Practical Opportunities in AMD Management

Inside...

Four years ago, only a select group of early adopters and key opinion leaders had real world experience using dark adaptation in AMD patients and suspects. Although several peer reviewed studies strongly confirmed the benefits of this testing, clinical experience lagged behind the overwhelming body of evidence. Such was the case when MacuLogix partnered with optometric leaders and AdaptDx® users to publish its first annual report on AMD in 2017.

There's no denying that 2020 is a unique year in our nation and in our profession. But one thing is certain: with regard to AMD, we are no longer in uncharted territory, attempting to navigate uncertain terrain. On the contrary, this year's report celebrates yet another milestone in AMD diagnosis with the introduction of the wearable, artificial intelligence-driven AdaptDx Pro™ guided by Theia™.

Although AMD is a devastating disease, the report that follows is saturated with hope and backed by the promise of clear, published scientific evidence. Indeed, we have come a long way in four years. The path forward is bright, heavily traveled and undeniably in the best interests of our patients and our practices.

A Supplement to
REVIEW® OF OPTOMETRY
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When Opportunity Knocks

By Pamela A. Lowe, OD, FAAO, Dipl. ABO

For far too long, our profession has viewed age-related macular degeneration (AMD) as a disease that cannot be addressed in optometric settings. Conversely, I feel strongly that AMD is one of optometry's biggest opportunities to impact patient lives and build stronger, more profitable practices.

Here's why:

1. *There is an obvious demand. AMD is more prevalent than glaucoma and diabetic retinopathy combined.*
2. *There is an obvious need. AMD is easy to miss during a clinical exam.*
3. *With a limited budget and equipment, early AMD is easier to diagnose—especially now that a wearable artificial intelligence-driven device is available.*
4. *There are proven treatments that span the entire disease continuum.*
5. *High-quality AMD patient care in an optometric practice can be beneficial to optometrists' bottom lines.*

1. Data Demonstrates Massive Demand for Optometric AMD Care

Statistically, AMD is more prevalent than glaucoma and diabetic retinopathy combined. In fact, you should have three times as many AMD patients as you do glaucoma patients in your practice! Currently, 58,000 eye care professionals are licensed to perform comprehensive eye exams; 40,000 of these are optometrists, 18,000 are ophthalmologists.[1] Retinal specialists account for about 10% of all ophthalmologists. Imagine if all of these patients with AMD tried to make an appointment with a retinal specialist. Chances are, they would wait a very long time for an exam. More importantly, retina specialists generally see the more advanced cases of AMD—not the 85% or more who are in the early to intermediate stages of disease.

Optometrists are on the front line for AMD, and now is the time to embrace the responsibility. One study found that 69% of patients are unaware that they have AMD until they are diagnosed with late-stage disease,[2] with another study showing that up to 78% of patients when first diagnosed already have 20/50 or worse best corrected visual acuity, including 40% with 20/200 or worse.[3,4] These are our patients and we are in a position to change these outcomes. With improved practice protocols to proactively identify and monitor disease progression, we can potentially eliminate sending patients to the retina specialist with such poor vision.

2. Studies Show an Urgent Need for a More Proactive Response

Put simply, optometrists are not diagnosing AMD as often as we could and should be. Historically, this failure to diagnose was largely due to a lack of available diagnostic tools. After all, we are great clinicians, but research demonstrates that observing the macula with

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Olathe, KS

AdaptDx Model: Tabletop & Headset
Testing Protocol: All patients over age 60 as part of a comprehensive exam. If they pass, I generally test every other year. Those who fail return for the Extended Test. I also test any patient under age 60 with any night- or dark-related vision issues, as well as any patient who asks about AMD and/or has a family history.
% Failed: Just under 40%
ROI: Don't forget to look at the indirect benefits. For instance, patients who fail the Rapid Test come back for the Extended Test, an exam and an OCT.
Advice: It's hard to understand what you are missing until you prove it to yourself. If you have patients over the age of 60, you have plenty of AMD patients to justify AdaptDx testing.

a 90D lens and evaluating fundus photos for small drusen and pigmentary changes isn't easy. For example, a study published in *JAMA Ophthalmology* showed just how often diagnoses are missed by optometrists and ophthalmologists alike—even when the doctors were aware that their findings would be double-checked by trained graders.[5] This cross-sectional study, which included 1,288 eyes (644 adults) from patients enrolled in the Alabama Study on Early Age-Related Macular Degeneration (ALSTAR),[6,7] revealed that doctors are missing AMD about 25% of the time. Also quite concerning is that 30% of the undiagnosed eyes in the study already had intermediate-stage disease with large drusen, a well-known risk factor for progression to advanced disease.[5]

When you consider the poor outcomes that often result from delayed diagnoses, there is no question that we need to take a more proactive approach and utilize tools that improve our diagnostic acumen. Use of dark adaptation testing in primary eye care practices would significantly increase the likelihood of diagnosing AMD in affected cases,[4] while also making diagnosis simple and fast. Imagine if you could refer at-risk CNV patients with BCVA of 20/20—in both eyes. With early detection, diagnosis, and close monitoring, you can. With dark adaptation (DA) testing, the number of AMD patients identified in our practices can more accurately reflect the true incidence of disease in this country.

