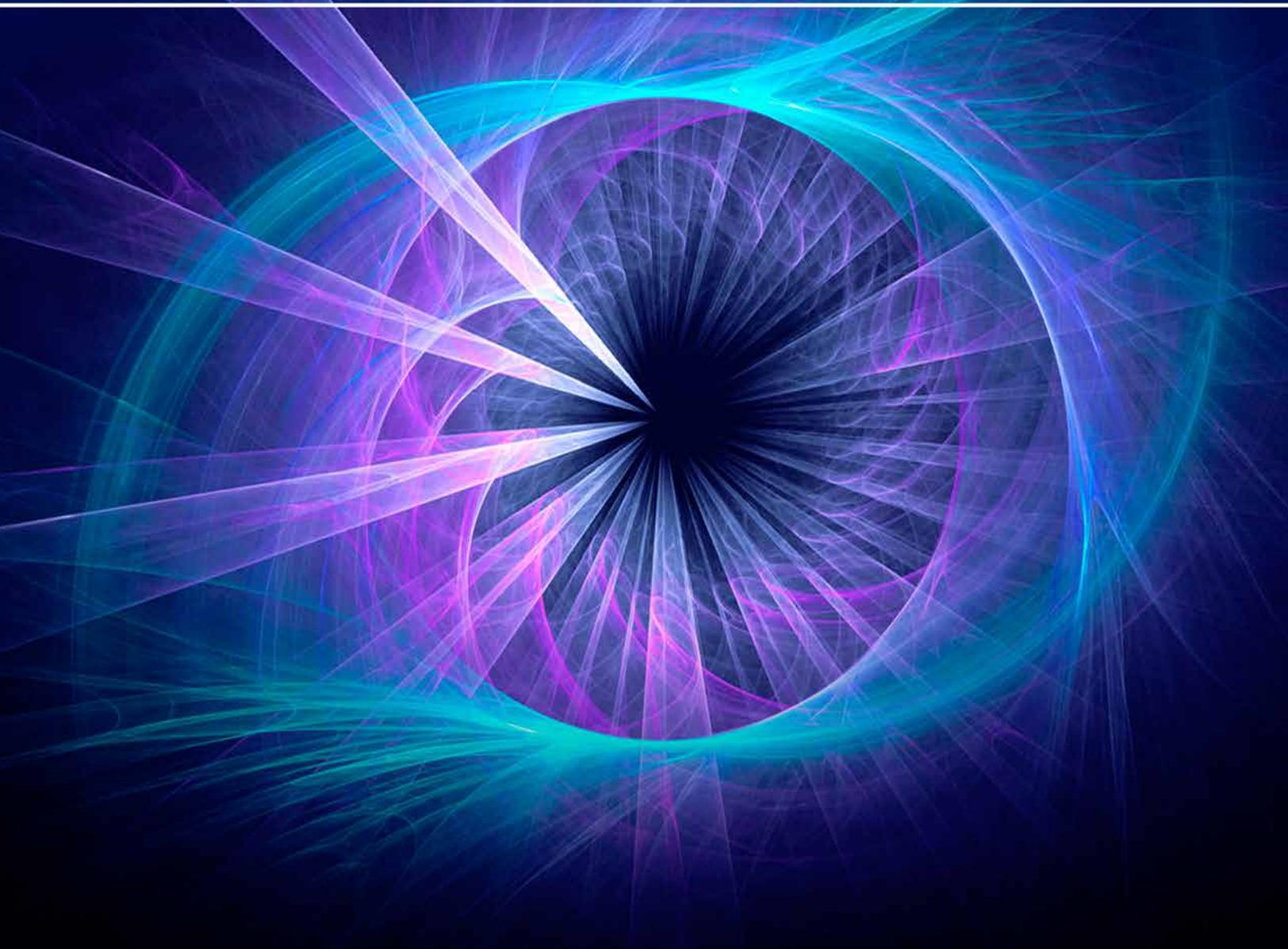




Ophthalmology at Mayo Clinic

Advancing the standard of care



Mayo Clinic Ophthalmology – Advancing eye care for 100 years



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Dharmendra (Dave) R. Patel, M.D.



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Miguel E. Mulet, M.D.

Dear Ophthalmology Colleagues:

There are more ophthalmology treatment options for our patients than ever before. Mayo Clinic clinicians and researchers, collaborating with many of you through multicenter trials, are confirming new and effective ways to treat complex eye conditions such as age-related macular degeneration, glaucoma, corneal diseases, amblyopia and strabismus.

Looking ahead, we're working on treatments that have the potential to dramatically improve outcomes or offer new treatment choices for patients who today have limited options to maintain or restore vision.

In 2015, Mayo Clinic's Department of Ophthalmology marks its 100-year anniversary. We've compiled this overview to share our current activities and contributions to the field, especially in areas of complex eye conditions. With specialists and subspecialists covering every area of medicine, we're well-prepared to provide coordinated and timely care that involves multiple disciplines. In most cases, patients with complex needs are evaluated, undergo testing and leave Mayo Clinic with a treatment plan within a few days. After diagnosis, treatment or surgery, many of our patients return to their home care team for ongoing management.

Please take a few minutes to learn more about Mayo Clinic, our ophthalmology practice, research and education. Our aim is to share what we're doing in the interest of advancing eye care worldwide.

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About Mayo Clinic

This year, patients from more than 135 countries will come to Mayo Clinic. They come because of a 150-year tradition of continually striving to provide safer, better and more efficient care for every patient.

Mayo Clinic was the first integrated, not-for-profit medical group practice in the world. Doctors from every medical specialty work together to provide whole-person care for patients. The care providers are united by a common philosophy that *the needs of the patient come first*.

Patients (2013): Nearly 1.3 million patients treated

Hospital admissions	131,000
Hospital days of patient care	608,000

Staff (2013): More than 4,100 physicians and scientists; 52,000 administrative and allied health staff

Research (2013):

Active human research studies	8,698
New human research studies approved by Institutional Review Board	2,526
Research and review articles in peer-reviewed journals	5,673
Funding (in millions)	\$645

Locations: Campuses in Phoenix/Scottsdale, Arizona; Jacksonville, Florida; and Rochester, Minnesota. Mayo Clinic Health System serves 70 communities in Georgia, Iowa, Minnesota and Wisconsin.

Mayo Clinic's mission: To inspire hope and contribute to health and well-being by providing the best care to every patient through integrated clinical practice, education and research.

Mayo Clinic shares innovations across the spectrum of ophthalmology



Jose S. Pulido, M.D., watches as a 15-year ocular cancer survivor rings the “cured” bell.

Referral center for ocular tumors

Mayo Clinic is a prominent referral center of ocular tumors and has been a leader in advancing the treatments for these complex diseases. The integrated, multidisciplinary practice is ideal for patients who require deliberate and coordinated care with ocular oncologists, radiation oncologists, hematologists and neuroradiologists.

Mayo Clinic will open proton beam facilities on its Rochester campus in 2015 and on the Arizona campus in 2016. These facilities will provide the possibility for novel treatments for ocular tumors and the opportunity to complement Mayo Clinic’s proton beam collaboration with the University of Florida in Jacksonville.

