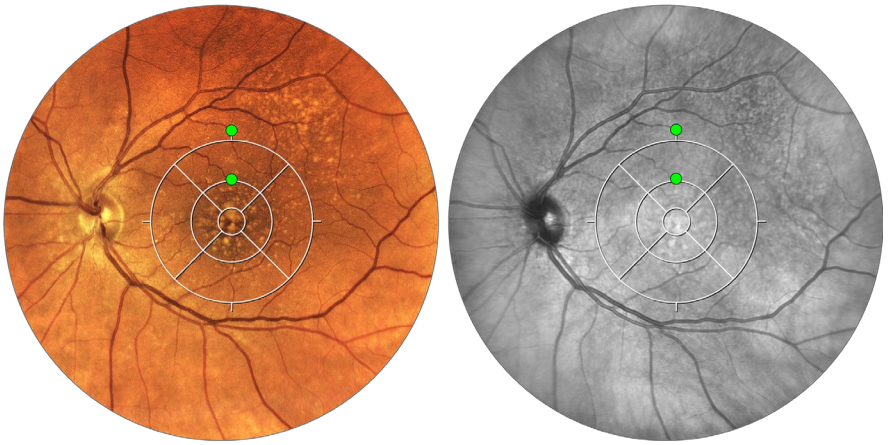
News in Review

COMMENTARY AND PERSPECTIVE



WHERE IT BEGINS. *(Left) Color fundus image of drusen. (Right) SDDs, seen via near-infrared reflectance. Rod-mediated dark adaptation tested at 5 degrees (bottom spot), where rods are sparse, slows more than at 12 degrees (top spot), where rods are numerous and SDDs begin.*

RESEARCH

Night Vision Testing and Emergence of AMD

NIGHT VISION TESTING AT SPECIFIC locations in the retina may help researchers pin down the point of transition from the eye's normal aging to intermediate age-related macular degeneration (AMD).

Two decades ago, researchers at the University of Alabama at Birmingham found that rod-mediated dark adaptation (RMDA) worsened as patients developed early and intermediate AMD. Now, they have found that RMDA takes place more slowly close to the fovea than in areas farther away from the fovea, where rods are numerous and where subretinal drusenoid deposits (SDDs, also called reticular pseudodrusen) are prominent.[1]

"Our data show that AMD is potentially more addressable at early stages of disease than in geographic atrophy [GA], currently the only stage of non-neovascular AMD for which there is a regulatory endpoint," said Christine Curcio, PhD.

Unmet clinical need. Despite evidence that RMDA worsens with AMD and that the area under the fovea plays a critical role in AMD progression, the goal of improving vision in patients with AMD remains largely unmet.

"We think RMDA testing could be used in clinical trials to track the ability of interventions to affect AMD progression at early stages," said Cynthia Owsley, PhD, MSPH. She added, "We also believe that RMDA is the best functional test for validating imaging tests, which are likely to be favored clinically because they take less time than behavioral measures like RMDA."

Study overview. This investigation was part of the Alabama Study on Early Age-Related Macular Degeneration 2 (ALSTAR2). The researchers examined RMDA (measured as rod intercept time) at 5 and 12 degrees in the superior retina of 438 adults (age, ≥60 years). Participants were recruited from three groups: those with early AMD (n = 129), those with intermediate AMD (n = 89), and those with normal macular health (n = 220).

One eye of each participant was tested with the AdaptDx (LumiThera) in a dark, light-tight room. The researchers also used multimodal imaging to identify SDDs, which start near 12 degrees in the superior retina.

Results. The results showed that rod intercept time was longer (i.e., poorer) at 5 degrees than at 12 degrees across all patient groups. In addition, differences in RMDA among groups were more pronounced at 5 degrees than at 12 degrees. In eyes with early and intermediate AMD, SDD presence was associated with slowed RMDA at 5 degrees. SDD presence at 12 degrees was associated with slowed RMDA only in eyes with intermediate AMD.

These findings "support a 'center-surround model' of deposit-driven AMD progression," Dr. Curcio said. She added that RMDA slowing at 5 degrees could be attributed to mechanisms associated with the accumulation of soft drusen and their precursors under the macula lutea throughout adulthood.