Use of dark adaptation testing in primary eye care practices would significantly increase the likelihood of diagnosing AMD in affected cases, while also making diagnosis simple and fast.

3. AMD Can Be the Easiest Diagnosis of the Day

The past several years have been a time of tremendous innovation in AMD. As a result, we have a much more in-depth understanding of disease pathogenesis and access to affordable tools to help us make a definitive diagnosis very early in the disease process. We now know that, as with glaucoma, structural changes are present in AMD prior to even the earliest clinical indicators of the condition. However, unlike using an OCT in glaucoma to detect these optic nerve changes before vision loss occurs on a visual field, we are unable to detect the earliest retinal damage in AMD with any of our currently available imaging devices. Instead, we need to find the functional biomarker of AMD to detect it at its earliest stages. Specifically, functional changes presenting as impaired dark adaptation take place several years before clinically evident damage to the eye has occurred. Better still, interpreting these functional changes in AMD is often much simpler than identifying the structural changes seen with early glaucoma.

Impaired dark adaptation is the first clinical biomarker for AMD and precedes visible presentation of drusen. In fact, this functional test enables eye care professionals to detect subclinical AMD with 90% accuracy three years before it can be observed clinically.[4] When you couple this test with your own clinical findings and structural measurements, it's obvious how much more confidence you will have in managing patients. In fact, managing AMD is infinitely easier than managing glaucoma. Glaucoma is complex and it is often extremely difficult to determine who will progress and who won't. Even IOP can sometimes be a false indicator. Still we follow our glaucoma suspects closely, though it's very likely their disease will progress quite slowly.

To enhance our ability to stage and monitor progression of AMD by looking at it clinically, we must consider

Glenn Corbin, OD
Wyomissing, PA

AdaptDx Model: Tabletop & Headset
Testing Protocol: All patients with night vision complaints and/or drusen
Tests per Week: >15
ROI: Based on over 60/month at $60/patient reimbursement, the instrument can be paid off in less than 1 year.
Advice: It has become our standard of care for confirming an AMD diagnosis in patients with drusen, especially when acuity is good or clinical findings are minimal. Dark adaptation testing should be considered a must-have for practices and would compare to diagnosing and treating glaucoma without a visual field.

other options—namely functional testing in the form of dark adaptation. Several peer-reviewed studies have shown that dark adaptation function is impaired from the earliest stages of AMD, with increasing impairment as the disease progresses.[8,9] Visual acuity loss is not a surrogate for dark adaptation testing because visual acuity is largely undisturbed during early disease,[10] whereas longitudinal data demonstrate that dark adaptation, as measured by Rod Intercept™ (RI™) time, exhibits significant change over four years among AMD eyes despite stable visual acuity.[11] Based on this and other research, as well as clinical observations and in accordance with the Preferred Practice Patterns of the American Academy of Ophthalmology,[12] it is clear that dark adaptation functional testing can overcome the practical challenges associated with diagnosing AMD using only traditional subjective clinical assessment.

4. There Are Effective Treatments for All Stages of AMD

Intravitreal injection (anti-VEGF) has become one of the most commonly performed procedures in the United States within any field of medicine.[13-15] But by the time a patient reaches this stage, significant damage and vision loss has likely already occurred. Just as we would never wait until late-stage disease to manage a glaucoma patient, we should not wait to treat AMD. Unfortunately, until recently, that was the trend. In fact, several studies have shown that doctors have been too passive when diagnosing and treating nonexudative AMD.[2,3,16] This mindset MUST change. Optometric care is significantly valuable in AMD, and it all begins with the earliest possible diagnosis. Knowing for sure that a patient has AMD makes all the difference in confident management and patient compliance.

For diagnosed patients, effective behavior modification, nutritional supplementation, and prompt anti-VEGF treatment reduce the incidence and progression of irreversible vision loss.[4] Although lifestyle changes, diet and exercise modification, systemic disease management, nutritional supplementation, retinal light protection, and more careful follow-up will not cure AMD, they have each been shown to slow or even halt the progression of the disease. This is extremely relevant to how we care for our patients. They want to know if they have a disease that we can do something about. Even if we can't make it go away, we can keep them safe by giving them the tools and attention they need to enjoy additional years of high-quality central vision, enhancing the odds of a better quality of life.

5. It Can Strengthen and Grow Your Practice

Performing dark adaptation is not only good for your patients, it has tremendous potential to grow your practice. Based on the disease prevalence, these patients are already in your practice. By using the right tools, you will start diagnosing a fair number of AMD patients. Once an AMD patient is diagnosed, your course of care and recommendations will be focused on slowing disease progression, which can lead to additional medical, nutraceutical and optical revenue for your practice. When we focus on what's best for our patients, we often realize it is also best for our practice.

Up to the point of advanced AMD, macular degeneration is well within the scope of primary optometric care. So, get passionate about improving visual outcomes and start managing AMD more proactively. It's a win-win for everyone.

Ryan Powell, OD

Kansas City, MO

AdaptDx Model: 2 Tabletops & 1 Headset
Testing Protocol: All patients over the age of 60 and any patient under the age of 60 who has a family history or a night vision complaint
Tests per Week: 12-15 tests
% Failed: 15-20%
ROI: The AdaptDx is essential to our priority to do the best we can for our patients. The ROI comes from the billing we do with the instrument directly, the supplements we start patients on to slow the rate of disease progression, the office visits we see for macular degeneration patients that we were missing before we had the AdaptDx, and the referral network our practice has built by being recognized by our patients as a practice that is leading the way in diagnosing macular degeneration at its earliest stages.
Advice: Our AdaptDx instruments easily pay for themselves. However, I do not think that comes close to representing the full ROI that this technology has for optometric practice and for our patients.

