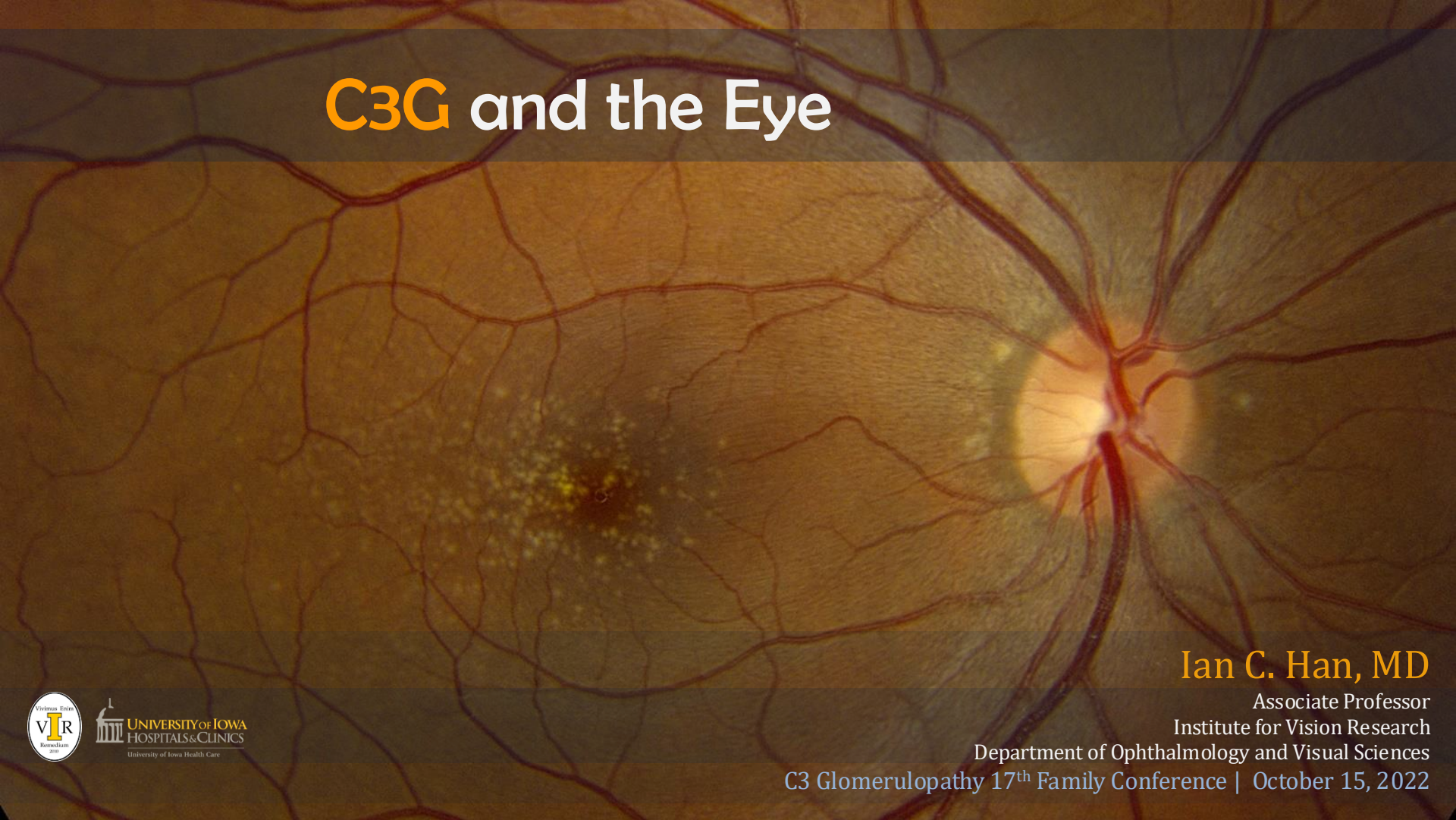
C3G and the Eye



Ian C. Han, MD

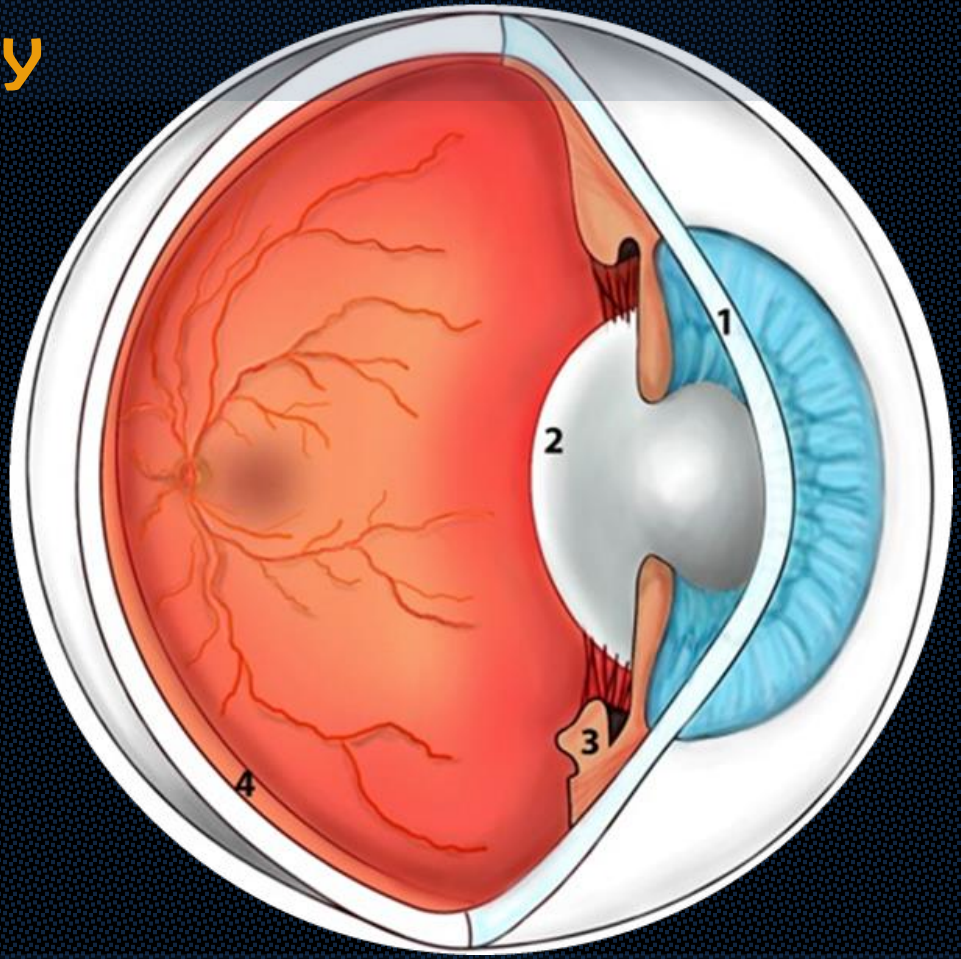
Associate Professor

Institute for Vision Research

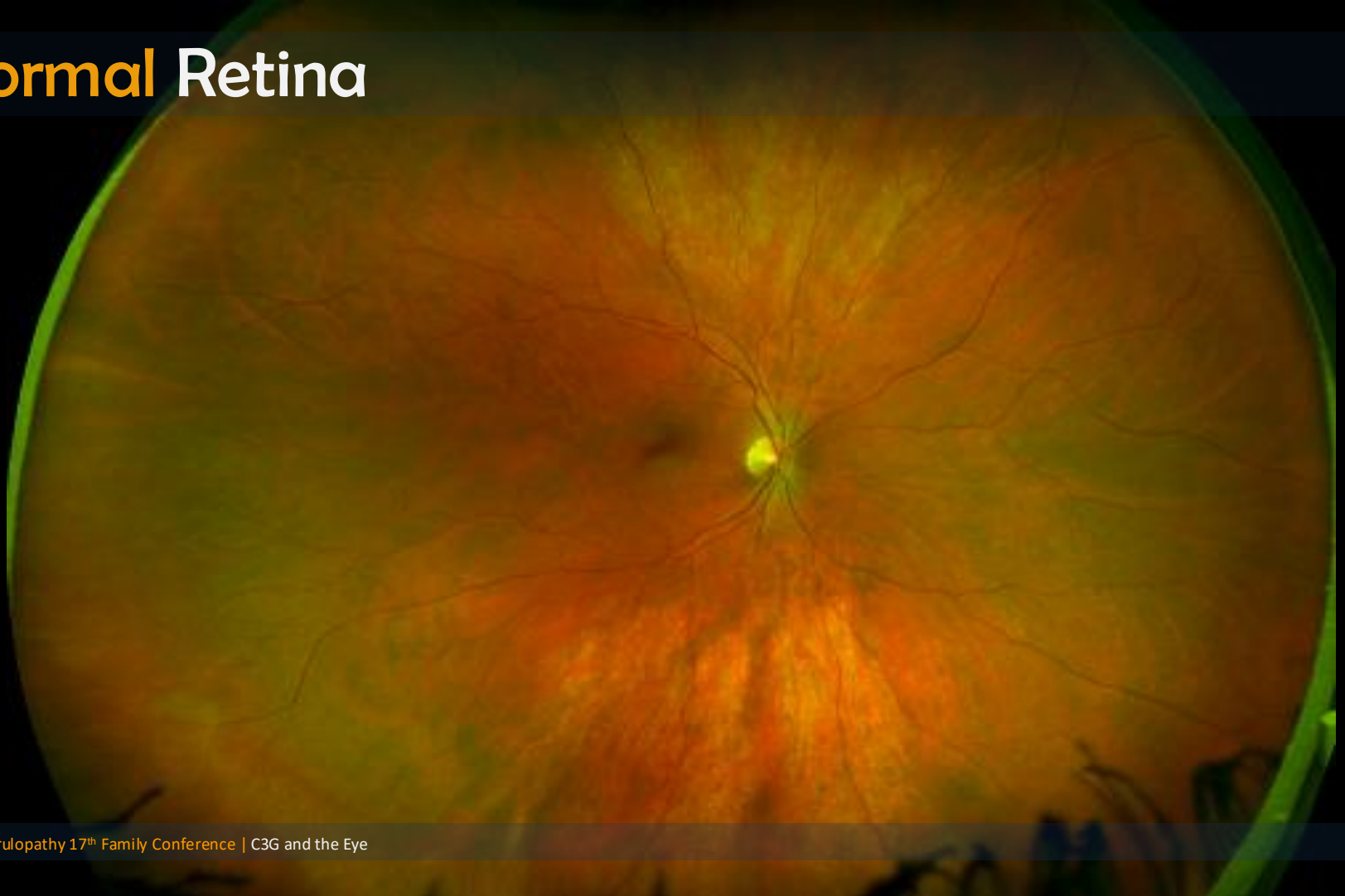
Department of Ophthalmology and Visual Sciences

