AMD 101

THE OD'S ROLE IN MINIMIZING BLINDNESS

Midwest Optometric Society – 2018

Leo Semes, OD, FAAO

Disclosures

Commercial Interest	Nature of Relevant Financial Relationship	
Maculogix	Honorarium	Speaker
Science Based Health	Honorarium	Speaker
OptoVue	Honorarium	Speaker
B&L	Honorarium	Advisor
Allergan	Honorarium	Advisor
Genentech	Honorarium	Advisor
Regneneron	Honorarium	Speaker
Shire	Honorarium	Speaker
ZeaVision	Honorarium	Advisor
Reichert/Ametek	Honorarium	Speaker
HPO	Stock options	Advisor

David Sackett, MD

- Widely regarded as the father of evidence-based medicine. (1938-2015)

Half of what you'll learn during training will be shown to be either dead wrong or out-of-date within 5 years . . .;

…the trouble is that nobody can tell you which half.

Optometric milestones . . .

- 1947: Optometrists begin staffing VA positions
- 1968: The LaGuardia Conference
- 1971: DPA legislation (Rhode Island)
- 1977: WV & NC pass therapeutic scope expansion
- March 1996 – California becomes 47th state

The rest is *progress* in limiting vision and sight loss

An expanded chronology can be found at: https://www.reviewofoptometry.com/article/legalizing-optometry#footnotes.
Accessed March 12, 2018

How important is vision?

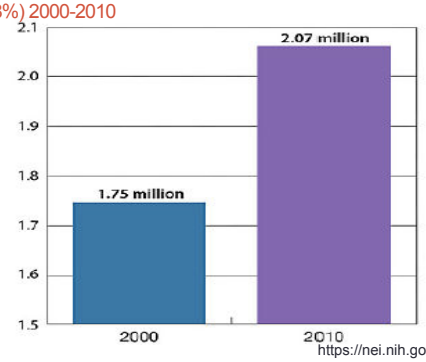
- Trans Am Ophthalmol Soc. 1999; 97: 473–511.PMCID: PMC1298275
- Vision and quality-of-life.
- G C Brown
- Objective:To determinetherelationshipofvisutalactuitylostoqualityof life.
- Design:Threehundredtwenty-fivepatientswithvisutallostoaminimum of 20/40 or greater in at least 1 eye were interviewed in a standardized fashion using a modified VF-14, questionnaire. Utility vlalues were also obtained using both the time trade-off and standard gamble mlethods of utilityassessment.
- MainOutcomneMeasuires:Best-correctedvisuialactuitywas correlatedwithl the visual function score on the modified VF-14 questionnaire, as well as with utility values obtainedc using both the time trade-off and standard gamblemethods.
- Results:Decreasinglevelsofvisionintheeyewithbetteracuitycorrelated directlywithldecreasingvisualfuinctionscoresonthemodifiedVF-14ques- tionnaire, as did decreasing utility values using the time trade-off method ofutilityevaluation.Thestandardgamblemethodofutilityevaluationwas notasdirectlycorrelatedwithvisionasthetimetrade-offmethod.
- Age,levelofeducation,gender,race,lengthoftimeofvisuallos,and thenumberofassociatedsystem-iccomorbiditiesdidnotsignificantlyafect thetimetrade-offutilityvaluesassociatedwithvisuallosinthebettereye. The level of reduced vision in the better eye, rather than the specific dis-easeprocesscausingreducedvision,was relatedtomeanutilityvalues.
- Theaveragepersonwith20/40visioninthebetterseeingeyewaswil-ingtotradle2ofevery10yearsoflifeinreturnforperfectvision(utiility valueof0.8),whiletheaveragepersonwithcountingfingersvisioninthe bettereyewas willingtotra(leapproximately5ofevery10remntainingyears oflife(utilityvalueof0.52)inreturnforperfectvision.

Vision is *this* important

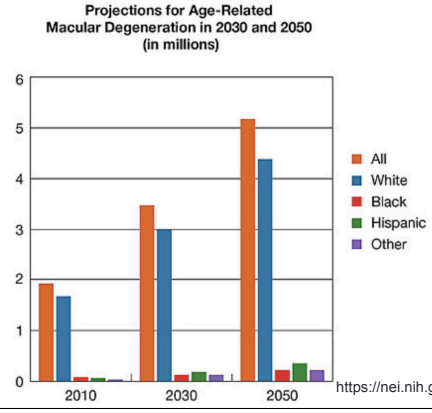
- The average person with 20/40 vision in the better-seeing eye was wiling to trade 2 of every 10 [remaining] years of life in return for perfect vision,
- while the average person with CF vision in the better eye was willing to trade approximately 5 of every 10 remaining years of life in return for perfect vision.

G C Brown. Vision and quality-of-life.Trans Am Ophthalmol Soc. 1999; 97: 473–511.

Decadal *increase* in AMD cases (18%) 2000-2010



https://nei.nih.gov/eyedata/amd



https://nei.nih.gov/eyedata/amd

February was established AMD awareness month in 2008 by Prevent Blindness

maculogix AMD AdaptDx® AMD Excellence Program℠ Resources About Us Contact Us

AMD

28 Facts about AMD

February is AMD Awareness Month! As the AMD experts, we will share 28 facts about macular degeneration, one every day. Follow us on social media so that you don't miss any – some of these might surprise you!