Anatomy and Pathogenesis of AMD

Understanding These Basics Will Make Disease Management Simple

By Julie Rodman, OD, MSc, FAAO

As many of the other articles in this report explain, poor AMD outcomes are driven, in large part, by how difficult it is to detect and properly grade drusen. However, even our currently accepted grading systems are insufficient in fully describing the degree of damage our patients have from AMD.[17] The reality is that we simply cannot diagnose what we cannot see. The pathogenesis of AMD is such that disease destruction begins years before we can see it clinically, and detecting progression is made difficult by the subtlety of structural changes and the lack of reduction in Snellen acuity. Fortunately, functional testing can alert us to these sometimes undetectable physical changes, ensuring that we are vigilant in monitoring patients for change that can quickly result in vision loss.

Functional testing can alert us to undetectable physical changes, ensuring that we are vigilant in monitoring patients for change that can quickly result in vision loss.

How AMD Starts

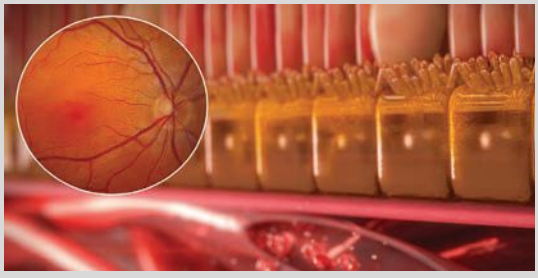
AMD represents a pathologic stage of an otherwise normally occurring deteriorative process.[18] As you know, drusen and subretinal drusenoid deposits become clinically visible at 30µm while changes in RPE cells are substantially smaller.[19] In AMD specifically, damage takes place before we can detect it using structural tests like optical coherence tomography (OCT) and fundus autofluorescence; and too often the harm it's caused comes as an alarming surprise during a regularly scheduled annual exam. That's because drusen are not the earliest-stage markers for AMD. They are visible structural evidence of a pathological process that has been underway for quite some time.

Cholesterol that is locally produced by the RPE and deposited in Bruch's membrane as layers of basal linear and basal laminar deposits is accumulating beneath the surface long before it becomes the drusen we see using current structure-based methods of detection such as OCT.[20] Yet all along the way as this process unfolds, the cholesterol buildup is causing inflammation, oxidative stress, and disruption of oxygen and nutrients such as Vitamin A to the outer retina and photoreceptors.[21] Rhodopsin is the pigment in rod photoreceptor cells that allows us to see dim light. As rhodopsin regeneration is diminished, patients will cite problems with night vision despite very good visual acuity in early disease.[10] As the disease progresses, the cholesterol layer continues to build, eventually thickening to a stage where the tell-tale drusen can be clinically visualized. Therefore, the drusen we finally see are just the proverbial tip of an iceberg of much larger cholesterol deposition.

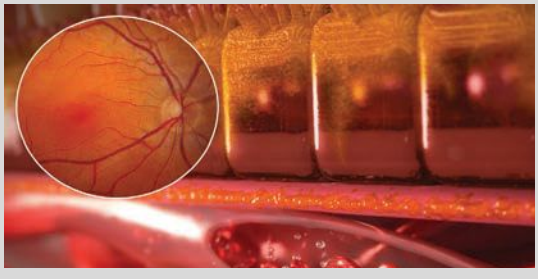
Claudio Lagunas, OD
The Woodlands, TX

AdaptDx Model: Tabletop & Headset
Testing Protocol: Patients 50 or older with a night vision complaint
Tests per Week: 10-12
% Failed: 25%
ROI: At 10-12 tests per week, our AdaptDx Pro will be paid for in about 1 year
Advice: Impaired dark adaptation is a biomarker for AMD. Therefore, it can tell you if a patient has or doesn't have the disease. Knowing up to 3 years before we can find it with OCT, retinal imaging or dilated fundus exams is critical in saving vision and having better outcomes. My patients deserve to know and deserve the best technology...do yours?

The Functional and Structural Progression of AMD

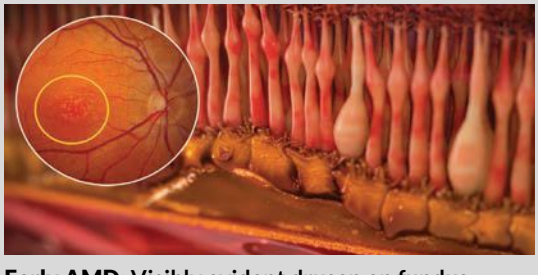


No AMD: Normal fundus appearance. Healthy choriocapillaris, Bruch's membrane, RPE, and photoreceptors.



Subclinical AMD: Normal fundus appearance. Invisible layers of cholesterol are forming along Bruch's membrane, blocking transport of vital nutrients and impairing dark adaptation function.

Subclinical AMD: Normal fundus appearance. Cholesterol continues to build, along with functional impairment.



