perhaps prevent that from going to late, and that's part of the makeup of people who eat a good diet. And even if you have early disease and developing from the early changes of macular degeneration, we found there was a 25 percent reduction. So, you can eat away your risk by having a very good diet.

This is also true ... it's interesting—we not only did macular degeneration look; we also had patient do a cognitive function testing, and in that case, we asked the patients—especially in AREDS2—at baseline, and every 2 years we tested them with a battery of tests that gave us an idea of the cognition asking about memory recall, looking at executive function, asking them to subtract seven from 100 backwards, and naming certain things with fluency. So, all that gave us a really good measure of their cognition, and guess what happened? The Mediterranean diet was also important there, too. So, the higher adherence, the more likely you have a Mediterranean diet, the less you have cognitive impairment.

So, it's seems like the brain and the eye are really tied together; these, I think, are important findings that really help us. So, I think this is something we have to take seriously. This is something we can do ourselves, and what does that mean? Well, what really drove it was the fish intake and how much you need to take. Well, it's two servings of fish a week, which is not a huge amount, but for some people, it's hard to get that fish twice a week. And you can open up a can of tuna, and that would count for one serving. So, fish was really important, but the overall diet is very important. Taking lots of fruits and vegetables as part of the Mediterranean diet is an important aspect of this, and we were delighted to find that. But we're not the only people—only researchers—who found ... that other researchers have looked at other data, especially in Europe, where they found similar findings, and so, in fact, I think it is very important for us to think about that as some of our, our recommendations for patients as to what to do with making sure your diet is in good shape.

MICHAEL BUCKLEY: Dr. Chew, we have several questions about the AREDS supplements themselves. One is: When you're in the vitamin aisle of a supermarket or a pharmacy, it can feel kind of overwhelming. How does someone know they're getting the correct product?

DR. EMILY CHEW: I'd like to say that look for the type AREDS2. That's more likely to give you what we tested, and there was a patent on it—there isn't a patent anymore—and, you know, vitamins are not regulated, so quite often they're not exactly what they say they are. So, if you see the AREDS2 on it, it's more likely that you're going to get the

real McCoy, and that's what you should be taking. For some people, they may not be able to tolerate certain things. For example, I know I have patients who can't tolerate the zinc because it does cause some GI upset; in other words, their bowels can get a little bit messed up with it. There's only a very few people who feel … who have that problem, and sometimes they just get the vitamins, and leave out the zinc. But, by and all … for most—almost 99 percent—of the people, if you look for AREDS2, that is a pretty good guarantee that you're in pretty good shape, and that's a good brand to have.

MICHAEL BUCKLEY: A few more questions kind of along that line. A listener is wondering: Can AREDS reverse vision damage that has already occurred?

DR. EMILY CHEW: No, we don't reverse damage. We certainly … where we can reverse damage is when patients have the wet form of macular degeneration, and they get the injections of the so-called … you've heard of Avastin®, you've heard of Lucentis® and Eylea®—all those things that are a part of the macular degeneration treatment; that's very powerful. So, people who lose vision in the wet form that can get treatment, there is hope—it's something like 40 percent will actually improve their vision—so that's true, but the supplements are only preserving what you've got now, and so it's important to start at the stage right before you lose vision.

MICHAEL BUCKLEY: Is the AREDS for people with dry AMD or wet? Where does it fall in the patient's progression?

DR. EMILY CHEW: So, believe it or not, it's for both. If you have good vision in one eye and you have wet on the other, there's a good chance you'll also be helped by taking the AREDS supplement. Those are patients we tested. People with wet or dry in one eye, like very severe disease in one eye—especially the wet and the fellow eye—definitely you can take that. People who have good vision, who've been told they have something called a dry form—although that's not very well defined—they are also helped by that, as well, too. So, it's a combination of both. But the really severe dry type where the center is involved, the vision's very poor; it may be more difficult. I think you should speak with your doctor to see whether it helps or not, but even those patients who have so-called dry in both eyes but have not terrible vision but still reasonably good vision, they may still be helped by it. So, the AREDS2 can be successful in reducing the risk of more vision loss in the future.