01 **78% of AMD patients have irreversible vision loss by the time they seek treatment**

According to recent studies, as many as 78% of patients are first diagnosed with AMD having already suffered irreversible vision loss. Nearly half of them are first diagnosed with an acuity of 20/200 or worse. These studies prove that AMD is not adequately detected by our current methods.

1. Cervantes CastañedaRA, et al. Eye (Lond). 2008;22(6):777-781.
2. Chen TW, et al. Ophthalmology. 2004;111(2):250-255.
3. Chevrenaud O, et al. European Journal of Ophthalmology 2014; 24 (1): 44-47.

02 **February was established as AMD Awareness Month in 2008 by Prevent Blindness**

Prevent Blindness, the nation's leading volunteer eye health and safety organization dedicated to fighting blindness and saving sight, established AMD Awareness Month. The mission behind this is to disseminate information and promote regular testing. When caught in its initial stages, we're better able to prevent vision loss that occurs as the disease progresses. Early detection and treatment are critical. Visit Prevent Blindness page about AMD.

MEDPAGE TODAY

Ophthalmology > Ophthalmology

This Year's Top Eye Stories: Detergent Burns, Solar Retinopathy, and More

— The most viewed articles from JAMA Ophthalmology in 2017

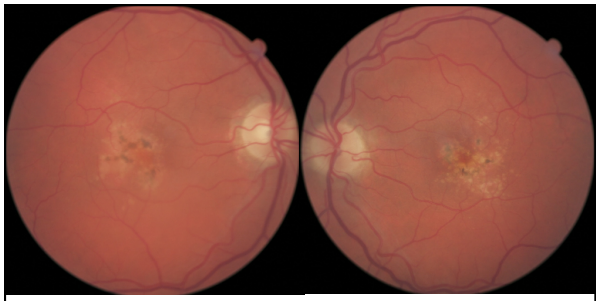
AMD Undiagnosed in Primary Eye Care

In a sample of 1,288 eyes considered normal by primary eye care practices, 320 (24.8%) had age-related macular degeneration (AMD) that fundus photography and trained raters discovered.

A total of 30% of these eyes, all in patients 60 and older, had AMD with large drusen that would have been treatable with nutritional supplements had it been diagnosed, according to an investigation by David C. Neely, MD, of the University of Alabama at Birmingham, and colleagues.

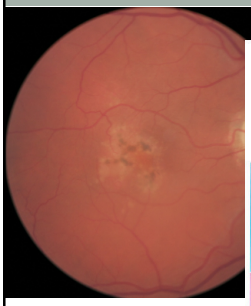
Undiagnosed AMD was associated with older patient age (OR 1.06), male sex (age-adjusted OR 1.39), and less than a high school education (age-adjusted OR 2.40). The prevalence of undiagnosed AMD was not different for ophthalmologists and optometrists.

AMD is a significant public health concern and this study "suggests that AMD is sometimes not diagnosed in older adults receiving a dilated comprehensive eye examination in primary eye care despite its presence," the authors wrote. Improved

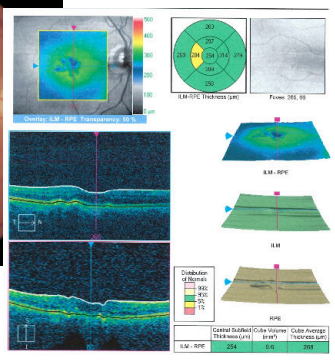


20/60 20/40

"I woke up in the middle of the night and I couldn't see the middle number on the digital clock with my right eye.



20/60



73 yo White Male

- Followed for 2+ years for dry AMD (pre-AREDS)
- Taking 6 mg Lutein/day + Centrum Silver
  - And a host of medications
- BCVA 20/40+, 20/40+ (at baseline)
- Drusen and pigment changes in each macula

Name	Strength
Atenolol	25 mg
Triam/HCTZ	37.5 - 25 mg
Lorazepam	0.5 mg
Tylenol	500 mg
Ecotrin	81 mg
Lutein	6 mg
Centrum Silver	
Robitussin-DM	

Name	Strength
Warfarin (Coumadin)	2.5 mg
Ancept	5 mg
Lovastatin	40 mg
Lorazepam	0.5 mg
Tylenol	500 mg
Robitussin-DM	

Underdiagnosis of early AMD

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

JAMA Ophthalmol. 2017;135(6):570-575. doi:10.1001/jamaophthalmol.2017.0830
Published online April 27, 2017.

Underdiagnosis of early AMD

RESULTS The sample consisted of 1288 eyes from 644 participants (231 [35.9%] male and 413 [64.1%] female; mean [SD] age, 69.4 [6.1] years; 611 white [94.9%]) seen by 31 primary eye care ophthalmologists or optometrists. A total of 968 eyes (75.2%) had no AMD, in agreement with their medical record; 320 (24.8%) had AMD despite no diagnosis of AMD in the medical record. Among eyes with undiagnosed AMD, 32 (10.0%) had hyperpigmentation, 43 (13.4%) had hypopigmentation, 249 (77.8%) had small drusen, 250 (78.1%) had intermediate drusen, and 96 (30.0%) had large drusen. Undiagnosed AMD was associated with older patient age (odds ratio [OR], 1.06; 95% CI, 1.04-1.09; $P < .001$), male sex (age-adjusted OR, 1.39; 95% CI, 1.02-1.91; $P = .04$), and less than a high school education (age-adjusted OR, 2.40; 95% CI, 1.03-5.62; $P = .04$). Prevalence of undiagnosed AMD was not different for ophthalmologists and optometrists (age adjusted OR, 0.99; 95% CI, 0.71-1.36; $P = .94$).

