

Glaucoma



Chats

Glaucoma 101: Exploring the Science Behind This Sight-Stealing Disease

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Transcript of teleconference with Dr. Qi Cui, MD, PhD, Associate Professor of Ophthalmology, University of Pennsylvania, Scheie Eye Institute

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

MS. KACI BAEZ: Hello, and welcome to today's Bright Focus Glaucoma Chat. My name is Kaci Baez, and on behalf of BrightFocus Foundation, I'm pleased to be here with you today as we discuss "Glaucoma 101: Exploring the Science Behind This Sight-Stealing Disease." Our Glaucoma Chats are a monthly program, in partnership with the American Glaucoma Society, designed to provide people living with glaucoma and the family and friends who support them with information straight from the experts. All vision Chats presented by BrightFocus are also available to listen to as podcasts on the go on YouTube, Spotify, iHeartRadio, Amazon Music, Apple Podcasts, and Pandora.

BrightFocus Foundation's National Glaucoma Research program is one of the world's leading nonprofit funders of glaucoma research and has

supported nearly \$51 million in scientific grants exploring the root causes, prevention strategies, and treatments to end this sight-stealing disease, and is currently supporting 38 active research projects across the globe in the quest for a cure.

Now I would like to introduce today's guest speaker, Dr. Qi Cui, MD, PhD, is a board-certified and fellowship-trained glaucoma specialist at the Scheie Eye Institute at the University of Pennsylvania. She attended medical and graduate school at the University of Rochester Medical Scientist Training Program and completed an ophthalmology residency at the University of California, San Francisco, followed by a surgical glaucoma fellowship at Wills Eye Hospital. Dr. Cui is involved in both clinical and basic science research. The Cui Lab seeks to understand pathogenic mechanisms contributing to glaucoma and seeks to identify novel therapies for glaucoma. Welcome, Dr. Cui. We're so excited to have you here today with us.

DR. QI CUI: Thank you, Kaci. It's a pleasure to be here today.

MS. KACI BAEZ: Thank you so much. So, we'll just dive right in. Most everybody on the call is familiar with glaucoma, but could you just start us off with an overview of what is glaucoma?

DR. QI CUI: Sure. Let me give you the textbook definition to start off with. Glaucoma is a heterogeneous group of eye diseases, all with characteristic changes to the optic nerve as a result of loss of retinal ganglion cells, which are neurons of the eye. And this results in progressive and, unfortunately, often permanent vision loss.

MS. KACI BAEZ: And how do you know if you have glaucoma? At what age is it most prevalent or should you get screening?

DR. QI CUI: Yeah, so that's the difficulty with glaucoma in many instances. Glaucoma is often called "the silent thief of sight." And by that, we mean that a lot of people who have glaucoma, especially early glaucoma or high-risk glaucoma suspects, do not know that they have glaucoma. And here is where early screening and going to an eye doctor to get examined so someone can look at the back of the eye and look at the

optic nerve and look at the retina is really important. Glaucoma tends to be more prevalent as we get older, so one of the risk factors associated with glaucoma is age. So, as we get older and older, glaucoma becomes much more prevalent in the population. So, in somebody who is 30 years old, glaucoma is not very prevalent, but by the time we get to 80 or 90 years old in certain population, it can be 5 percent to 10 percent of the population. So, the take home here is get screened early. We recommend yearly eye exams, in general, but particularly if someone has a family history of glaucoma or you are aware that you do have a risk for glaucoma, then get screened early and get regular follow-up.

MS. KACI BAEZ: Thank you. And so in terms of how glaucoma works, what part of the eye is affected by glaucoma? Does glaucoma affect your central vision when you have severe glaucoma?