C3 Glomerulopathy 17th Family Conference | October 15, 2022

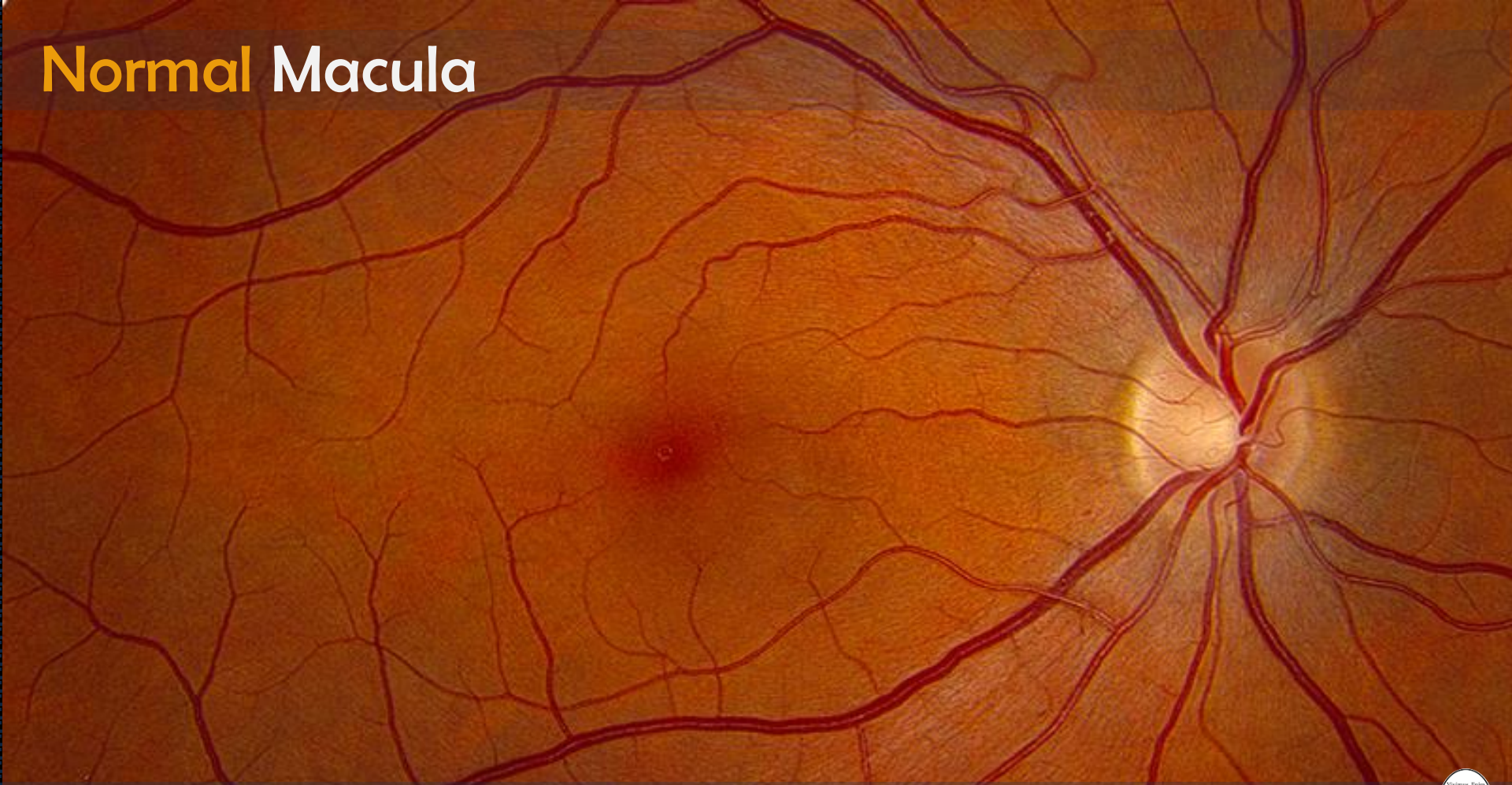
Eye Anatomy



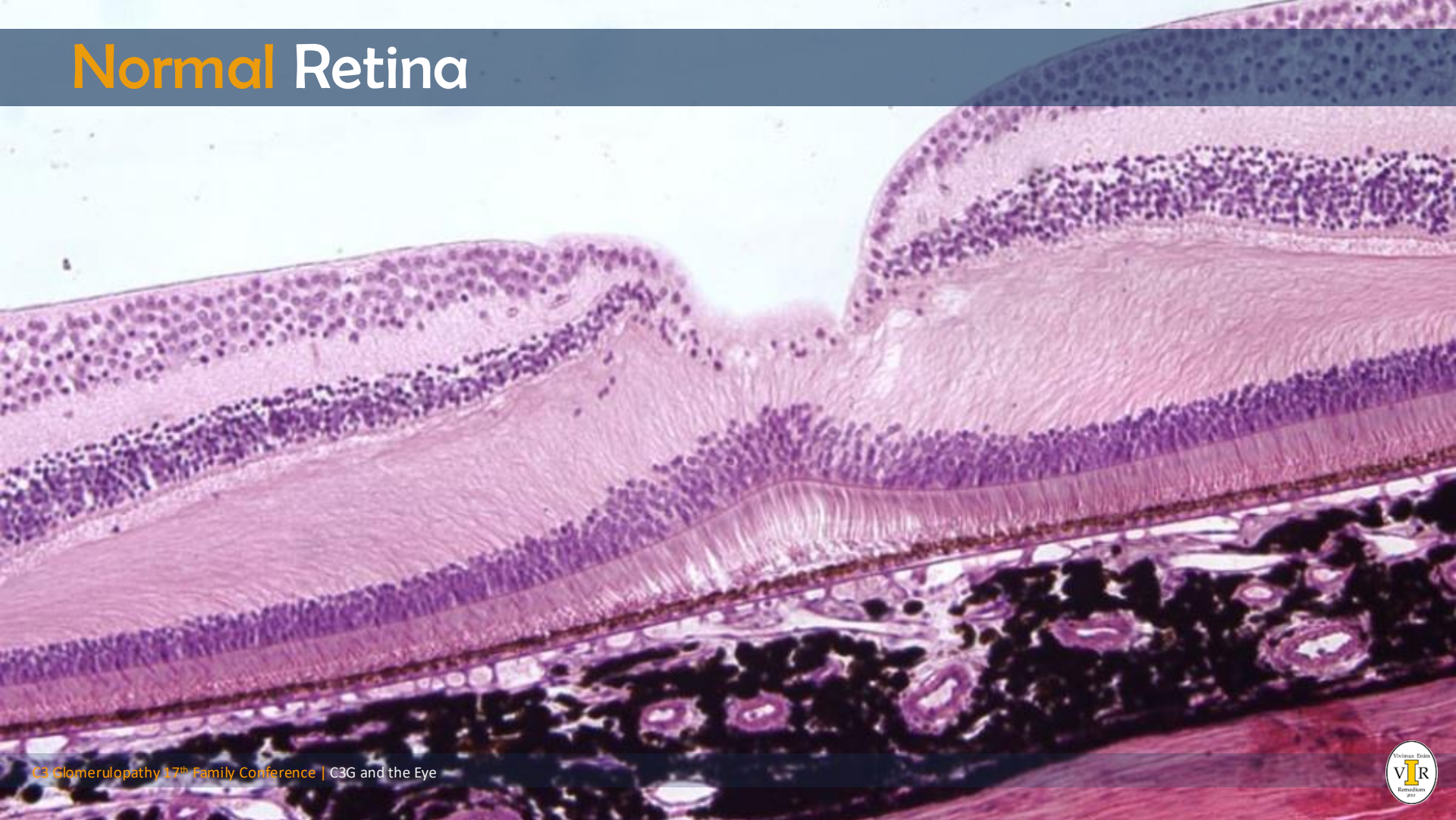
Normal Retina