MICHAEL BUCKLEY: That's interesting. Another listener is wondering: Can you take AREDS proactively? Let's say, someone like myself that doesn't have AMD, could I start taking it proactively to help me as I age?

DR. EMILY CHEW: What we find is that, when we look at our patients in AREDS, the first study, we had patients who had no disease, and we didn't even give them that supplement. And then, the second group with people with what we call early disease and then the intermediate and then late disease, those with early disease was not helped. Only when they got to the intermediate stage did that help. So, the answer is no. It doesn't help everyone, and the most important thing you need to do is go and see your eye doctor. Do you have a family history of macular degeneration? Are you worried about macular degeneration? You should see an eye doctor and have your pupils dilated with some eye drops that makes the pupils large. You can't read well, but they can look in better … have a better view of what the retina looks like and make that diagnosis. If you have a diagnosis of intermediate AMD, then you should take the AREDS supplement. So, the answer is no; it's not for everyone. I get that answer … that question often when children who bring their parents in and say, "My father has terrible macular degeneration; should I be taking this?" I'd say, "Well, the most important thing for you is to have your eyes examined, and if you don't have that, at this point, you should have regular exams to check for any onset of it. Once it starts with the intermediate form, then you should take the AREDS supplements."

MICHAEL BUCKLEY: That really tees out the question we've gotten from a few people today about family history. We hear a lot these days about genetic testing in the news or products advertised on TV or whatever. Is there a role for genetic testing in AMD?

DR. EMILY CHEW: I think there's a strong role, but that role is for research, and we do a lot of that. And a lot of our work in AREDS went in there … was based on genetic testing. Genetic testing is hugely important for us to understand why the disease happens, and it may give us clues as to where the treatment might be helpful. And the problem with the genetics in macular degeneration is that it's not like the typical genetics. So, all of us know about Down syndrome. Down syndrome is where chromosome 21 has a defect, and it's a very specific area, and when you have it, you get a Down's child. It's not the same in macular degeneration. That disease in Down's is called monogenetic—one gene—whereas in macular degeneration, we have 34 different areas in the whole genome and 52 different varieties of that, so there's a huge number of genes that are involved, although two very specific ones are important—complement factor H and ARMS2 in chromosomes 1 and 10 are really important—and they account for most of the genetic burden. But having that information doesn't help predicts what happens completely in the future.

So, we know that you can get the genetic testing, but what does it mean? For example, people … if it's a complex disease, it means that it could be affected by environment, and you already heard that diet is really important. And for someone who is a smoker,

smoking has a really huge impact on macular degeneration. It increases your risk quite dramatically, and the more you smoke, the more likely you have it. It's almost like having a larger dose, the more you can get it. So, those things affect your body and your environment, so even sometimes if you have the gene, you may not even have the disease because you're healthy living, there are other things that are ongoing, and the genes aren't all just harmful genes—there are protective genes. There are certain genes that help you, so the interpretation of the genetic information is very difficult in this complex disease, so we don't recommend that patients get the genetic testing.

One of my colleagues, Dr. Ed Stone, who is at The University of Iowa, has done a lot of work in this, and he's very knowledgeable in genetics, and he said, "You know, even though my mother has macular degeneration, I don't do genetic testing because …" and he shows examples of people who get macular degeneration and have no genetic bearing at all. So, you might be lulled into a false sense because your genetics looks good, but in actuality, you might have it, or people who have … who get the genetic testing and found they have the gene but yet they never get the disease, that gives them such a burden of worry. So, it's a very complex situation. I would only do it with a doctor, talking to them about what that might mean, and even most physicians don't have the training to actually interpret a lot of this very complex genetic information, and that would be very important to have. And most people who do genetic testing in their practices will have a genetic counselor, and most doctors don't have a genetic counselor who would help interpret the data and talk to the patients. So, the answer is "no" for routine use for clinical practice, but for research, it's hugely important and very important to do.

