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### Diabetic Retinopathy: Understanding the Impact on Patient Lives and the Need for Timely Diagnosis and Referral

Announcer: This activity is provided in partnership with the National Eye Institute, of the National Institutes of Health, of the US Department of Health and Human Services. The National Eye Health Education Program of the NEI is acknowledged for its important contributions to this initiative.

Dr. Austin-Clayton: Vision loss caused by diabetic retinopathy can have a significant impact on a patient's quality of life. As Associate Director for Research on Women's Health at the National Institutes of Health, we are asking healthcare providers to help us improve our efforts in protecting vision by taking more assertive action on behalf of our patient with diabetes. The acronym ASSERT-D was created as a reminder to be more proactive in the screening, referral, and treatment of diabetic retinopathy in patients with diabetes. This initiative is both a wakeup call and a call to action to healthcare professionals to be more proactive. What does being proactive and taking action look like in practice, and why is this initiative so important?

Welcome to CME on ReachMD. I am Dr. Janine Austin-Clayton, Director of the NIH Office of Research on Women's Health and a practicing ophthalmologist. Today I am joined by Drs. Paul Chous, Anne Peters, and Charles Wykoff. It is great having you all on the program today.

Dr. Peters: Thank you so much for having me.

Dr. Wykoff: Hi, great to be here.

Dr. Chous: It is a real pleasure to be here

Dr. Austin-Clayton: Dr. Peters, can you start us off by telling us about the prevalence of diabetes and its implications for health?

Dr. Peters: Because more people are getting diabetes, obviously more people are at risk for having diabetic retinopathy, and the most recent statistics show that in the United States one in ten adults are living with diabetes, both diagnosed and undiagnosed. Sadly, some of those people do not even know they have diabetes, and the others obviously do. One of the big issues is that it is not the same in every population, the rates of diabetes, so Hispanic individuals and African-Americans are at higher risk for diabetes, and they are also at higher risk for diabetic complications. Not only are you going to see more people with diabetes, we are going to see more higher-risk people with diabetes, and over the next 30 years, the rate of people with diabetes is going to keep increasing. If rates of obesity go up as they have been, by 30 years from now, one in three adults in the United States will have diabetes.

Dr. Austin-Clayton: Dr. Wykoff, what is the impact of diabetes on the eye health of these patients?

Dr. Wykoff: Diabetes is a growing global challenge, and I think a key to remember here is that the longer patients live with diabetes, the more likely they are to develop diabetic retinopathy. I think we need to change our thought process here and really consider that diabetic retinopathy is a when a problem not an if problem for most people with diabetes if they live long enough. If you look at the longest epidemiologic studies that we have, well over a majority of patients will ultimately develop diabetic retinopathy.

Dr. Austin-Clayton: Dr. Peters, what other factors are associated with diabetic retinopathy that we should be aware of?

Dr. Peters: First and foremost, good glycemic control is vital, and good glycemic control early on really makes a huge difference. That means we need to diagnose patients early in their disease so we can keep them under tight control throughout. Patients who have had a very long duration of diabetes are obviously at very much increased risk of having diabetic retinopathy because the risk of retinopathy is related both to glycemia and duration of disease. Hypertension is a risk factor as are elevated lipid levels, so controlling blood pressure is very important and that is also incredibly important for reducing risk of diabetic nephropathy as well. Any other vascular complication also increases the risk for diabetic retinopathy. The way I look at it is somebody with one complication, whether it is retinopathy, nephropathy, vascular disease is somebody who is also at risk to have another complication, so we need to look very carefully to assess those patients and then treat them for all the complications they might have. From my perspective, the best thing we can do is identify patients with prediabetes early and frankly prevent diabetes. If we cannot do that, at least early diagnosis will allow us to do early screening and therefore identify patients who need treatment for retinopathy earlier.

Dr. Chous: Just to reiterate, diabetes duration is the biggest risk factor for developing diabetic retinopathy. The longer a patient has it, the higher the risk. Long-term control of diabetes is really important beyond diabetes duration, and I think it is important for all of us to remember that patients with good metabolic control now can still develop sight-threatening diabetic retinopathy. It is not simply what your hemoglobin A1c is today but what it was 20 years ago vis a vis metabolic memory protecting us from developing more severe diabetic retinopathy. You do not develop skin cancer for instance because you were out in the sun last weekend. It happens from a lifetime of exposure, and the same thing is true with respect to diabetic retinopathy.