Early AMD: Visibly evident drusen on fundus evaluation. Functional impairment continues to worsen.

Making Sense of What We Can't See

Nothing can replace a comprehensive dilated exam. Likewise, fundus photography, OCT and other structural tests have a critical place in practice because they help us document and measure clinically detectable drusen. But just because we don't see it, doesn't mean it's not there. Rather, it means we need to consider other ways to detect it. This is where functional testing is most valuable.

Functional testing not only makes us aware of what we can't see—it measures the effects of clinically invisible damage by reliably measuring patients' ability to dark adapt. Remember, early cholesterol accumulation impairs normal transport of vitamin A across Bruch's membrane and creates a localized vitamin A deficiency which results in poor night vision. Unlike characterizing the risk associated with small drusen, a patient's ability to dark adapt can be easily measured in any office setting using an automated dark adaptometer like the AdaptDx or AdaptDx Pro.

The AdaptDx devices test retinal function that has been shown in clinical trials to aid in the identification of patients at all stages of AMD—even when they have no visible structural signs of disease. It does this by revealing impaired dark adaptation function that is 90% specific and 90% sensitive for the presence AMD, sometimes at least three years before it becomes clinically evident.[10] This is significant because it means we can actively take part in the patient journey and do everything possible to protect patients' vision before structural damage has occurred. Because functional impairment of the rod photoreceptors happens in the earliest stages of AMD, dark adaptation becomes affected before visual acuity declines,[10] which means we can be there every step of the way, ensuring that when and if aggressive injection therapy is needed, the referral can potentially be made before lines of vision are lost.

Knowledge Is Power

When you know that a patient has AMD, you have a duty to treat that patient. Indeed, there is no magic bullet for patients with early-stage AMD, but the same can be said of almost any degenerative disease. We can't completely stop AMD in its tracks nor can we make it go away, but as with almost every other disease, we manage it. If we can get a head start, that's great news for our patients.

So how do we manage AMD when we detect it early using dark adaptation? The same way we would if we knew the patient had AMD based on structural findings. In other words, the treatment of AMD should be initiated at first detection. Why? Because based upon our current understanding of AMD pathogenesis, the stages of subclinical, early, and intermediate AMD all represent different clinical manifestations of the same underlying disease process. From a pathophysiological standpoint AMD is AMD—regardless of stage or how long the disease has progressed. Although the deposits may not become visible drusen for several years after their formation, damage is well underway. As such, the following treatments should be offered to patients—even at the earliest stages of AMD:

- **Prescribe smoking cessation programs.** Smoking is the largest modifiable risk factor for the progression of both CNV and GA,[22] yet in one study, 90% of patients with AMD were not advised to stop smoking.[23] Although most patients have been counseled on the ill effects of smoking, most don't realize that it affects their eyes and potentially their vision.
- **Prescribe nutritional supplementation.** Although there is extensive debate about which supplements are most appropriate, evidence strongly suggests prescribing them because, on average, treated patients have better outcomes than untreated patients.[24-26]
- **Discuss lifestyle modifications with respect to diet and exercise.** Following a healthy diet, exercising regularly and maintaining overall health are sound goals for all patients.[26] These lifestyle choices may act synergistically to prevent or delay onset or progression of AMD. One study found that women who followed a healthy diet, engaged in physical exercise, and avoided smoking had substantially lower risk of early AMD compared with women who did not follow these healthy lifestyles.[27,28]
- **Systemic disease management.** Several systemic conditions carry an increased risk of the development of AMD based on epidemiological studies—and it is our job to educate patients on how overall health can impact eye health. Cardiovascular disease, diabetes, hypercholesteremia, and obesity have all been associated with increased risk of AMD and/or progression of AMD.[29-32] Body mass index and abdominal obesity are independent risk factors for progression to advanced AMD. [29]
- **Prescribe retinal light protection.** Epidemiological evidence suggests that chronic sunlight exposure increases the risk of incident AMD and its progression.[33] Based on increased study in this area, you may also want to consider recommending HEVL-blocking eyeglass lenses.

Finally, for a patient with AMD, more frequent retinal examinations are recommended. Moving from a 12-month follow-up interval to a six-month (or even shorter in some cases) follow-up interval may be useful for monitoring disease progression.[12] More frequent visits provide the clinician increased opportunity to detect CNV before visual acuity loss.

An Easy and Obvious Choice

As optometrists, we aren't faced with a lot of clear-cut decisions. We make tough calls all day long. For example, we try to fight contact lens over-wear using every trick in the book; we assess risk in patients with glaucoma and try to decide if they need to start or switch drops; we consider investments in new in-office treatments for patients with ocular surface disease. Making the call to treat AMD is easy. With every early diagnosis and timely intervention, we empower our patients to take control of their ocular health and potentially delay or prevent blindness from AMD.

Jessica Marshall, OD
Holmdel, NJ

AdaptDx Model: Tabletop
Testing Protocol: All patients with a complaint of difficulty with night vision over age 50
Tests per Week: 15-20
% Failed: 60%-70%
ROI: Assuming we have 50 failed tests in a month, we are looking at an additional ~107K in revenue for the practice.
Advice: The ROI has been great for us. More importantly, because we see patients more frequently, our doctor-patient relationships have become even stronger.