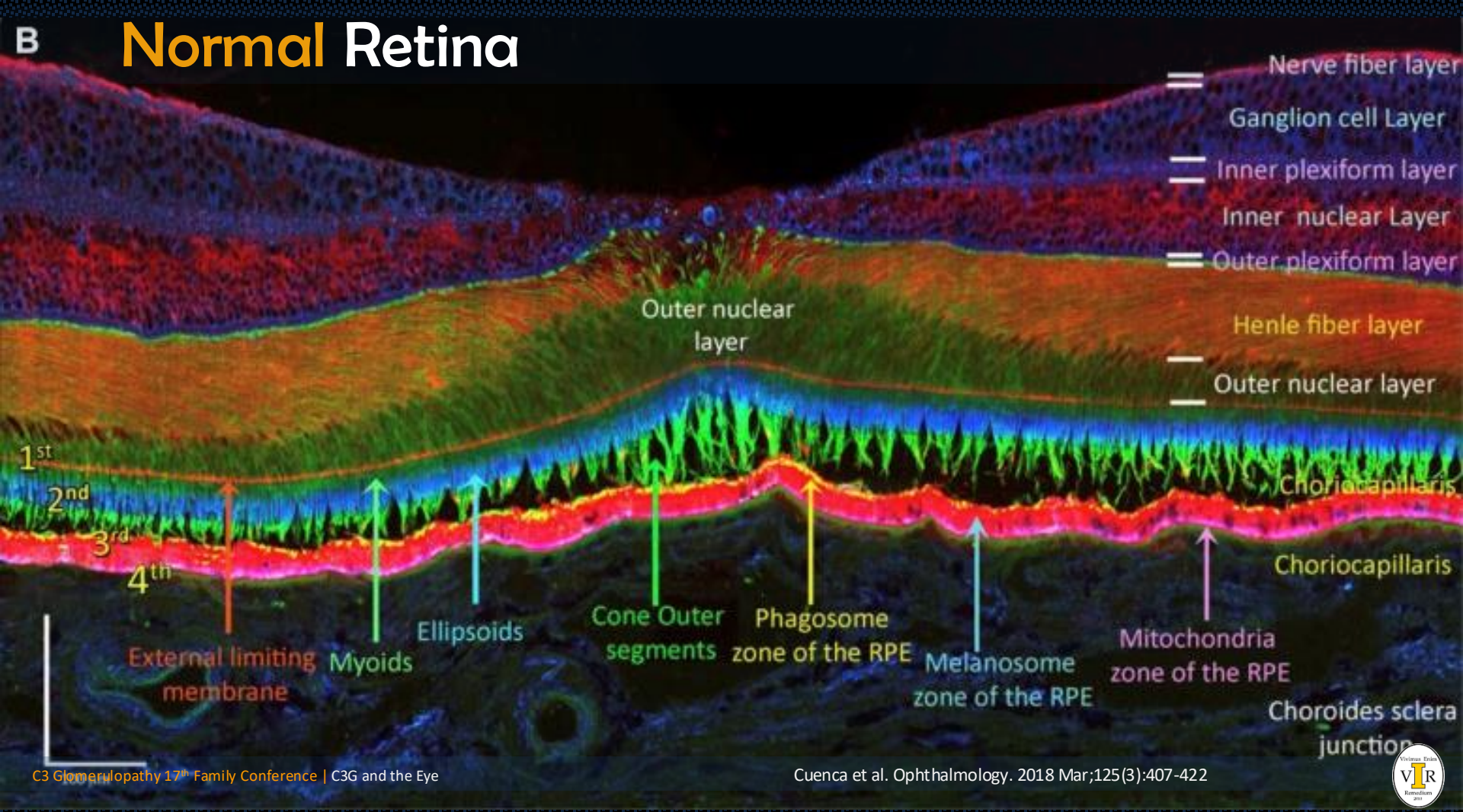


Normal Macula



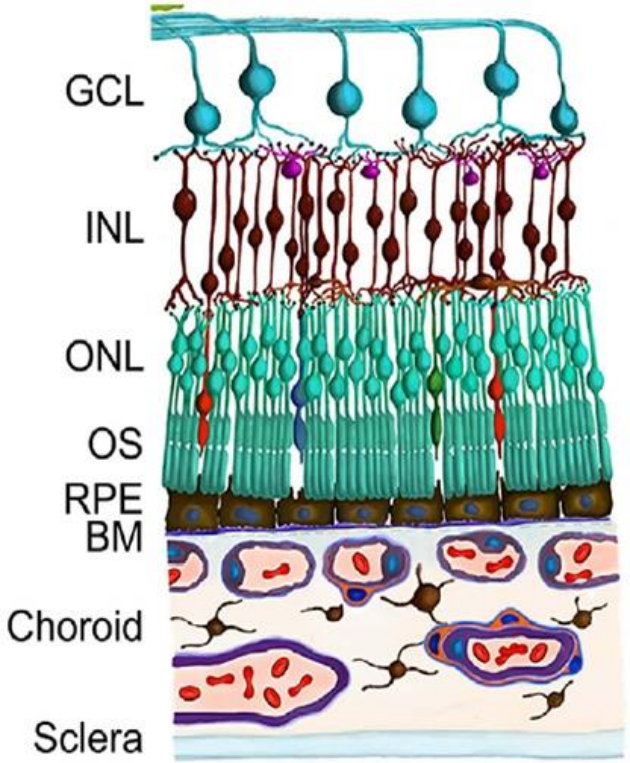
Normal Retina



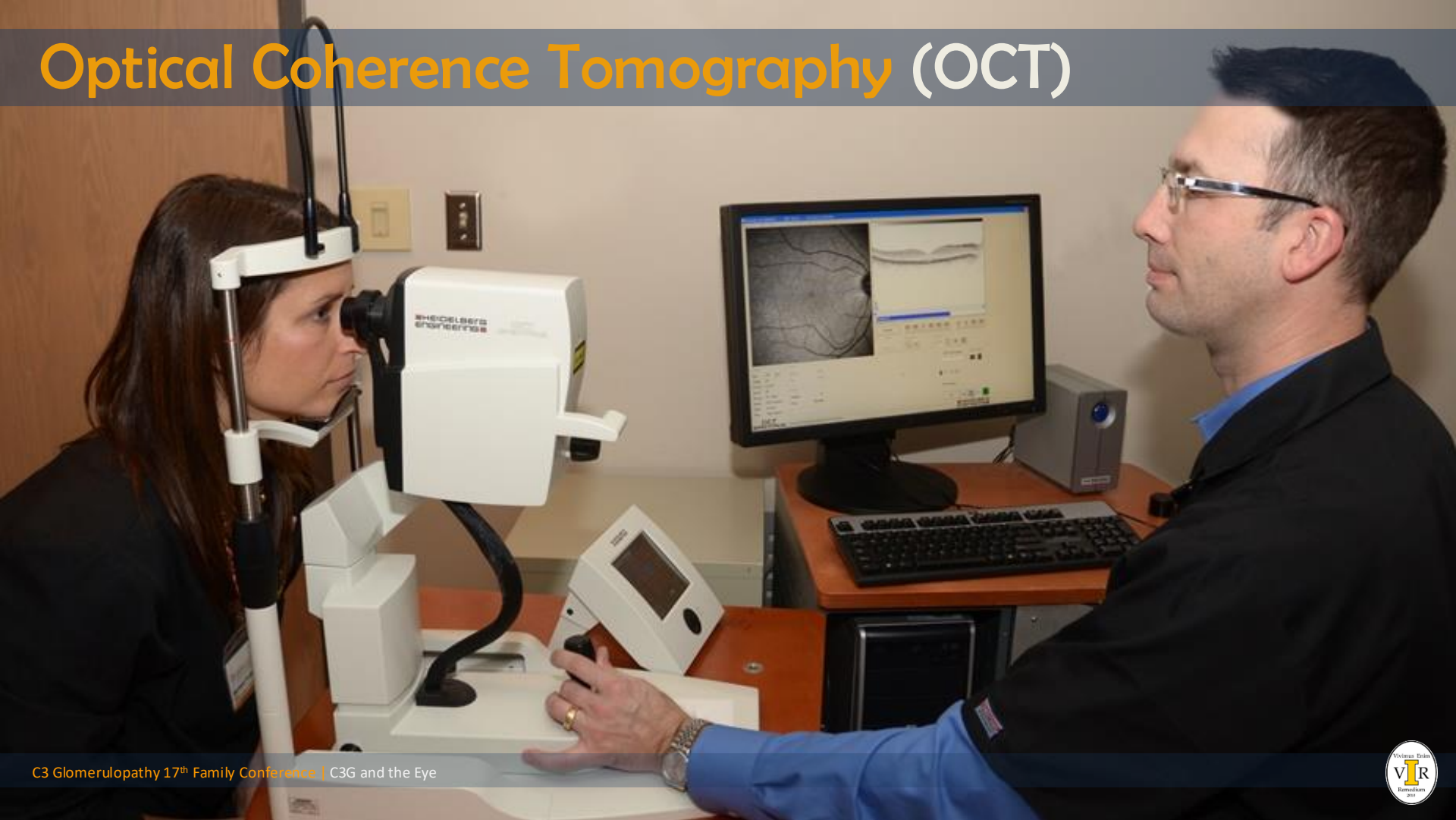