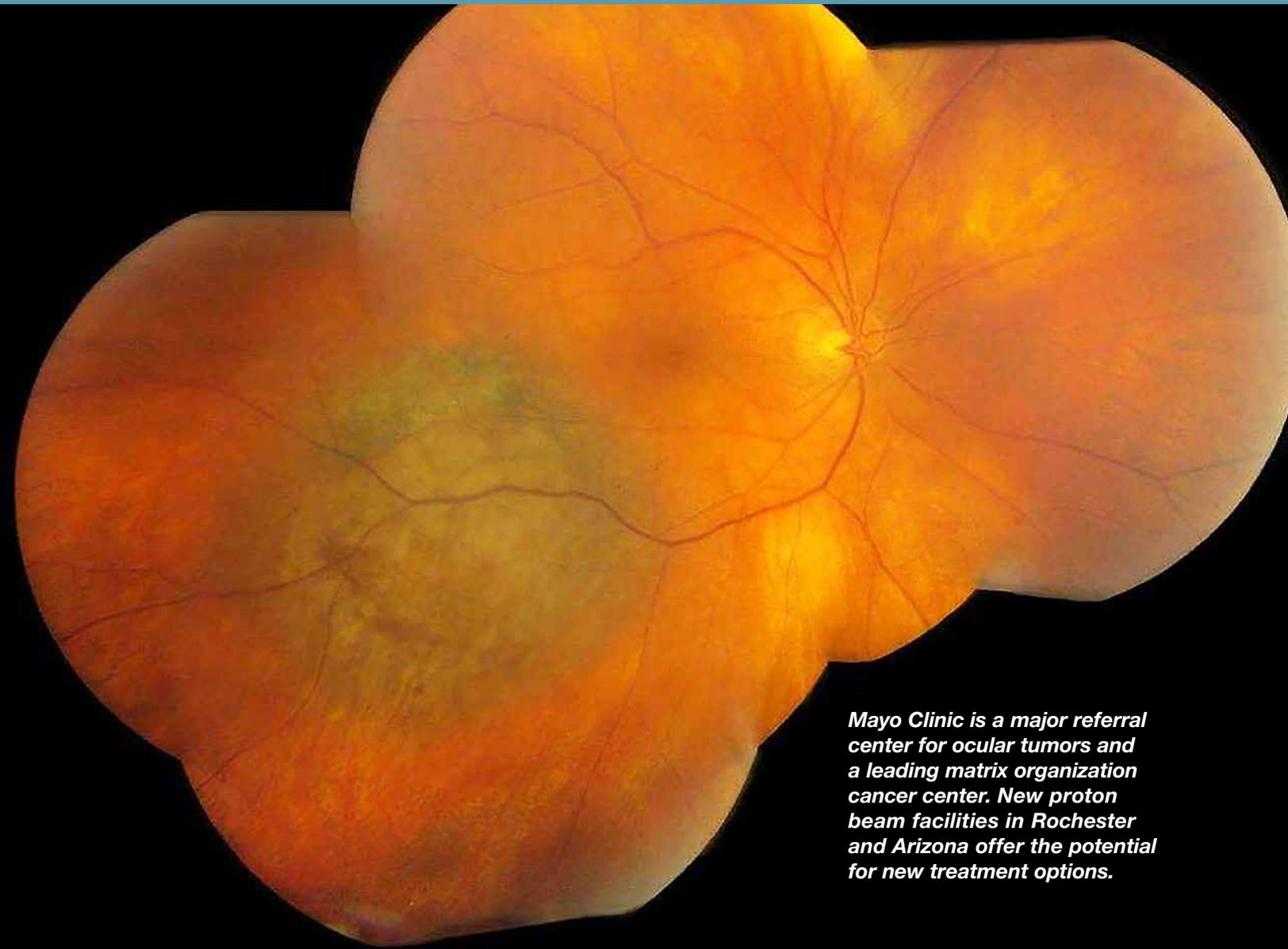
Advancing cancer treatment options

Vitreoretinal lymphoma. A combination of intravitreal methotrexate and rituximab can improve vitreoretinal lymphoma, according to a Mayo Clinic study. Treatment results can be followed by tracking interleukin-10 levels in aqueous humor of treated eyes.

A clinical trial is underway to test whether the oral medication pomalidomide is beneficial to treat recurrent vitreoretinal lymphoma.

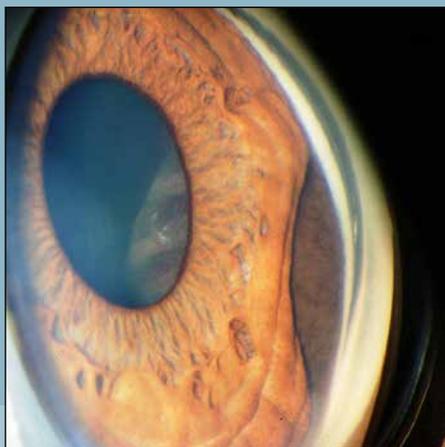
Novel plaques for iris melanoma. Mayo Clinic ocular and radiation oncologists have modified gold alloy-backed plaques used for treating anterior eye tumors. The outer collimating lip reduces the dose to surrounding tissues while the inner lip protects the cornea and surrounding sclera. As a result, much lower doses can be used.

Uveal and skin melanomas. Mayo Clinic researchers are using transgenic mice to test vaccine strategies that could help in the treatment of uveal and dermal melanomas. The transgenic mice spontaneously develop melanocytic tumors that can then be followed for their response to immune interventions.



Mayo Clinic is a major referral center for ocular tumors and a leading matrix organization cancer center. New proton beam facilities in Rochester and Arizona offer the potential for new treatment options.

Image reprinted from International Journal of Radiation Oncology • Biology • Physics, Vol. 78, No. 4, RM Thomson, et al. Modified coms plaques for ¹²⁵I and ¹⁰³Pd iris melanoma brachytherapy, pages 1261-1269, Copyright 2010, with permission from Elsevier.



Mayo Clinic has developed modified gold alloy-backed plaques to treat iris melanomas. This novel design allows for lower radiation doses to be delivered to the eye.

Mayo Clinic hallmark: Collaboration on complex care needs

Multidisciplinary teams of experts collaborate on providing exactly the care needed for patients with complicated ophthalmology concerns. Most patients are evaluated, undergo testing, see specialists as needed and leave with a treatment plan within a few days. Patients who need oculoplastics and orbital surgery benefit from specialists working together:

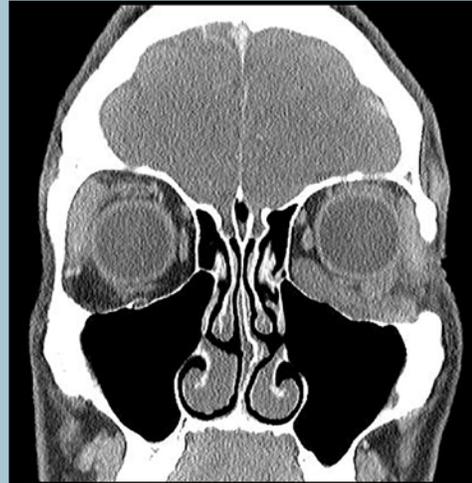
IgG4-related sclerosing disease. This fibro-inflammatory condition, which can mimic a tumor, may be first detected around the eyes. It was initially described in patients with autoimmune pancreatitis but has since been recognized in many other sites throughout the body. Orbital surgeons work with gastroenterologists and hematologists to address this condition — without surgery. More than 20 patients with orbital IgG4-related sclerosing disease have been biopsied and treated while another 20 patients have been identified through the Mayo Clinic Biorepositories Program and referred for treatment.

Benign and malignant orbital tumors. Orbital surgeons work with neuroradiologists, otorhinolaryngologists, neurosurgeons, plastic surgeon, medical oncologists and radiation oncologists to diagnose, manage and treat primary orbital tumors, those with extraorbital/intracranial extension and adjacent sinus tumors that extend into the orbit both in adults and children.