Key Points

Question To what extent is age-related macular degeneration (AMD) undiagnosed by primary eye care physicians when AMD is actually present?

Findings In this cross-sectional study, 320 of 1288 eyes had AMD despite no diagnosis of AMD in the primary eye care medical record, including 30.0% with undiagnosed large drusen.

Meaning As treatments and monitoring strategies for early AMD are refined in the future, these data suggest that improvements for correct, prompt identification of AMD seem to be warranted if subsequent interventions for early AMD safely avoid vision loss.

Table 2. Patient Characteristics Associated With Undiagnosed AMD in Primary Care and Whether the Physician Was an Ophthalmologist or Optometrist*

Characteristic	AMD (N = 1288 Eyes) Not Present and Not Diagnosed (n = 1259)	Present But Not Diagnosed (n = 313)
Age, mean (SD), y	69 (6.7)	71 (6.9)
Visual acuity, mean (SD), logMAR [Snellen]	0.04 (0.07) [20/25]	0.04 (0.07) [20/25]
Visual acuity, logMAR (Snellen)		
<0.0 (<20/20)	272 (29.3)	111 (36.2)
≤0.0 (≤20/20)	656 (70.7)	196 (63.8)
Sex		
Male	327 (33.8)	135 (42.2)
Female	641 (66.2)	185 (57.8)
Race/ethnicity		
White, non-Hispanic	915 (94.5)	307 (95.9)
Other	53 (5.5)	13 (4.1)
General cognitive status		
≥24 (Nonimpaired)	944 (97.5)	316 (98.8)
<24 (Impaired)	24 (2.5)	4 (1.3)
Education level		
AREDS nutritional supplement use	similar % among diagnosed/"overlooked"	
Yes	21 (2.2)	7 (2.2)
No	947 (97.8)	313 (97.8)
≥ 1 (choroidal neovascularization)	NA	0 (0.0)
Smoking status		
Current	46 (4.8)	14 (4.4)
Former	393 (40.7)	139 (43.4)
Never	527 (54.6)	167 (52.2)
AREDS nutritional supplement use		
Yes	21 (2.2)	7 (2.2)
No	947 (97.8)	313 (97.8)
Pseudophakia	187 (33.3)	78 (41.1)
Family history of AMD	70 (7.2)	30 (9.4)
Time since primary care eye examination, mo		
<6	281 (29.8)	85 (27.6)
6-12	385 (40.9)	139 (45.1)
>12	276 (29.3)	84 (27.3)
Primary eye care physician type		
Ophthalmologist	360 (37.9)	118 (37.9)
Optometrist	591 (62.2)	193 (62.1)

Abbreviations: AMD, age-related macular degeneration; AREDS, Age-Related Eye Disease Study; CARMS, Clinical Age-Related Maculopathy Staging; NA, not applicable.
* Data are presented as number (percentage) of eyes unless otherwise indicated.

Table 3. Eyes With Macular Characteristics Indicative of AMD Noted During Fundus Photograph Grading[a]

Characteristic	Eyes, No. (%) (N = 320 Eyes)
≥10 Small drusen	249 (77.8)
Intermediate drusen	250 (78.1)
Large drusen	96 (30.0)
Hyperpigmentation	32 (10.0)
Hypopigmentation	43 (13.4)
Drusenoid retinal pigment epithelial defect	2 (0.6)
Serous retinal pigment epithelial defect	0
Geographic atrophy	1 (0.3)
Choroidal neovascularization	0
Disciform scar	0

*Categories not mutually exclusive, so %-ages do not add to 100

AMD STAGING REVIEW
(AND UPDATE)

Derived from the AREDS, CARMS and the European System

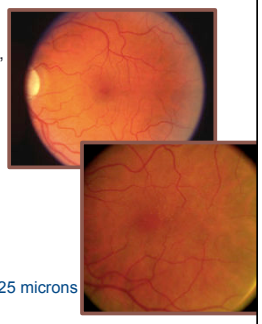
Make a careful distinction

- Specification *vs.* • Performance
- 17" brakes
- 460 HP

Simplified AREDS Staging (specification)

Category 1
- No or few drusen (<63 microns*), no pigment abnormalities, neither eye Wet
- 0% risk of Wet at 5 yrs

Category 2
- Intermediate drusen (<125 microns*), mild pigment abnormalities, neither eye Wet
- <2% risk of Wet at 5 yrs

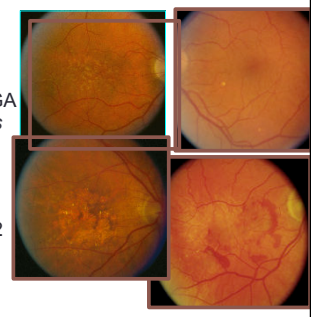


*Note: Central retinal vein is approximately 125 microns

AREDS Staging

Category 3/Intermediate
- Combo of extensive intermediate or *any* large druse, or GA
- *18% risk of Wet in 5 yrs*