Dr. Austin-Clayton: Dr. Peters, what are the key things that healthcare providers can say and do for their patients regarding diabetic retinopathy?

Dr. Peters: From my perspective, the whole focus of our current ADA guidelines only involves patient engagement, and I think we need both patient and provider engagement here. I first of all discuss with the patient when did they last go, and then I have a conversation about why go now. A lot of people will say, as you heard earlier, I do not have symptoms, this is not an issue. Again, bringing it back to this is really about your eyes. Even if you are not feeling like you need to go to an eye doctor right now, it is really important because we can do something about it. A lot of times my patients think that it is futile, that they cannot do anything. They may have family members who had loss of vision. They get very discouraged. I really spend a lot of time working with patients to understand that this is something that they can do to empower them to really want to go have their eyes checked. I find that works. Again, as a provider, I bug them every time I see them, and as their diabetes specialist, I see most patients every three months. I have a lot of opportunity to bug them to come and talk about it. I think it is just an important piece of the visit, and I actually have patients write down on a form before they see me, and I know a lot of offices to this electronically but we are still in paper mode for writing down patient notes. I always say when was your last appointment with your eye professional, and then they write it down, and then I can see it and validate when they last went.

Dr. Austin-Clayton: Dr. Wykoff, how effective is screening?

Dr. Wykoff: In the United Kingdom, diabetic-associated eye diseases used to be one of the number one causes of blindness among adults, but that has now subsequently fallen out of the number one slot because of their optimized screening protocols, emphasizing that screening really works. An important point to recognize is that screening should be performed regardless of symptoms. The reality is across the United States we are simply not screening the majority of diabetic patients for diabetic retinopathy. There is data that as few as a third of patients with diabetes come in for screening before they have visual symptoms. I think that there is a misconception that patients with diabetes really do not need eye screening until they have symptoms. That could not be further from the truth. The reality is that diabetic retinopathy in all of its stages is much more readily treatable the earlier it is diagnosed, and that often means when a patient is asymptomatic. It is critical that all patients with diabetes receive the screening that they need and that they deserve as soon as they are diagnosed with diabetes as an adult.

Dr. Austin-Clayton: Dr. Peters, they say an ounce of prevention is worth a pound of cure. What can we as healthcare providers do to prevent diabetic retinopathy?

Dr. Peters: The problem is that a lot of patients do not get screened or followed early enough so they actually have undiagnosed diabetes for a period of time estimated up to four to seven years before they are actually diagnosed. During that time with undiagnosed diabetes, they can be developing retinopathy such that by the time someone actually gets the diagnosis of diabetes, the clinical diagnosis, they may already have retinopathy. This is why I am such a big advocate of identifying prediabetes before they even get to this stage of diabetes and having this risk because I think it is very important to turn the clock back to start early and then prevent progression and certainly in those patients make sure they are going to see the eye doctor as they begin to develop diabetes because this can happen early on, and people need to be very aware of that risk.

Dr. Austin-Clayton: Turning to you now, Dr. Chous, what are the stages of vision-threatening diabetic retinopathy?

Dr. Chous: There are really two vision-threatening forms of diabetic retinopathy. Center-involved diabetic macular edema, where the central 1 mm of the macula gets fluid edema, cystic spaces, and the like. That is really the leading cause of a significant vision loss in diabetes. Then proliferative diabetic retinopathy, which leads to new blood vessel growth on the optic nerve or the retina fibrovascular traction that can detach the retina and result in severe permanent vision loss, including blindness. What we need to worry about most is any non-proliferative retinopathy that is accompanied by diabetic macular edema but also patients that have severe non-proliferative diabetic retinopathy, which was pretty clearly defined by ETDRS, the Early Treatment Diabetic Retinopathy Study. I think it is important for us to remember that patients with severe NPDR, about 50% of them develop proliferative retinopathy within the next 12 months. That is why it is important for clinicians to be aware of when patients cross over into the severe level of disease progression.

