



Wet AMD Treatments: Updates, Challenges, and Future Innovations

January 29, 2025

1:00 PM EDT

Transcript of Teleconference with Dr. Charles C. Wykoff

The information provided in this transcription is a public service of BrightFocus Foundation and is not intended to constitute medical advice. Please consult your physician for personalized medical, dietary, and/or exercise advice. Any medications or supplements should be taken only under medical supervision. BrightFocus Foundation does not endorse any medical products or therapies.

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 so pleased to be your host for today's Macular Chat, called, "Wet AMD Treatments: Updates, Challenges, and Future Innovations." We're partnering with the American Society of Retina Specialists, or ASRS, for today's Chat, so this is really exciting.

Macular Chats are a monthly program designed to provide people living with macular degeneration and family and friends who support them with information straight from the experts, like the wonderful expert that we have today. BrightFocus Foundation's Macular Degeneration Research Program has supported nearly \$53 million in scientific grants exploring the root causes and potential prevention, treatment, and ultimately leading towards, we hope, a cure for macular degeneration, and is currently investing in 49 active projects across the globe.

So, without further ado, I'm so pleased to introduce today's guest speaker,

Dr. Charles C. Wykoff, who has both an MD and PhD and is Director of Research at Retina Consultants of Texas™; also Chairman of Research, Retina Consultants of America™; the Deputy Chair of Ophthalmology for the Blanton Eye Institute at Houston Methodist Hospital; and Clinical Professor of Ophthalmology at Weill Cornell Medical College. He's passionate about translational research and accelerating drug and device development. He's published over 325 peer-reviewed manuscripts and serves on multiple scientific and medical advisory boards, safety monitoring committees, and global steering committees for endeavors spanning the innovative process from early to late-stage development. And he also serves on the ASRS Executive Committee and Board of Directors. His guiding philosophy is to build and strengthen innovative, ethical teams focused on developing new approaches to improving outcomes for people with blinding diseases. So, Dr. Wykoff, thank you so much for joining me today.

CHARLES WYKOFF: Hey, great to be here. So glad that you guys are in this space. You guys do fantastic work. It's great to be on to talk about something that's very important, that I'm passionate about and something that's central to the mission of the ASRS also, which is patient education, patient awareness, and the ability to access timely and appropriate treatments. So, really looking forward to this discussion. Thanks.

DIANE BOVENKAMP: Absolutely. It sounds like this is really a great nexus of our two organizations getting together and doing something that we're really passionate about to help the community. The first question that I have here will be one of questions that have come in from some of our Chat attendees. I'll just go down this list here, and we can always add more information later. Just to start us off, can you explain what is so-called "wet AMD" and how it differs from other types of AMD, or age-related macular degeneration?

CHARLES WYKOFF: Yeah, super important question. If you start at a high level and you look across the United States, we deal with vision loss and visual impairment. And there's different ways to categorize that, but when you look at macular degeneration—and it gets confusing because there's a lot of terms and they get confusing—but macular degeneration

is the same thing as age-related macular degeneration. People often abbreviate it AMD for age-related macular degeneration. That category of diseases—because there's multiple within AMD—but that category is the most common cause of irreversible blindness in our country. It's like the big player, and actually it causes more visual blindness than all the other things combined, so it's like the big player in our country. And then if you break that down further, you think, "Well, who's at risk for it?" Well, you really can't have it before the age of 50. And then after the age of 50, it increases substantially the risk every decade of life.

And there's two major forms of it. This is where it gets important for the treatments, is that there's a wet kind and a dry kind of AMD. And this is where the terms get a little confusing, because for most things in the world, if they're wet, then they're not dry, right? If you have a car that's dry, it's either dry or wet. And in Houston, where I am, when it rains, everything gets wet and it's no longer dry. So, patients often think, "Well, I have the wet. That means I don't have dry anymore." But that's not right. You can have both. So, you can have the dry form and the wet form. It gets confusing. But the wet form is basically when you get abnormal scar tissue and blood vessels that grow in the back of the eye. And that's the most common cause of rapid, progressive, severe vision loss, where you get scar tissue that just takes over the part of our central vision responsible for reading and all the detailed things that we like to do with vision. And the good thing is there are great treatments for that that have been around for 20 years now. And in the dry form, the other form, the more appropriate term, which we're using more and more in the field, is geographic atrophy. And the word "atrophy" is the key component there, where the retina begins to die, where it dies away and it doesn't come back. And there are a couple drugs now that are approved to slow that process down, but it's the wet form that the majority of people out there are currently still being actively treated for.

