Optometry's Role in Age Related Macular Degeneration

-Early Detection and Effective Treatment

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Financial Discloser

Speakers Panels

- Allergan Pharmaceuticals
- Bausch & Lomb/ Valeant Pharmaceuticals
- BioTissue
- Maculogics
- Optovue
- Shire

Multi-factorial nature of AMD

Non-modifiable risks

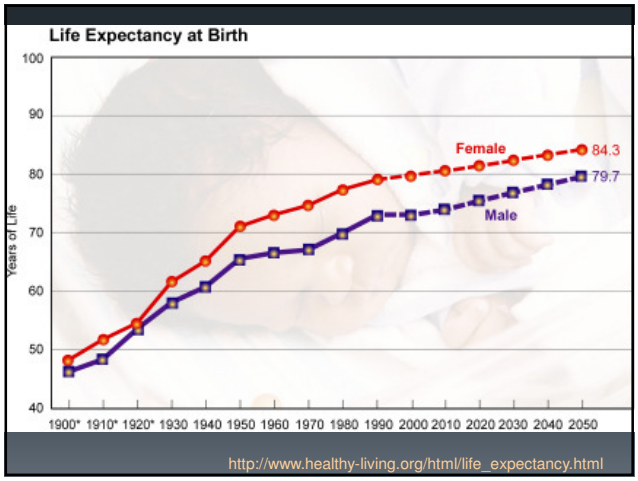
Family Hx	3-4X increased risk of AMD
Genetics	genetic predisposition may account for 50% of AMD
Race	increased risk for Caucasians
Age	2% risk in middle age 30% risk over age 70

Life Expectancy*

- US 78.6 years
- US Male 76.1 years
- US Female 81.1 years

✓Dropped for 2nd year in a row for the second time in history

**National Vital Statistics System, Mortality*



Multi-factorial nature of AMD

Modifiable risks

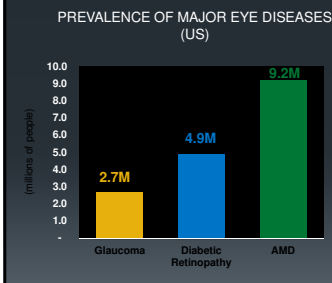
- Ultraviolet and Blue Light exposure
- Smoking 2-3X increase risk
- Nutrition beware "partially-hydrogenated vegetable oils, sugars
- Hypertension (uncontrolled) 1.5X increased risk
- Obesity 2X increased risk
- Alcohol intake and excessive omega 6's
- Hypercholesterol

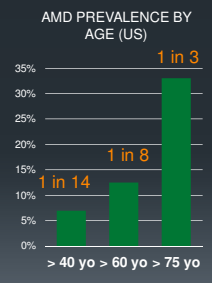
Modifiable risks

- Ultraviolet and Blue Light exposure
- Smoking
- Nutrition
- Cardiovascular disease
- Medications
- Alcohol intake

AMD is a Major Health Problem in the US

- Clinical AMD is more prevalent than Glaucoma and Diabetic Retinopathy combined



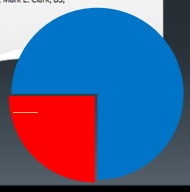


Primary Eye Care Misses Visible Disease in >25% of Patients Using Standard Workup

JAMA Ophthalmology | Original Investigation

Prevalence of Undiagnosed Age-Related Macular Degeneration in Primary Eye Care

David C. Neely, MD; Kevin J. Bray, MD; Carrie E. Huisingh, MPH; Mark E. Clark, BS; Gerald McGwin Jr, PhD; Cynthia Owsley, PhD



25% of "normal" patients had AMD!

Early Treatment Can Slow Disease Progression

Smoking Cessation is the First Step!