Cuenca et al. Ophthalmology. 2018 Mar;125(3):407-422

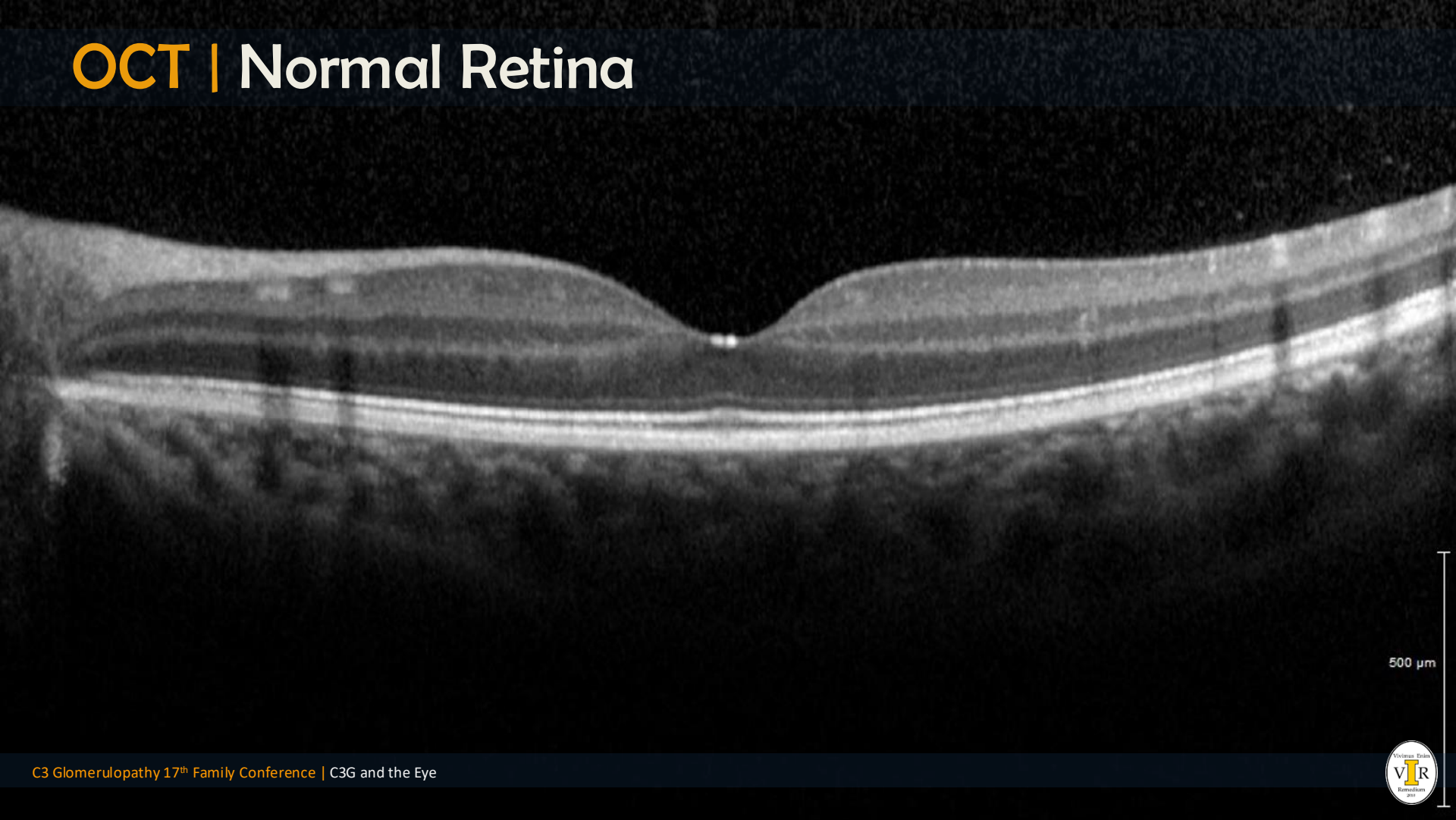
Normal Retina



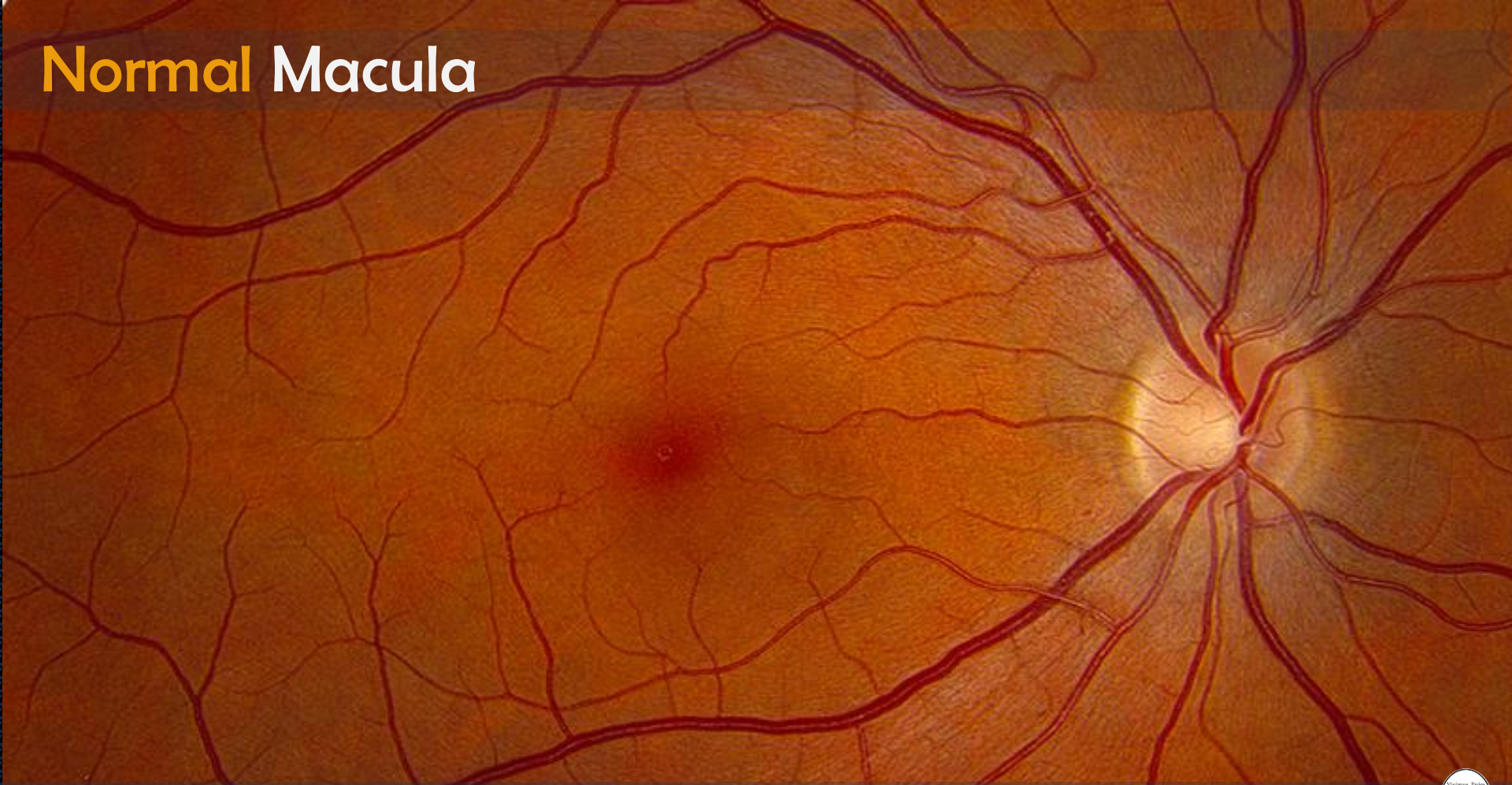
Optical Coherence Tomography (OCT)