Dark Adaptation Testing is Proven to Find Treatable AMD

By Jeffry Gerson, OD, FAAO

Earlier in my career, I was not fully confident in diagnosing AMD on the appearance of drusen alone. I knew that even the smallest druse was a harbinger of AMD, yet I was hesitant to give a patient a diagnosis of AMD. Instead, like many of my colleagues, I would say, "You might have some early signs of AMD." For the patient, that was neither definitive nor reassuring.

Then, a few years ago, I incorporated dark adaptation (DA) testing into my practice. Based on the science, it was clear that functional testing could change the way I diagnose and treat AMD. To be clear, impaired dark adaptation is not an indication of risk. Delayed rod-mediated dark adaptation in older adults with normal macular health is associated with incident early AMD three years later, and thus is a functional biomarker for early disease.[10] In fact, the Preferred Practice Patterns of the American Academy of Ophthalmology indicate that an initial patient history should consider difficulties in dark adaptation.[12] As this paper details, impaired dark adaptation has been found in numerous cross-sectional studies of AMD and may be used as an aid in the diagnosis and staging of AMD.[4]

To prove it to myself, I did a simple study with my own patients. I tested 100 patients over the age of 60 who had no visible indications of drusen. In the end, I was shocked to discover that 38 of them failed the dark adaptation test—which meant they had subclinical or early AMD that I would have otherwise missed. This drastically changed the way I thought about the disease and my approach to patient care. Today, I schedule every patient over 60 for an AdaptDx test, so I can find the functional biomarker of AMD as early as possible. This gives me the confidence to diagnose disease and have a deeper discussion around treatment, while providing my patients with vital information about their health.

Importantly, the definitive AMD diagnosis made possible by the AdaptDx dark adaptometer helps secure patient buy-in with critical lifestyle changes, such as smoking cessation, while also increasing the likelihood that patients will comply with a more frequent follow-up schedule. Offering a true AMD diagnosis, versus hypothetical conversations about risk, also helps inform supplementation recommendations and other interventions. *(See guidelines on page 11).*

Several peer-reviewed studies have shown that dark adaptation function is impaired from the earliest stages of AMD, with increasing impairment as the disease progresses.

Rod Intercept: An Established Measurement of Disease Severity

The science proving that Rod Intercept™ (RI™) times correlate strongly with both the presence of AMD and disease severity has long been known. RI, as measured by the AdaptDx and AdaptDx Pro, is the number of minutes it takes for the eye to adapt from bright light to darkness at a standard threshold stimulus level. Indeed, several peer-reviewed studies have shown that dark adaptation function is impaired from the earliest stages of AMD, with increasing impairment as the disease progresses.[8,9]

RI is a simple and objective measurement of retinal function:

- An RI of less than 6.5 minutes indicates normal dark adaptation consistent with healthy photoreceptor function.
- An RI of 6.5 minutes or higher indicates impaired dark adaptation, most often due to AMD in patients over age 50, unless there is a pre-existing hereditary retinal degeneration or significant vitamin A deficiency, which is rare in the United States.[8,34,35]

When compared with older adults with normal macular health, patients with early-phase AMD have delayed dark adaptation.[7,8,10,35,36] Studies also indicate that the

higher the RI, the worse the AMD. In fact, a significant worsening of dark adaptation in eyes with early or intermediate AMD over a 12-month period can occur without a change in visual acuity or fundus appearance.[7,37] Further, in patients over age 50, declines in dark adaptation function correlated with patient-reported functional deficits and were accelerated in eyes with greater AMD severity.[11] Finally, dark adaptation has been identified as a suitable outcome measure in early-to-intermediate AMD.[38]

High Sensitivity and Specificity

Prior to the release of the AdaptDx, methods for measuring dark adaptation were time intensive (> 30 minutes) and not very patient or technician friendly, making them unsuitable for everyday clinical use.[4] Conversely, the AdaptDx devices can help you identify patients with AMD in as little as 6.5 minutes using the Rapid Test protocol.

In 2014, researchers at Penn State College of Medicine, Massachusetts Eye and Ear Infirmary and the University of Tennessee published their findings in the peer-reviewed ARVO Journal, *Investigative Ophthalmology & Visual Science* and, since that time, numerous investigations have supported these findings.[4] To calculate the diagnostic sensitivity and specificity for the Rapid Test, dark adaptation was measured by using the AdaptDx dark adaptometer in two groups: subjects with normal retinal health and subjects with AMD. Subjects were assigned to their group by clinical examination and grading of fundus photographs. Sensitivity was defined as the percentage of AMD subjects who exhibited a Rod Intercept > 6.5 minutes. Specificity was defined as the percentage of normal subjects who exhibited a Rod Intercept ≤ 6.5 minutes. In the study results:

- Diagnostic test sensitivity was calculated to be 90.6% (115/127, P < 0.001). The 95% CI for diagnostic sensitivity had a lower bound of 85.1% and an upper bound of 100%.
- Diagnostic test specificity was calculated to be 90.5% (19/21, P = 0.0271). The 95% CI for diagnostic specificity had a lower bound of 72.9% and an upper bound of 100%.