DIANE BOVENKAMP: Yeah. So this atrophy, it's kind of like a pothole, I guess, is in your retina, right? And so, it's typically in the macula, right, in the center.

CHARLES WYKOFF: Yeah.

DIANE BOVENKAMP: So, people have trouble looking at things because it's not a peripheral vision thing. It's a central vision issue, right?

CHARLES WYKOFF: Great question. Yeah. And it's in the name, you're right. So, when we say "macular degeneration," the macula's just a place, right? It's like Chicago or San Francisco or Dallas or whatever. It's just a location in the back of the eye. So, macular degeneration is degeneration of the macula. It's a very nonspecific term, actually, even though it means a very specific disease process. And the macula, you're 100 percent right, it's responsible for our good central vision. So, when you look at a book or at your family's faces or you're watching a game on television or you're reading your report card, whatever you're doing with your vision, that's your macula that you're using. And so, when that tissue doesn't work, it's a problem. And that's when people start to say, "Wait, wait, wait. I can't see well enough to drive, and I can't see my kids' faces." So, macular degeneration takes away that central vision.

But what macular degeneration usually does not do, and this is really important for patients to understand, it usually doesn't make people go, like, eyes-closed, darkness blind. The word blind is a really scary word for, I think, everybody, myself included. No one wants to be blind, but there are different ways to talk about blindness. There's something called legally blind, and then there's what most people think of when they hear blind, which is eyes-closed darkness. That is true blindness, and does not generally happen. That is exceedingly rare. I would, in fact, say it does not happen, full stop, with macular degeneration. Like, that will not make you go eyes-closed darkness blind without treatment. What it will do, though, is it can make you go legally blind, which is where your vision is worse than 20/200 in both eyes. And that means that you can't legally drive, it's very difficult to read, it's hard to do a lot of the things that we're used to with our good central vision. And that's why treatment is so important, because if we diagnose and treat the wet form of this disease early, most people can actually maintain useful vision for many, many years—in fact, most of their life.

DIANE BOVENKAMP: Right. Okay, so this is really good to know. And will everyone diagnosed with age-related macular degeneration develop the

wet form? Or do some people kind of stall?

CHARLES WYKOFF: Yeah, great question. So, when I say it's the most common cause of irreversible vision loss, the majority of that is due to the wet form, but there's a lot of people out there that have macular degeneration that never go blind. They never develop the wet form, and they never need treatment, actually. The majority never need treatment, and those patients typically have what's called either early or intermediate macular degeneration. Remember, I said this gets confusing with the terms. But it's basically an early stage of the dry, where there's not atrophy. There's no pothole, as you mentioned, right. I think that's a good way to think about it. The retina is still intact, it's still working, but there's a few signs, and there's some evidence that there's some early stage or intermediate stage of macular degeneration. And when you catch it at that stage, there are three things that we know that slow it down at that stage.

The most important is not to smoke. We know that smoking is like fuel on the fire for this disease process, and we know that from twin studies. There's fascinating data looking at identical twins where the genetics are obviously the same between two different people, and if one twin smokes and the other one doesn't, the one that smokes gets macular degeneration about a decade earlier. So, really, smoking is like fuel on the fire here, so don't smoke. And then I also would say, I have some patients that are like, "Look, doc, I love you, but I'm going to smoke," and I say, "Okay, I get that. I respect that, but even less is more." So, we have data that even less smoking will decrease your risk rather than more, so fewer cigarettes. A half a pack a day is better than a full pack a day.

And then beyond smoking, it's vitamins that everybody talks about, and there is data that a certain regimen can slow the progression from intermediate dry to the wet form of the disease. There's more recent controversial data that the vitamins can slow the advanced dry form, also. I think that still needs more work to understand that. We are convinced, as a field overall that the vitamins work to help slow the development of the advanced form of the disease, the wet form. So it's definitely important to take the vitamins also. They're called AREDS2. Happy to talk more about that.

And then the third thing I always advise to people, in addition to no smoking, take the vitamins, is to keep your heart healthy. There's some data to suggest that optimal cardiovascular risk factor control—things like blood pressure, cholesterol—can minimize the risk of progression of the disease also.

DIANE BOVENKAMP: Yeah, I've heard it said, "If it's good for your heart, it's good for your eyes."

CHARLES WYKOFF: I think that's a good way to put it, absolutely. Yeah.

DIANE BOVENKAMP: We can put links to the information we talk about today, including AREDS2, pictures of what wet and dry AMD look like at different stages and links to our information and also the ASRS website, as well on the transcript.