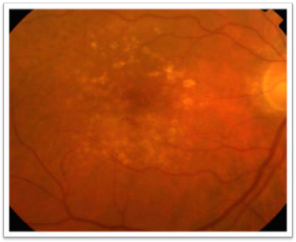
Category 4/Advanced/ High Risk
- One eye with Wet or BCVA worse than 20/32 from Dry



http://www.nei.nih.gov/amd/background.asp

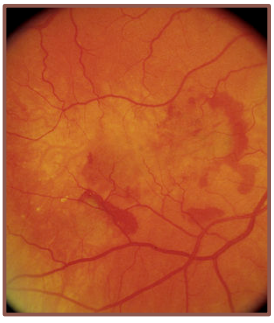
LS

Dry AMD



- The clinical presentation of "Dry," plus development of either:
  - subretinal choroidal neovascular membranes (CNVM)
  - subretinal hemorrhage
  - RPE detachment

Wet AMD



- The clinical presentation of "Dry," plus development of either:
  - subretinal choroidal neovascular membranes (CNVM)
  - subretinal hemorrhage
  - RPE detachment

Natural Course of AMD

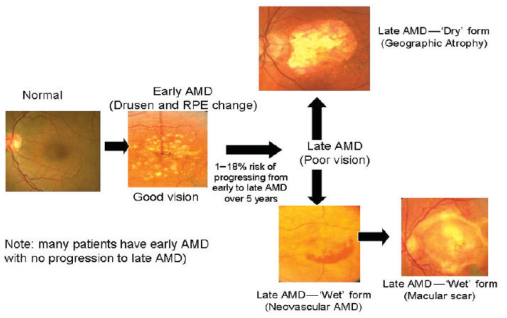


Fig. 1 Classification of age-related macular degeneration.

British Medical Bulletin 2008;85

Emily Chew quote regarding prophylaxis

" It would be great to have the opportunity to study primary prevention of AMD.

I think the pathways to drusen and then from drusen to advanced disease might be quite different.

Those pathways need to be elucidated…."

STAGING RISK FOR VISION LOSS SECONDARY TO AMD

A multi-factorial disease

Simplified AREDS, STARS (European).

First steps to having an impact on vision loss from AMD

Table 1. Five-Year Rate of Developing Advanced AMD in AREDS Participants by Drusen Size and Degree of Pigmentary Abnormalities

Drusen Size	Pigmentary Abnormalities None	Pigmentary Abnormalities One Eye	Pigmentary Abnormalities Both Eyes
None or small drusen	0.4% (4/1017)	0% (0/64)	12.5% (1/8)
Intermediate drusen one eye no large drusen	0.5% (2/449)	5.0% (5/101)	12.9% (4/31)
Intermediate drusen both eyes no large drusen	2.1% (4/187)	12% (6/50)	20% (7/35)
Large drusen one eye	3.9% (11/283)	10.1% (17/168)	25.6% (30/117)
Large drusen both eyes	13% (27/208)	27.3% (48/176)	47.3% (150/317)

AMD = age-related macular degeneration; AREDS = Age-Related Eye Disease Study.

Ferris FL, et al. Ophthalmology. 2013 Apr;120(4):844-51

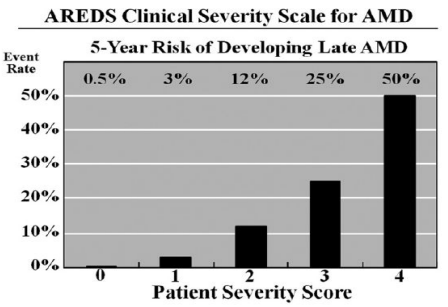


Figure 3. Graph showing age-related eye disease clinical scale for age-related macular degeneration (AMD), demonstrating the 5-year risk of developing advanced AMD for various risk groups. AREDS = Age-Related Eye Disease Study. Ferris FL, et al. Ophthalmology. 2013 Apr;120(4):844-51

Simplified risk scoring system (Rapid assessment of risk from STARS) (highlights)

- Age (>85)
- Family history of AMD
- Hyperopia
- Cataract surgery
- North African ethnicity (vs. Caucasian)
- *History of atherosclerosis*
  - History of smoking (former, </= 10 yrs)
  - History of MI

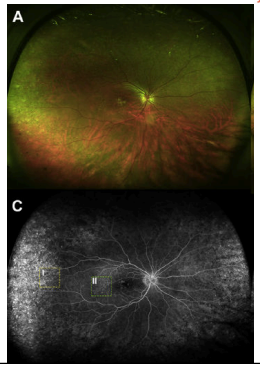
Citation: Delcourt C, Souied E, Sanchez A, Bandello F; for the STARS Survey Group. Development and validation of a risk score for age-related macular degeneration: for the STARS questionnaire. *Invest Ophthalmol Vis Sci*. 2017;58:6399–6407. DOI: 10.1167/iovs.17-21819

EARLIEST IDENTIFICATION OF AMD

What you can t see may be harmful!

Why are mammograms performed?

Cuticular drusen – not just in the posterior pole anymore

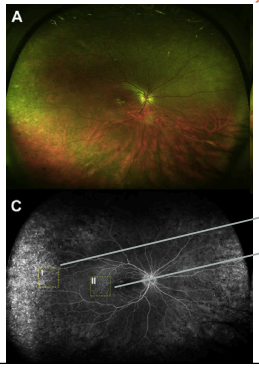


Ultrawide color and FA imaging of a 51 YO with *peripheral* cuticular drusen.

Note RPE abnormalities (hyper and hypo)

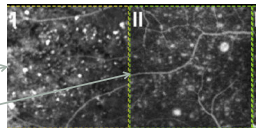
Balaratnasingam C, et al. Cuticular Drusen: Clinical Phenotypes and Natural History Defined Using Multimodal Imaging. Ophthalmology. 2018 Jan;125(1): 100-118.