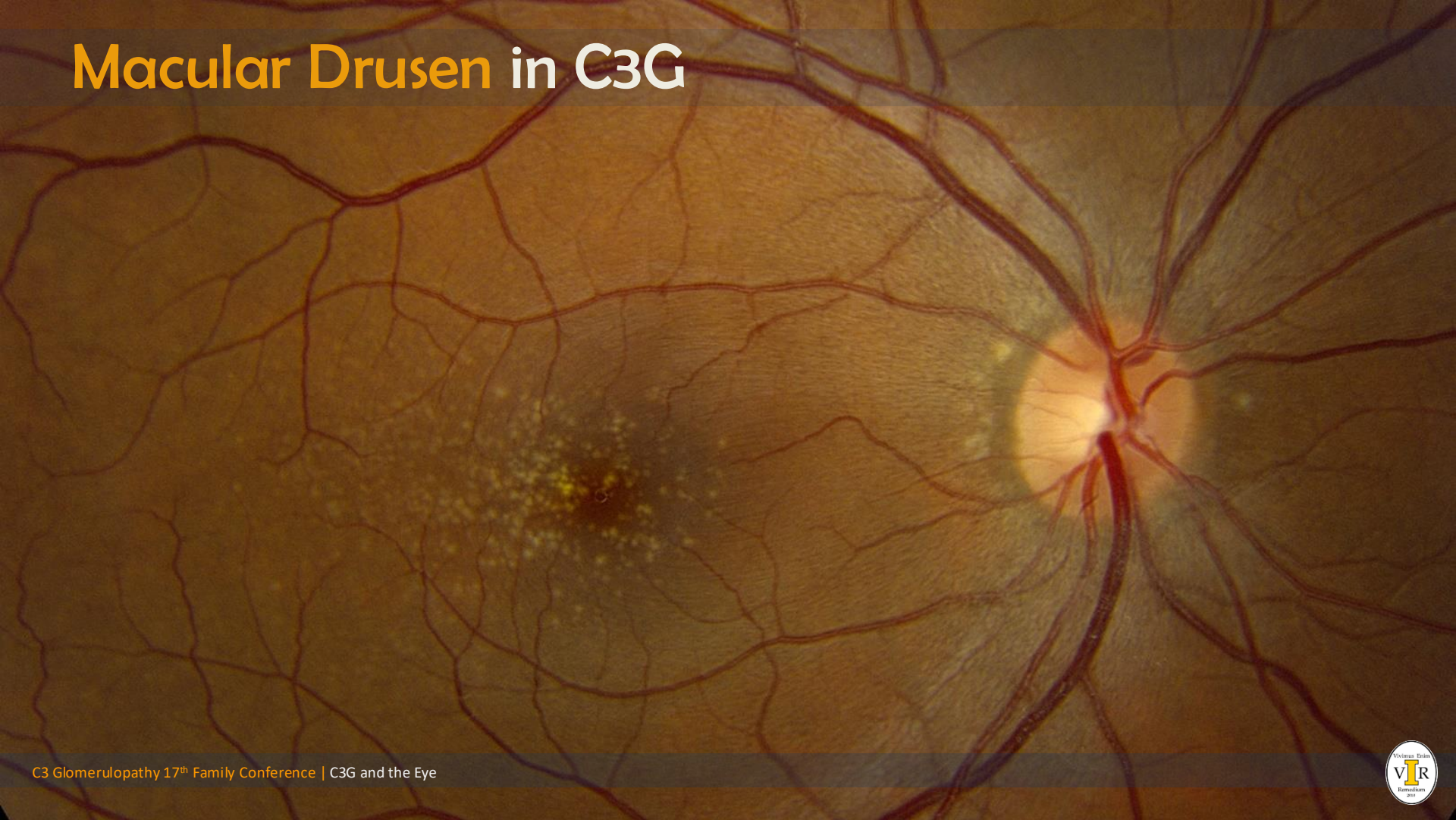
OCT | Normal Retina



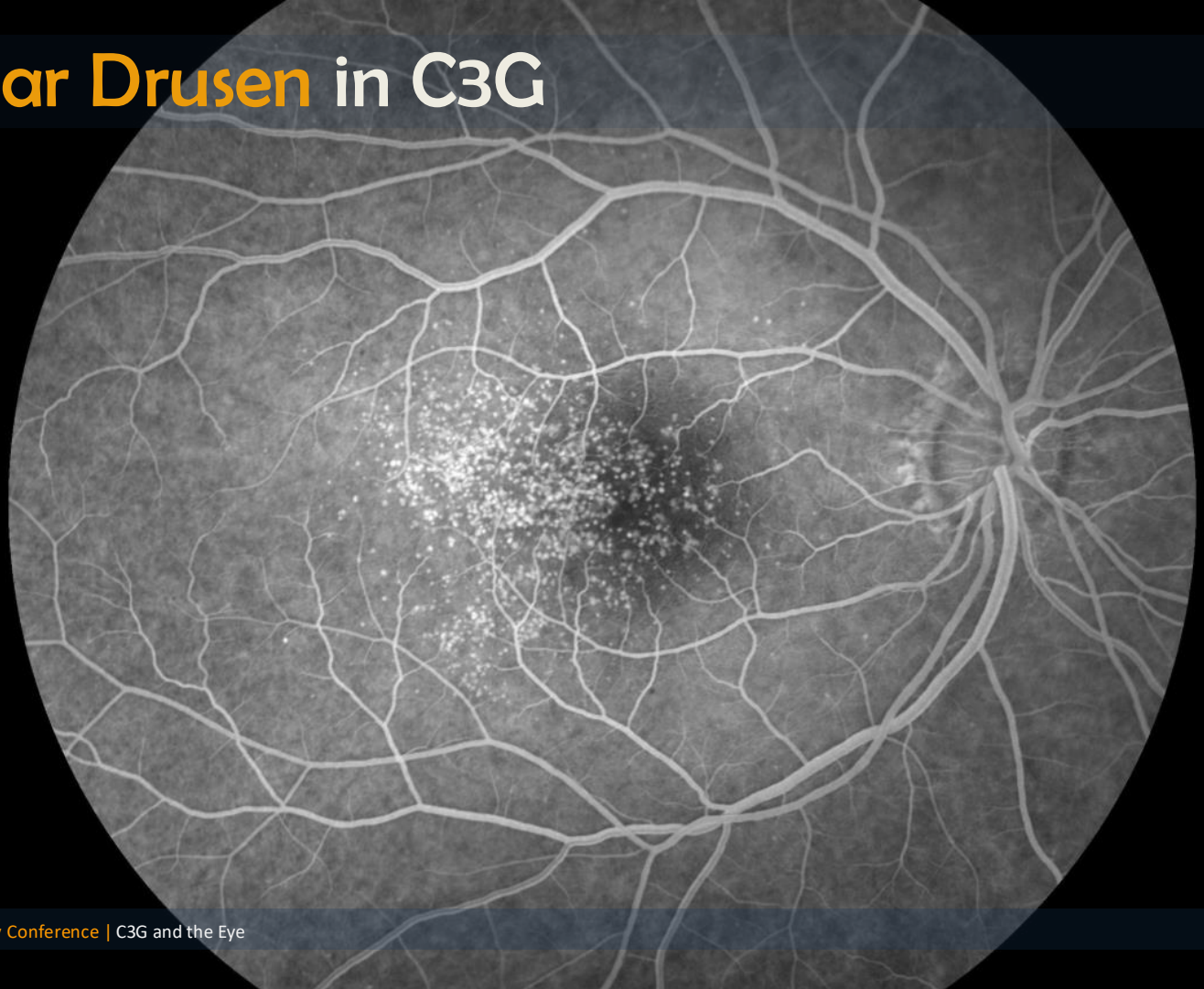
Normal Macula



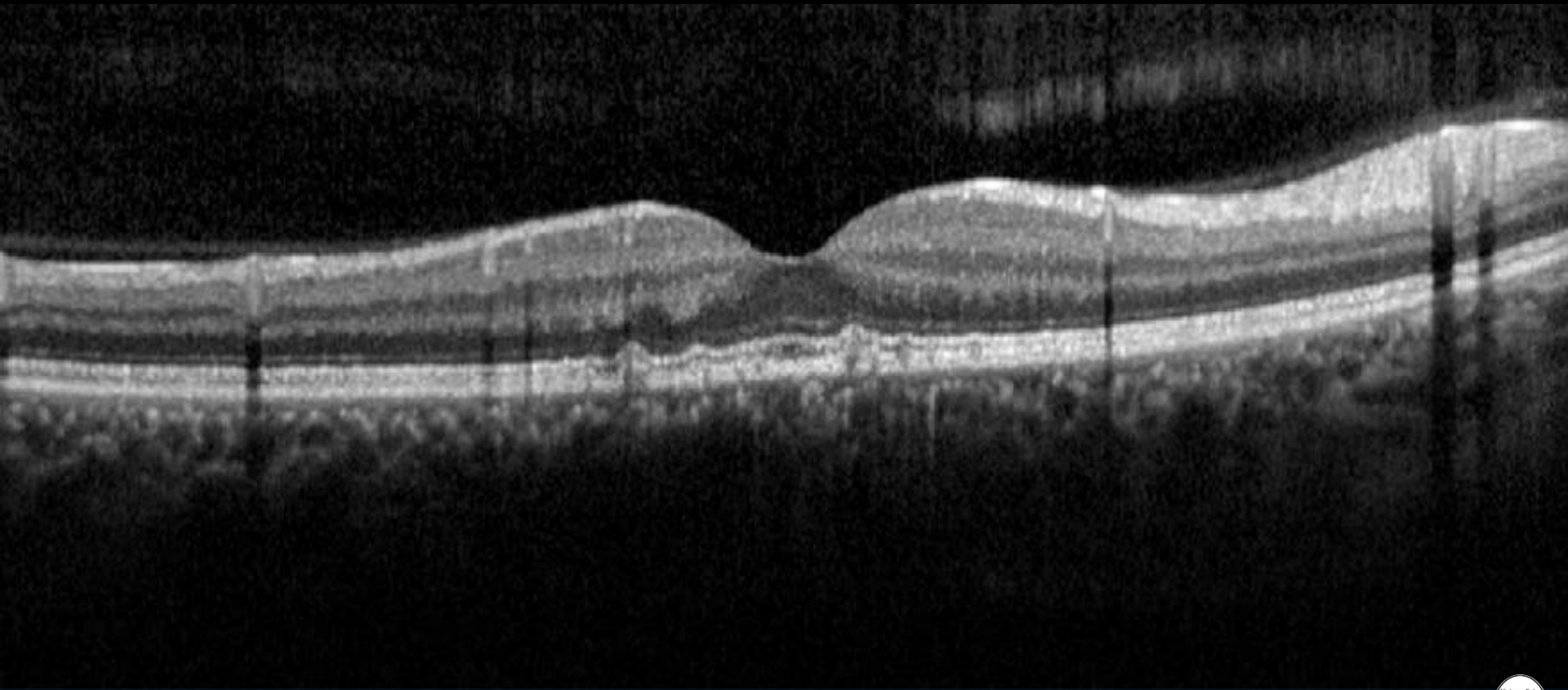
Macular Drusen in C3G



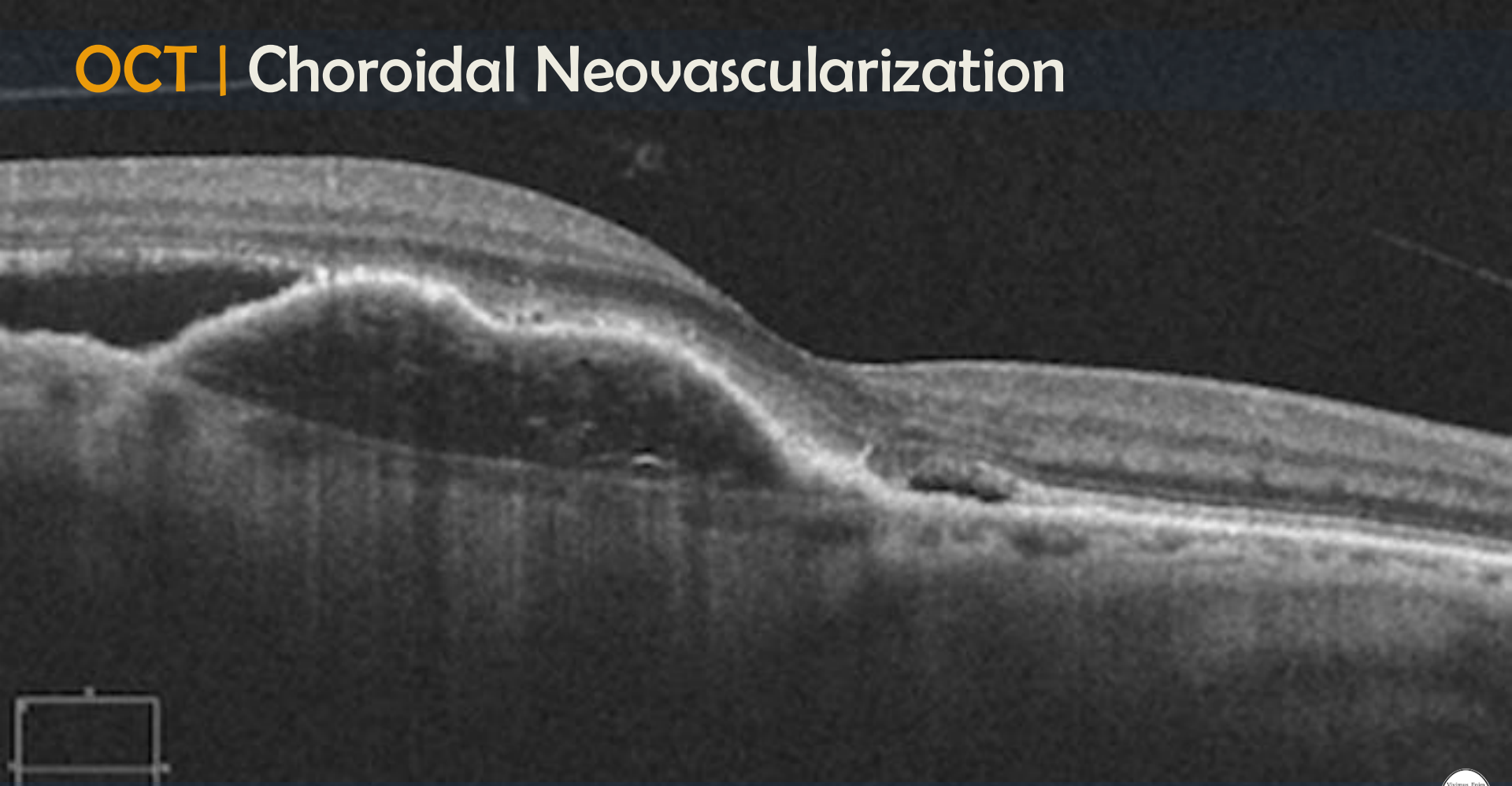
Macular Drusen in C3G

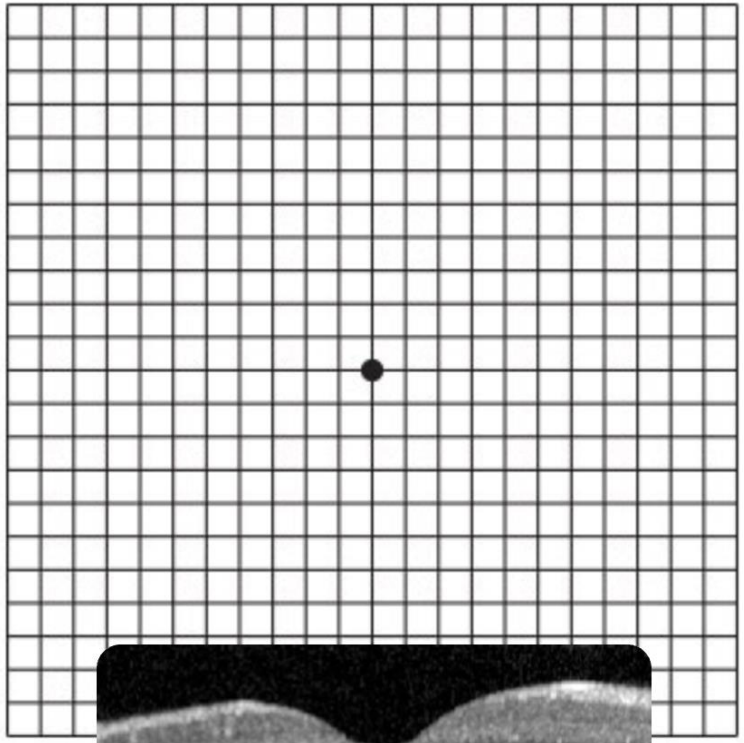


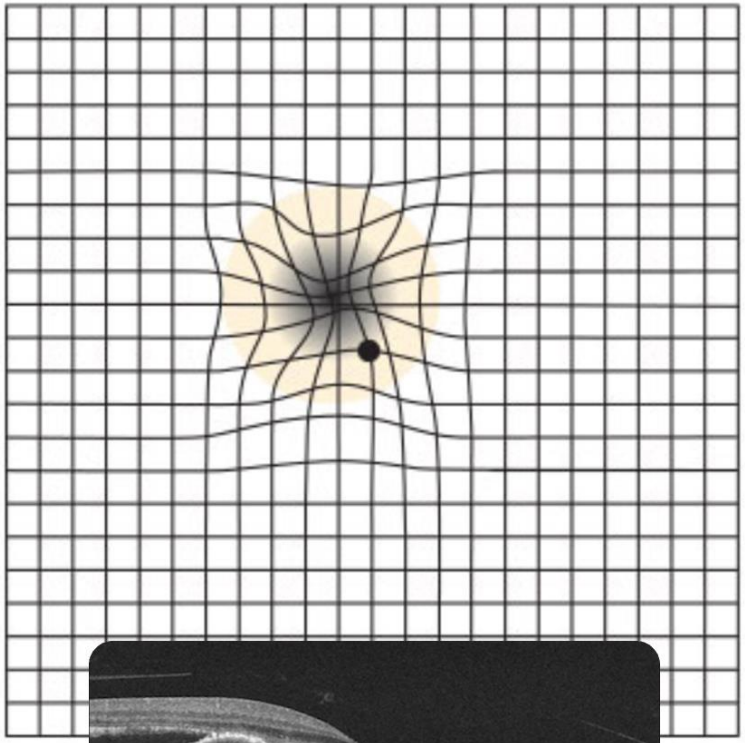
OCT | Macular Drusen in C3G

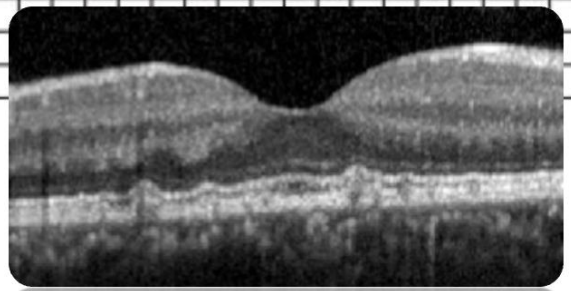


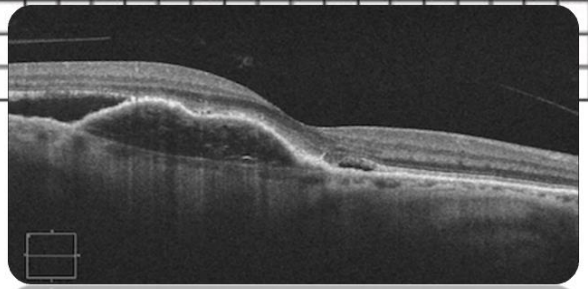
OCT | Choroidal Neovascularization



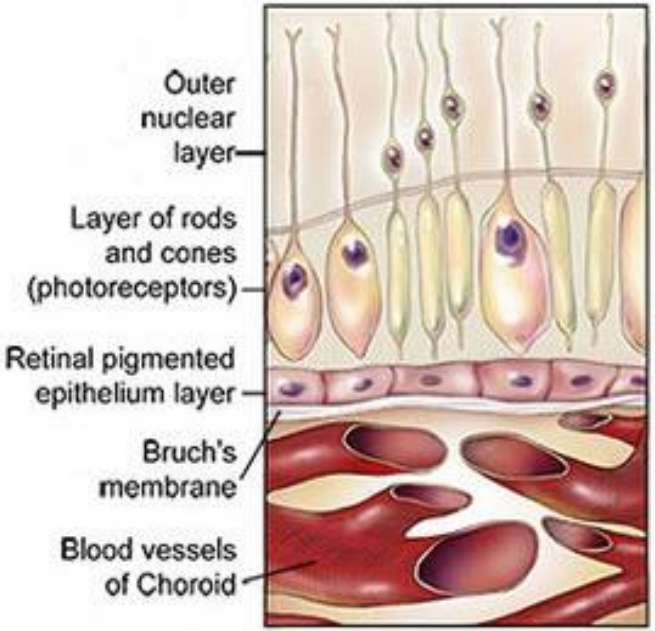




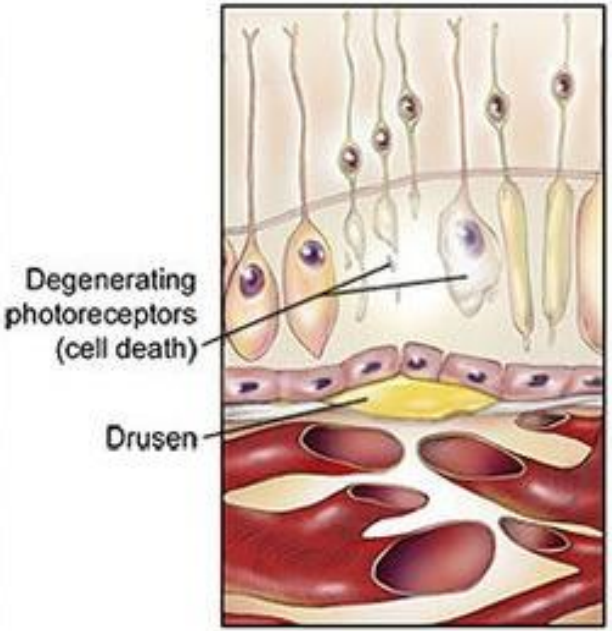




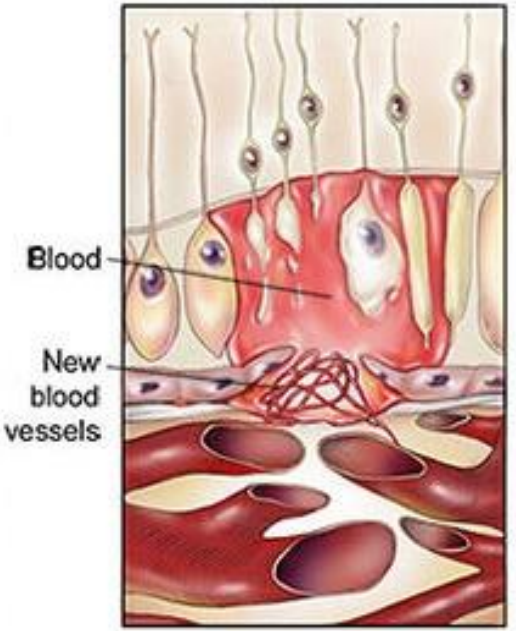
Drusen and Choroidal Neovascularization



Normal



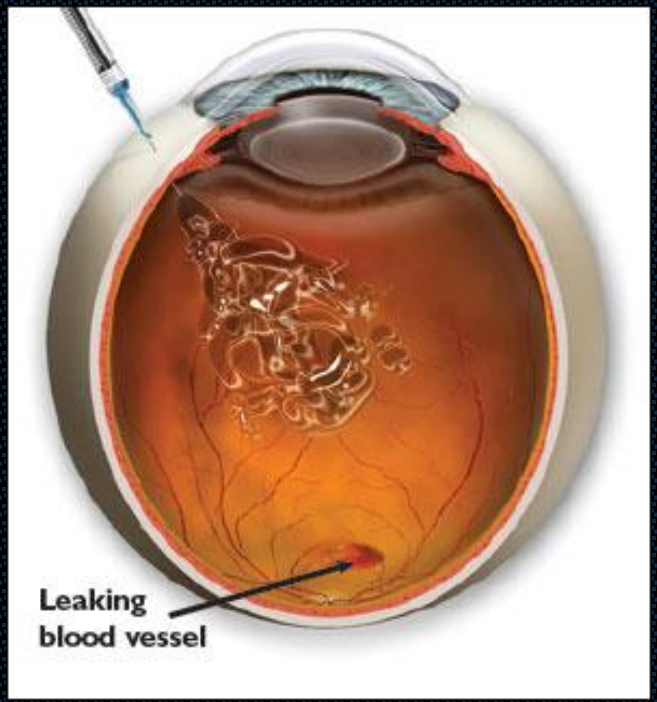
Drusen



Choroidal Neovascularization

Adapted from: https://www.brightfocus.org/macular/infographic/what-macular

Prevention | Treatment



Complement C3 Inhibitor Pegcetacoplan for Geographic Atrophy Secondary to Age-Related Macular Degeneration

A Randomized Phase 2 Trial