Granulomatosis with polyangiitis (formerly Wegener's granulomatosis). Orbital surgeons, otorhinolaryngologists, pulmonary specialists and rheumatologists collaborate to diagnose and treat this formerly fatal disorder that can involve the eye or orbit, sinuses, lungs, and kidney.

“Being able to call upon the skills of the internists or fellow surgeons within Ophthalmology and in other specialties is a win-win for both the patient and the clinician.”

— James A. Garrity, M.D.



Recurrent orbital varix



Post valsava

Case history: Surgery with super glue (cyanoacrylate) improves quality of life

Patient presentation. Patient experiences frequent, severe eye pain and is hospitalized frequently for pain — up to 30 days a year.

Diagnosis. Orbital varix.

Treatment. Ophthalmologists and interventional neuroradiologists collaborate by injecting cyanoacrylate tissue adhesive into the varix to minimize bleeding while it is surgically removed.

Outcome. Significantly diminished pain and no hospitalizations after removal.

Neuro-ophthalmology expertise and tradition

Patients with complex neuro-ophthalmologic conditions benefit from coordinated care between multiple specialists:

Multiple sclerosis. Neurologists, neuro-ophthalmologists, strabismus surgeons, low-vision specialists, speech therapists and physical therapists work together to diagnose and manage all manifestations that multiple sclerosis may have on the eyes and the rest of the body.

Paraneoplastic neurological syndromes. Ophthalmologists work with neurologists and retina specialists to diagnose and treat uncommon paraneoplastic neuropathies and retinopathies.

Pituitary tumors. Ophthalmologists coordinate with endocrinologists, neuro-oncologists, neurosurgeons and radiation oncologists to minimize damage to the chiasm, optic nerves and cavernous sinuses. Treatments offered include:

- Endoscopic transnasal transsphenoidal surgery
- Transcranial approach (craniotomy)
- External beam radiation
- Gamma knife stereotactic radiosurgery

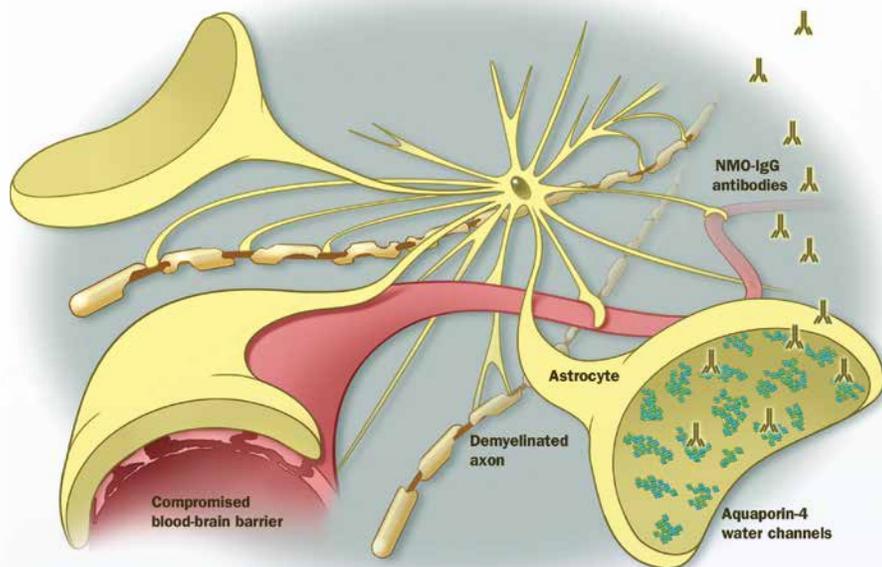
Biomarker identified for neuromyelitis optica (NMO)

Mayo Clinic researchers identified NMO-IgG, the first-ever biomarker that is specific and sensitive for any form of central nervous system inflammatory demyelinating disease.

- NMO-IgG is 99 percent specific and 70 percent sensitive for neuromyelitis optica, helping to distinguish it from multiple sclerosis.
- More than 900 patients with this rare condition have been treated at Mayo Clinic.

“The biggest single advantage we offer patients is immediate access — under one roof — to whatever specialist they need.”

— Jacqueline A. Leavitt, M.D., neuro-ophthalmologist



The target molecule of the neuromyelitis optica (NMO) antibody, NMO-immunoglobulin G (NMO-IgG), is aquaporin-4. This molecule occurs in particles and clusters that reside on the end-feet of the astrocytes which surround the blood vessels, the tight junctions of which constitute the blood-brain barrier. The astrocyte end-feet also encircle axons at the nodes of Ranvier. Mayo Clinic scientists suspect that damage to astrocyte end-feet by the NMO-IgG autoantibody contributes to myelin damage and also compromises the blood-brain barrier.

Name-making leaders in neuro-ophthalmology

Hollenhorst plaques

Mayo Clinic ophthalmologist Robert Hollenhorst, M.D., (1913-2008), determined an association between cerebro- and coronary vascular diseases and cholesterol plaques in retinal blood vessels. He first described what are now called Hollenhorst plaques in 1961 and noted that their intra-arterial location was related to carotid artery disease.

Kearns-Sayre syndrome

Thomas Kearns, M.D., (1922-2011), joined Mayo Clinic in 1947. His research defined Kearns-Sayre syndrome, which was first identified in a case report he co-authored in 1958. Kearns-Sayre syndrome (KSS) is a rare neuromuscular disorder that is the result of abnormalities in mitochondrial DNA. Dr. Kearns also made contributions to advance understanding of retinal changes of carotid artery disease (venous stasis retinopathy).

Sharing expertise in uveitis diagnosis, treatment

Mayo Clinic ophthalmologists have advanced training in uveitis diagnosis and treatment for the most complex ocular inflammatory conditions.

Mayo Clinic specialists offer:

- Comprehensive evaluation of new or chronic uveitis
- Coordinated care with rheumatology, infectious disease, neurology, for complex or systemic conditions
- Advanced ocular imaging and testing customized to the needs of the patient
- Laboratory studies of aqueous, vitreous and other specimens (PCR, cytology, microbiology) to complement the diagnosis of complex and unusual conditions

Uveitis treatment resources

- Smith WM. Uveitis treatment: Going beyond the Medrol dose pack. Presentation at the Mayo Clinic Ophthalmology Retina Update and Case Conference; September 2012; Rochester, Minn. www.youtube.com/watch?v=ols-RT-X7Oo.
- Immunosuppressive agents may enhance corticosteroid treatments for uveitis. Mayo Clinic Ophthalmology Update. 2013;3. www.MayoClinic.org/medical-professionals/publications/ophthalmology-update.



Wendy M. Smith, M.D., coordinates care for patients with complex uveitis and ocular inflammatory diseases with specialists in rheumatology, infectious diseases, neurology, and other specialties.

Treating common and rare retinal disorders

Mayo Clinic's ophthalmologists offer comprehensive care for common and rare retinal disorders. Clinicians and researchers have developed or implemented advances that are easier for patients, from retinal injections coordinated with a patient's hometown ophthalmologist to elimination of facedown positioning for macular hole repair.

In addition, doctors are developing or using breakthrough treatments — retinal transplants and prostheses — to restore vision to the blind.

Idiopathic macular hole repair: Facedown positioning not necessary

Mayo Clinic researchers have found that macular hole surgery can be performed without facedown positioning with results equivalent to surgery in patients who practice facedown positioning. The single-procedure macular hole closure rate was 100 percent and there were no reported complications. The postoperative visual acuities were equivalent to those previously reported with facedown positioning. Patients reported great satisfaction in avoiding the burden of facedown positioning.