CHARLES WYKOFF: Yeah, absolutely. And toward that point, I'd make two extra points. One is vitamins can be confusing too, because there's tons of different companies that make the vitamins. And just make sure whatever you're taking as a patient that it has the right amount of the six vitamins and minerals that have been proven together to slow the progression. Every company patents their own little combination, but most of them have approximately the right concentrations. We can put a link to the ASRS patient handout all about this. It's really helpful. The ASRS really tries to be a partner for patients to help them get educated about this disease and all retinal diseases. And there's a really good educational resource page on the ASRS website that we'll give you links to that describes retinal diseases and conditions that is very digestible and understandable, and you can download it. And I think that would be a great link to add.

DIANE BOVENKAMP: That's absolutely fantastic. I mean, the more you can read about this, the more you're empowered, so that's great.

CHARLES WYKOFF: Absolutely.

DIANE BOVENKAMP: So, how do people know if they have wet AMD versus dry AMD? How is it diagnosed, and are there any signs or symptoms that people can notice?

CHARLES WYKOFF: Yeah, this is a good one, because it is important that, I think, everybody over the age of 50 probably gets a regular eye exam, at least partially because you want to look for these early signs of macular degeneration before you're symptomatic. Because you really should start taking the vitamins before you have the advanced form of the disease. You want to prevent that advanced form. And really, you can only know if you have those early stages by doing an eye exam. And what I think is most useful and what we recommend as ASRS is a dilated fundus exam, where they dilate your pupil and take a comprehensive look inside your eye. I think I would start over the age of 50—and certainly before that it can be useful also—but after that. And then from there, if you need more specialized evaluations or treatments, you can see a retina specialist, but there are a lot of types of eye care professionals, including optometrists and general ophthalmologists, that can do comprehensive dilated eye exam. The key is just making sure that you are getting a full, comprehensive dilated eye exam, and then get referred to an appropriate retina specialist when and if macular degeneration is diagnosed and needs to be managed.

DIANE BOVENKAMP: Yeah. I'm really glad that you mentioned that having a dilated eye exam is important, because I know that you can go to an optometrist to get things tested, but if you don't have your eyes dilated, essentially, you're missing looking at some of the retina, so it might be hiding there.

CHARLES WYKOFF: Yeah.

DIANE BOVENKAMP: In addition, one of the things, too, that BrightFocus provides, is a magnet, printout or PDF of something called an Amsler grid. Can you tell them about that? Because it's kind of cool.

CHARLES WYKOFF: Yeah.

DIANE BOVENKAMP: And it's really a low-tech way of monitoring.

CHARLES WYKOFF: Yeah, absolutely. So, two thoughts there. One is: Completely agree with you. I mean, the field of eye care, again, like all things, can be confusing. But I and we at the ASRS view it very

collaboratively. We work closely with general ophthalmologists, with optometrists, with glaucoma specialists, with neuro-ophthalmologists, with pediatric ophthalmologists—lots of different eye care specialists out there, and many of them can do a dilated eye exam. You just want to make sure that you're getting the appropriate exam.

DIANE BOVENKAMP: Yeah, great.

CHARLES WYKOFF: Right. And then, related to Amsler grid, great question. So, the Amsler grid, you can download them online for free. They're just a little grid. It's approximately 6 by 6 inches or so that has a bunch of little lines on it, both horizontal and vertical lines, like a checkerboard. And then you want to look at it right in the middle. There's a little dot in the middle of it. You look with one eye, and then you close one eye and look with the other eye. You look back and forth, and when looking at that central dot, you're trying to appreciate if all the lines look straight. Because if any of the lines look wavy or crooked or broken or missing, that could mean that you have a problem in your macula. And one of those problems could be macular degeneration. And so, that can certainly be useful screening for anybody for many different diseases, but once we know people have an early stage of macular degeneration, we're trying to pick up an early symptom, an early sign of wet AMD development, the advanced form. And that's where the Amsler grid has really been proven to be useful, where patients are screening themselves at home on their vision with that chart on their refrigerator, wall, or a door, then they can often pick up early signs of bleeding when they start noticing some crooked or distorted or missing lines. So, you really want to be screening yourself at home. I think that that is useful for patients to think about.

DIANE BOVENKAMP: Right. And we can give you a 1-800 number or our email address. You can even get a magnetic form of that grid from us.

I just wanted to go back over all those different types of doctors and health care professionals you were talking about. I think that ASRS has a Find a Retina Specialist tool, right? There are many different types. Can you tell us about that?