DR. QI CUI: So, in terms of which part of the eye is affected by glaucoma, as I already mentioned, the cells that are affected by glaucoma are called retinal ganglion cells, and they reside in the back of the eye in the retina. The retinal ganglion cells are the innermost layer of cells in the retina. So, after dilation, when someone goes to my office and I look in the back of the eye, the innermost layer of the retina is the retinal ganglion cells. I don't see the cells, but sometimes I can see the axons of the cells, which all come together to make up the optic nerve. So, that is part of the eye that is actually affected by glaucoma. Having said that, however, sometimes the pathophysiology of what causes glaucoma, what causes the pressure inside the eye to elevate, has to do with the front of the eye, and that's part of the eye called the angle. So, the drainage angle is where the fluid, which is the aqueous humor inside the eye, naturally drains out of the eye. And if the angle is not open, not patent, there's something occluding it, then the pressure inside the eye can elevate, and that is a major risk factor for glaucoma. In terms of whether glaucoma can affect your central vision when you have severe glaucoma, unfortunately, it can. And in the majority of glaucoma sufferers, it does not affect central vision until later on in the disease process. But in a subset of glaucoma, typically associated or what we call normal-tension or low-tension glaucoma, central vision or the part of the vision that's responsible for reading and for high-acuity vision can be affected a little bit earlier.

MS. KACI BAEZ: You mentioned low-tension glaucoma. Understanding that glaucoma is a group of different types of diseases that come with different risks and maybe affect different people differently, could you provide us with an overview of what are the different types of glaucoma, and how do we distinguish from each of them?

DR. QI CUI: Yeah, absolutely happy to. Broadly speaking, glaucoma is divided into open-angle and angle-closure glaucoma or closed-angle glaucoma, and what that means is we're referring to the part of the eye that's called the anterior chamber drainage angle that I was just referring to. So, this is the part of the eye where the aqueous humor, which is the fluid that is produced by our eyes, naturally drains out of the eye after it's done its job. If that angle is occluded, meaning that we don't have a clear visualization of the anterior chamber drainage angle, then we talk about angle-closure or closed-angle glaucoma. If that angle is broadly open, then we talk about open-angle glaucoma. So, those are the two broad types. And the way we can tell whether somebody is at risk for open-angle glaucoma versus angle-closure glaucoma is by doing an examination technique called gonioscopy. And what this is is we use a prism lens on top of the eye that will allow us to look into the angle and see what the architecture of the angle looks like. If the angle looks narrow or potentially occludable, then we're a little bit more worried about closed-angle or angle-closure glaucoma. If they look nice and open, but someone does look like they have other risk factors for glaucoma on either examination or a medical history, then we're a little bit more worried about open angle. Now, there are different subcategories of, particularly, open-angle glaucoma, such as pseudoexfoliative glaucoma and pigment dispersion syndrome. So, broadly speaking, though, we characterized glaucoma based on the structure of the angle.

MS. KACI BAEZ: Okay, thank you. Are some people more at risk than others for these different types?

DR. QI CUI: Yes. Absolutely. That is, unfortunately, the case that some people are more risk than others for different types of glaucoma. Certainly, when it comes to angle-closure or closed-angle glaucoma, if someone has a more narrow angle, then they're at risk for that category

of glaucoma. As many of you probably already know, glaucoma, unfortunately, does have a genetic component, and there are a lot of genes that's been characterized to potentially confer higher risk for open-angle glaucoma or closed-angle glaucoma. There are also systemic diseases and risk factors, personal risk factors that are associated with glaucoma, such as high and low blood pressure. Diabetes has been shown to be a risk factor for glaucoma, sleep apnea, cardiovascular disease. A lot of these systemic risk factors can cause somebody to be at higher risk for glaucoma, as well. And here, once again, it's important to see an eye care provider so they can evaluate not only the eye but these systemic and potentially genetic risk factors. The other thing is, if there's a family history of glaucoma, then somebody might be at higher risk for glaucoma, and that is something that's important to make the eye care provider aware of, as well.

MS. KACI BAEZ: Thank you. It's always important to understand your family history when it comes to health and to be open and honest with your medical care provider, because everybody's different, so go get your eyes examined.

DR. QI CUI: Absolutely.

MS. KACI BAEZ: That's an important message. And so, in the world of glaucoma, why is elevated intraocular pressure, or IOP, something to be concerned about? Do all people with glaucoma have elevated IOP?