Retinal prosthesis: New option for legally blind patients

Mayo Clinic plans to offer a retinal prosthesis to patients who have suffered severe vision loss due to advanced

retinitis pigmentosa. The implanted epiretinal prosthesis includes a miniature camera, attached to a patient's eyeglasses, that wirelessly sends visual signals to electrodes implanted within the eye to restore rudimentary vision. Post-implantation, patients report improved navigation ability in familiar and unfamiliar environments. Mayo Clinic ophthalmologists expect to conduct their first implantations in 2015.

Research highlights

- Iezzi R, Kapoor, KG. No facedown positioning and broad internal limiting membrane peeling in the surgical repair of idiopathic macular holes. *Ophthalmology*. 2013;120:1998.
- Kapoor KG, Hodge DO, St Sauver JL, Barkmeier AJ. Oral fluoroquinolones and the incidence of rhegmatogenous retinal detachment and symptomatic retinal breaks: a population-based study. *Ophthalmology*. 2014;121(6):1269.

Ophthalmologists routinely treat:

- Retinal tears to complex, recurrent retinal detachments with proliferative vitreoretinopathy
- Common and uncommon retinal vascular diseases
- Epiretinal membrane and macular holes
- Central serous chorioretinopathy
- Inherited retinal degenerations, including Best disease, retinitis pigmentosa, cone dystrophy and Stargardt macular dystrophy
- Complex ocular trauma

"This technique has allowed several patients with macular holes for up to 15 years to undergo successful surgery that had been deferred due to unwillingness or inability to position facedown."

— Raymond Iezzi Jr., M.D., vitreoretinal surgeon

Finding ways to restore or prevent vision loss due to eye diseases and trauma

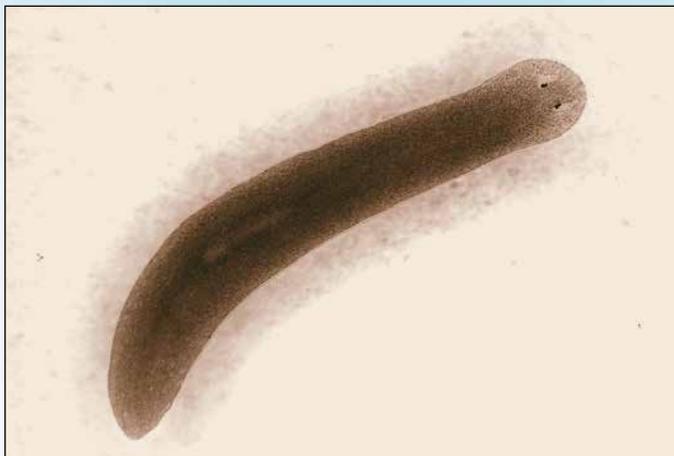
Laboratory researchers at Mayo Clinic are focused on three areas, developing:

- New treatment options for inherited retinal disease where few or no options exist
- New drugs aimed at previously unrecognized targets to lower intraocular pressure, the only proven strategy to slow vision loss due to glaucoma
- Ways to restore vision by regenerating eye tissue, or even whole eyes, by using stem cells
- Possible use of stem cell derived RPE transplants to replace defective RPE cells

Using RPE cells *in vitro* to find treatments for Best disease

In clinical studies, researchers are modeling Best disease and other diseases due to mutations in *BEST1* by using induced pluripotent stem cells generated from skin and differentiated into retinal pigment epithelium (RPE) cells. These cells allow for:

- Evaluation of disease activity in culture
- Evaluation of drugs for treatment of the disease
- Possible development of gene therapy



This illustration shows a planarian of the species S. mediterranea. The two darkly pigmented spots on the planarian's head in the upper right corner of the photo are its eyes.



Alan D. Marmorstein, Ph.D., is leading regenerative ophthalmology through research with induced pluripotent stem cells and planaria flatworms.

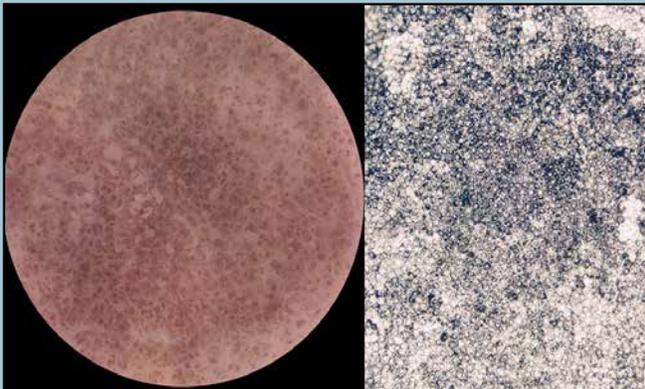
Regenerative therapies

Learning from planaria

Planaria are two-eyed flatworms with a remarkable ability to regenerate their eyes. Mayo researchers are using planaria to understand genetic control of eye regeneration with the goal of inducing human stem cells to regenerate different types of complex eye tissues or even whole eyes. This approach could offer novel regenerative therapies for complex eye disease or trauma.



The Center for Regenerative Medicine builds on Mayo's extensive research resources and clinical practice and includes discovery science, translational research and clinical application.



Retinal pigment epithelial (RPE) cells grown from induced pluripotent stem (iPS) cells are pigmented and form monolayers of cells that are nearly indistinguishable from RPE cells in the eye.

Mayo Clinic Center for Regenerative Medicine

Efforts in the Mayo Clinic Center for Regenerative Medicine span the spectrum of discovery science, translation research and clinical applications. Work includes:

Accelerated regenerative medicine clinical trials

Ongoing trials are studying neurodegenerative diseases, heart failure, peripheral vascular disease, congenital heart disease and kidney disease.

Growing organs

Using a patient's own cells, whole new organs, such as lungs, are being reconstructed.

Constructing scaffolds

Using donor tissue and biodegradable synthetics, researchers are building bioscaffolds to construct new organs.

Developing smart stem cells

This innovation guides adult stem cells, isolated from the patient's bone marrow or fat, to become another tissue — for example, new heart tissue or bone.

Bioengineering stem cells

One method takes skin cells called fibroblasts and reprograms them into induced pluripotent stem (iPS) cells, which can differentiate into virtually any tissue in the body.

"The longer term goal is to take what we learn from planaria to literally program human stem cells to grow human eyes."

— Alan D. Marmorstein, Ph.D., ophthalmology researcher

Fuchs' dystrophy: Identifying the genetic defect



Keith H. Baratz, M.D., led the research team that identified the first genetic association of the common variant of Fuchs' endothelial corneal dystrophy.

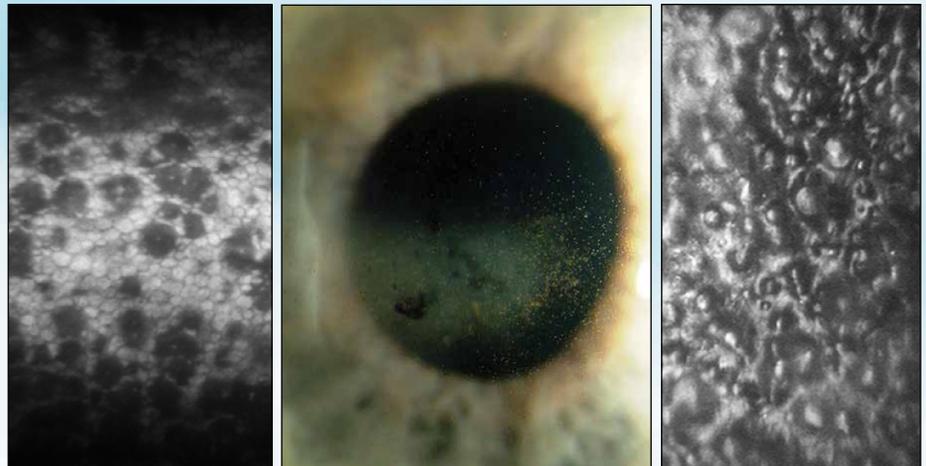
Mayo researchers first identified the specific gene and genetic defect (trinucleotide repeat expansion in the transcription factor 4 gene) that is probably the major contributor to adult-onset Fuchs' endothelial corneal dystrophy in most families.