- **SMOKING IS THE LARGEST MODIFIABLE RISK FACTOR FOR AMD.**
- Current smokers carry a **2.5 to 4.8X** higher risk than non-smokers for late AMD[1]

90% of patients with AMD were not advised to stop smoking[2]

<50% of smokers know that smoking may contribute to blindness[3]

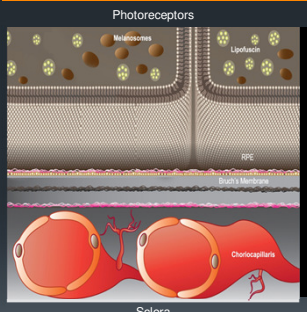
Classification of AMD is Based on Retinal Structure

- The Beckman Committee Classifies AMD Into 4 Stages[1]

Progression

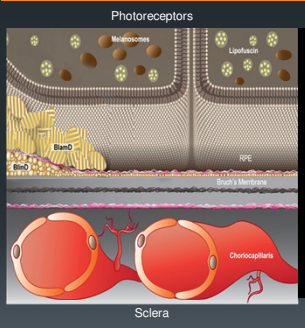
No AMD	• No drusen or small drusen ≤ 63 µ • No AMD pigmentary abnormalities
Early AMD	• Medium drusen > 63 µm and ≤ 12 • No AMD pigmentary abnormalities
Intermediate AMD	• 1 large druse > 125 µm and/or • Any AMD pigmentary abnormalitie
Advanced AMD[2] forms	Geographic atrophy; Neovascular AMD

However, AMD May be Lurking Below the Surface



A healthy macula shows no signs of drusen or oxidative stress

Cholesterol Starts Coating the Macula Before Drusen Form

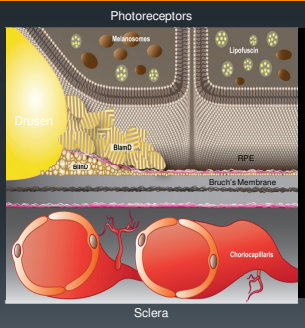


Panmacular cholesterol (Basal Laminar Deposits and Basal Linear Deposits) starts to build up along Bruch's Membrane

While not visible with imaging- this layer of cholesterol is:

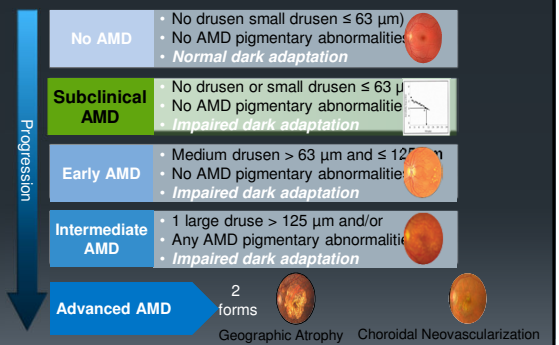
- Causing oxidative stress and inflammation
- Impairing normal transport, including that of vitamin A
- Affecting photoreceptor health

Visible Drusen is Just the Tip of the Iceberg



Like icebergs, peaks of cholesterol become clinically **visible drusen** several years after damage has begun

Comprehensive Classification System: Structure + Function



Contemporary recommendations for nutritional supplementation

Age Related Eye Disease Study

- Reduced risk of progression with formula vs. placebo
- Results / Specific recommendations
- Limitations (The Beta-carotene effect)

Age Related Eye Disease Study 2

- Analysis for a new formulation of supplements
- Reduced risk assessment for new formulation
- Limitations
  - ✓The influence of Omega-3s in that cohort
  - ✓The effect of the antioxidant component
  - ✓The result of substitution of Lutein and Zeaxanthin for Beta-carotene
  - ✓The influence of the formula supplier on the reported outcomes

Other component results from the Tri-continent Consortium

The Rotterdam Study

- First significant indication of prophylactic effects from supplementation

Other component results from the Tri-continent Consortium

The Blue Mountains Eye Study

- Supported the prophylactic effects but to a lesser extent than Rotterdam
- Emphasis on dietary habits

Omega 3 for the benefit of ocular tissue

- Dry eyes
- AMD
  - ✓DREAM STUDY

Diagnosis of early AMD

Clinical evaluation is often insufficient

- 25- 30% of early (Subclinical) AMD missed among a cohort of 1288 eyes based on clinical observation AND practitioner evaluation of fundus photography*.
- Final determination proven with advanced clinical testing employing dark adaptation

Diagnosis of early AMD

- Impaired dark adaptation identified emergence of clinical manifestations three years before clinical signs became evident
- These results and emerging histopathological studies leads to a new paradigm to explain sub clinical findings that precede manifest clinical observations

Clinical Testing of Dark Adaptation Practical

AdaptDx

The only functional test for measuring dark adaptation quickly and effectively in a clinical setting with objective results.