DR. QI CUI: That's a great question. If someone has been to the doctor's office and has been evaluated for glaucoma, you've probably heard the term "elevated intraocular pressure." And the reason for that really stems from this study that was conducted first in 1994, the Ocular Hypertension Treatment study. In this study, patients were randomized to either receive intraocular pressure–lowering medication or to not receive intraocular pressure–lowering medication. They found that about a 20 percent reduction of the intraocular pressure halved the risk for developing glaucoma over the course of 5 years. This study—and it is still ongoing—really informed our understanding of the treatment of glaucoma, namely that elevated intraocular pressure is a modifiable risk factor for glaucoma. So, many of our treatments^{3/4}whether they are medical, surgical, laser^{3/4}by

and large, aimed at lowering intraocular pressure. And so, that's why we talk about intraocular pressure a lot, and we talk about lowering intraocular pressure.

As to whether everybody has elevated intraocular pressure who have glaucoma, that is not actually true. There is a subcategory of glaucoma, as I already mentioned, called normal-tension glaucoma or low-tension glaucoma, where when we check the pressure inside the eye in these patients, the pressure is not considered high. So, they're typically under 21 millimeters of mercury, but we do see evidence of glaucoma. And this is an important distinction because it does not mean that if someone has "normal intraocular pressure", that they do not have glaucoma. It really depends on the rest of the exam and the other risk factors associated with glaucoma. Incidentally, there has been a different study working at this subpopulation of patients, and this also found that even though pressures are normal in these normal-tension glaucoma patients, lowering intraocular pressure also decreases their risk of having developed glaucoma and glaucoma progression.

MS. KACI BAEZ: Yes, an important example of the complexities of this disease and the many factors at play.

DR. QI CUI: Absolutely.

MS. KACI BAEZ: Yes, we often get some of the same questions during these programs from our listeners. One question we got for this program that I know we've discussed before, but we want to address it again because these are really important questions: Will I ever totally lose my sight by having glaucoma? And it's connected to the question of what happens to our vision as glaucoma progresses?

DR. QI CUI: Yeah, that is a good and important question. Glaucoma can cause complete blindness, unfortunately, but it does not cause that in everyone. As we already talked about, everybody's risk for glaucoma and glaucoma progression is different. So, the appropriate treatment for everybody and what they need in order to prevent the glaucoma from progressing is also different. So, yes, can glaucoma cause people to completely lose their vision? The answer is, unfortunately, yes. But will

glaucoma cause everyone who has glaucoma to lose vision? The answer for that is definitely no. I apologize, Kaci, can you remind me what the second part of the question is?

MS. KACI BAEZ: Oh, sure. And just thinking about what happens to our eyesight as glaucoma progresses. I know you mentioned it is different for everyone.

DR. QI CUI: Yeah. It is different for everyone, and it's one of those experiences that can be difficult to characterize for people who have not experienced it. George Spaeth and other physicians at Wills Eye has done a lot of good research on this topic in terms of: What are the symptoms experienced by glaucoma patients as their glaucoma continues to worsen? A lot of times when we talk about is loss of peripheral vision, and this results in a "tunnel vision." And some of the studies that Dr. Spaeth and his cohorts have looked at, where they've shown this is not entirely the case. What can happen is that people start to lose contrast sensitivity. And what that means is the different colors seem a little bit less vivid, the details become a little bit fuzzier, they need more light to be able to see. Overall, things become, for a lack of better description, more washed out. That can very well be the experience of some of these patients who are suffering from glaucoma. But as glaucoma becomes more severe, people can develop scotomas, and that means parts of the vision where they're not able to see through as well, that look either black or gray. That can certainly happen, and that's more noticeable when they're closer to their central vision. But, ultimately, it's a little bit of an amorphous change to their vision, and because it happens so gradually, not everyone appreciates it as an acute change. And this can make glaucoma a little bit harder to diagnose and to know this, even when it is already approaching severe stage.

MS. KACI BAEZ: Thank you. Some other questions that we get that are pretty popular amongst people interested in glaucoma or people who have glaucoma is: Can vision lost to glaucoma be restored? And can the damage to our optic nerve be reversed?