- Fuchs' dystrophy remains the most common indication for corneal grafting in the United States, but little is known regarding its pathogenesis. Trinucleotide repeat expansions are also found in a select group of neurological degenerations such as Huntington's disease, myotonic dystrophy and Friedreich's ataxia.
- Current research at Mayo Clinic involves the analysis of disease transmission within families, the evaluation of genetic tests to identify young individuals at risk, studies of the biology of normal and diseased cultured corneal endothelial cells, and the generation of induced pluripotent stem cells from Fuchs' dystrophy patients.
- Identification of the Fuchs' gene is allowing investigators to determine the biochemical pathways that are involved in the disease and to identify the mechanism underlying the disease process.

In vivo corneal imaging

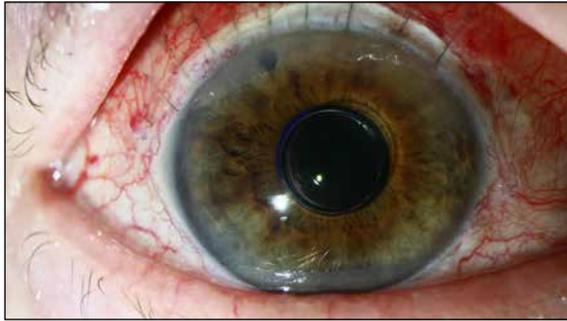
Early disease manifestations are being uncovered in patients with Fuchs' dystrophy through the use of imaging technology.

Mayo researchers are leaders in *in vivo* corneal imaging and have applied their expertise to determine early changes that occur in the anterior cornea in Fuchs' dystrophy. These changes are present by confocal microscopy of corneas that otherwise appear clear by slit-lamp examination, but become chronic and affect visual outcomes even after endothelial keratoplasty.



Mayo Clinic is a prominent referral center for Fuchs' dystrophy, providing clinical and transplantation expertise, and the option for patients to participate in leading genetic and imaging research. Confocal and specular microscopy has revealed early anterior corneal abnormalities in Fuchs' dystrophy in addition to the classic posterior guttata.

Implantable miniature telescope improves vision for advanced macular degeneration



An intraocular telescope greatly improved vision for this Mayo Clinic patient.

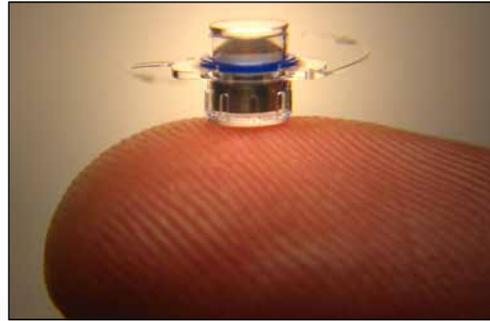


Photo courtesy of VisionCare Ophthalmic Technologies

Mayo Clinic’s cornea surgeons are some of the first in the United States to implant intraocular miniature telescopes for patients with advanced age-related macular degeneration. The telescope magnifies and projects high-resolution images onto healthy photoreceptors, resulting in increased independence, improved ability to engage in everyday activities, and

the ability to recognize faces and facial expressions. Patients benefit from Mayo’s integrated and coordinated care by streamlining evaluations for the procedure between retina specialists, low-vision experts, cornea specialists, and a dedicated team of occupational therapists for pre- and postoperative training.

“We are fortunate to have loyal patients who are eager to participate in cross-sectional and prospective clinical studies, including over the long-term.”

— Sanjay V. Patel, M.D.



Tracking outcomes since the first refractive surgeries

Mayo Clinic surgeons have been performing refractive cornea surgeries since 1998 and have tracked outcomes of those very first patients and thousands of patients since then. Long-term prospective and randomized trials have improved the understanding of the effect of refractive surgeries on the cornea’s curvature, clarity, cellularity, and thickness, while correlating these to visual function.

Research highlights

- Wieben ED, Aleff RA, Tosakulwong N, Butz ML, Highsmith WE, Edwards AO, Baratz KH. A

common trinucleotide repeat expansion within the transcription factor 4 (*TCF4*, E2-2) gene predicts Fuchs’ corneal dystrophy. *PLOS One*. 2012;7:e49083.

- Patel SV, McLaren JW. In vivo confocal microscopy of Fuchs’ endothelial dystrophy before and after endothelial keratoplasty. *JAMA Ophthalmology*. 2013;131:611.
- Patel SV, Diehl NN, Hodge DO, Bourne WM. Donor risk factors for graft failure in a 20-year study of penetrating keratoplasty. *Archives of Ophthalmology*. 2010;128:418.

Corneal transplants

Restoring vision, even for patients with previous transplant failures

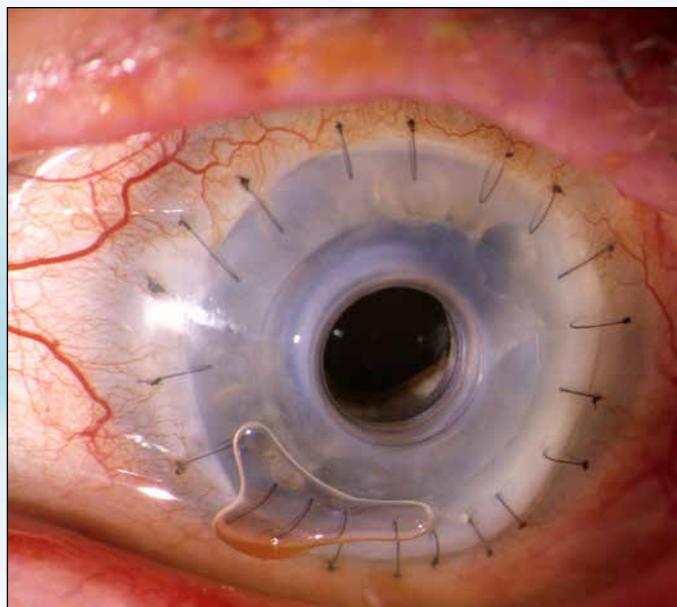
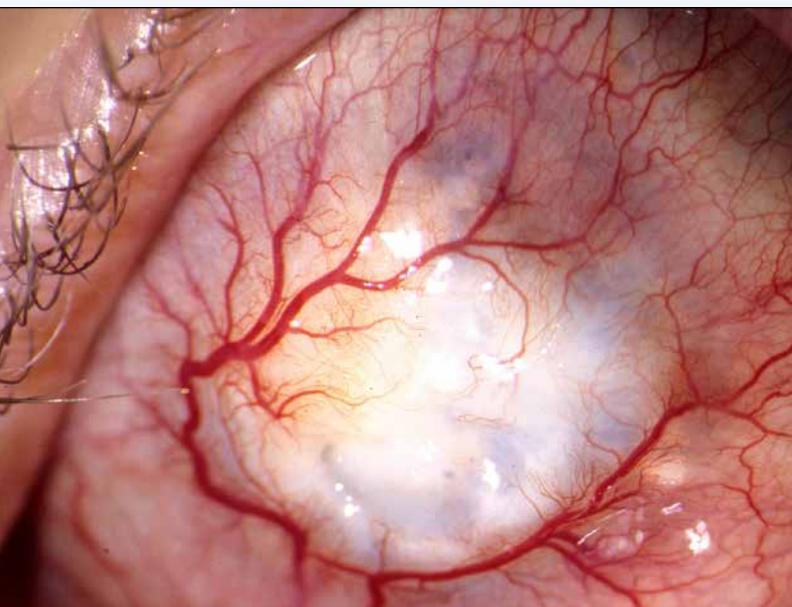
Cornea surgeons at Mayo Clinic continue to refine selective tissue transplantation to treat diseases including Fuchs' dystrophy and keratoconus.