Cuticular drusen – not just in the posterior pole anymore



Ultrawide color and FA imaging of a 51 YO with *peripheral* cuticular drusen.

Note RPE abnormalities (hyper and hypo)



Peripheral and posterior pole patterns are similar

Here's what's interesting about this cohort (240 eyes, 120 patients)

Demographic and clinical features of the cohort are summarized in Table 1. Mean age at first visit was 57.9±13.4 years (median, 58.2 years; range, 22.6–90.9 years; $P = 0.060$, Shapiro-Wilk test, normal distribution; Fig S3, available at

methods

Ophthalmologic National Hospital (Paris, France). Included eyes demonstrated the characteristics of cuticular drusen phenotype in at least 3 of 4 imaging methods: color photography, OCT, FA, and fundus autofluorescence (FAF), using the following criteria (Fig 2): color photography—multiple yellow or pale, uniform, and round accumulations under the RPE[1,15]; FA—discrete hyperfluorescence that corresponded to drusen during the early arteriovenous phase, conferring a starry-sky appearance[1,3,18]; fundus autofluorescence (FAF)—drusen characterized by central hypoautofluorescence and a rim of hyperautofluorescence[19]; and OCT—drusen localized beneath the RPE and characterized by RPE elevations.[20]

Multi-modal imaging of drusen in young patients (Denmark)

Table 1 Frequency and distribution of drusen in the fovea, parafovea and perifovea in 21 healthy participants with small hard drusen in at least one eye on colour fundus photographs

	Age (years) *Mean (SD)*	Eyes with drusen	Drusen within 0°–2° (%)	Drusen between 2° and 5° (%)	Drusen between 6° and 10° (%)
All (21)	23.2 (4.5)	27	10.2	37.3	52.5
Male (8)	25.4 (6.4)	10	6.8	18.6	33.9
Female (13)	21.9 (2.0)	17	3.4	18.6	18.6

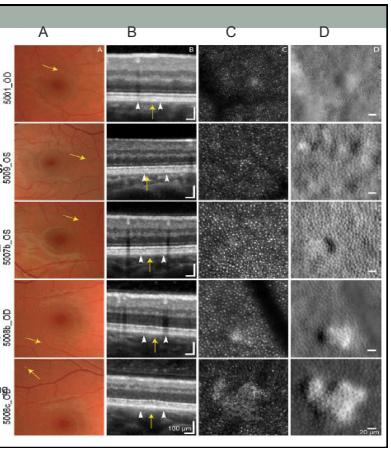
Pedersen HR, et al. Multimodal imaging of small hard retinal drusen in young healthy adults. Br J Ophthalmol. 2018 Jan;102(1):146-152.

4 imaging modes

A. Fundus photogrpahy
B. SD-OCT
C. AOSLO Adaptive optics scanning laser ophthalmoscopy, confocal
D. AOSLO, split detection

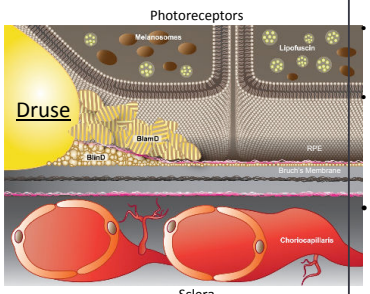
Conclusions.
Small hard drusen could arise from single RPE lesions or a small cluster of 2-3 RPE cells.

Pedersen HR, et al. Multimodal imaging of small hard retinal drusen in young healthy adults. Br J Ophthalmol. 2018 Jan;102(1):146-152.



What do you notice about the water's surface?

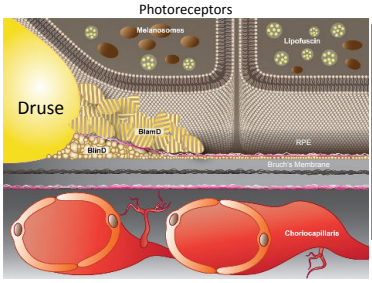
AMD Pathogenesis



Curcio CA, Johnson M. Structure, function, and pathology of Bruch's membrane. In: Ryan SJ, et al, eds. *Retina, Vol 1, Part 2: Basic Science and Translation to Therapy*. 5th ed. London: Elsevier; 2013:466–481.

- Cholesterol deposition BlinD and BlamD
- These deposits eventually become clinically visible drusen
- These extracellular cholesterol deposits affect photoreceptor health, causing inflammation and predisposing to CNV
- In addition, they **impair nutritional transport**, including that of ***vitamin A,*** across Bruch's membrane

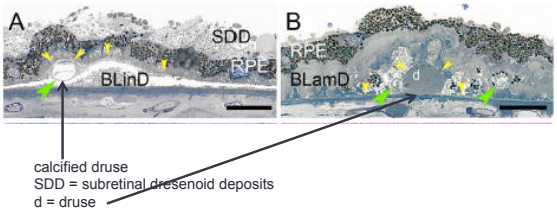
AMD Pathogenesis



Curcio CA, Johnson M. Structure, function, and pathology of Bruch's membrane. In: Ryan SJ, et al, eds. *Retina, Vol 1, Part 2: Basic Science and Translation to Therapy*. 5th ed. London: Elsevier; 2013:466–481.