Looking ahead. In a follow-up study, Dr. Owsley said, the ALSTAR2 researchers are planning to examine whether RMDA slowing at 5 degrees can predict AMD progression. As part of this investigation, they will correlate imaging findings with photoreceptor function. *—Christos Evangelou, PhD*

1 Owsley C et al. *Ophthalmol Science.* 2023;3:100272.

Relevant financial disclosures: Dr. Curcio—Heidelberg Engineering: S; NIH: S. Dr. Owsley: Co-inventor of AdaptDx device; NIH: S.

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NEURO-OPHTHALMOLOGY

Optic Neuritis: NMOSD and MOGAD Treatment Evolves

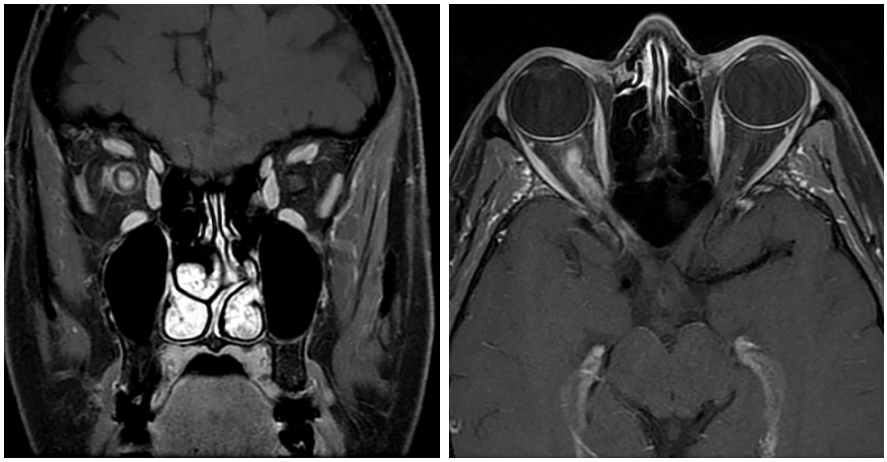
OPTIC NEURITIS (ON) IS MOST OFTEN associated with multiple sclerosis (MS), but it can also be a symptom of other autoimmune disorders, including neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD).

"Early diagnosis of NMOSD and MOGAD is crucial, as it impacts the course of treatment, clinical outcomes, and morbidity," said Negar Moheb, MD, at the Mayo Clinic in Rochester, Minnesota.

Fortunately, scientific knowledge of NMOSD and MOGAD continues to expand. "Our understanding of NMOSD has been growing since the discovery of the aquaporin-4 [AQP4] antibody in 2004, which was found to be both a biomarker and pathologic cause of the disease," said John J. Chen, MD, PhD, also at the Mayo Clinic. More recently, he said, MOG antibodies were found to be a biomarker of MOGAD.

Key points in diagnosis and treatment. In a comprehensive review of current diagnostic and treatment options for these atypical forms of ON,[1] Drs. Chen and Moheb highlighted the following key points for clinicians:

- NMOSD-ON is associated with poor visual outcomes. Therefore, early treatment with high-dose corticosteroids and plasma exchange are recommended for acute attacks. All patients with NMOSD-ON require long-term treatment with an immunotherapeutic agent, such as rituximab or one of the recent FDA-approved monoclonal antibody treatments.
- MOGAD-ON is usually responsive to high-dose corticosteroids and has a generally favorable visual outcome. However, some cases are corticosteroid dependent or have a relapsing disease course and require long-term maintenance therapy; options include IV immunoglobulin or tocilizumab.
- Because treatments for NMOSD-ON and MOGAD-ON are different from those for MS and other forms of ON, AQP4 and MOG antibodies should be checked in any patient with ON unless he or she has classic features of MS (both clinically and radiologically). For instance, Drs. Chen and Moheb wrote, the periventricular white-matter lesions typically seen in MS are rare in NMOSD-ON.



MOGAD-ON. *Magnetic resonance imaging shows prominent longitudinal enhancement of the right optic nerve in a patient with MOGAD-ON.*

On the research front. Strategies to diagnose and treat NMOSD-ON and MOGAD-ON are actively evolving, as multiple clinical studies are in progress or have recently concluded, Dr. Chen noted. For instance, he said, the FDA approved eculizumab, inebilizumab, and satralizumab for the treatment of NMOSD, based on results of three trials that reached completion in 2019. And two clinical trials are now enrolling patients with MOGAD to investigate rozanolixizumab and satralizumab, Dr. Moheb said. *—Patricia Weiser, PharmD*

1 Moheb N, Chen JJ. *Eye* (Lond). Published online March 16, 2023.

Relevant financial disclosures: Dr. Chen—Horizon: C; UCB: C. Dr. Moheb—None.