CHARLES WYKOFF: Yeah. Right, this is where eye care does get confusing, because I think there's, sort of, two major types of eye care professionals, and then there's lots of subcategories. But one is optometry versus ophthalmology. That comes up a lot. And they work very collaboratively in most cases across the country for patients' benefits. Overall, I think the major difference is that ophthalmologists have gone to medical school and they are full medical physicians, whereas optometrists are specialized in the eyes. And then within ophthalmology, there's many different categories. There are glaucoma specialists, there are neuro-ophthalmologists, there are cornea specialists, etc. And then I am a retina specialist. So, retina specialists are people that take care, comprehensively, of the retina and vitreous and all diseases that involve the retina and vitreous inside and in the back of the eye. And the most common causes of irreversible blindness involve the retina. Today, we're focused on AMD. But the other big ones, just to list them out there, are diabetic retinopathy and all of the associated manifestations, like diabetic macular edema, there's retinal vein occlusion, there's retinal detachments. There's a lot of things that can happen to the retina, and, again, it can be confusing in the eye care space. And so, we think it's really important to make sure there's a place to go representing the entire country to find a retina specialist. And it's a really useful website because you can search by city, by state, by ZIP code, or you can type in the name of retina specialist if you've heard of one and see where they go. So, it's a very comprehensive way to access where retina specialists can be found. And we're well represented across every urban center in the country and almost all regions of all states.

DIANE BOVENKAMP: Perfect. And I know we have that link on our website, but we'll also put it at the end of this Chat transcript. Thank you. So, can you give us an overview of the treatments that are currently available for wet AMD? And generally, how do they work?

CHARLES WYKOFF: Yeah. So, one of the most important developments in eye care, I would say, was the development of the class of medications that we use to treat this. And they're called anti-VEGF medications. And so, we'll unpack what that means, but the short summary is these are medicines given by injections into the eyeball, so it sounds barbaric. It sounds like, "Oh, my goodness. You're going to put a what in my where?"

And patients kind of look at you cross-eyed the first time you mentioned it, but that's exactly what it is. It's a needle that goes inside of the eye and injects the medicine directly inside of the eye. And it is extremely well tolerated. Every procedure that any physician does has risk with it, so there is some risks, and we can talk about those. But overall, it's extremely well tolerated by patients, but this is one of the key reasons why it's so important that a well-trained physician is doing these procedures—a retina specialist is doing these procedures—because you want to make sure that they're very used to doing these, and this is what retina specialists do.

So, to back up now and unpack that a little bit more, a VEGF stands for vascular endothelial growth factor. And there is a molecule inside the eye called VEGF that drives the development of this bleeding process with macular degeneration. And it turns out that medications that block that molecule—again, anti-VEGF medications—work really well to stabilize the abnormal blood vessels and the abnormal scar tissue, prevent it from getting bigger, and in many cases, can improve the active bleeding process in the back of the eye. There's 15 years—plus worth of data showing that these medications are highly effective—actually 20 years' worth of data now, 2 decades worth of data—showing that these medications are highly effective when used appropriately by the appropriate type of physician to get optimal outcomes for patients. And they are, they're injections inside of the eye. Most people need them once a month at the beginning. And then, in many cases, patients can receive fewer than every-month injections. Some people, a minority of patients, do need ongoing monthly injections for a long time, but many patients are able to go longer between the injections—6 weeks, 8 weeks, 10 weeks, 12 weeks, even longer in some cases.

And we are now up to a large number of medications in this class. There are multiple different companies that have medications in this class, and they are all effective. Some might be more effective in some eyes than others, and the ASRS is very supportive of patient and physician choice so that we can use the right medicine in the right patients at the right time. But as a general rule, these medications work very well for this disease process, especially when the disease is diagnosed early in the

development of the neovascular or wet or bleeding process.

DIANE BOVENKAMP: I like what you said there, “the right medication in the right patient at the right time.” I think that’s the definition of personalized medicine. And as you said at the beginning, you know, AMD is experienced differently by different people, and so definitely having a choice to use one drug versus another is very important.

CHARLES WYKOFF: Yeah, I agree. Absolutely.

DIANE BOVENKAMP: Yeah. And then just before I go to the next question that we have, one thing for people who might be squeamish about eye things or not know about eye anatomy. It’s not like the eye is like a water balloon where if you put a needle in there, the water’s not going to escape or something. I would think of maybe the eye is more like a grape. I know that you mentioned the vitreous before.

CHARLES WYKOFF: Right. Yeah.