MICHAEL BUCKLEY: I appreciate you clarifying that. You mentioned your research on AREDS and research of other colleagues, and I want to talk for a minute about clinical trials. I think in the last year, we've all become very familiar with clinical trials in terms of the COVID-19 vaccine and just amazingly impressed at how it all worked. How does something like the COVID-19 trials, how does that process compare to the clinical trials in vision research? And how or why should someone consider volunteering?

DR. EMILY CHEW: Well, clinical trials are hugely important for deciding whether treatment is important or not, and that's why the COVID-19 vaccine was so amazing. I mean, 30,000 people volunteered in a drop of a hat, and we got information that was so useful in getting the vaccine out to people. I mean, that could not have been possible … of course, the basic science and the lab work had to be done first, but that is really fast … really fast-tracking things very rapidly and very important.

So, with most studies and most pharmaceutical companies and even our government,

what we do is test this, and the clinical trials are the gold standard because we ... that flipping of the coin—whether you get it or not—is the most powerful tool we have in testing whether that specific thing you're testing—whether it's a pill or an injection or some lifestyle or some surgical treatment—that can determine whether it's good or not, and only through that very rigorous science can we determine whether treatments are good or not, and COVID-19 has really shown how important clinical trials are.

Macular degeneration is the same way. The injections that we've had, the anti-VEGF therapy of the Avastin for the wet form, that came about because of their rigorous clinical trials that went over a number of years before we got to this. Most clinical trials or most drugs that start from the beginning to the end take almost 2 decades to get through. A clinical trial is hugely important, and for those of you who are willing to be part of that process, we applaud you, and I really ... I follow patients for ... AREDS is now almost 30 years old, and we've got patients who are still with us and who participated from the very beginning and have given so much of their time and really very altruistically think, saying, "This may not be good for me, but it may help my family or someone down the road, someone who comes behind me." So, that altruistic attitude has really helped us. And having been in clinical trials helps you be alert to what new treatments might be possible, and there's some real good things that can be for both the researcher and the actual participant. But the participants are to be highly applauded for such a laudable goal for them to be participating, and we certainly need patients, such as patients who are affected with this disease, who are willing to undergo.

And, of course, I have to explain that these treatments are things that researchers don't really understand. If we know the answer, we wouldn't be doing a clinical trial. We really want to know whether it's good or not, and so we have that. It's what we call equipoise; we don't know whether it's good or not, but that trial is the gold standard, and it helps giving treatment to people—to yourself to all the way, whoever comes before us—so, it's really important.

MICHAEL BUCKLEY: I really appreciate you articulating the benefits so clearly. So, Dr. Chew, we just have time for a couple more questions. When you talk about research, you've obviously had a lot of great accomplishments. What do you think is next for the field of vision research? What's next from the perspective of the National Eye Institute at NIH or just the field of vision research? What's the next frontier that you and your colleagues want to get to?

DR. EMILY CHEW: I think the next frontier ... well, there are a number of things. For macular degeneration specifically, I want to address the fact that we have good

treatment for the wet form of macular degeneration; we don't have it for the dry, but we are working towards that. There are a number of companies and a number of researchers who are working on seeing what the reason may be for the dry-form macular degeneration, and hopefully, we're getting close to finding something that would be very helpful to reduce the burden of blindness from that aspect of it.

But I think the overarching new technology that's really important in not only macular degeneration but throughout all of medicine and especially vision health, vision health, in particular, is very geared to this; it's the use of artificial intelligence or deep learning. That is really phenomenal work where the machines are detecting things that humans cannot detect. It's really quite amazing. So, what does that mean? It means that we could perhaps detect diseases in a different way earlier, with different parameters with less of the … and we also know that there's going to be a shortage of physicians coming up, unless we can address that. This will help us be better physicians. We can diagnose things better. We can detect things better. We can also predict who might go on to disease, and so, that might help us in clinical research.

We can enroll patients who clearly are the ones we want to be able to treat right away. So, those are important things. And we can also, in clinical practice, where we know a patient is going to progress, we may see them more frequently and offer them help in an earlier stage. So, this AI, or artificial intelligence/deep learning, is all across the field. But especially for ophthalmology, we do a lot of photographs and the image processing for this artificial intelligence, having the images, is a really important part. They teach the machine how to recognize certain things; the machine learns by itself. So, that's a huge, huge, huge aspect.