In effect, early precursors to AMD cause a localized deficiency of vitamin A, and **dark adaptation [DA]** is the best measure of this change

Histology of basal linear and laminar deposits (still specification)



Pilgrim MG, et al. Subretinal Pigment Epithelial Deposition of Drusen Components Including Hydroxyapatite in a Primary Cell Culture Model. Invest Ophthalmol Vis Sci. 2017 Feb 1;58(2):708-719.

IMPAIRED DA IS DIRECTLY RELATED TO SUBCLINICAL ANATOMICAL CHANGES

Let's look at *visual performance*

The discussion boils down to . . .

• Specification	*vs*	• Performance
• 460 HP		• 100MPH to speed limit
• 17" brakes		• 0-60 MPH in 4.2 sec.

1202 eyes (958 normal, 244 with early AMD), as graded by AREDS classification.

- Data collection (*Specification*)
  - Color Fundus Photography [CFP],
  - IR reflectance imaging,
  - Fundus autofluorescence [FAF] *and*
  - SD- OCT (Spectralis)
- Visual function testing (*Performance*)
  - BSCVA (photopic)
  - Contrast and light sensitivity
  - Mesopic visual acuity
  - Low-luminance deficit and
  - Rod-mediated dark adaptation

Neely D, et al. ASSOCIATION BETWEEN VISUAL FUNCTION AND SUBRETINAL DRUSENOID DEPOSITS IN NORMAL AND EARLY AGE-RELATED MACULAR DEGENERATION EYES. Retina. 2017 Jul;37(7):1329-1336.

Subretinal drusenoid deposits (SDD)

- SD-OCT – primary triage
  - Followed by the grading of the 3 en-face imaging modalities. [CFP, IR, FAF,]
- Criteria for SDD at the eye level(clinically) required identification on > 1 en face modality and OCT

or

- on >2 en face modalities in the absence of OCT findings (called strict criteria)

Neely D, et al. ASSOCIATION BETWEEN VISUAL FUNCTION AND SUBRETINAL DRUSENOID DEPOSITS IN NORMAL AND EARLY AGE-RELATED MACULAR DEGENERATION EYES. Retina. 2017 Jul;37(7):1329-1336.

Results (prolonged rod-intercept time (RIT)

- Visual function/performance testing failed to distinguish between eyes with *vs*. those without SDDs, with the exception of Dark Adaptation.

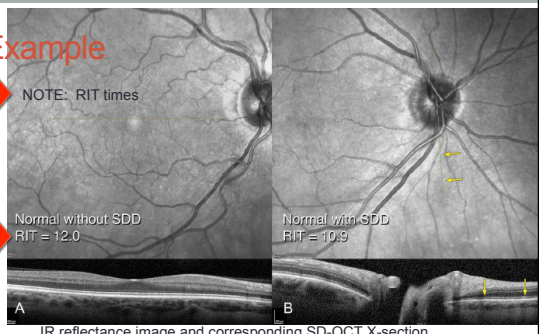
Table 2. Visual Function Stratified by SDDs' Presence Versus Absence for the Total Sample

Visual Function	N Eyes	M	SD	M	SD	*P*	Age-Adjusted *P*
Rod-mediated dark adaptation, rod-intercept time, minutes†	547	14.1 (9.3)		11.4 (6.4)		0.0019	0.0511
Visual acuity, logMAR	1,202	0.056 (20/22)	0.13	0.043 (20/22)	0.13	0.1964	0.7029
Low-luminance acuity	1,202	0.362 (20/46)	0.12	0.353 (20/45)	0.13	0.3464	0.9702
Low-luminance deficit	1,202	0.307 (0.11)		0.310 (0.10)		0.6566	0.6118

Rod-mediated dark adaptation, rod-intercept time, minutes† 547 14.1 (9.3) 11.4 (6.4) 0.0019 0.0511

Neely D, et al. ASSOCIATION BETWEEN VISUAL FUNCTION AND SUBRETINAL DRUSENOID DEPOSITS IN NORMAL AND EARLY AGE-RELATED MACULAR DEGENERATION EYES. Retina. 2017 Jul;37(7):1329-1336.

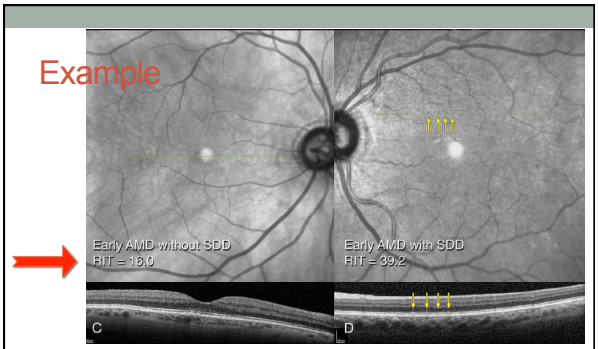
Example



IR reflectance image and corresponding SD-OCT X-section
Left: Normal macula Right: Normal macula with subtle SDD

Neely D, et al. ASSOCIATION BETWEEN VISUAL FUNCTION AND SUBRETINAL DRUSENOID DEPOSITS IN NORMAL AND EARLY AGE-RELATED MACULAR DEGENERATION EYES. Retina. 2017 Jul;37(7):1329-1336.