DIANE BOVENKAMP: So, the eye is so solid. Nothing is going to, like, come out or anything if a needle is put in the eye. The retina is just kind of like the grape peel, right, like a very, very thin thing at the back, right?

CHARLES WYKOFF: Yeah. That’s a good analogy. It is. The eye is, you know, it’s pretty small. If you actually cup your fingers and you touch your middle finger to the tip of your thumb, that’s about how big the eyeball is in a circle. And it’s a sphere, right, it’s a ball. And so, when you put a needle in the eye, you inject a tiny amount of fluid. The volume is actually usually about 50 to 100 microliters. That’s what it is, which is 0.05 mL, so it’s a tiny volume. But you’re right, when you put fluid in the eye, you can actually change the physiology of the eye. So, the pressure of the eye will go up a little bit right away, and that’s, again, why it’s really important to make sure that the people doing the injections are retina specialists so that they’re well informed and well educated about exactly how to do the procedure safely and know the best way to execute that. And then, I think the other thing is that there is, just to talk about it again, there are risks with these procedures. And those risks are small. The patient should definitely know what they are. I would raise two, sort of, categories. One is things that

are very common and not vision threatening. So, usually after injection, the eye is going to be a little sore. It's going to be, kind of, a little itchy, scratchy, burny for a few minutes to a few hours. It's kind of like after you get a vaccine, your COVID booster, your arm is kind of sore for a little bit. Sometimes the eye can feel like that afterward. And then, the other category are vision-threatening problems, things like infections in the eye or retinal detachments or cataract—those things are much less common but really important that you're seeing a retina specialist who can manage those things and can communicate with you about what to look out for if any of those bad things happen so they can be identified and managed appropriately.

DIANE BOVENKAMP: Absolutely. The whole 10,000 hours thing. You put it in, and you know how to handle any situation.

CHARLES WYKOFF: Yeah, absolutely.

DIANE BOVENKAMP: Yeah. And so, one listener question is, "Once I start these injections, will I always have to have these injections for the rest of my life?" That's a very interesting question.

CHARLES WYKOFF: It's a great question. It comes up all the time, and there's so many ways to peel back the layers of the answer there. I'll give you a few of the comments I make to patients, then happy to dive in. The first is, I try to make the comparison to blood pressure medicine or medicine for diabetes or medicine for thyroid dysfunction. There are so many things in modern medicine where we, as physicians, are pretty good at treating things. We have great options for blood pressure management, right? Hypertension is super common in our country, so it's very readily managed. Same thing with high cholesterol. But the problem with all of those is that the pills that we take—I take a pill myself for cholesterol—they're not a cure, right? If I don't take my Lipitor® or whatever someone's taking, the cholesterol is going to go back up. Same thing with the blood pressure. And that's intuitive. We get that because you just take a pill. It's no big deal to take a pill every day. People do it. But if you forget for a while or you run out, your blood pressure's going to go back up. People understand that.

Unfortunately, it's the same thing for these eye problems that we're injecting these medications for in many patients. Not all patients, but many of them need this chronically over a long period of time. And it's so much easier to take a pill, but the shot is unfortunately having the same problem. The medication is just wearing off. And when it goes away, the shot was never a cure, the disease comes back, and it's active. And so, that's why people often need these shots repeatedly. So, that's what I think is the simplistic way to say it. The other even more simplistic phrase I use a lot is, "These shots are forever for now." And what I mean "for now," there's a tremendous amount of excellent research going on in the field, and the ASRS plays a really important part in that research, highlighting the research, presenting the research, funding the research in many cases. And I think that that we have great partners in industry that are really creating, in collaboration with ASRS and ASRS membership, the future of what retina can look like. And there's a lot of promising therapeutics that are truly going to be more durable, I believe. And maybe one day we can get to a quote-unquote cure for patients. Maybe not, but I'm hopeful that we will be able to. So, the research is great, so want to give that hope to patients, because we've seen ... just as a sidebar, when I started practicing in about 2010, 2011, there were three medications FDA approved to treat this disease. Today, I think we have, like, 13 different options that are FDA approved to treat AMD, both wet and dry forms of AMD. So, the field has developed a tremendous number of new options for therapies, and the future is even brighter. So, to the patient, I would say, I'm sorry, but in many cases you do need regular injections. But the future is bright, and let's just keep giving the shots now so that when we have something better, you can benefit from it.

DIANE BOVENKAMP: Absolutely. Don't give up hope. We're funding research, and BrightFocus funds research, too. And we're funding so many different—

CHARLES WYKOFF: Love that.

DIANE BOVENKAMP: —ways. I think we'll talk about that. I think the last question I'm going to ask you will be about what's coming down the pipeline in clinical trials.

