ALSTAR Study

Delayed dark adaptation indicates subclinical AMD at least three years before it is clinically evident

The ALSTAR study, published in *Ophthalmology*,1 prospectively tracked two cohorts of adults age 60 and older: one having abnormal dark adaptation at baseline and one having clinically normal retinal health at baseline. Three years later the subjects with abnormal dark adaptation at baseline exhibited clinically detectable AMD at twice the rate of individuals with normal dark adaptation at baseline and had advanced beyond the earliest stages of AMD at eight times the rate. The relationship between dark adaptation impairment and incident AMD was robust and not affected by aging or smoking status. The study demonstrates that dark adaptation impairment indicates subclinical AMD at least three years before it is clinically evident.

Subclinical AMD is the earliest stage of AMD
During the subclinical phase of AMD, retinal pigment epithelium (RPE) cells secrete cholesterol deposits into the RPE/Bruch's membrane complex throughout the macula. These initial deposits are clinically undetectable and precede the appearance of drusen. The early lesions impair retinoid transport in the retina which in turn impairs dark adaptation. Consequently, abnormal dark adaptation is the first clinical sign of AMD pathogenesis.

Dark adaptation as a functional biomarker for AMD
Although the ALSTAR study was not designed to evaluate dark adaptation as a screening test for AMD, it is tantalizing that with only three years of follow-up, the sensitivity to identify incident AMD was already 33%. It is expected that continued follow-up will show the actual sensitivity for incident AMD is much higher. The sensitivity of dark adaptation to detect clinically evident cases of AMD rises to 91%.

Taken as a whole, these results demonstrate that dark adaptation is clinically useful to identify patients in the earliest stages of the disease when risk reduction strategies are most effective.

About the ALSTAR study
The Alabama Study on Early Age-Related Macular Degeneration (ALSTAR study) was led by Cynthia Owsley, Ph.D., at the University of Alabama at Birmingham (UAB) School of Medicine. It prospectively tracked 325 adults age 60 and older with normal macular health.

Results:
• At baseline, all 325 subjects had normal retinal health as verified by clinical examination and grading of fundus photographs using the AREDS classification severity system.
• However, abnormal dark adaptation was found in 24% of the subjects at baseline. Dark adaptation measurements were made using MacuLogix® AdaptDx® dark adaptometer.
• Three years later, the cohort of subjects with abnormal dark adaptation were two times more likely to have AMD (age adjusted RR = 1.99, p = 0.03) and eight times more likely to have advanced beyond the very earliest stage of AMD.
• Subjects with more severe dark adaptation impairment tended to exhibit more severe AMD at follow up (p = 0.024).
• All eyes with the most severe AMD at follow-up exhibited impaired dark adaptation at baseline.