Outcomes research. Mayo Clinic has been a leader for high-quality prospective outcomes research of corneal transplantation, including a 20-year prospective study of penetrating keratoplasty and prospective studies of visual outcomes after endothelial keratoplasty. In a recent study, patient-reported outcomes were evaluated after different keratoplasty techniques for Fuchs' endothelial dystrophy. Results showed that penetrating keratoplasty is associated with improved quality of life similar to endothelial keratoplasty at three years after surgery.

Keratoprosthesis — Artificial cornea

Mayo Clinic surgeons have performed keratoprosthesis procedures since 1995. Mayo Clinic is:

- One of the first centers to offer keratoprostheses to patients with multiple failed corneal transplants or chemical injuries. Specialists commonly perform keratoplasty or keratoprosthesis procedures in combination with glaucoma and vitrectomy surgery. Recently, they have restored useful vision to patients with severe vision loss from repeated graft failure due to congenital corneal opacities, hypotony and silicone oil keratopathy.
- One of the few referral centers to routinely offer visual rehabilitation through keratoprosthesis surgery for patients with immunobullous diseases, such as mucus membrane pemphigoid.



A team-based approach, combining cornea, vitreoretinal and glaucoma surgeons, has restored sight to the blind through complex keratoprosthesis surgery.



Dharmendra (Dave) R. Patel, M.D., treats a patient with Intense Pulsed Light (IPL) therapy at Mayo Clinic's campus in Arizona. Patients who have exhausted other treatment options for evaporative dry eye have experienced symptom relief with IPL.

Intense Pulsed Light therapy provides dry eye relief

Ophthalmologists at Mayo Clinic's campus in Arizona are successfully treating evaporative dry eyes with Intense Pulsed Light (IPL) therapy.

IPL uses bursts of light directed at the lower eyelids and upper cheek areas to heat meibomian glands that are blocked with stagnant secretions, followed by manual expression of the gland secretions.

Most patients require monthly treatments for four months to see full results, but many notice transient improvement after a single treatment. The benefit appears to last six to 12 months.

Ophthalmology surgeries and procedures at Mayo Clinic, 2013

Rochester, Minnesota

Surgeries: 5,094

Procedures: 20,700

Jacksonville, Florida

Surgeries: 727

Procedures: 2,845

Phoenix/Scottsdale, Arizona

Surgeries: 822

Procedures: 675

Mayo Clinic Health System

Surgeries: 5,897

Procedures: 9,893

Strabismus in adults and children

Ways to better understand, diagnose and treat strabismus

Treatments

Botulinum toxin to treat convergence insufficiency

Mayo Clinic strabismus surgeons and collaborators have found that botulinum toxin injection to a lateral rectus muscle improves reading symptoms in convergence insufficiency beyond the duration of the pure pharmacologic effect. Botulinum toxin injections can be performed under topical anesthesia in the office and are proving very useful in the management of adult convergence insufficiency.

Managing torsion using intraoperative monitoring

In many strabismus conditions, the objective is to either treat torsional diplopia or prevent its occurrence. Mayo Clinic strabismus surgeons have developed a method of monitoring the torsional position of the eyes during surgery by marking the limbus at 12 and 6 o'clock at the start of the procedure. This method reduces the incidence of torsional and vertical diplopia post-transposition procedures and allows identification of superior oblique involvement in thyroid eye disease, reducing the incidence of postoperative torsional surprises.



Michael C. Brodsky, M.D., a specialist in pediatric neuro-ophthalmology and strabismus, has established a 3-D video-oculography program to better understand pediatric strabismus.

Diagnostic tool

3-D video-oculography sheds light on pediatric strabismus

Mayo Clinic strabismus researchers are using video-oculography to noninvasively record eye movements in children with strabismus and nystagmus. Video-oculography uses light in the infrared wavelengths to detect positional (horizontal, vertical and torsional) and velocity changes of the two eyes that cannot be detected on clinical examination. Data gathered could help direct surgical treatment with unprecedented precision.

Multidisciplinary eye care for children

Pediatric specialists in neurology, endocrinology, neurosurgery and oncology routinely work together with pediatric ophthalmologists to provide inpatient and outpatient care for children with complicated eye disorders, including:

- Pediatric cataracts
- Double vision
- Pediatric glaucoma
- Retinoblastoma
- Retinopathy of prematurity
- Strabismus
- Amblyopia

Child-focused inpatient care is provided at Mayo Eugenio Litta Children's Hospital, an 85-bed facility on Mayo Clinic's campus in Minnesota.



Mayo Eugenio Litta Children's Hospital in Rochester, Minnesota, offers general, specialty and intensive care for children as well as neonatal intensive care.

Strabismus research

Measuring quality of life, functional improvement

Adult Strabismus 20 (AS-20)

- The Adult Strabismus 20 (AS-20), a questionnaire to assess the impact of strabismus on a patient's health-related quality of life (HRQOL), was developed at Mayo Clinic. Now used internationally, the AS-20 has become the standard measurement tool to assess patients over time or after treatment.
- New Mayo Clinic research, using the AS-20, assessed both psychosocial and functional concerns in adult strabismus patients who do not have diplopia. Results show that in addition to the improvement in psychosocial HRQOL, there were unexpected marked improvements in functional HRQOL. These data indicate functional benefits of adult strabismus surgery, in addition to restoration of normal alignment, even when patients don't have diplopia.
- The AS-20 questionnaire is available without charge for clinical practice or research at http://pedig.jaeb.org/ViewPage.aspx?PageName=Other_Forms.

Diplopia Questionnaire

- Mayo Clinic strabismus surgeons have developed a new quantitative method of assessing and scoring the severity of a patient's diplopia. The Diplopia Questionnaire is useful for clinical assessment of individual patients and for clinical studies where diplopia is an outcome measure.
- The Diplopia Questionnaire is available at http://pedig.jaeb.org/ViewPage.aspx?PageName=Other_Forms.

The genetics of strabismus

Strabismus has a hereditary component, yet little is known about the genetic links to the disease. At Mayo Clinic, researchers are now enrolling two- and three-generation families in a study to better understand the genetic causes of strabismus.

Incidence of adult-onset strabismus

In the first of its kind population-based study of adults diagnosed with strabismus over a 20-year period, a research team at Mayo Clinic quantified the incidence and types of new-onset strabismus. The most prevalent forms were: paralytic (44 percent of cases), convergence insufficiency (16 percent), small-angle hypertropia (13 percent) and divergence insufficiency (11 percent).

