Optometry’s Role in Age Related Macular Degeneration

*Early Detection and Effective Treatment*

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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 "partially-hydrogenated vegetable oils, sugars"
- Hypertension 1.5X increased risk (uncontrolled)
- Obesity 2X increased risk
- Alcohol intake and excessive omega 6’s
- Hypercholesterolemia

**AMD is a Major Health Problem in the US**

**Clinical AMD** is more prevalent than Glaucoma and Diabetic Retinopathy combined.

**Prevalence of Major Eye Diseases (US)**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Prevalence</th>
<th>Age Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glaucoma</td>
<td>2.7M</td>
<td>&gt; 40 yo</td>
</tr>
<tr>
<td>Diabetic Retinopathy</td>
<td>4.9M</td>
<td>&gt; 60 yo</td>
</tr>
<tr>
<td>AMD</td>
<td>9.2M</td>
<td>&gt; 75 yo</td>
</tr>
</tbody>
</table>

**AMD Prevalence by Age (US)**

- 1 in 14
- 1 in 8
- 1 in 3

Sources: 
- https://www.aao.org/newsroom/eye-health-statistics
Primary Eye Care Misses Visible Disease in >25% of Patients Using Standard Workup

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.²

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

<50% of smokers know that smoking may contribute to blindness.²

Classification of AMD is Based on Retinal Structure

- The Beckman Committee Classifies AMD Into 4 Stages.¹

No AMD
- No drusen or small drusen ≤ 63 µm
- No AMD pigmentary abnormalities

Early AMD
- Medium drusen > 63 µm and ≤ 125 µm
- No AMD pigmentary abnormalities

Intermediate AMD
- 1 large druse > 125 µm and/or
- Any AMD pigmentary abnormalities

Advanced AMD² Terms
- 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

Progression

- **No AMD**
  - No drusen or small drusen ≤ 63 µm
  - No AMD pigmentary abnormalities
  - Normal dark adaptation

- **Subclinical AMD**
  - No drusen or small drusen ≤ 63 µm
  - No AMD pigmentary abnormalities
  - Impaired dark adaptation

- **Early AMD**
  - Medium drusen > 63 µm and ≤ 125 µm
  - No AMD pigmentary abnormalities
  - Impaired dark adaptation

- **Intermediate AMD**
  - 1 large druse > 125 µm and/or
  - Any AMD pigmentary abnormalities
  - Impaired dark adaptation

- **Advanced AMD**
  - Geographic Atrophy
  - Choroidal Neovascularization

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

Other component results from the Tri-continent Consortium

The Rotterdam Study
- First significant indication of prophylactic effects from supplementation

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

High
- **Sensitivity:** Correctly identified 90.6% of confirmed AMD cases
- **Specificity:** Correctly identified 90.5% of confirmed normal cases
- **Accuracy:** 90.6% overall

Applicable ICD-10 Codes

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

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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

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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

**SAMPLE DARK ADAPTATION PROGRESSION OVER TIME**
(Rod Intercept in minutes)

<table>
<thead>
<tr>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.5</td>
<td>8.2</td>
<td>8.4</td>
<td>12.3</td>
</tr>
<tr>
<td>15.0</td>
<td>17.0</td>
<td>17.1</td>
<td>17.5</td>
</tr>
<tr>
<td>18.5</td>
<td>19.5</td>
<td>19.5</td>
<td></td>
</tr>
</tbody>
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Baseline
Case 2: Subclinical AMD

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

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 AREDS nutritional supplements

WET AMD
- Choroidal Neovascularization (CNV)
  - Cause: angiogenesis
  - Lower risk of progression by 35% with anti-VEGF

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.

Sources:
- Loewenstein A. Retina. 2007;27:873-878
New technology-improved outcomes and reduced preventable blindness

<table>
<thead>
<tr>
<th>CURRENT OUTCOMES</th>
<th>IDEAL OUTCOMES</th>
</tr>
</thead>
<tbody>
<tr>
<td>w/o AdaptDx</td>
<td>w/ AdaptDx</td>
</tr>
<tr>
<td>Poor Outcome</td>
<td>Good Outcome</td>
</tr>
<tr>
<td>78%</td>
<td>100%</td>
</tr>
<tr>
<td>60%</td>
<td>90%</td>
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<td>40%</td>
<td>80%</td>
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<tr>
<td>20%</td>
<td>60%</td>
</tr>
<tr>
<td>0%</td>
<td>40%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
</tr>
</tbody>
</table>


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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