In short, this study found that the AdaptDx Rapid Test protocol can be used to detect abnormal dark adaptation associated with AMD and that the diagnostic sensitivity and specificity with this Rapid Test were both greater than 90%, which is comparable with longer-duration research protocols studied earlier.[4,8,39]

Gary Kirman, OD
Hummelstown, PA

AdaptDx Model: 1 Tabletop & 3 Headsets
Testing Protocol: All patients 55 and older as well as those younger with night vision complaints or a strong family history of AMD
Tests per Week: 30 tests per week
% Failed: 45%
ROI: 6 months
Advice: Improve the quality of your examination, save sight and prolong patients' independence with earlier AMD detection and intervention plans.

Beginning an AMD treatment for a patient with marked visual loss may result in a poorer visual outcome when compared to patients with better baseline visual acuity at time of first injection.

Earlier Detection and Intervention Can Make a Big Difference

We are fortunate to live in a time when there are several treatments for late-stage wet AMD. However, by the time injections commence, vision has most likely already been compromised. In fact, it has been clearly established that beginning an AMD treatment for a patient with marked visual loss may result in a poorer visual outcome when compared to patients with better baseline visual acuity at time of first injection.[16,40,41]

Because visual acuity is so closely correlated with treatment delay,[16,42] retinal specialists are increasingly interested in early detection. Likewise, every optometrist's goal should be to diagnose AMD in its earliest stages and monitor disease progression more closely to refer patients at the first sign of choroidal neovascularization (CNV)—before significant vision is lost. With proactive treatment and monitoring, our primary goal is to delay or avoid the onset of CNV. But with this approach, if CNV does occur, we are far more likely to achieve improved outcomes in partnership with our patients and retina specialists.

Damon Dierker, OD
Indianapolis, IN

AdaptDx Model: Tabletop & Headset
Testing Protocol: Symptomatic patients and patients with any fundus findings indicative of possible early AMD
Tests per Week: 10
% Failed: 70%
ROI: With the AdaptDx Pro headset, our testing is up approximately 100%
Advice: AMD is the leading cause of adult blindness in the United States. We should be doing everything we can to diagnose it and manage it early to reduce risk of bad outcomes.

As was reported in a 2014 natural history study published in *Optometry and Vision Science*, AMD patients can exhibit a significant change in DA speed in 12 months, which is a serious concern given the correlation between DA impairment and disease severity that's been well established for many years in multiple cross-sectional studies.[7,37] For example, a study of 325 patients age 60 and older found that those with normal macular health were approximately twice as likely to develop early AMD 3 years later if they had abnormal rod-mediated DA at baseline.[10] This is important on multiple levels. First, consider the danger that these patients face if they aren't seen for 12 months. Knowing that a patient has delayed dark adaptation alerts us to the importance of more frequent follow-up, so vision is not lost unnecessarily. Second, dark adaptation delays are associated with difficulty and emotional distress when performing visual activities under dim illumination and at night (driving, reading, detecting objects, ambulatory mobility.)[43,44] We should not sit idly, pretending a problem does not exist when we know that there is a very real problem. Vigilance is essential as early AMD patients age. For now, progression may be inevitable, but it is our duty to impress upon patients the need for follow-up, and to advise them on options, such as supplements and smoking cessation, that are intended to slow disease progression.

Second eye outcomes provide yet another example of the positive impact of earlier diagnoses. Research demonstrates second eye outcomes could be potentially better than the first eye with careful monitoring.[16] There are several reasons for this, the most obvious of which involves closer monitoring, which is spurred by our knowledge of the patient's much higher risk. When we know a patient has AMD, we proceed differently and we take steps to prevent disease progression in the fellow eye, a strategy that appears to work.[16] Dark adaptation makes this even easier because it tells us whether or not AMD exists in the other eye, even before vision declines. These patients are not ticking time bombs in the hands of doctors who utilize dark adaptation testing.

The great news is that major research utilizing dark adaptation continues on a global scale.[11,34,38,45] For example, these two multi-year studies are using the AdaptDx device as a clinical endpoint:

- ***MACUSTAR:*** The AdaptDx was selected as a key testing device in the MACUSTAR project, a five-year study aimed at reducing the disease burden of AMD worldwide. Currently funded with more than 16 million euros from the European Union and leading European pharmaceutical companies, the investigation expects to enroll 750 patients at 20 clinical study centers in seven countries across Europe.
- ***AMD Ryan Initiative Study (ARIS):*** Led by the National Eye Institute, this study is designed to follow 500 people over five years to learn more about the natural history of early AMD and identify biomarkers of disease progression well before it advances and causes vision loss. All ARIS participants will undergo routine spectral-domain optical coherence tomography (SD-OCT); and visual function will be measured by dark-adapted fundus perimetry and dark adaption with the AdaptDx.

No Room for Doubt

AMD is a devastating disease, but the damage can be mitigated with early diagnosis, proactive treatment and regular monitoring. This wasn't possible a decade ago. We were often forced to somberly accept poor outcomes and significantly diminished quality of life in our patients. We can change these outcomes because we now can use dark adaptation in conjunction with the clinical exam and imaging technology to help us monitor for disease progression and identify those patients who are most at risk for developing advanced, vision threatening AMD.