Sensitive and specific

JOHNS HOPKINS UNIVERSITY

VE RI TAS HARVARD

PENNSTATE HERSHEY College of Medicine

High Sensitivity: Correctly identified **90.6%** of confirmed AMD cases

High Specificity: Correctly identified **90.5%** of confirmed normal cases

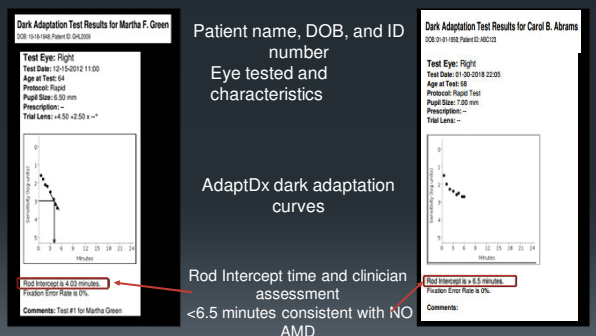
High Accuracy: **90.6%** overall

Applicable ICD-10 Codes

Code	Description
E50.5	Vitamin A deficiency with night blindness
H35.30	Unspecified macular degeneration
H35.31XX	Non-exudative age-related macular degeneration
H35.32XX	Exudative age-related macular degeneration
H35.36X	Drusen (degenerative) of macula
H35.50	Unspecified hereditary retinal dystrophy
H35.52	Pigmentary retinal dystrophy
H35.53	Other dystrophies primarily involving the sensory retina
H35.54	Dystrophies primarily involving the RPE
H53.60	Unspecified night blindness
H53.61	Abnormal dark adaptation curve
H53.62	Acquired night blindness
H53.63	Congenital night blindness
H53.69	Other night blindness

First Coast LCD 33925 limits reimbursement in Florida, Puerto Rico and the Virgin Islands to ±50.5, H35.50, ±35.52, H35.53, H35.54, H53.60, H53.61, H53.63 and H53.69

The AdaptDx Report-Simple, Objective



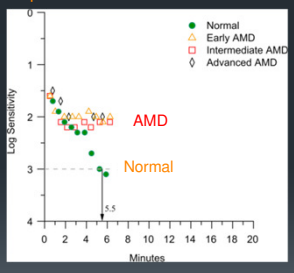
Patient name, DOB, and ID number
Eye tested and characteristics

AdaptDx dark adaptation curves

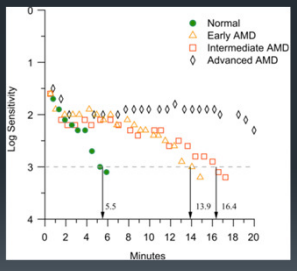
Rod Intercept time and clinician assessment
<6.5 minutes consistent with NO AMD
>6.5 minutes consistent with AMD

