

Ophthalmology Update

Ophthalmology News From Mayo Clinic Vol. 16, No. 1, 2026

JUNE 2026

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Keratoconus: Early Intervention Can Halt Progression

As a disorder that arises from abnormal corneal biomechanics, keratoconus causes thinning and subsequent protrusion of the cornea. The resulting optical irregularities lead to a progressive reduction in visual function. Growing global awareness, increasing research, improved diagnostic capabilities and expanding treatments have made it possible to detect keratoconus at earlier stages. As a result, available therapies are now able to meaningfully reduce or even halt the progression of the disease.

A comprehensive assessment is required when evaluating a patient for keratoconus. “We’ll typically begin with a detailed history, vision testing and a clinical corneal examination,” says Ashlie A. Bernhisel, M.D., an ophthalmologist and cornea surgeon at Mayo Clinic in Rochester, Minnesota. “This is followed by advanced corneal imaging to confirm the diagnosis, stage the disease and determine whether progression is occurring.”

Patient evaluation includes refraction, slit-lamp examination, keratometry, corneal tomography and corneal topography. “Because these tools measure corneal shape and thickness, they can detect keratoconus even in its earliest stages,” Dr. Bernhisel says. “Serial imaging over time can also help determine whether the disease is stable or the rate at which it’s progressing.”

Research has shown that genetic and environmental factors play a role in the pathogenesis of keratoconus. However, it remains a complex and highly variable



Figure. Dr. Bernhisel performs corneal transplant surgery.

condition. “Along with the genetic component, there are additional risk factors that are not yet fully understood,” says Keith H. Baratz, M.D., a cornea surgeon at Mayo Clinic in Rochester, Minnesota. “Having certain conditions such as Down syndrome, Ehlers-Danlos syndrome and severe allergies can also increase the risk of developing keratoconus. A lot of eye rubbing may also contribute to worsening of keratoconus.”

While there is no known cure for keratoconus, advancements in early detection can significantly improve a patient’s prognosis. “If it starts during childhood or teen years, progression tends to be faster,” Dr. Baratz says. “Early detection is crucial and allows us to offer certain treatments, such as corneal cross-linking, at an earlier stage and prevent further visual decline.”

Though keratoconus often emerges during puberty and progresses through

the third decade of life before stabilizing, pediatric-onset keratoconus tends to be more aggressive. “Keratoconus can have a major impact on a young patient with the potential to cause serious visual disabilities,” Dr. Baratz says. “The earlier the intervention, the greater the potential we have to prevent that.”

Treatment is tailored for each patient and is dependent on disease stage and symptoms. “Early cases may be managed with glasses or soft contact lenses, while more-irregular corneas often benefit from rigid, gas-permeable, hybrid or scleral lenses,” Dr. Bernhisel says. “For progressive disease, corneal collagen cross-linking is used to stabilize the cornea, and advanced cases may require surgery such as corneal transplantation.” (Figure)

Since its inception in the late 1990s, corneal cross-linking has grown from a compelling concept to the standard of care for eligible patients. In this procedure, the cornea is saturated with riboflavin eye drops and treated with ultraviolet light. This stiffens the cornea to prevent further shape changes, potentially reducing the risk of progressive vision loss by stabilizing the corneal collagen early in the disease.

“Treatment has moved from primarily surgical solutions to less invasive, preventive approaches,” Dr. Bernhisel says. “Cross-linking can halt progression in many patients, while modern contact lens designs provide excellent visual rehabilitation without surgery. As a result, long-term outcomes and quality of life have improved for many patients.”

Precision Diagnosis of MOG Antibody-Associated Disease Is Critical for Timely, Targeted Therapy



John J. Chen,
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Myelin oligodendrocyte glycoprotein (MOG)-associated disease (MOGAD) is a rare antibody-mediated inflammatory demyelinating disorder of the central nervous system. The phenotypic overlap between MOGAD and related diseases can hinder clear diagnostic separation and delay targeted treatment.

“Because MOGAD is a distinct condition with a different immune system pathology, accurate diagnosis is essential for patients in terms of prognosis and management,” says John J. Chen, M.D., Ph.D., a neuro-ophthalmologist at Mayo Clinic in Rochester, Minnesota.

Symptoms of MOGAD include vision loss, eye pain, muscle weakness, confusion, seizures and headaches — which can resemble related disorders such as multiple sclerosis (MS) and neuromyelitis optica spectrum disorder.