AMD Staging, Treatment and Management Guidelines

	Subclinical AMD	Early AMD	Intermediate AMD	Advanced AMD
Functional Testing (Average Rod Intercept*)	**RI >** 6.5 The diagnostic specificity and sensitivity of the 6.5 minute cut-point for the presence of AMD is greater than 90%	**12.9** (+/- 6.1)	**16.6** (+/- 5.2)	**19.0** (+/- 4.5)
	Dark adaptation speed is correlated with disease severity. The AdaptDx Pro Extended Test is a useful aid for staging AMD severity based on these average RI times.			
Structural Imaging	• No drusen or small drusen ≤ 63 µm • No pigmentary abnormalities	• Medium drusen > 63 µm and < 125 µm • No pigmentary abnormalities	• 1 large druse > 125 µm and/or • Pigmentary abnormalities	• Geographic atrophy (GA) or • Choroidal neovascularization (CNV)
Treatment Guidelines**	• Prescribe smoking cessation program • Prescribe nutritional supplementation • Discuss lifestyle modifications with respect to diet and exercise • Discuss systemic disease management • Prescribe blue light protection • Prescribe UVA and UVB protection	• Monitor smoking cessation compliance • Monitor nutritional supplementation • Review diet and exercise regimen • Partner with primary care provider on systemic disease management • Check blue light protection • Reinforce UVA and UVB protection	• Monitor smoking cessation compliance • Review vitamin and supplement recommendations • Discuss diet and exercise regimen • Manage systemic diseases with primary care provider • Re-evaluate optical protection	• Low vision rehabilitation for GA • Anti-VEGF injections for CNV
Frequency of Exams	**Every 6-12 months** to monitor for rapid progression with clinical exam, imaging and dark adaptation testing	**Every 6 months** to monitor for rapid progression with clinical exam, imaging and dark adaptation testing	**Every 3-6 months** to monitor for CNV with clinical exam, imaging and dark adaptation testing	Refer to retina specialist at first sign of CNV and continue to closely monitor the fellow eye

* Jackson, G. R., Scott, I. U., Kim, I. K., Quillen, D. A., Iannaccone, A., & Edwards, J. G. (2014). Diagnostic Sensitivity and Specificity of Dark Adaptometry for detection of Age-Related Macular Degeneration. Investigative Ophthalmology & Visual Science, 55, 1427–1431.

** Practical Guidelines for the Treatment of AMD, published as a supplement to Review of Optometry in October, 2017

AMD Practice Guidelines

By Paul Karpecki, OD, FAAO

I've been fortunate to be on the forefront of many advances, including the breakthrough in diagnosing and managing AMD with the 2014 release of the AdaptDx. As with any new technology, there are often a few early adopters who are the real-life testers and help us figure out the best way to implement testing in practice. The same goes for dark adaptation. With this in mind, MacuLogix brought 25 AdaptDx users together in January 2019. Our goal was to discuss and debate the real-life application of AdaptDx testing. After two days of discussion, this diverse group of optometrists came to a consensus on AMD standards of care in optometry.

1. **The goal of managing AMD is to preserve visual function—not to wait until vision has already been lost.** We often see patients with a few small drusen, but we rarely know for sure what those drusen will mean for the patient down the road. In the absence of a definitive AMD diagnosis, many of these patients would be seen only once per year. The result: CNV seems to develop without warning and the patient loses vision before being referred for injections. That was old world optometry. Now we can refer on time based on earlier detection and regular monitoring, prompted by AdaptDx tests.
2. **Dark adaptation testing can overcome the practical challenges associated with diagnosing AMD using only traditional subjective clinical assessment.** Subjective assessment of AMD prior to CNV is exceedingly complex. In fact, a study published in *JAMA Ophthalmology* revealed that optometrists and ophthalmologists miss AMD about 25% of the time.[5] In performing dark adaptation, we are obtaining the critical puzzle piece and eliminating the guesswork that used to make AMD diagnosis and management so difficult. Now, we simply use the AdaptDx to test patients over a certain age or who have drusen, difficulty seeing at night, or other risk factors.
3. **Optometrists must establish improved practice protocols to proactively identify early disease and monitor it on a regular basis to ensure that CNV is detected as soon as it occurs.** As many as 78 percent of AMD patients seek their first treatment after having already suffered irreversible vision loss in one eye, and nearly half of them have an acuity of 20/200 or worse.[2,3] This is an unacceptable statistic that doctors with access to dark adaptometry have the power and tools to change. Patients who are monitored with the AdaptDx potentially have a much better opportunity to have a timely referral to a retina specialist at the first signs of CNV because the doctors who use this technology are identifying the patients who require more frequent follow up.
4. **Optometrists can, and should, recommend treatments that make a meaningful difference.** As described above, knowledge is our most powerful tool and, for patients with AMD diagnoses confirmed by dark adaptation, the best thing we can do is watch them more closely. That said, a confirmed AMD diagnosis also gives us more confidence in suggesting supplements and blue blocking lenses for example. It also helps encourage better patient compliance with lifestyle changes such as smoking cessation and diet.
5. **The treatment of AMD should be initiated at first detection, regardless of the stage.** Without knowing whether a patient has AMD, we might not suggest any treatments. Conversely, when we are armed with the knowledge that a patient has AMD—no matter how early in the disease process—we definitely should intervene by prescribing lifestyle changes, such as diet and exercise modification, better systemic disease management, nutritional supplementation, retinal light protection, and more careful follow-up. While the current early- and intermediate-stage treatments will not cure AMD, they have each been shown to slow or even halt the progression of the disease, allowing patients to enjoy additional years of high-quality central vision.