DR. QI CUI: Yeah, as I mentioned, I do basic science and clinical research in glaucoma, as well. That is something we're all striving for; that is the

Holy Grail. We would love to be able to restore lost vision in glaucoma and other eye diseases, as well. As of right now, we do not have a way to restore retinal ganglion cells and regrow retinal ganglion cells in the eye after they have been damaged and they have died. And because of this, unfortunately, the answer is that we are not able to restore lost vision as of right now in glaucoma. But there is a lot of active research going on in terms of vision restoration, trying to regrow retinal ganglion cells, and encourage their axons to go through the optic nerve and reconnect with the brain, allowing us to pick up visual information once again and send it to our brain. And I am hopeful that potentially the next 5 to 10 years, we will have made very good progress along those lines.

MS. KACI BAEZ: And there are treatments available for glaucoma that many of our listeners may be familiar with. We've had entire episodes on glaucoma treatments, but could you briefly summarize the types of treatments that are currently available for glaucoma?

DR. QI CUI: Yeah, absolutely, happy to do it. In terms of treatment for glaucoma, broadly speaking, we have medical treatment, we have laser procedures, and we have surgical treatment. And medical treatment—many of our listeners are probably familiar with this—are typically eye drops. So, these are different classes of medication that's been formulated as an eye drop to be applied directly to the cornea. And the goal for all of these medications is to lower the pressure inside the eye, and this is done by encouraging the aqueous humor to either flow throughout the angle more effectively or flow through parts of the eye and through the lymphatic drainage more effectively, or else to encourage the eye to produce less aqueous humor and thereby decreasing the pressure inside the eye. Laser procedures, the specific ones that I'm thinking of, are selective laser trabeculoplasty or argon laser trabeculoplasty. These lasers are applied directly to the drainage angle, and this results in basic restructuring of the drainage angle matrix, cellular matrix, in that area to encourage drainage of the fluid from the angle. And this can be done in the clinic, and it typically is done with the same level of effectiveness at about one to two eye drops. And finally, we have surgeries. Once again, the purpose of these surgeries is to lower the pressure inside the eye, and this can be done by either directly targeting the drainage network by

opening up the drainage network a little bit more, allowing the aqueous humor to flow out of the angle, or else by creating an alternative pathway for the fluid inside the eye to drain out of the eye into the connective tissue around the eye. So, those are, broadly speaking, the different categories of treatment options. And they can be very effective for a large proportion of glaucoma patients.

MS. KACI BAEZ: Thank you. In terms of treatment, many of our listeners are curious about how lifestyle interventions, such as diet or nutrition, or different types of healthy lifestyle factors. How do those play a role in glaucoma disease management or risk reduction? One of our listeners has also inquired about plant-based foods and glaucoma.

DR. QI CUI: Yeah, I mean, that's a great question, and we are still learning a lot of information—new information—as far as that's concerned. As we had already talked about, certain systemic diseases, like high blood pressure, diabetes, sleep apnea, cardiovascular diseases, can cause a higher risk for glaucoma and glaucoma progression. So, certainly, making sure systemic diseases are well controlled is helpful. In terms of plant-based diet, I think there is a significant amount of evidence out there to suggest that leafy green vegetables and a diet that is rich in antioxidants may be beneficial for glaucoma. And the reason for that is there is a whole class of literature looking at oxidative stress as a cause of glaucoma, and there is a lot of literature suggesting that by decreasing oxidative stress, we may be helping to prevent progression of glaucoma and worsening of glaucoma. And leafy green vegetables certainly have a lot of antioxidants in them, so having a healthy diet, low inflammatory diet can certainly be helpful.

MS. KACI BAEZ: Feels like everything is connected to inflammation.

DR. QI CUI: It can be. Yeah.

MS. KACI BAEZ: Thanks. Yeah, lots of leafy green vegetables. And BrightFocus also has recipes for healthy eating, for brain and vision health on its website at www.BrightFocus.org. So, I know that your lab is dedicated to finding new treatments for glaucoma. Could you tell us a little bit about your current work and the association between glaucoma

and neurodegenerative conditions?