David S. Liao, MD,[1] Federico V. Grossi, MD, PhD,[2] Delphine El Mehdi, PhD,[2] Monica R. Gerber, MD, PhD,[2] David M. Brown, MD,[3] Jeffrey S. Heier, MD,[4] Charles C. Wykoff, MD, PhD,[5] Lawrence J. Singerman, MD,[6] Prema Abraham, MD,[7] Felix Grassmann, PhD,[8,9] Peter Nuernberg, PhD,[10] Bernhard H.F. Weber, PhD,[8] Pascal Deschatelets, PhD,[2] Robert Y. Kim, MD,[2] Carol Y. Chung, PhD,[2] Ramiro M. Ribeiro, MD, PhD,[2] Mohamed Hamdani, MS,[2] Philip J. Rosenfeld, MD, PhD,[11] David S. Boyer, MD,[12] Jason S. Slakter, MD,[13,14] Cedric G. Francois, MD, PhD[2]

Purpose: Geographic atrophy (GA), a late stage of age-related macular degeneration (AMD), is a major cause of blindness. Even while central visual acuity remains relatively well preserved, GA often causes considerable compromise of visual function and quality of life. No treatment currently exists. We evaluated the safety and efficacy of pegcetacoplan, a complement C3 inhibitor, for treatment of GA.

Design: Prospective, multicenter, randomized, sham-controlled phase 2 study.

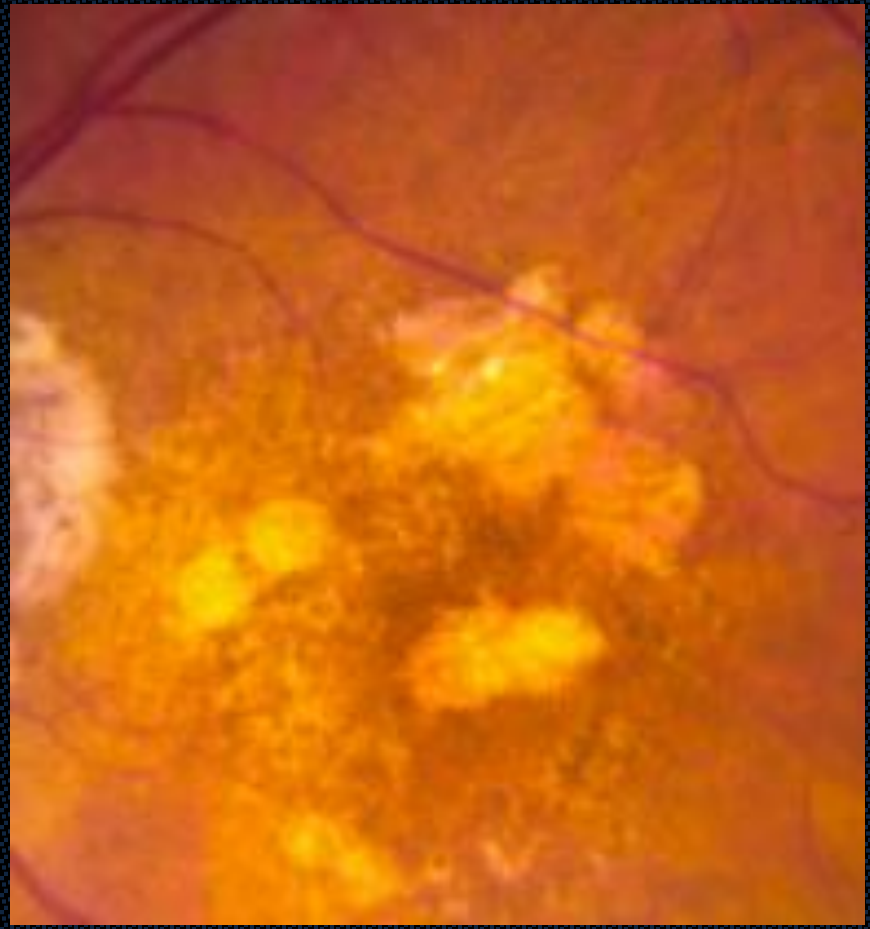
Participants: Two hundred forty-six patients with GA.