CHARLES WYKOFF: Yeah.

DIANE BOVENKAMP: So, I put that as a teaser so people will listen until the end. So, one more question is: How does a provider determine which treatment to choose? And especially, I guess, I'll also add in there, you mentioned at the beginning some people have dry and wet, so do you treat that differently if a person has both diseases?

CHARLES WYKOFF: Yeah, the core principle here that I believe strongly and the ASRS strongly supports is choice—patient choice first and foremost, physicians choice right along with that. We want patients to be able to get the right medicine at the right time and access it. And unfortunately, as patients are experiencing more and more, there are a lot of demands and challenges in our health care system. We have a fragmented system. It's great in many ways, but it has its challenges. And we're seeing increasingly that private payers are driving treatment decisions that may interfere with a patient's or retina specialist's ability to provide patients with what they believe is the most effective treatment in a timely fashion.

And just to get really specific about it for a moment, patients, especially with Medicare Advantage, can have trouble with step therapy in some cases. In some cases, step therapy has referred to as "fail first," which involves the insurer requiring a patient to try and fail a specific medication or drug before covering others, and usually that is driven entirely by cost. And for patients with wet AMD, typically that first-step therapy is often Avastin® or bevacizumab. To be clear, Avastin/bevacizumab is a good therapeutic. It works. It can definitely improve the problems of wet AMD in the back of the eye. The challenges with it, though, are many. First of all, it is not FDA approved for ocular use. It's not been approved for the management of wet AMD. It must be repackaged, and that process does add some degree of risk. There have been outbreaks of infections, for example, from repackaging situations in the past. Those outbreaks are exceptionally rare, but it wouldn't be fair to say that they don't happen. And therefore, some doctors may choose a different drug, or some patients may choose a different drug.

And so, we believe that step therapy wastes valuable time and can put

patients' eyesight at risk. And we really believe that patients should have the right to choose the medication they want to start with from day one. And the ASRS—and you also, I'm sure as an organization, I don't mean to single out the ASRS, it's just the organization I work closely with—and many physician organizations across medicine are definitely opposed to step therapy and are actively, continuously working to put patient autonomy and patient choice first in order to preserve that patient–physician relationship. And we continue to seek for legislative and regulatory solutions to curb or, hopefully, eliminate step therapies. And we've seen some progress recently. It's an active space. And I would just encourage patients to continue to be educated about what their choices are and about what their insurance plans are doing, with their physicians in collaboration, so we can continue to move this space forward and get patients what they need.

DIANE BOVENKAMP: Exactly. And I think that one of the things that you said is choice. If you do have a choice, I think people should look at their insurance. And if they do have step therapy, or if your drug is not covered, then people can always choose to get another insurance if they do have that choice. So knowledge is key. Knowledge is empowerment, so I like that.

CHARLES WYKOFF: Absolutely. Yeah.

DIANE BOVENKAMP: You mentioned Avastin, and yeah, I think that seems to be because it is the lowest cost of all of them. A lot of times that is the option that people do go for, but recently there has been a shortage of Avastin. And so, how does that impact the overall landscape of treatments?

CHARLES WYKOFF: Yeah, I'm so glad you bring this up. This is an interesting situation, and it kind of comes in waves, right? For a while, the Avastin supply chain across the United States was pretty stable and there was no problem. And then this past fall, 2024, the largest producer of repackaged Avastin in the U.S. decided to suspend production. And we had no warning. At least I certainly didn't, and the ASRS, we didn't know this was coming. And all of a sudden it was upon us, and we had a lot of physicians and a lot of patients that had difficulty accessing Avastin for a

short period of time there. And it's still lingering into 2025 about access issues. So, it's not easy to get access to Avastin because it's, again, not FDA approved, it requires these repackaging pharmacies, and they all can be a little different about how you access it, so it can be challenging for many reasons. And many but not all of the Medicare Advantage plans have an understanding and have eased step therapy requirements during this situation. But for those that haven't, retina specialist practices are having to scramble, still, in some cases, to get the drug or try to secure exceptions for patients.

You know, it's worth patients and physicians knowing that you can appeal the step therapy requirements if there are challenges accessing the drug that is required in the step therapy—almost always Avastin. And this is another key place where the ASRS is actually here to help and be a patient advocate. So, if you look at the ASRS website, there's a Patient Access section. We can put the email here at the bottom here, but I see Monica Horton is the person on our team that helps shepherd this, and she's fantastic at helping individual patients understand their situation and access challenges and overcoming those. So, again, I agree with you, empowerment, knowledge will empower patients and just be aware. And there are organizations like yours and like ours, the ASRS, that can help patients.