RETINA

Indian Health Service Sees DR Success

OVER THE PAST 30 YEARS, THERE HAS been a notable decline in the incidence and progression of diabetic retinopathy (DR) in American Indian and Alaska Native individuals, researchers report.[1]

The decline coincides with the success of Indian Health Service (IHS) diabetes-related programs, particularly the teleophthalmology program for diabetic eye disease, noted Dara Shahon, MD, at the Phoenix Indian Medical Center in Arizona. And it raises the possibility of extending the follow-up interval for selected individuals.

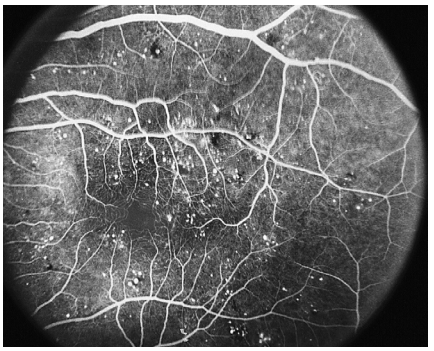
A retrospective cohort study. The researchers analyzed medical records of 8,374 individuals with diabetes who were seen for a baseline appointment and at least one follow-up visit between Jan. 1, 2015, and Dec. 31, 2019. At baseline, patients at 75 IHS primary clinics in 20 states either had no evidence of DR or had mild nonproliferative diabetic retinopathy (NPDR).

Of these patients, 18% had mild NPDR or worse at follow-up; 6.2% had an increase of 2 or more steps in DR over time; and .1% developed proliferative diabetic retinopathy (PDR). Of new DR cases, 65.5% were mild NPDR. Of those with mild NPDR at baseline, 27.2% developed a more severe DR level, with 2.3% progressing to severe NPDR or worse.

Who progressed? Characteristics associated with DR incidence, as well as occurrence of a ≥2 step increase in DR level, included diabetes duration of 15 or more years, a higher HbA1c level, and diabetes therapy (including diet, insulin, or combination treatment).

Regarding the latter, patients on insulin had 4.5 times the rate of a ≥2 step increase in DR, compared to patients

Courtesy of John J. Chen, MD, PhD, and Negar Moheb, MD



GAINS. *The rates of DR incidence and progression among those served by the IHS are now comparable to estimates of non–American Indian and non–Alaska Native populations examined in the last 20 years.*

on diet therapy alone. Notable characteristics associated with any progression from mild NPDR included longer diabetes duration, higher HbA1c level, and presence of peripheral neuropathy.

Imaging mattered. Eyes were imaged nonmydriatically with either ultra-widefield (UWF) imaging or digital fundus photography. Although the study did not conduct a head-to-head comparison of the two modalities, it found that patients imaged with fundus photography at baseline and UWF at follow-up had 2.2 times the rate of a ≥2 step increase in DR level compared to patients imaged with fundus photography only at both stages. This finding may reflect the ability of UWF to identify predominantly peripheral lesions.

While the researchers were unable to comment on the superiority of one imaging modality or the other, Dr. Shahon said, "We are quite pleased" with the low rate of UWF images deemed ungradable.

No changes to protocol. The findings suggest a possibility of extending follow-up intervals from yearly to alternate years for certain low-risk patients. This would conform to the American Diabetes Association's biennial follow-up protocol,[2] but it runs contrary to the Academy's guidelines.[3]

However, any change in protocol would require further evaluation, said Dr. Shahon, who is currently studying adherence to teleophthalmology recommendations for follow-up care and regular screening. Potential candidates for less frequent follow-up would include those who have no NPDR at baseline, are imaged consistently with UWF, and adhere to current screening recommendations, Dr. Shahon said. She added that HbA1c results and cardiovascular status must also be considered.

For now, she stressed the value of teleophthalmology for assessing how patient populations change. "Rates do change over time and need to be updated." —*Miriam Karmel*

1 Fonda SJ et al. *JAMA Ophthalmol.* Published online March 9, 2023.

2 Solomon SD et al. *Diabetes Care.* 2017;40(3):412-418.

3 Flaxel CJ et al. *Ophthalmology.* 2020;127(1):P66-P145.

Relevant financial disclosures: Dr. Shahon—None.

See the financial disclosure key, page 8. **For full disclosures,** including category descriptions, view this News in Review at aao.org/eyenet.