Research highlights

- Saunte JP, Holmes JM. Sustained improvement of reading symptoms following botulinum toxin A injection for convergence insufficiency. *Strabismus*. 2014;22:95.
- Martinez-Thompson JM, Diehl NN, Holmes JM, Mohny BG. Incidence, types and lifetime risk of adult-onset strabismus. *Ophthalmology*. 2014;121:877.
- Liebermann L, Hatt SR, Leske DA, Holmes JM. Improvement in specific function-related quality-of-life concerns after strabismus surgery in nondiplopic adults. *Journal of AAPOS*. 2014;18:105.
- Holmes JM, Hatt SR, Bradley EA. Masked Superior Oblique Involvement in Thyroid Eye Disease: Avoiding Postoperative A-Pattern Exotropia and Intorsion. *JAAPOS* 2012;16:280.

AS-20
Date: ___/___/___
MM DD YY

Name: _____

1) I worry about what people will think about my eyes
Never Rarely Sometimes Often Always

2) I feel that people are thinking about my eyes even when they don't say anything
Never Rarely Sometimes Often Always

3) I feel uncomfortable when people are looking at me because of my eyes
Never Rarely Sometimes Often Always

4) I wonder what people are thinking when they are looking at me because of my eyes
Never Rarely Sometimes Often Always

5) People don't give me opportunities because of my eyes
Never Rarely Sometimes Often Always

6) I am self-conscious about my eyes
Never Rarely Sometimes Often Always

7) People avoid looking at me because of my eyes
Never Rarely Sometimes Often Always

8) I avoid looking at others because of my eyes
Never Rarely Sometimes Often Always

"Our AS-20 and Diplopia questionnaires are particularly useful in clinical practice because you can see at a glance what is bothering the patient. They are also great research tools."

— Jonathan M. Holmes, M.D.

Glaucoma: Advancing frontiers in clinical practice and research

Mayo Clinic is a leading center for the management of complex eyes with glaucoma, requiring collaborative care with other subspecialties to provide the best outcomes for patients. In addition, Mayo Clinic has a rich heritage of glaucoma research and continues to investigate and develop novel mechanisms of and therapies for glaucoma.

Clinical practice

Mayo Clinic clinicians have well-established routines to coordinate the care of patients with glaucoma after keratoprosthesis and corneal transplantation, pediatric glaucoma, neovascular glaucoma, uveitic glaucoma, and glaucoma associated with retinal disease and surgery. Patients with complex ocular diseases are managed with traditional incisional procedures, novel surgical techniques and the latest imaging modalities. Mayo uses an integrated care team model to serve patients with all severities of glaucoma.

Novel surgical techniques

In 2006, Mayo Clinic was one of the first centers to offer minimally invasive glaucoma surgery (MIGS). Based on this experience, Mayo Clinic researchers have helped to identify exfoliative glaucoma patients as a group that may be particularly amenable to ab interno trabeculotomy. Mayo Clinic researchers are involved in ongoing studies to understand the mechanisms of action of novel MIGS devices in humans.

Glaucoma surgeons at Mayo Clinic also offer canaloplasty and trabecular bypass stents, based on the needs of the patients. These techniques are being used with positive results in patients with:

- Open-angle glaucoma
- Stable glaucoma who require cataract procedures

Imaging

In addition to standard imaging techniques in glaucoma, Mayo Clinic offers expertise in ultrasound biomicroscopy to objectively diagnose and manage angle-closure glaucoma. Ultrasound biomicroscopy remains the gold standard for evaluating angle configurations and anatomy, and can identify patients at risk through darkroom testing.



Syril K. Dorairaj, M.D., uses ultrasound biomicroscopy to help diagnose angle-closure glaucoma.

Integrated care team model

A physician-led, team-based care model developed at Mayo Clinic serves patients with all severities of glaucoma across a large region. The model is being evaluated for improved adherence to the American Academy of Ophthalmology guidelines. Delivery of this model of care through the Mayo Clinic Health System may serve as a foundation for other institutions nationally.

Glaucoma research

Glaucoma researchers at Mayo Clinic lead their fields in aqueous humor dynamics and the molecular basis of glaucoma. Novel therapies and mechanisms of disease are actively under investigation.

Cerebrospinal fluid pressure and glaucoma

Patients with primary open-angle glaucoma have decreased cerebrospinal fluid pressure compared with the normal population, according to retrospective studies performed by Mayo researchers and collaborators. This suggests that low cerebrospinal fluid pressure may be a risk factor for glaucoma. Mayo researchers have developed an animal model to test this hypothesis and are further investigating the association between cerebrospinal fluid pressure and glaucoma in patients.



Michael P. Fautsch, Ph.D., has developed an animal model to determine the role of cerebrospinal fluid pressure in glaucoma, and is evaluating ATP-sensitive potassium channels as a novel therapeutic target for reducing intraocular pressure.

Novel treatment lowers intraocular pressure, protects optic nerve

A new class of pharmacologic agents might become a novel treatment for lowering intraocular pressure while also providing protection to the optic nerve.

Researchers have studied ATP-sensitive potassium (K_{ATP}) channels and found that K_{ATP} channel openers reduce intraocular pressure in a human organ culture model and *in vivo* animal models. This class of drugs also offers neuroprotective properties.

Aqueous humor and intraocular pressure variability dynamics in humans

Researchers at Mayo have developed novel techniques for measuring the factors that contribute to intraocular pressure (IOP). This includes a novel device for objectively measuring episcleral venous pressure in humans for the first time. Using this device and other Mayo-developed devices for aqueous humor dynamics studies, Mayo researchers have recently uncovered the reasons for the circadian pattern of IOP. They are now focusing on understanding mechanisms of action of existing and novel therapies for glaucoma

Glaucoma-induced blindness decreasing

Mayo Clinic researchers have found that blindness due to glaucoma is declining. Researchers found that the probability of glaucoma-related blindness in at least one eye over 20 years decreased from 26 percent for subjects diagnosed in 1965-1980 to 14 percent for subjects diagnosed in 1981-2000.

Other research

- **Genetics of glaucoma.** Mayo researchers are involved in several multicenter studies to understand the genetic basis of glaucoma. This includes studies investigating primary open-angle glaucoma, exfoliative glaucoma and low-tension glaucoma.
- **New pathway to regulate intraocular pressure.** Mayo researchers recently discovered a new pathway regulating intraocular pressure, involving bicarbonate

and soluble adenylyl cyclase. The pathway is being characterized in animal models to help define new therapeutic targets for treating glaucoma.

Research highlights

- Malihi M, Moura Filho ER, Hodge DO, Sit AJ. Long-term trends in glaucoma-related blindness in Olmsted County, Minnesota. *Ophthalmology*. 2014;121:134.
- Chowdhury UR, Holman BH, Fautsch MP. ATP-sensitive potassium (K_{ATP}) channel openers diazoxide and nicorandil lower intraocular pressure in vivo. *Investigative Ophthalmology & Visual Science*. 2013;54:4892.
- Chowdhury UR, Holman BH, Fautsch MP. A novel rat model to study the role of intracranial pressure modulation on optic neuropathies. *PLOS One*. 2013;18:e82151.

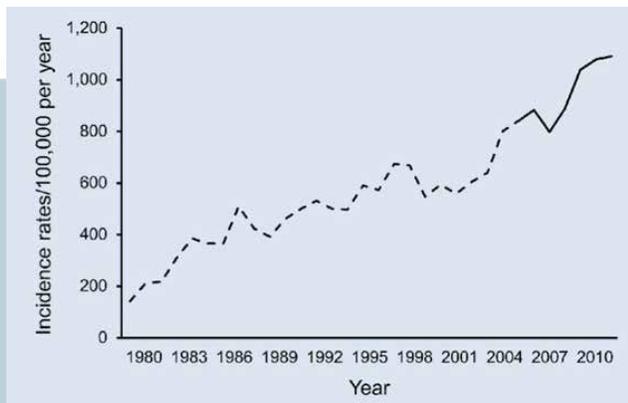
“The risk of blindness from glaucoma has decreased by half over the last 40 years. While this is encouraging, many patients still go blind. This is the motivation for our ongoing efforts to better understand glaucoma and to develop novel medical and surgical therapies.”