“MOG antibody-associated disease can often be differentiated from MS by the absence of scar formation and the tendency of lesions to resolve,” says Eoin P. Flanagan, M.B., B.Ch., a neurologist at Mayo Clinic in Rochester, Minnesota. “High-positive MOG

antibody levels in the blood are strongly indicative of MOGAD, but spinal fluid testing can be useful in uncertain cases.”

Mayo Clinic offers the first coordinated, multidisciplinary clinic in the world that is devoted specifically to MOGAD. Patients receive a comprehensive assessment including:

- **Standard ophthalmic testing.** Tests include visual acuity, pupillary exam, visual fields and optical coherence tomography (OCT).
- **Neuroimaging.** MRI of the orbits and brain assesses optic nerve inflammation (Figure) and looks for brain lesions suggestive of alternative diagnoses such as MS.
- **Serological testing.** Blood testing looks for antibodies to aquaporin-4 (AQP4) and MOG unless the presentation is classic for MS-associated optic neuritis.
- **Cerebrospinal fluid (CSF) studies.** Lumbar puncture may be considered to evaluate for oligoclonal bands supporting an MS diagnosis. CSF testing for MOG antibodies can identify an additional subset (about 10%) of patients with MOGAD who are seronegative in blood.

Mayo Clinic researchers originally discovered the AQP4 antibody in 2004, and Mayo Clinic was the first center in the United States to offer clinical MOG antibody testing — providing institutional expertise in antibody-mediated demyelinating disorders.

“Early availability of the live cell-based MOG assay at Mayo Clinic, before it was widely accessible in the U.S., resulted in an unparalleled cohort of clinical samples and biospecimens,” Dr. Chen says. “This has enabled foundational insights into the clinical spectrum, imaging features and outcomes of MOGAD.”

Patients are typically treated initially with high-dose intravenous corticosteroids. When they have severe optic neuritis or inadequate response to steroids, plasma exchange is frequently offered. Plasma exchange is an escalation therapy that removes circulating pathogenic antibodies and has been shown to improve outcomes in severe inflammatory attacks.

“Timing is critical,” Dr. Chen says. “Early treatment, especially prompt corticosteroids and timely escalation to plasma exchange in severe cases, can significantly influence visual outcomes.

Graduating Residents: Building on a Solid Foundation

Mayo Clinic’s Ophthalmology Residency training program provides an essential foundation in clinical, surgical and academic ophthalmology. This foundation ensures that graduates are well prepared to excel in comprehensive clinical practice or pursue further subspecialty training. In addition to learning clinical care, residents and fellows participate in innovative research, quality improvement, advocacy and educational opportunities.

“Residents have distinctive interests, aspirations and goals,” says Matt R. Starr, M.D., a vitreoretinal surgeon and program director for the Ophthalmology Residency at Mayo Clinic in Rochester, Minnesota. “They might aspire to pursue a subspecialty fellowship, seek a career in academic medicine or be interested in pursuing comprehensive ophthalmology.

Rapid referral is particularly important for patients with profound vision loss, bilateral involvement, poor steroid response or atypical imaging features.”

Mayo Clinic’s collaborative network regarding MOGAD extends nationally and internationally to accelerate discovery and harmonize clinical approaches. Current research efforts include:

- Participation in industry-sponsored, randomized clinical trials for relapsing MOGAD.
- A multicenter, PCORI-funded randomized trial (TIMELY PLEX) evaluating early versus rescue plasma exchange for severe optic neuritis and transverse myelitis. This trial spans multiple U.S. sites and has the potential to change standards for acute escalation therapy.
- Ongoing translational studies focused on disease pathogenesis, including cytokine and complement biology, and advanced imaging biomarkers such as OCT angiography and ultrahigh-field 7T MRI.

As a tertiary referral center for complex and treatment-refractory optic neuritis and MOGAD, Mayo Clinic offers multidisciplinary expertise, advanced imaging, gold standard

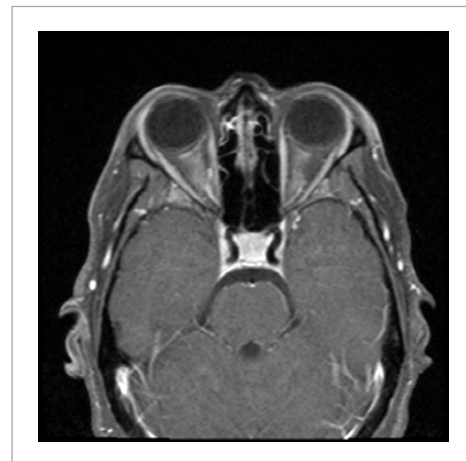


Figure. MRI of the orbits shows bilateral longitudinal enhancement of the optic nerves with perineural enhancement that is classic for MOGAD optic neuritis.