DR. QI CUI: Yeah, I would be happy to. So, in my lab work, our current focus is on a class of medications called GLP-1 receptor agonist, and that's a mouthful, but many of you will have heard of sort of, generic name, which is Wegovy® and Ozempic® and semaglutide. So, this class of medication has been getting a lot of press lately for weight loss, and it's also used to treat diabetes. What we found in our lab, and others as well, is that this class of medication decreases neural inflammation inside the eye. And what prompts us to look at this is they have also been looking at this class of medication for treating neurodegenerative conditions, like Alzheimer's, Parkinson's disease, and Huntington's disease, and we have identified similar pathways between our animal models of glaucoma and some of these neurodegenerative conditions. Now, they're obviously not the same disease, but some of the pathways specifically related to neuroinflammation are similar. And what we've shown is that GLP-1 receptor agonists may serve to decrease neuroinflammation or inflammation inside the eye in response to elevated intraocular pressure. And this could potentially be a viable treatment for glaucoma. Now, lots of work still remains to be done, and we are looking to see whether we can develop this into a clinical trial. But I think the initial information or the initial studies are relatively promising.

And then, the second thing that we've looked at is looking at existing health database information to see whether there's any connection in the use of this class of medication for treating diabetes and risk for glaucoma. And what we found is that type 2 diabetic patients who are using GLP-1 receptor agonist medications, as opposed to a different kind of diabetic medication, appear to have lower risk for developing glaucoma. So, that's also a piece of information that suggests these medications may be beneficial. So, I'm very excited by this work. Whether or not this ends up being a treatment that we can rely on for glaucoma remains to be seen, but I am hopeful.

MS. KACI BAEZ: That's really exciting, and research can take a while to see the benefits, but I think if you look at the course of history, research does pay off. And so, there's a lot to be hopeful about in vision research,

and thank you for diving into that. And BrightFocus has funded a lot in the space devoted to neurodegeneration, because it's all connected.

DR. QI CUI: Yeah, absolutely.

MS. KACI BAEZ: Yeah, it's all connected. It's so fascinating. And so, what are you most excited about in terms of promising glaucoma research for a cure?

DR. QI CUI: Oh, that's a good question. I'm really excited now that we have basically two general avenues of research. My lab's focus is on neuroprotection, so our goal is to prevent glaucoma from getting worse. But there are a lot of other researchers, other labs out there looking at neuroregenerative pathways. So, not only are we trying to prevent glaucoma from becoming evident and progressing, but other researchers are also looking into whether they can restore vision after glaucoma has already caused some damage. So, I think those avenues of research are really important, and they will work in combination with each other to, hopefully, advance our understanding of glaucoma. Personally speaking, I feel there's a lot we still don't understand, even as somebody who treats glaucoma, about glaucoma, and the research along that field has never been so robust. And I'm really excited to see what we're going to find in the next 5 to 10 years. So, I think there's a lot of promise.

MS. KACI BAEZ: That is so exciting. There's so much in the pipeline.

DR. QI CUI: Absolutely.

MS. KACI BAEZ: So, thank you for everything that you've shared with us. Yeah, it's been so informative when you have a condition like glaucoma to just get as much information as possible. We have a few more questions before we wrap up, just a couple more that I'd like to ask just before we jump off. And so, one question is: Can you have glaucoma in only one eye?

DR. QI CUI: Yes, this can happen. In fact, in a lot of people, glaucoma severity is asymmetric. Many of my patients have glaucoma that's affecting their vision in one eye, and in the other eye, they may only be a glaucoma

suspect, which means that we're watching that eye carefully, but they do not have glaucoma that is affecting their vision as far as we're aware of. The difference between somebody who's a high-risk glaucoma suspect and a glaucoma, it's a fine line. A lot of times because glaucoma takes a number of years in a lot of people to manifest themselves, we may not know if somebody will ultimately develop glaucoma as they get a little bit older, so they will remain in that glaucoma suspect category until and when or if the glaucoma manifests itself. But certainly, glaucoma can be asymmetric, and especially in those who have other cause for glaucoma, for example, trauma. Prior ocular trauma can cause glaucoma. And if the trauma only occurs in one eye, then that would be the eye that's affected and the other eye can be perfectly healthy.