And then, of course, we all have electronic medical records—so, what we call big data science—getting all these data together and trying to figure out what may be important, and we have a lot more power—the computing power. The computers are so much more powerful because of the more recent developments in that. That's allowed us to do all this, and now the burgeoning of a different discipline of the computer scientists, as well as the biomedical field, we're just trying to get together and really learn a lot from each other, and hopefully, we'll make this a better field and a better life for all of us in terms of both the actual practice of medicine, the research part; and hopefully, we can have something that would be equitable and even the patients will be using this, as well—and they are, already, in some of the devices that are being used. So, this is a huge, huge development that I see as a very important development in the future.

MICHAEL BUCKLEY: It's a really exciting time for vision research. Dr. Chew, it's been

just a fantastic conversation. It's really so exciting to hear about all of the progress being made. And, as we conclude, I was wondering if you could share with listeners some sort of a bigger-picture lesson that you've learned in your career, or maybe one thing that you wish your patients knew or all Americans knew about vision health, or any kind of concluding remarks you'd like to leave us with today?

DR. EMILY CHEW: Well, I think vision health is obviously crucially important for all of us—the quality of life is really important, as many surveys show that patient would rather have very disabling disease compared to having vision loss because it affects the quality of life. And I think the most important thing is, if some of this can be really … we're empowered to take care of ourselves, and I think one of the most important things for all of us who confront some of these diseases, it's the importance of living well. And sometimes it's not so easy for us to say, but having good nutrition, exercise—that is crucially important—and stopping smoking. These are just healthy living styles that really can help us in so many aspects of our life, not only for vision, but really for general health. So, I think that's something that we haven't been taught in preventive medicine when we were in school. We were very focused on specific treatment, but I think taking this very seriously, the nutrition and make sure you exercise both for our brains and for all the other aspects we go on. I think the big picture is that, I think, nutrition will become very important as we do more work, and there's a lot of interest in going forward. We're doing a lot of work in genetics and precision medicine and precision nutrition. So, overall, I think we can do a lot for ourselves by really … no matter what your circumstances are, to try and strive to teach those things to your family and to those around you to lead by example—to be a model of good living.

MICHAEL BUCKLEY: It's great advice for all of us. We'll be back next month, July 28, with Dr. Joshua Dunaief from the University of Pennsylvania Medical School, and he'll be answering a wide range of questions from our listeners about all things related to AMD.

When the call concludes, you can leave a message for anything else that we might be able to help you with. You can always call us at (800) 437-2423. Again, that's (800) 437-2423. You can always find resources on our website, BrightFocus.org.

Dr. Chew, I just want to thank you on behalf of BrightFocus and our listeners. This has been tremendously enlightening to help navigate the world of diet and nutrition and vitamins supplements. I really appreciate your generosity and your clarity, and you also gave us a lot of hope for the future of vision research, so I just want to thank you so much for taking the time to be with us today.

DR. EMILY CHEW: Well, thank you for having me. It's always an honor to be here. Thank you very much.

MICHAEL BUCKLEY: Thank you. On behalf of the BrightFocus Foundation, this concludes today's BrightFocus Chats. Thanks for being with us.

Useful Resources and Key Terms

BrightFocus Foundation: (800) 437-2423 or visit us at www.BrightFocus.org. Available resources include—

- Macular Chats Archive
- Clinical Trials: Your Questions Answered
- Healthy Living and Macular Degeneration: Tips to Protect Your Sight
- How Low Vision Servives Can Help You
- Macular Degeneration: Essential Facts
- Research funded by Macular Degeneration Research
- The Top Five Questions to Ask Your Eye Doctor
- Overview of Macular Degeneration
- Treatments for Macular Degeneration
- Resources for Macular Degeneration

Helpful low vision tools or resources mentioned during the Chat include—

The National Eye Institute's Office of Science Communications, Public Liaison and Education responds directly to requests for information on eye diseases and vision research in English and Spanish. They cannot provide personalized medical advice to individuals about their condition or treatment.

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