

Clinical Update

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Impact of Glaucoma and its Treatment on the Cornea

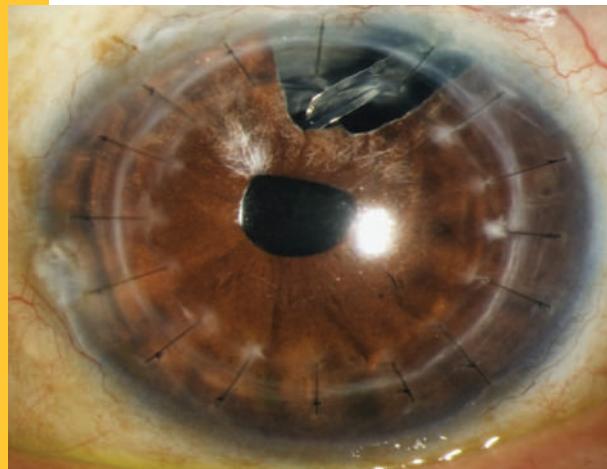


Photo credit: David Hollander, MD, MBA

Clear corneal graft with tube in place

Glaucoma and how it is treated – from topical eye drops to incisional and laser glaucoma surgeries – can negatively affect the cornea, notes JoAnn A. Giaconi, MD, assistant clinical professor in the Jules Stein Eye Institute's Glaucoma Division, who recently conducted a review of the ways in which glaucoma and its treatments affect corneal health.

The complex interrelationship between glaucoma and the cornea is seen in the measurement of intraocular pressure (IOP). Normally, one assumes that a thick cornea overestimates IOP. However, in the case of corneal edema, such as from acutely elevated IOP, excess corneal hydration leads to false underestimations of actual IOP, Dr. Giaconi explains. Corneal decompensation and edema can be the result of glaucoma itself or of glaucoma treatment and its complications. Corneas most at risk are those that already have compromised endothelial function and

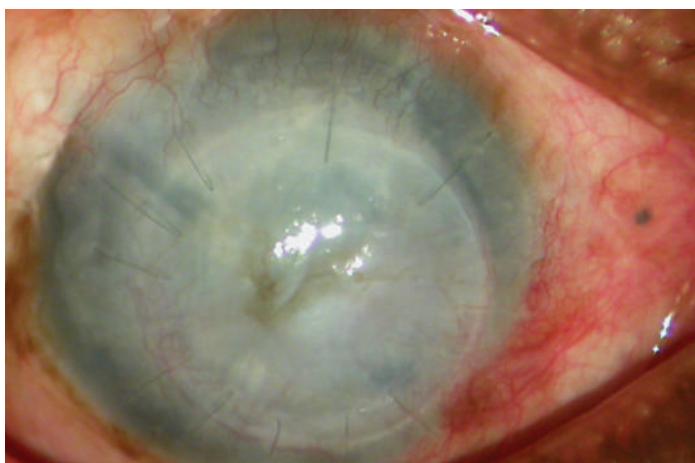
density, which may not be clinically appreciated, Dr. Giaconi notes.

Tube Shunts Increase Risk for Corneal Transplant Failure

A primary concern for the cornea is the presence of tube shunts, which have been associated with an increased risk of corneal transplant failure. "This association raises many questions," says Dr. Giaconi, who conducted a retrospective review of penetrating keratoplasty in eyes with Ahmed valves alongside colleagues in the cornea and glaucoma divisions. "Is it the physical presence of the tube shunt that's causing the problem, is it inflammation induced by the tube shunt surgery, or is it the underlying diseases that are causing these corneal transplants to fail – and, in turn, are these issues that would cause a normal cornea to fail in the presence of a tube?" These questions are important to sort out because tube shunts are being used as first-line surgery by an increasing number of surgeons since the TTVT (Trabeculectomy versus Tube Shunt) trial. Because tube shunts were previously reserved for eyes with refractory glaucomas, where endothelial cell density may be reduced from previous surgical and endothelial insults, research is needed to determine whether tube shunts negatively affect healthy endothelium in native corneas, Dr. Giaconi says. She is currently conducting such a study, comparing the endothelial effects of trabeculectomy with antimetabolite to tube shunts in patients without corneal transplants.

IMPACT OF GLAUCOMA AND ITS TREATMENT ON THE CORNEA

(continued from page 1)



Failed corneal graft with several tubes in place

Photo credit:
David Hollander, MD, MBA

The most damaging effect of incisional glaucoma surgery on the cornea occurs if anterior chamber collapse allows the central cornea to touch the lens postoperatively, which can result in loss of more than half of the endothelial cells. In addition, Dr. Giacconi explains, antimetabolites used as adjunctive treatment for trabeculectomy have the potential to be toxic to the cornea. Both mitomycin-C and 5-Fluorouracil have been found in aqueous humor after being externally applied – a potential concern in eyes with an unhealthy endothelium, Dr. Giacconi says.