— Arthur J. Sit, M.D., glaucoma specialist

New developments in cataract treatment

Mayo Clinic ophthalmologists are:

- Optimizing intraocular lens measurement accuracy with individualized formulation to determine lens power
- Assessing the addition of femtosecond laser-assisted cataract surgery
- Performing intracameral antibiotic injections to decrease the risk of postoperative endophthalmitis



Age- and sex-adjusted rates of cataract surgery among residents of Olmsted County, Minnesota, 1980 to 2011, by year. The solid line represents 2005 to 2011, and the dashed line represents 1980 to 2004.

Going up: Incidence of cataract surgeries

It's not a surprise, but incidence of cataract surgery has steadily increased over 32 years. Additionally, second-eye surgery is performed sooner and more frequently. Between 2005 and 2011, 60 percent of study participants had second-eye cataract surgery within three months of first-eye cataract surgery, more than double the 28 percent rate recorded between 1998 and 2004.

The Mayo Clinic study was conducted using data from the Rochester Epidemiology Project (REP).

Rochester Epidemiology Project

The REP is a research consortium to collect, link and store medical record information for people living in Olmsted County, Minnesota, and southeastern Minnesota. Started in 1966 by Mayo Clinic, this resource includes medical information of nearly all people living in Olmsted County and is a virtually unparalleled resource for epidemiology studies.

The Department of Ophthalmology uses the REP database for retrospective studies to analyze disease trends and clinical outcomes.

Optometry highlights at Mayo Clinic

Scleral lenses

Mayo Clinic optometrists are successfully using commercially available scleral lenses to manage moderate to severe ocular surface diseases and advanced corneal ectatic disease. The scleral lens fitting process can be completed efficiently for most eyes by using diagnostic trial lenses. The service has provided a critical alternative option for many patients with severe or complex diseases of the cornea and ocular surface, by restoring vision or preventing vision loss or loss of the eye.

Researchers are now studying the fitting characteristics and pathophysiologic effects of these lenses, and patient-reported outcomes.

Vision rehabilitation services

Mayo Clinic offers a wide array of integrated services to maximize a patient's remaining vision.

Services are tailored for patients with eye disease, including those with vision and perception concerns due to traumatic brain injury and neurological conditions. Patients benefit from numerous aids and technologies to use their remaining vision, dedicated occupational therapists who educate individual patients to master techniques, and coordinated teamwork between providers in physical medicine and rehabilitation, neurology, ophthalmology, and others.

Research highlights

- Schornack MM, Pyle J, Patel SV. Scleral lenses in the management of ocular surface disease. *Ophthalmology*. 2014;121:1398.
- Siemsen DW, Brown WL. Vision rehabilitation of persons with age related macular degeneration. *Seminars in Ophthalmology*. 2011;26(3):65.

Training the next generation



Resident Victoria I. Lossen, M.D., develops cataract surgical skills in one of Mayo Clinic's three simulation centers.

Residencies

More than 410 physicians have completed the Mayo Clinic Ophthalmology Residency in its 100-year history. The residency includes:

- Clinical and surgical rotations in comprehensive ophthalmology and all subspecialties, staffed by more than 30 full-time faculty
- Chief resident rotations at Mayo Clinic and at the Veterans Administration Medical Center, Minneapolis
- Opportunity to develop academic, educator, and leadership skills, working alongside dedicated mentors
- Participation in professional organizations and specialty meetings providing interaction with colleagues regionally and nationally

"Our residents leave as outstanding ophthalmologists, ready to provide comprehensive care, pursue subspecialty training or academic careers."

— Andrew J. Barkmeier, M.D.



Andrew J. Barkmeier, M.D., consults with residents Sejal R. Amin, M.D., and Aarika L. Menees, M.D. Residents receive high-quality medical and surgical training with a balance of autonomy and supervision.

Fellowships

Fellowship programs at Mayo Clinic include Oculoplastic and Orbital Surgery, Pediatric Ophthalmology and Strabismus, Vitreoretinal Disease and Surgery, and Glaucoma.

Continuing medical education (CME)

Mayo Clinic offers two or more CME courses for ophthalmologists every year. Visit www.Mayo.edu/cme/ to find offerings.

Specialty and community-based care

Rochester, Minnesota. This is Mayo Clinic's largest campus and the foundation of the ophthalmology practice with specialists in every area of eye care and surgery.

Jacksonville, Florida. Mayo Clinic is one of the few health care centers in the Southeast to offer proton beam therapy for ocular cancers. Care providers also have expertise in anterior segment surgery and imaging, oculoplastic and orbital surgery, and vitreoretinal disease and surgery.

Phoenix/Scottsdale, Arizona. Ophthalmologists offer general and advanced ophthalmology diagnostic

procedures and medical, laser and surgical therapies for a wide range of eye disorders. Ophthalmologists have specialized training in glaucoma, retinal diseases, and laser and vitreoretinal surgery.

Mayo Clinic Health System. Mayo-owned clinics, hospitals and other health care facilities serve the health care needs of people in more than 70 communities in Georgia, Iowa, Minnesota and Wisconsin. The community-based ophthalmologists and optometrists, paired with the resources and expertise of Mayo Clinic, allow patients in the region to receive the highest-quality health care close to home.

Mayo Clinic Health System provides care in 70 communities



“With the close collaboration of our colleagues in Rochester, Mayo Clinic Health System ophthalmologists and optometrists provide the best possible care in the most appropriate setting.”

— Miguel E. Mulet, M.D.

Mayo physicians lead top ophthalmology journals

Ophthalmologists share expertise in many ways



George B. Bartley, M.D., editor-in-chief, *Ophthalmology* and Thomas J. Liesegang, M.D., editor-in-chief, *American Journal of Ophthalmology*

The Department of Ophthalmology at Mayo Clinic has a strong leadership heritage with past and current faculty members serving in important internal and external leadership roles. Currently, George B. Bartley, M.D., and Thomas J. Liesegang, M.D., are editors-in-chief of *Ophthalmology* and the *American Journal of Ophthalmology*, respectively.

Ophthalmology faculty members have served in internal senior leadership roles, including chief executive

officers of Mayo Clinic. Other faculty members are leaders in the American Academy of Ophthalmology, the American Board of Ophthalmology, the American Ophthalmological Society and the Minnesota Academy of Ophthalmology. Mayo Clinic ophthalmologists also participate in journal editorial boards, the National Institutes of Health and other study sections, multicenter trial planning and writing committees, and as leaders of multicenter trial networks.

“Serving as a journal editor is just that: service. The overriding goal is to serve society by publishing new research that will improve patients’ lives.”

— George B. Bartley, M.D.

Contact Us

Mayo Clinic welcomes inquiries and referrals, and a request to a specific physician is not required to refer a patient.

Phoenix/Scottsdale, Arizona

866-629-6362

Jacksonville, Florida

800-634-1417

Rochester, Minnesota

800-533-1564

Resources

MayoClinic.org/medicalprofs

Clinical trials, CME, Grand Rounds, scientific videos and online referrals

Sign up for Ophthalmology Update, a free e-newsletter published several times a year for physicians.

Mayo Clinic Ophthalmology Mission

"Improve lives by creating, delivering, and teaching unsurpassed innovative care in a unique integrated and collaborative patient-focused environment."

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