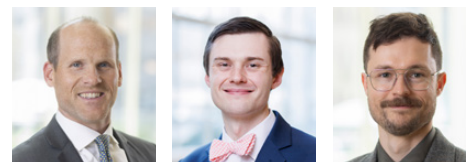
antibody testing, research and participation in cutting-edge clinical trials.

“Optic neuritis is no longer a single disease entity,” Dr. Chen says. “Early, accurate phenotyping has important implications for prognosis and treatment. Early identification and referral of these disorders can prevent misdiagnosis and allow for timely therapeutic intervention and consideration of clinical trial enrollment — all of which can meaningfully improve patient outcomes.”

Regardless of the end goal, our dedicated faculty of physician educators offers invaluable mentorship to maximize each resident’s potential.”

Mayo Clinic’s clinical and academic environment uniquely positions graduates to contribute to the field of ophthalmology throughout their career. The internship curriculum includes three months of clinical ophthalmology and nine months of ophthalmology-customized broad patient care experiences across internal medicine and surgical subspecialties.

“Residency at Mayo Clinic provides an incredibly solid foundation,” says Grayson B. Ashby, M.D., a chief Ophthalmology resident at Mayo Clinic in Minnesota. “In addition to the steady support we receive from the faculty, we’ve experienced a phenomenal



Matt R. Starr, M.D. Grayson B. Ashby, M.D. Darrell Kohli, M.D.

breadth and depth of opportunities that we'll continue to build on throughout our careers."

Residents' comprehensive clinical and surgical ophthalmology training encompasses a wide spectrum of ophthalmic care, with focused clinical experience and didactics in diverse subspecialty areas, including cataract, neuro-ophthalmology, pediatric ophthalmology, ocular oncology and vitreoretinal surgery (Figure).

"I feel blessed to have had good mentors throughout residency," Dr. Ashby says. "For example, I've had the opportunity to work with Brian G. Mohny, M.D., on about a dozen different papers over the last six years. He's really helped shape how I view myself as a budding academic ophthalmologist and how I approach patient care. So many people in the department have been very supportive."

"After graduation, I anticipate there will be a learning curve when navigating a new environment and getting used to the autonomy," says Darrell Kohli, M.D., a chief Ophthalmology resident at Mayo Clinic in Minnesota. "The training at Mayo Clinic prepares residents for comprehensive practice. I feel confident that by the end of this final year, I will feel prepared surgically and medically to treat a wide range of patients while also understanding limits — and recognizing when to reach out with questions or refer for subspecialty help."

Dr. Kohli will be joining SSM Health Fond du Lac Regional Clinic in Fond du Lac, Wisconsin, and he will practice general ophthalmology.

"My goal is to have a relatively comprehensive medical practice and perform surgery that will encompass a mix of cataracts and some oculoplastics procedures," Dr. Kohli says. "I look forward to developing this practice and joining my wife, who is an OB-GYN in the same multispecialty group."

Dr. Ashby's post-residency plans include a fellowship in pediatric ophthalmology and strabismus at Vanderbilt Eye Center in Nashville, Tennessee, and he shares the anticipation for what lies ahead.



Figure. Resident practicing a microsurgical procedure on an anatomical model.

"Big picture, I hope to work as an academic pediatric ophthalmologist," Dr. Ashby says. "Which would ideally give me the opportunity to continue pursuing my research interests while also working with residents and fellows both in clinic and in the operating room."

Although stepping into postgraduation life brings its own hurdles, Dr. Ashby and Dr. Kohli recognize the promising possibilities waiting in the next chapter of their careers.

"I feel very comfortable and ready to go on to fellowship and to build on the foundation that I've been given here," Dr. Ashby says. "It's definitely a change of pace, but it's something I'm looking forward to."

"I will always appreciate the bonds I've formed with my co-residents," Dr. Kohli says. "Residency can be a challenging yet rewarding time — contributing to the strength and enduring quality of the relationships formed."

As ophthalmology continues to evolve, graduating residents are eager to shape what comes next.

"It's an exciting time to join the field," Dr. Ashby says. "With ophthalmology being a smaller, relatively competitive specialty overall, pediatric ophthalmology in particular is an area with significantly unmet needs. Given the general trends of incoming ophthalmology residents, retention, retirement, growing populations and more, it will take some creative thinking on how to expand our field in the future while continuing to meet current patient needs."



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Cover Image

Human multicolored iris of the eye animation concept. Credit: CG Alex

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