Methods: Patients with GA were assigned randomly in a 2:2:1:1 ratio to receive intravitreal injections of 15 mg pegcetacoplan monthly or every other month (EOM) or sham intravitreal injections monthly or EOM for 12 months with follow-up at months 15 and 18. Area and growth of GA were measured using fundus autofluorescence imaging.

Main Outcome Measures: The primary efficacy end point was mean change in square root GA lesion area from baseline to month 12. Secondary outcome measures included mean change from baseline in GA lesion area without the square root transformation, distance of GA lesion from the fovea, best-corrected visual acuity (BCVA), low-luminance BCVA, and low-luminance visual acuity deficit. The primary safety end point was the number and severity of treatment-emergent adverse events.

Results: In patients receiving pegcetacoplan monthly or EOM, the GA growth rate was reduced by 29% (95% confidence interval [CI], 9–49; $P = 0.008$) and 20% (95% CI, 0–40; $P = 0.067$) compared with the sham treatment group. Post hoc analysis showed that the effect was greater in the second 6 months of treatment, with observed reductions of 45% ($P = 0.0004$) and 33% ($P = 0.009$) for pegcetacoplan monthly and EOM, respectively. Two cases of culture-positive endophthalmitis and 1 case of culture-negative endophthalmitis occurred in the pegcetacoplan monthly group. New-onset investigator-determined exudative AMD was reported more frequently in pegcetacoplan-treated eyes (18/86 eyes [20.9%] and 7/79 eyes [8.9%] in monthly and EOM groups, respectively) than in sham-treated eyes (1/81 eyes [1.2%]).

Conclusions: Local C3 inhibition with pegcetacoplan resulted in statistically significant reductions in the growth of GA compared with sham treatment. Phase 3 studies will define the efficacy and safety profile further.



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Early onset macular drusen and C3 glomerulopathy (formerly type II membranoproliferative glomerulonephritis-associated drusen)

Ben J. Janson, MD, Thomas A. Oetting, MS, MD, Elliott H. Sohn, MD

October 9, 2017


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