DIANE BOVENKAMP: And I think just before we move on, I think that you, the ASRS, and AAO is working with the Centers for Medicare & Medicaid Services to try and ameliorate this situation. And you probably have more information about that on your website, too, right?

CHARLES WYKOFF: Yeah, absolutely. This is a key, active place of ongoing dialogue. The ASRS has been very active with both directly interacting with payers but also, at a very high level, interacting with organizations like CMS, the government agency that oversees Medicare Advantage plans. And I think overall that we had a conversation with CMS directly, as the ASRS, when this shortage was happening with Avastin last fall and explained the situation in detail, and they did listen. And CMS sent a letter to plans recommending that they suspend Avastin first-step therapy policies until the shortage is resolved. And we have seen some progress

on that, but again, if any patients are still experiencing challenges with access, please let us know, and we're here to help.

DIANE BOVENKAMP: Great. Okay. So, this is great to know, that there's a source of information. They can get info from BrightFocus, they can get information from ASRS for some advocacy and help with that. But also, if an individual is not satisfied with their current treatment, do you have any advice on the best way to approach a conversation with their doctor about other options? Because really, what's key is the relationship and the decision that's made jointly between the person who's being treated and their health care provider, right?

CHARLES WYKOFF: Yeah, absolutely. I think the two layers of comments that I would make are: While these medications are excellent, they have truly changed the epidemiology of vision loss in our country and in many countries around the world. I cannot understate how important they are to us as physicians and to patients. They're not perfect. So, there are definitely a lot of patients still with macular degeneration that are receiving the appropriate treatment that are experiencing progressive vision loss. And sometimes we're just at the end of the rope, and that's where one of the questions we'll get to will be the future, but we're at the end of our rope, and the medications really have done the best they can, but patients still have imperfect vision. And so, it's worth understanding what is the severity of your disease, how are you responding to the anti-VEGF therapies that you're getting, and then asking, "Is there a different therapy I could switch to?" Because there are different therapeutics in this class with different concentrations, different molar concentrations of anti-VEGF capacity—in other words, different amounts of drug in the injections. Some of the different molecules block different growth factors in a different to VEGF-A. And so, it's worth talking with your provider about: Could there be other choices within this class that might be worth trying to see if you can get better outcomes? And then the other thing that we talked about peripherally a little bit, but it's just the dry component of this. And this is where it gets challenging, because you can have an eye or a patient that's responding beautifully to anti-VEGF therapy, but they're experiencing progressive vision loss, and it's due not to the wet disease, but now to the dry component, the geographic

atrophy component is now, sort of, the primary driver of vision loss in some eyes. And that's where it's worth talking with your provider: Could you be right for some of those therapeutics that are FDA approved to treat and slow down that dry component?

DIANE BOVENKAMP: Yeah, and there's a few drugs that are out there right now, and they basically target these proteins in the complement system, I guess C3 and C5 and whatever, to try and, like what you were saying, kind of reduce that response, like what you would get from inflammation, from a vaccine or whatever.

CHARLES WYKOFF: Yeah. You know, it's interesting. Again, I like to take things just at a high level first. The anti-VEGF class of medications, I don't think there's any retina specialist that would argue that they're fundamentally important, and every retina specialist, I think, would use them. The anti-complement therapeutics are a little more controversial. There's more discussion there in the field because we have two medicines that are FDA approved. Both of them have been shown to slow the progression of the geographic atrophy form, but the main challenging thing there is that the clinical trials to date have not shown a visual benefit in any of the prespecified outcomes. In other words, we can't look at patients and say, based on the data, that you're going to see better at the end of 2 years of treatment, than if we don't treat you. And that's sort of a tough position to be in. What we can say is that if we treat you with these drugs for the geographic atrophy form, we are going to slow the progressive loss of tissue in the back of your eye. And many physicians, I think, reasonably believe that that's going to long-term protect more visual function, but we need more data to try to better understand exactly what that functional benefit is for patients. And that's why it is still a controversial topic in the field.

DIANE BOVENKAMP: Exactly. And I think there's a lot of follow up being done that'll be presented annually. They're doing the monitoring, and I think that at the very least, if you can try and prevent the damage from being started, that's at least a start—or the damage from being continued—that's at least a start. But it would be great if we could, like, gain seven lines of reading like we do with some of the VEGF inhibitors,

right?