AMD Causes Major Impairment of Dark Adaptation

Rapid Test: ≤6.5 minutes

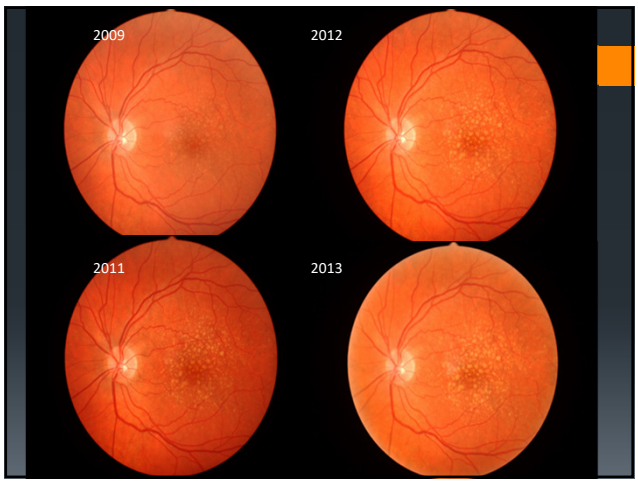


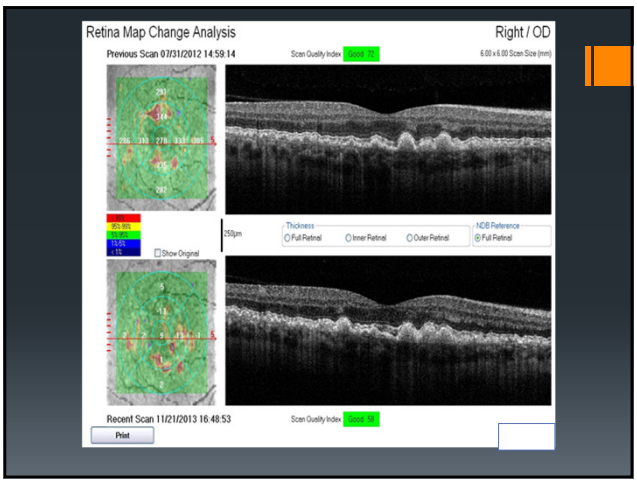
Extended Test: ≤20 minutes



Diagnosis of early AMD

- OCT utilization in the diagnosis and monitoring of AMD patients





Current histopathological paradigm for AMD -clinical findings of prolonged dark adaptation

- Deposits of lipids in Bruch's membrane interfere with normal active transport from the choroid to the outer retina
- Certain nutritional deficiencies account for these deficiencies that result in impaired (prolonged) dark adaptation
- Impaired dark adaptation can be quantitated by a time perspective and clinically is related directly to levels of AMD

Proven effectiveness for early intervention

Optometry as a proactive partner in treating AMD

- Identifying early changes in the retina may be crucial to identifying the candidates at highest risk for vision loss from AMD
- This may account for as many as 30% of all patients over the age of 50 years seen in a primary care setting
- Treating patients by adjusting variable risk factors to improve these patients prognosis has been proven to be effective based on evidence from large international clinical trials.

Additional Treatments for All Stages of AMD

Nutritional Supplementation
Patients treated with supplements have better outcomes than untreated patients due to:
1. Beneficial effects of the supplements
2. Increased compliance with care

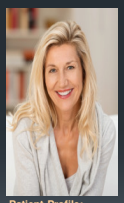
Systemic Disease Management
Cardiovascular disease, diabetes, high cholesterol, and obesity have all been associated with increased risk and/or progression of AMD

Lifestyle Modifications with Respect to Diet and Exercise
- Omega fatty acids
- Mediterranean diet
- Exercise

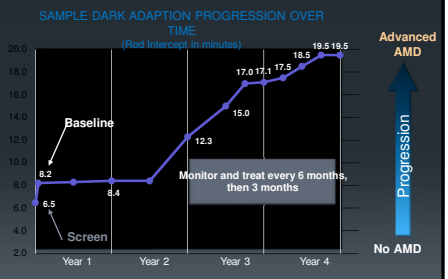
Retinal Light Protection
Chronic sunlight exposure increases the risk of incident AMD and its progression
- Full-spectrum UV protection
- High Energy Visible Light (HEVL) / Blue Light blocking lenses

AdaptDx -Monitor and Treat AMD Proactively

- Goal: Improve AMD Patient Outcomes

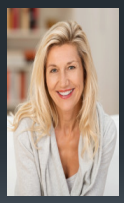


Patient Profile:
- Jane Doe, Age 59
- No family history of AMD
- Presents with no drusen, but complains of night vision issues