Example

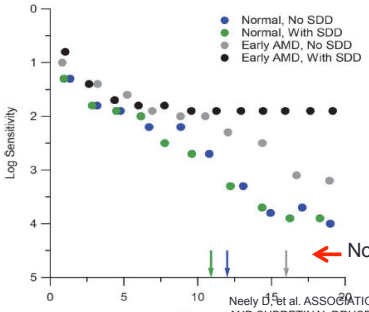


IR reflectance image and corresponding SD-OCT X-sections
Left: Early AMD Right: Early AMD with subtle SDD

NOTE RIT times

Neely D, et al. ASSOCIATION BETWEEN VISUAL FUNCTION AND SUBRETINAL DRUSENOID DEPOSITS IN NORMAL AND EARLY AGE-RELATED MACULAR DEGENERATION EYES. Retina. 2017 Jul;37(7):1329-1336.

DA results for 4 representative cases



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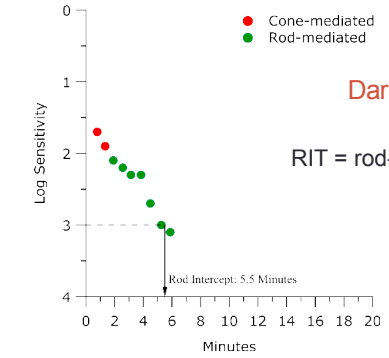


Dark Adaptation

RIT = rod-intercept time

Jackson GR, et al. *Vision Res.* 1999;39(23):3975-3982.
Leibrock CS, et al. *Eye (Lond).* 1998;12(pt 3b):511-520.

Conclusion

- Eyes with clinically normal ocular health and early AMD who have been identified with SDDs warrant careful scrutiny because of their increased risk for incident early AMD *and* its progression. (LS)

Neely D, et al. ASSOCIATION BETWEEN VISUAL FUNCTION AND SUBRETINAL DRUSENOID DEPOSITS IN NORMAL AND EARLY AGE-RELATED MACULAR DEGENERATION EYES. Retina. 2017 Jul;37(7):1329-1336.

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

Impaired dark adaptation is NOT a risk factor.

It IS the earliest manifestation of disease.

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

Performance !

AAO Preferred Practice Pattern® for AMD

History

An initial history should consider the following elements:

- Symptoms[176]
  - Metamorphopsia
  - Decreased vision
  - Scotoma
  - Photopsia
  - Difficulties in dark adaptation
- Medication and nutritional supplement use
- Ocular history[12,177,178]
- Medical history[12,177,178] (including any hypersensitivity reactions[162,179])
- Family history, especially family history of AMD[76,180]
- Social history, especially a quantitative smoking history [37-41]

American Academy of Ophthalmology. "Preferred Practice Pattern for AMD." (2015)

ALSTAR Study

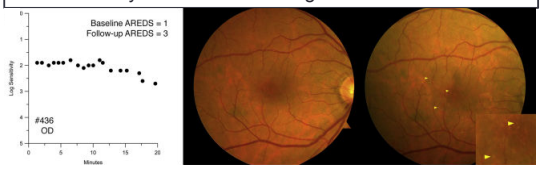
Prospective Study of Subclinical AMD

Sample consisted of 325 adults without clinically detectable AMD. At baseline, 24% of the subjects exhibited impaired dark adaptation. AMD status determined at 3-year follow-up visit.

Owsley, C et al. *Ophthalmology.* 2016;123(2):344-351.

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 **2X** likely to develop clinically evident AMD and **8X** likely to advance beyond the earliest stage of AMD.



Owsley, C et al. *Ophthalmology.* 2016;123(2):344-351.

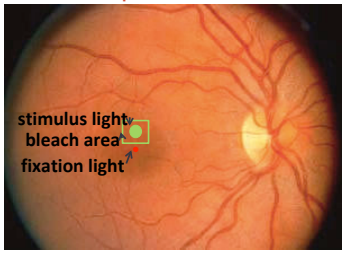
AdaptDx

First dark adaptometer for rapid (practical), routine clinical use

Simple, objective tool to measure dark adaptation as earliest functional correlate of macular dystrophies

Two clinical protocols
- ≤6.5-minute rapid test (for quick assessment)
- ≤20-minute extended test (for benchmarking)

How AdaptDx® Works



DA impairment extends across the entire macula.

The stimulus location shown is the first and most severely affected by AMD.

This is where the AdapDx tests

The AdaptDx is Easy to Use and Administer

- ✓ No prior adaptation or pupil dilation required
- ✓ Low patient burden
- ✓ Automated analysis
- ✓ Objective output (Rod Intercept)
- ✓ FDA 510(k) Cleared

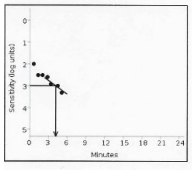
Applicable ICD-10 Codes

Code	Description
E50.5	Vitamin A deficiency with night blindness
H35.30	Unspecified macular degeneration
H35.31	**Non-exudative age-related macular degeneration**
H35.32	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 E50.5, H35.50, H35.52, H35.53, H35.54, H53.60, H53.61, H53.63 and H53.69

Case Example 3: 67 WM

Test Eye: Left
Test Date: 02-09-2017 14:45
Age at Test: 68
Protocol: Rapid Test
Pupil Size: 6.50 mm
Spherical Correction: --
Cylindrical Correction: --

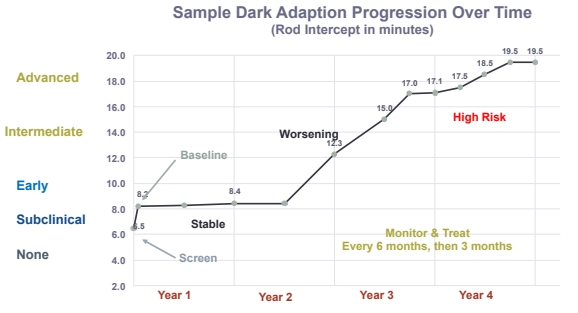


Rod Intercept is 4.21 minutes.
Fixation Error Rate is 0%.

