Age-Related Macular Degeneration and Emerging Treatments – with Advice from Dr. Ajay Kuriyan on Balancing Research with Clinical Responsibilities

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Age-related macular degeneration (AMD) is a chronic disease of the central retina and a leading cause of vision loss worldwide. Although the early stages of AMD may present asymptomatically, the disease may progress and lead to severe visual impairment via geographic atrophy ("late dry") or neovascular ("wet") AMD. In geographic atrophy (GA), there is progressive atrophy of the retinal pigment epithelium (RPE), choriocapillaris, and photoreceptors due to lipofuscin (Drusen) accumulation between the RPE and Bruch's membrane.[1] These Drusen deposits grow and create an inflammatory and metabolically dysfunctional environment for the photoreceptors supplying the macula (**Figure 1**).[2] Eventually, the photoreceptors die off, and central vision is lost. In the wet form of AMD, choroidal neovascularization occurs, which leaks blood, fluid, and lipids leading to fibrous scarring and loss of vision (**Figure 2**).[3]

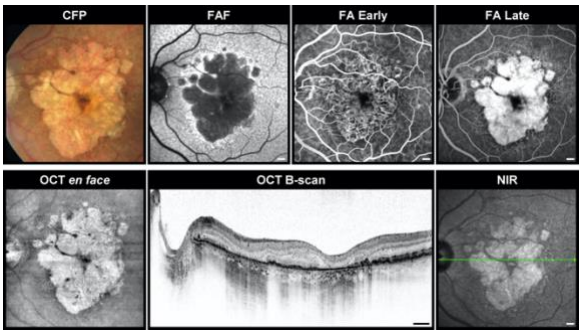

Figure 1. *Example images of geographic atrophy (GA) from 1 eye using color fundus photography (CFP), fundus autofluorescence (FAF), fluorescein angiography (FA), near-infrared reflectance (NIR), and spectral-domain OCT. Scale bars = 500 µm.*[4]

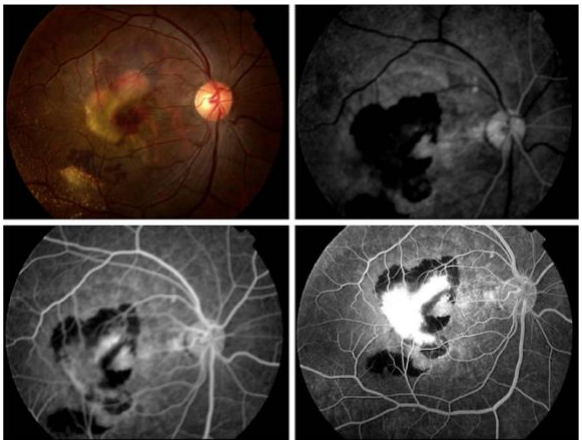

Figure 2. *Example images of choroidal neovascular membrane in AMD depicted in fluorescein angiography. Images show early hyperfluorescence with progressively increasing hyperfluorescence on successive images, surrounded by hypofluorescence due to blockage from subretinal hemorrhage.*[5]

"For a long time, there has been nothing for them, so these [developments in research] are very exciting."

Dr. Ajay Kuriyan
Figure 3

There are several ocular, lifestyle, and genetic risk factors associated with AMD. Ocular risk factors include lighter iris pigmentation, previous cataract surgery, and hyperopic refraction.[6-8] Lifestyle risk factors include cigarette smoking, obesity, sunlight exposure, low dietary intake of vitamins (e.g. A, C, E, Zinc) and omega-3 fatty acids, and cardiovascular disease.[9-11] Additionally, researchers have found many genes to be implicated in the pathogenesis of AMD, including *CFH*, *CF1*, *CFB*, *HTRA1*, *ABCA4*, and *APOE*.[3]

Although the aforementioned risk factors may impact anyone, AMD is far more common in elderly individuals. In a recent meta-analysis of white adults aged 40 and older, the prevalence of early AMD was 6.8% and late AMD 1.5%.[11] Studies have indicated that late AMD was 9-10 times more prevalent in white patients than in black patients, yet the prevalence of AMD in Asian patients was similar to that in white patients.[12-14] AMD is the most common cause of blindness among those aged 65 and older and of European-descent.[15]

AMD was considered untreatable for a long time, but the development of drugs that inhibit vascular endothelial growth factor (VEGF) revolutionized the treatment of wet AMD.[16-18] In 2006, landmark clinical trials indicated that monthly injections of ranibizumab (Lucentis) prevented vision loss in 95% of patients, and improved vision significantly in 40% of patients.[19]

While treatments such as these exist for wet AMD, more research is needed in treating the late-stage form of dry AMD, which is currently untreatable.

Dr. Kuriyan believes some of the most exciting progress in ophthalmology will come from emerging research on GA. While many clinical trials have proven unsuccessful, clinical trials from Apellis and Ivaric Bio show promising results.[20,21] "For a long time, there has been nothing for them (i.e. his patients with geographic atrophy), so these [developments in research] are very exciting" (**Figure 3**). As someone who treats many retinal disorders like AMD, Dr. Kuriyan is passionate in conducting research on new and improved treatments.

An Interview with Dr. Kuriyan

Dr. Ajay Kuriyan is an attending with Mid Atlantic Retina at Wills Eye Hospital. He completed his undergraduate and medical training at the University of Rochester before completing his residency and retina fellowship at Bascom Palmer Eye Institute in Miami.

Dr. Kuriyan's initial advice to aspiring physicians is to "get inspired." Dr. Kuriyan was initially inspired by research involving scarring. Research into the scarring process is vital in all fields of medicine, but one area in ophthalmology where the scarring process is particularly important is in proliferative vitreoretinopathy (PVR). PVR is a blinding disease process characterized by fibrotic membranes that develop on the retinal surface or within the retina and is the leading cause of recurrent retinal detachments.[22,23] Dr. Kuriyan and colleagues have showed promise in using amniotic membranes – which have anti-inflammatory and anti-scarring properties – to inhibit PVR formation *in vitro*.[25] Their team is now optimizing a model to remove the matrix component of amniotic membranes, solubilize it, and inject the solution into the vitreous of the eye to prevent PVR.

In addition to being inspired by your work, Dr. Kuriyan recommends to "work your passions into your clinic." Dr. Kuriyan has found it valuable to use his time in the operating room (OR) to contribute toward his research. He has pioneered the start of a vitreous 'BioBank' at Wills, where a portion of vitreous is saved during each retinal surgery where vitreous is removed. Dr. Kuriyan and others plan to analyze proteomics between vitreous samples, which might provide insight into the biochemical functioning of pathological eye processes like PVR. Dr. Kuriyan reports that patients are "excited to become a part of the study." Not only is collecting samples a productive and engaging use of time for Dr. Kuriyan, but it is a "great way to get patients thinking and interested in research."

Like most of his colleagues, Dr. Kuriyan typically works four days in the retina clinic at Wills Eye Hospital with one full day in the OR. Aside from the BioBank

proteomics project he contributes to in the OR, most of his research is done on slower clinic days, the evenings, and occasionally the weekends.

Dr. Kuriyan's last portion of advice to medical students was to take the time to "ask questions and learn how to answer them." Even if medical students are helping with someone else's project, Dr. Kuriyan advises to learn the art of asking research questions as it will help down the road as an attending in coordinating research projects.

If medical students are not passionate about research – no worries. "There are lots of ways to help your institution," including teaching, administration, and service. "Follow your interests and talents."

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