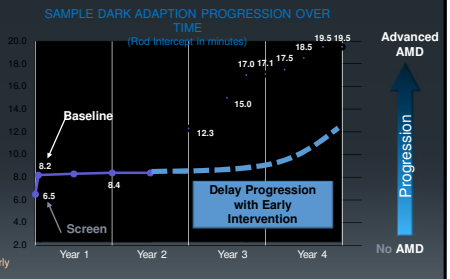


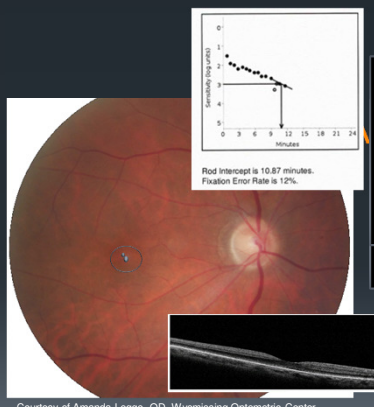
AdaptDx -Monitor and Treat AMD Proactively

- Goal: Delay Progression of AMD



Patient Profile:
- Jane Doe, Age 59
- Subclinical AMD diagnosed early
- Treatment plan: Anti-oxidants and more frequent exams





- 65 Year old female
- 20/20 OU
- No AMD family Hx
- Nonsmoker
- Subtle drusen
- Unremarkable OCT
- Abnormal dark adaptation

Courtesy of Amanda Legge, OD, Wyomissing Optometric Center

Dark Adaptation Is **NOT** a Risk Factor for AMD

Genetic testing and **macular pigment density (MPOD)** can indicate a heightened risk for developing AMD, but neither indicates the actual presence of disease.

Impaired dark adaptation is NOT a risk factor. It is the earliest manifestation of disease.

Early Detection & Timely Intervention Can Preserve Sight: There Is No Cure, So The Focus is on Delaying Progression

DRY AMD

Early, Intermediate & Late AMD

- Cause: oxidative stress and inflammation
- **Lower risk of progression by 30% with** AREDS2 nutritional supplements

10%-15% *of Patients progress to Wet AMD*

WET AMD

Choroidal Neovascularization (CNV)

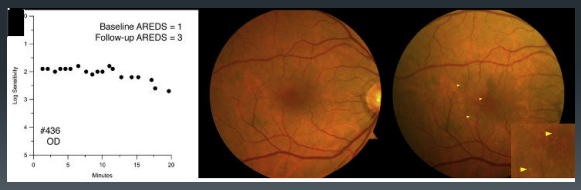
- Cause: angiogenesis
- **Lower risk of progression by 35% with** anti-VEGF

BAUSCH + LOMB PreserVision · AREDS 2 · BAUSCH + LOMB Ocuvite · I-Caps · LUCENTIS · EYLEA · AVASTIN (off label)

Sources: Age-Related Eye Disease Study Research Group. *Arch Ophthalmol* 2001;119(10):1417-1436. | Age-Related Eye Disease Study 2 Research Group. *JAMA*. 2013;309(19):2005-2015. | Boyer DS, et al. *Ophthalmology*.

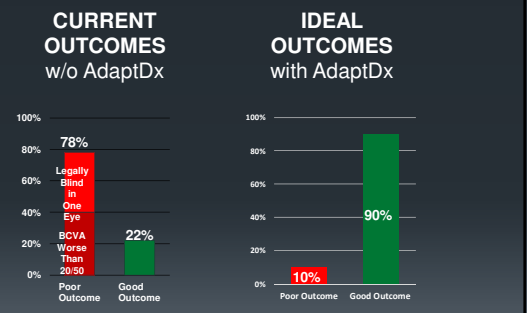
ALSTAR Study Results

- Impaired dark adaptation identifies subclinical AMD at least **three years before** it can be seen with other methods.
- Subjects with impaired dark adaptation were **two times** as likely to develop clinically evident AMD and **eight times** as likely to advance beyond the earliest stage of AMD.



Owsley, C et al. *Ophthalmology. In press;* 10.1016/j.ophtha.2015.09.041.

New technology-improved outcomes and reduced preventable blindness



Summary-Optometry's Role in AMD

- Identify Risk Factors
- Modifiable Factors
- Diagnose Early
- Monitor Regularly
- Nutritional Supplements
- Blue Light Education

Thanks

- Brian E Mathie, OD, FAAO
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