Dr. Austin-Clayton: Dr. Wykoff, can you tell us how the treatments of diabetic macular edema and diabetic retinopathy have evolved over time?

Dr. Wykoff: Thirty years ago, we only had lasers to treat diabetic retinopathy. Lasers still today play an important role in managing diabetic retinopathy both NPDR with DME as well as proliferative diabetic retinopathy. Fortunately, today we have more than just lasers. We squarely live in the pharmaceutical era. There are four medications that are FDA approved to be given by direct intraocular injection, and there are other medicines that can be used off-label to treat many different forms of diabetic retinopathy. The key is that patients get diagnosed earlier. Originally, we were treating patients with proliferative diabetic retinopathy and center-involved DME with visual acuity loss with again both lasers and pharmaceutical agents, but now we have more and more data supporting the use of pharmaceutical agents earlier in the diabetic retinopathy process. There is a phase 3 trial called PANORAMA that was recently reported top-line data showing that with regular treatments, you can dramatically improve the anatomy in eyes with diabetic retinopathy that is earlier than previously accepted stages to initiate treatment. The field is really at a crossroads right now. How do we manage these eyes with milder forms of diabetic retinopathy, these high-risk non-proliferative diabetic retinopathy eyes? We now have data to guide that management discussion with patients. The key being that most of these patients are asymptomatic at this stage of the disease. Please do not wait until patients develop symptoms to get the screening that they deserve.

Dr. Austin-Clayton: Those are all excellent points. To put this all together, I am going to ask each of you to tell us each of your biggest takeaways for our audience. Dr. Peters?

Dr. Peters: I want to be sure that patients are empowered to go see their eyecare specialist. I want to encourage patients to go see their optometrist or their ophthalmologist for regular screening and stress the fact that this is just part of one of the things they do to maintain their health. It is not scary. It is not awful. In fact, it is the opposite. It helps ensure that they have good visual acuity for the rest of their lives. I make sure that patients who have retinopathy are encouraged to continue follow-up and understand the importance of treatment, and then I work with each patient to discuss what is going on and really discuss their status and work in conjunction with their optometrist and/or their ophthalmologist. I think it is very important that endocrinologists and primary care doctors work together with the eyecare specialists who are seeing their patients.

Dr. Austin-Clayton: How about you, Dr. Chous?

Dr. Chous: For optometrists, really the key is to refer patients that have any degree of non-proliferative retinopathy when it is associated with diabetic macular edema. Beyond that now, given the new evidence about anti-VEGF therapy, refer patients to retina specialists sooner than we would have heretofore. When patients develop moderately severe non-proliferative diabetic retinopathy or even moderate non-proliferative retinopathy, those patients really ought to be referred to a retina specialist for further evaluation. The other thing that I think is key for optometrists is to remember prevention is the best way to prevent blindness from diabetes. If you do not get diabetes, you are not going to go blind from diabetes. Talking with patients who are at high risk about lifestyle strategies to prevent the disease and also to remember to send a note along to primary care providers if you detect evidence of diabetic eye disease so that patients can achieve the optimal metabolic control.

Dr. Austin-Clayton: And you, Dr. Wykoff?

Dr. Wykoff: I certainly echo what Dr. Peters and Dr. Chous have said. From a treating physician's perspective, a retina specialist's perspective, the key that I want patients and healthcare providers in general to understand is that we have highly effective treatments for diabetic retinopathy. We live in an era where patients really should not be going blind from diabetic retinopathy. We can manage many different stages of this disease, but the overarching principle is the earlier these patients get access to the treatments that they need and the treatments they deserve, the better outcomes can be achieved. Make sure everyone with diabetes is getting the screening that they need.

Dr. Austin-Clayton: Those are the most important messages for us to take away today as we work proactively as healthcare

professionals to take care of the needs of our patients with diabetes. On behalf of myself and the National Eye Institute at the National Institutes of Health, I would like to thank Drs. Paul Chous, Anne Peters, and Charles Wykoff for talking to me today to talk about what we can do to help protect the vision of our patients with diabetes. It was great speaking to all of you today.

Dr. Peters: Thank you.

Dr. Chous: It has been my pleasure. Thank you so much.

Dr. Wykoff: Thanks. Great to be here.