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Understanding Supplement Research

By Steve Ferrucci, OD, FAAO

Based on AREDS2 research,[46] most doctors advocate supplementation in patients who have intermediate-stage or worse AMD. However, controversy abounds regarding the use of supplements in patients who have early or subclinical stage AMD. Currently, in patients with early disease, no definitive guidelines exist defining precisely which vitamins and nutrients doctors should recommend. Despite this unfortunate lack of consensus, one thing is certain: Evidence strongly suggests that patients with AMD should be prescribed some form of nutritional supplement.[24-26]

AREDS2 authors never stated that supplements are useless in patients with early disease because that was outside the scope of the study and could not possibly be extrapolated from the data based on the study's inclusion criteria.

Contrary to what you may have heard, the AREDS2 authors never stated that supplements are useless in patients with early disease because that was outside the scope of the study and could not possibly be extrapolated from the data based on the study's inclusion criteria. Patients with early disease were not included in AREDS2 to begin with. To directly quote the paper, "Enrollment was restricted to people between the ages of 50 and 85 years at high risk of progression to advanced AMD with either bilateral large drusen or large drusen in one eye and advanced AMD in the fellow eye."[46] That means both eyes had to be at the intermediate stage, or one eye at the intermediate stage and one eye at the advanced stage.

Conversely, the original AREDS research did investigate early disease and found no statistically significant benefit to supplementation with the original formula. But, as you know, the original AREDS formula, containing beta-carotene and devoid of lutein and zeaxanthin, is no longer recommended. Since publication in 2001, and following the many years of research that went into AREDS2, we have discovered so much more about AMD pathogenesis and about the role of carotenoids and antioxidants.

This leaves us with an important choice about what to do for our patients who present with early disease. Do we wait to prescribe supplements until the patient's AMD progresses to a worse disease state simply because AREDS1 supplements were not found to be of significant benefit? Or do we consider the risk-benefit ratio and prescribe a supplement that we know is inexpensive and safe at an earlier stage? Although practitioners favor certain formulas and brands, at the early stage, a carotenoid-based supplement seems to be an obvious choice.

The *Practical Guidelines for the Treatment of AMD* identify three primary options for appropriate nutritional supplementation.[47] The first option is to prescribe a macular pigment supplement (the carotenoids: lutein, zeaxanthin, meso-zeaxanthin). The second option is to prescribe a supplement containing both carotenoids and antioxidants, including zinc and vitamins C and E (e.g., an AREDS2 supplement). The third option is to prescribe a carotenoids supplement to patients with subclinical and early AMD, and a xanthophyll-antioxidant combination supplement to patients with intermediate AMD or patients that progress to intermediate AMD. It is beyond the scope of this report to dictate which of these is best for your patients. However, one fact is clear: Patients treated with supplements have better outcomes than those who are not.[24-26]

Wearable Technology Enables Modern AMD Care

By Claudio Lagunas, OD

The original AdaptDx automated dark adaptometer was introduced in 2014 and has since been used by more than 1,000 eye care professionals worldwide to help identify and monitor AMD. In 2020, MacuLogix introduce a radically new and elegantly simple way to measure dark adaptation. As a self-contained wearable headset with an on-board technician named Theia powered by artificial intelligence, the AdaptDx Pro is a true game changer in eye care.

Although the original and more traditional tabletop form of the dark adaptometer is easy to administer, it required a dark room, a modest footprint, and a dedicated technician. The AdaptDx Pro guided by Theia was designed from the ground up to easily fit into any practice workflow, while providing a completely reimagined user experience for the technician and the patient.

Years of development went into creating this one-of-a-kind medical device to make modern AMD management practical in almost any eye care setting. In fact, it creates a comfortable, personal dark room so patients can take the test anywhere in the office, in any light. Additionally, the medical grade hardware withstands all necessary disinfection, and the hygienic barrier that makes contact with the patient's face is designed for single use, offering a greater level of patient confidence in this new era of point-of-care testing.

Virtual Tech in a Portable Darkroom

Theia, the on-board technician, uses artificial intelligence to help ensure a consistent testing experience and reliable results. After your technician selects the testing protocol and places the device on the patient, Theia administers the test from start to finish. She gently and confidently guides the patient through the test using automated instructions and adaptive feedback.

The built-in cameras and pupil tracking software enable Theia to monitor the patient in real time, reminding the patient to stay focused on the fixation light, or open or close the eyes as needed. She also uses positive reinforcement to keep the patient engaged and on task. As Theia administers the test, your technician is free to work on other high-value tasks while easily monitoring testing progress by glancing at the interactive LCD screen on the device.

AdaptDx Pro guided by Theia

The Future of AMD Care Starts Today

There is no question that earlier models of AMD care delivery are inadequate and not doing enough to save patients from avoidable vision loss. However, practical challenges sometimes stood in the way of best practices. The AdaptDx Pro guided by Theia removes those barriers, offering a truly revolutionary way to measure dark adaptation quickly and effectively in virtually any clinical setting, without requiring too much additional staff or doctor time.

A better future for your patients, your technicians and your practice can start right now. Are you ready to join your colleagues in embracing progress and improving AMD care by welcoming Theia and the AdaptDx Pro into your practice?

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