RETINA INTERNATIONAL
Seeking A Cure For
Retinitis Pigmentosa, Macular Degeneration,
Usher Syndrome and Allied Retinal Dystrophies

Progression to Late-AMD (GA & Neovascular AMD)

Progression from early- to late- AMD and development of GA and/or neovascular AMD is a complex process. The underlying mechanisms that cause an eye to develop GA versus neovascular AMD are not fully understood. No reliable genetic or environmental risk factors have been identified to predict whether a patient will develop one form or the other.[1] Both types can occur simultaneously in the same eye, or simultaneously in different eyes.[2] It has in fact been suggested that GA and neovascular AMD are not mutually exclusive diseases, but that they lie on the same disease continuum. Eyes developing both types may in fact be at a more advanced stage than either GA or neovascular AMD alone.[2]

The rate of progression varies between patients; some people progress quickly to late-stage disease (either GA or neovascular AMD), whereas others may progress slowly over several years.[3]

Long-term epidemiological studies evaluating the natural history and progression of AMD, including the Blue Mountain Eye Study and Beaver Dam Eye study, have reported that the presence of large drusen and pigmentary abnormalities are associated with a greater long-term risk of developing late-stage AMD (either GA or neovascular AMD).[4] Recent studies have also reported the presence of reticular pseudodrusen (RPD) as a strong predictor for progression to late-stage AMD, particularly GA.[5, 6] RPD are subretinal deposits that appear on colour images as yellowish interlacing networks in the fundus. [7]

An analysis of an Australian community-based cohort (the Melbourne Collaborative Cohort Study) reported a prevalence of RPD of 0.41% in a population aged 48–86 years (87 of

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[2] Kaszubski P, Ben Ami T, Saade C, Smith RT. Geographic Atrophy and Choroidal Neovascularization in the Same Eye: A Review. Ophthalmic research. 2016;55(4): 185-193.
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[4] Joachim N, Mitchell P, Kifley A, Rochtchina E, Hong T, Wang JJ. Incidence and progression of geographic atrophy: observations from a population-based cohort. Ophthalmology. 2013;120(10): 2042-2050.
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[6] Finger RP, Chong E, McGuinness MB, Robman LD, Aung KZ, Giles G*, et al.* Reticular Pseudodrusen and Their Association with Age-Related Macular Degeneration: The Melbourne Collaborative Cohort Study. Ophthalmology. 2016;123(3): 599-608.
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21,130 participants). The study found that the presence of RPD was linked with development of late-stage AMD, and this association was stronger with GA than with neovascular AMD.[6] The precise role of RPD in the progression of AMD is still unclear. However, the strong correlation between the presence of RPD and GA, and the observation that GA lesions tend to develop in regions of the macula where RPD lesions exist, has led to the suggestion that RPD lesions are an early manifestation of the process leading to GA.[5]

The proportion of people reported to develop both GA and neovascular AMD in the same eye varies widely between clinical studies. The Beaver Dam Eye Study reported that among eyes with GA at baseline, 11% progressed to neovascular AMD after 5 years; the development of neovascular AMD was more frequent if it was present in the fellow eye.[8] Another study investigating the GA/neovascular AMD phenotype reported that GA usually occurs prior to the development of neovascular AMD. [1]

Epidemiological studies conducted for the US and UK populations have shown that GA and neovascular AMD occur with approximately equal prevalence, among people with late-stage AMD.[9, 10]

[8] Klein R, Klein BE, Knudtson MD, Meuer SM, Swift M, Gangnon RE. Fifteen-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye Study. Ophthalmology. 2007;114(2): 253-262.
[9] Rudnicka AR, Kapetanakis VV, Jarrar Z, Wathern AK, Wormald R, Fletcher AE*, et al.* Incidence of Late-Stage Age-Related Macular Degeneration in American Whites: Systematic Review and Meta-analysis. American journal of ophthalmology. 2015;160(1): 85-93 e83.
[10] Owen CG, Jarrar Z, Wormald R, Cook DG, Fletcher AE, Rudnicka AR. The estimated prevalence and incidence of late stage age related macular degeneration in the UK. The British journal of ophthalmology. 2012;96(5): 752-756.