AdaptDx by MacuLogix

Normal rod-intercept "R/C break"
RIT = 4.1 min. (OS)

The AdaptDx can Monitor AMD Progression



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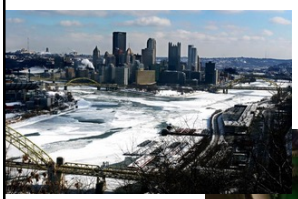
EARLY DIAGNOSIS – SO WHAT?

AMD Risk Factors

Non-Modifiable
Age (chronological)
Gender
Hereditary: ***Genetics***
Race/Pigmentation

Modifiable
Smoking
Cardiovascular disease
Dietary intake
Alcohol intake
Light exposure
Nutrition / MPOD



http://www.brooklineconnection.com/history/Facts/images/Point2014.JPG

NUTRITIONAL RECOMMENDATIONS

AREDS 2, Rotterdam, Tufts NE medical center

#1 Take-Home Message (AREDS 2)

Patients aged 50-85 years who are at high risk for progression of AMD, especially those who do not eat well, should use a supplement that contains 10 mg lutein, 2 mg zeaxanthin, and no beta-carotene

- L/Z was associated with additional reduction in risk for progression, beyond the original AREDS supplement:
  - By 26% in patients with low dietary intake of L/Z
  - By 18% L/Z vs beta-carotene
- Beta-carotene did not affect the risk for progression and significantly increased the risk for lung cancer

Age-Related Eye Disease Study 2 Research Group. *JAMA*. 2013;309(19):2005-2015.

report #23

"...dietary -3 long-chain polyunsaturated fatty acid intake is associated with a decreased risk of progression from bilateral drusen to CGA."

SanGiovanni JP, et al. The Relationship of Dietary -3 Long-Chain Polyunsaturated Fatty Acid Intake With Incident Age-Related Macular Degeneration Arch Ophthalmol. 2008;126(9):1274-1279.

Dietary antioxidants and AMD risk –corroborating evidence (Rotterdam Study)

- Results (4170 followed; 560 incident AMD @ 8-yr F/U)
- High dietary intake of vitamin E (whole grains, vegetable oils, eggs, nuts) and Zinc (meat, poultry, fish whole grains, dairy) was protective
- Above-median intake of C, E, beta-carotene (carrots, kale, spinach), and Zn lowered risk ~ 35%

Conclusion (Rotterdam Study)
"Dietary anti-oxidants may delay the development of early AMD and, possibly, of AMD in general."

Van Leeuwen R, et al. JAMA 2005; 294(24): 3101-7

Recommended Supplements for Age-related Macular Degeneration – *Tufts NE Medical Center*

- Lutein, 6-10 mg
- Vitamin C, 500 mg
- Vitamin E, 200 – 400 IU
- Vitamin D3, 1000 – 2000 IU
- Zeaxanthin, 2 mg
- May also include Zinc, 20 – 80 mg

Omega-3 fatty acids, 1000 mg (fish oil) if not eating fish

Macular Vitamin – PRN

Supplement Facts

Serving Size: 2 Tablets
Servings per Container: 30

Amount per Serving		% DV
Vitamin C (as ascorbic acid)	500 mg	833%
Vitamin E (as natural d-alpha-tocopheryl succinate with mixed d-alpha, d-beta, d-gamma and d-delta-tocopherols and tocotrienols	400 IU	1,333%
Thiamin (as thiamin mononitrate)	50 mg	3,333%
Riboflavin	50 mg	2,941%
Niacin (as niacinamide)	50 mg	250%
Vitamin B6 (as pyridoxine HCl)	50 mg	2,500%
Folate (as folic acid)	1,000 mcg	250%
Vitamin B12 (as cyanocobalamin)	1,000 mcg	16,667%
Biotin	50 mcg	17%
Pantothenic acid (as D-calcium pantothenate)	50 mg	500%
Zinc (as zinc oxide)	25 mg	167%
Copper (as copper oxide)	2 mg	100%
Lutein (from marigold flower extract) (FloraGLO®)	10 mg	*
Zeaxanthin	2 mg	*

* Daily Value (DV) not established.

Eye Omega Advantage -PRN

Supplement Facts

Serving Size: 4 Softgels
Servings Per Container: 30

Four Softgels Contain		% Daily Value
Calories (energy)	40	
Calories from Fat	35	
Total Fat	3.5g	5%*
Polyunsaturated Fat	2.5g	†
Cholesterol	10mg	3%*
Protein	<1g	
Vitamin D (as D_3 Cholecalciferol)	1000 IU	250%
Omega-3 Fatty Acids as TG**	2200mg	†
EPA (Eicosapentaenoic acid) as TG**	920mg	†
DHA (Docosahexaenoic acid) as TG**	920mg	†
Additional Omega-3 Fatty Acids as TG**	360mg	†
Lutein (free)	10mg	†
Zeaxanthin (free)	2mg	†

* Percent Daily Values are based on a 2,000 calorie diet
† Daily Value not established
** Superior Triglyceride Form

THANK YOU