CHARLES WYKOFF: Completely right. Yeah, I mean, if you take a patient with new macular degeneration that's the wet form and they have wet macular degeneration and they're bleeding in the back and they've lost vision, a lot of those patients, not all of them, but a lot of them, you're right. You give them a shot or two or a few, and the patient will say, "Yeah, Doc, I definitely see better." And sometimes they measure better, and sometimes they don't, but most patients will notice subjectively, yeah, there's some improvement if you catch it early in the disease process. Whereas with the dry form, it's totally the opposite. The conversation with those patients with the two drugs that are FDA approved is similar, which is, "We're going to slow the disease process." And I agree with you. I think it is a meaningful slowing here, but the problem is we're saying, "Look, we're slowing the process, we're not stopping it, and we're certainly not reversing it. And so, you're not going to get visual improvement, we think, in the vast majority of cases, and you may still notice progressive decline because, again, we haven't stopped it, we're just slowing it down."

DIANE BOVENKAMP: Great. Well, it'll be good to ... maybe we can check in with you in another year or two and see.

CHARLES WYKOFF: Yeah, your point, the future. I truly believe, and I tend to be an optimist, but the future is bright. I mean, we didn't have anything for geographic atrophy a few years ago, and now we have two medicines. You know, 25 years ago, there was nothing for wet AMD, and now we have 13 options, right? So, we will have more options over time, and I think we're going to get better. We're going to get better both in durability for the medications in wet AMD where they last longer. I think there's some exciting options coming in wet AMD where we can actually gain more vision because we've already said we're gaining some vision with these current therapeutics, but in some cases patients are not getting optimal outcomes. And we need new medications that actually improve the absolute amount of vision that patients are getting. And then, maybe the other side, or the third one I would add, is we're going to get better medications for geographic atrophy—things that slow the progression even more and things that ultimately, hopefully can improve visual

function.

DIANE BOVENKAMP: Great. And they might take the form of non-injections, right? Some injections, but maybe who knows, they might be the Holy Grail pill, or there might be eye drops, therapy—gene therapy. There's all these things that are in the works, so there's a lot to hope for the future. I agree.

CHARLES WYKOFF: Absolutely. There's three gene therapies in humans right now for dry AMD. There's multiple self-injectable therapies, so there's a Phase 3 trial right now for an injection that patients give themselves into their abdomen at home once a day.

DIANE BOVENKAMP: Wow.

CHARLES WYKOFF: Most patients would much rather have that than a shot in the eye. There's options for once-a-month, at home subcutaneous treatment. Patients who are used to using insulin, imagine just doing one of those little shots once a month at home, and that's potential option for geographic atrophy. Again, none of this is proven. It's all in clinical trials, but the hope is that some of these will be positive and will improve outcomes for patients and decrease the treatment burden that they have to experience. So, it is an exciting time, and I'm so thankful for groups like yours that support research and see the value in that, because if you look back over the last 20 years, we really have come a long way in retina. We're doing so much more for patients today than we were 20 years ago. And I'm a firm believer that that even as little as 5 years from now, but certainly 20 years from now, it's going to be a very different landscape of what we can offer patients with retinal diseases, including macular degeneration.

DIANE BOVENKAMP: Wow, I think I'm just going to end right there. That's a mic drop statement right there. So hopeful. So, thank you, Dr. Wykoff, for all the information you shared with us today. To our listeners, I sincerely hope you found today's Chat helpful. Our next Macular Chat will be Wednesday, February 26, on the topic of geographic atrophy. And I wanted to again, Dr. Wykoff, thank you so much for coming with us today. We know you have a busy clinic, and we appreciate giving us all the

information to give us hope today.

CHARLES WYKOFF: No problem. Great to be part of the conversations. Thank you for the partnerships.

DIANE BOVENKAMP: Great. Absolutely. And thanks again for joining us, and this concludes today's Macular Chat.

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](#)
- [Research funded by Macular Degeneration Research](#)
- [Macular Degeneration Overview](#)
- [Treatments for Macular Degeneration](#)
- [Macular Degeneration Resources](#)

American Society of Retina Specialists (ASRS): (312) 578-8760 or visit <https://www.asrs.org/home>. Available resources include—

- [ASRS Educational Resources](#)
- [ASRS Resources and Tools](#)
- ASRS' [Find a Retina Specialist](#) tool

For further assistance, contact Monica Horton at monica.horton@asrs.org

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

- [Amsler grid](#)
- [AREDS2 vitamins](#)
- [Anti-VEGF medications](#)
- [ASRS Help Stop Step Therapy](#)
- Avastin® (bevacizumab)