MS. KACI BAEZ: It shows the importance of getting that eye exam because everyone is different. Thank you. And one more question related to vision.

DR. QI CUI: Yeah, absolutely.

MS. KACI BAEZ: So, what makes my vision go dark and then get light again? Sometimes there's also a cloud or fogging, but it goes away.

DR. QI CUI: Yeah. So, a lot of things can cause these visual changes that people experience. If we're to assume that this is due to glaucoma—which it may not always be—but if we're to assume that it's due to glaucoma and severe glaucoma, then it could be related to the general health of the retinal ganglion cells. The retinal ganglion cells can be damaged, but they can still be functioning, so sometimes what can happen is their functional ability—the way they're functioning and carrying information from the front of the eye to the brain—can wax and wane a little bit. And that can cause some of this fogginess and change in vision, darkening that someone is experiencing. Having said that, I will just say a lot of things that's not related to glaucoma can cause these kinds of visual changes, so it may not be directly attributable to glaucoma in all cases.

MS. KACI BAEZ: Always important to discuss your symptoms with your health care provider, but thank you for that information.

DR. QI CUI: Yeah, absolutely.

MS. KACI BAEZ: And so, we have one more listener-submitted question. This is actually a really important question. I think we could probably spend a long time talking about it, but the question is: At what point does glaucoma become a disability?

DR. QI CUI: Oh, gosh, that is a really good question, and you're right, we can probably spend a lot of time talking about that. I think, from my perspective, when I talk to my patients about this, it really depends on their personal needs, right? So, we talked about eye diseases—I should say, we often talk about eye diseases affecting our activities of daily living. So, everybody's daily needs of what they need to do to get through the day and how they conduct their lives is different. So, someone can have very low visual needs, in which case glaucoma may not become a disability ever, even if it's relatively severe, when somebody else as a very high visual need, and their glaucoma can become a disability because it disrupts their life even when it's relatively mild. So, I think it's a hard question to answer in that sense, but I do think there is a personal component to that. And ultimately, if the glaucoma is affecting your life in a way that prevents you from doing what you need to do on a daily basis, then you can argue it is debilitating for you. So, it may not be a disability in the strictest sense of the word, but it can be debilitating for an individual person, even when the glaucoma is mild.

MS. KACI BAEZ: So important. Just an important reminder that everyone is different.

DR. QI CUI: Yeah, absolutely.

MS. KACI BAEZ: And once your life is affected, it just becomes a whole different ball game. Thank you, Dr. Cui. Do you have any final thoughts to share with our listeners today?

DR. QI CUI: Yeah, I mean, we talked a lot about this already, but glaucoma is one of those studies that is, unfortunately, incredibly frustrating. And it can be seemingly difficult to control for some patients, but just keep in mind, please, that not all glaucoma are created equal, right? Some people

will, unfortunately, lose vision because of glaucoma, but other people can do very, very well, and their glaucoma can be put under excellent control. The way to make that happen is just follow up with your eye care provider, make sure you go to regular appointments, discuss your symptoms and your concerns with your eye care provider. And that's the way to ensure we're able to provide you with the glaucoma care that is needed for each individual. But we talked about that a little bit already.

MS. KACI BAEZ: Absolutely. Just remember to communicate and ask questions. Such important information and insight that you shared today, Dr. Cui. Thank you so much.

DR. QI CUI: Thank you so much.

MS. KACI BAEZ: Yeah, so informative. And to our listeners, thank you so much for joining our Glaucoma Chat. We sincerely hope that you found it helpful. This is our last Glaucoma Chat for 2024. We look forward to next year and joining you on Wednesday, January 8. Thanks again for joining us today, and this concludes today's BrightFocus Glaucoma Chat.

Useful Resources and Key Terms

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

- [Glaucoma Chats Archive](#)
- [Research funded by National Glaucoma Research](#)
- [Overview of Glaucoma](#)
- [Treatments for Glaucoma](#)
- [Resources for Glaucoma](#)
- [Expert Advice for Glaucoma](#)

Helpful treatment options or resources mentioned during the Chat include—

- [Recipes](#) by BrightFocus Foundation
- Wegovy®
- Ozempic®
- Semaglutide