In comparison to incisional surgery, laser iridotomy and trabeculoplasty are believed to carry low risk of adverse effects, Dr. Giacconi notes. Although these treatments appear to have little effect on the endothelial density, two case series in Singapore and Japan have shown corneal decompensation after argon laser iridotomy. “The incidence in Asian countries is low, but it’s something to be aware of,” says Dr. Giacconi. “With an eye that has had underlying corneal disease and then high pressure for many days due to angle closure, the iridotomy could trigger further events leading to corneal failure.” Laser

trabeculoplasty poses no known danger to the endothelium.

Topical Medications Pose Danger for Some

Commonly used topical glaucoma medications that contain preservatives can also carry risks to the cornea, Dr. Giacconi notes. While usually not toxic to healthy endothelial cells, carbonic anhydrase inhibitors can lead to decompensation in corneas with compromised endothelium. Benzalkonium chloride, the most common ocular preservative, is toxic to corneal epithelium. Finally, chronic topical medication use may adversely affect corneal innervation, which might explain ocular surface side effects.

“Ophthalmologists should be aware that eye drops can have serious side effects in some people, whether it’s on their quality of life because their eyes are uncomfortable, or because the eye drops contribute to serious corneal problems,” Dr. Giacconi says. “The majority of patients do fine, but some are more sensitive or have underlying disease, and we need to pay close attention to the possibility that topical medications can cause major problems in these patients.”

Acute Angle Closure Attacks May Compromise Cornea

Elevated IOP itself can damage corneal endothelium, Dr. Giacconi notes, but it appears to be the duration of IOP elevation, and not the height of elevation, that is damaging. After 72 hours of acutely elevated IOP, significant endothelial cell losses are seen (average losses of 23-35%).

Hypoxic cell damage is believed to be the culprit in these losses. “In eyes that have suffered a prolonged angle closure attack with resulting endothelial cell damage, initiating subsequent treatment may risk corneal decompensation,” Dr. Giacconi says. “Before performing surgical procedures, it can be useful to measure the endothelial cell density to help stratify risk.” Less clear is the extent to which chronic and moderately elevated IOP affects the endothelium – it may lead to a decrease in endothelial cell density, but this decline does not appear to be clinically significant for most patients, Dr. Giacconi says.

Glaucoma specialists have been especially interested in the importance of the cornea since the Ocular Hypertension Treatment Study showed central corneal thickness to be a risk factor for the development of glaucoma. However, Dr. Giacconi points out, the cornea has always been important as it relates to glaucoma. “A compact and transparent cornea is required for a clear view of the optic nerve, for good visual acuity to perform visual fields, and for accurate measurements of intraocular pressure,” Dr. Giacconi says. “It’s important to take into account the interplay between the cornea, glaucoma, and their treatments.”

Clinical Research Center a Boon to JSEI's Patient-Based Studies

More than a decade after it was established at the Jules Stein Eye Institute (JSEI), the Clinical Research Center continues to serve as a valuable resource for faculty members who are conducting patient-based studies. By providing core services that facilitate the clinical research process – including assistance in preparing grant applications, designing and managing studies, and collecting and analyzing data – the center bolsters JSEI's research enterprise, enabling faculty to focus on the science rather than the business aspects of clinical research. Thanks to this infrastructure, Institute faculty are currently participating in more than 50 clinical studies.

The center's role in promoting important clinical research can be seen in two recent JSEI accomplishments:

Research Collaboration to Study Toxoplasmosis gondii

JSEI is collaborating with Dartmouth University and the Palo Alto Medical Foundation to study the effects of Toxoplasmosis gondii on the eye. *T. gondii* is a leading cause of preventable blindness; however, not everyone who contracts the parasite develops ocular disease, and the severity of ocular disease among those who do varies greatly. This collaboration aims to determine the relative significance of parasite vs. host genetics on ocular disease. Through the sharing of information and specimens, each site will have access to a larger study population coming from geographically distinct locations.

The Clinical Research Center is playing a key role, helping to provide the infrastructure and design

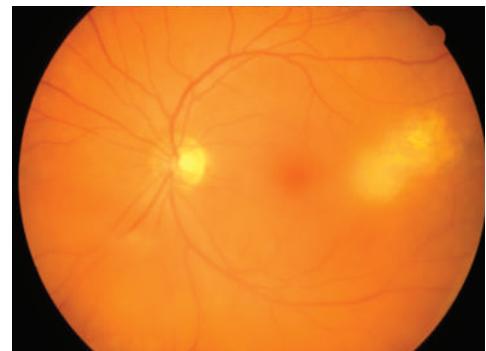
for the project and assisting in its future development and expansion. The study, headed at the JSEI site by Gary N. Holland, MD; Ralph D. Levinson, MD; and Raja Rajalingam, PhD, has the potential to contribute substantially to the prevention of ocular disease caused by *T. gondii* and create a network of investigators who can share information.

American Society of Retina Specialists Meeting: A Showcase for JSEI Clinical Research

The value of the Clinical Research Center could be seen at the 2008 annual meeting of The American Society of Retina Specialists in October, where JSEI residents, fellows, alumni and faculty presented 22 clinical research papers.

"The scale and scope of the retina research completed at JSEI over the last few years would not have been achievable without the Clinical Research Center, which helps us to navigate the complexities of today's research landscape," says Steven D. Schwartz, MD, who oversees most of the clinical research performed in JSEI's Retina Division as the division's chief.

At the meeting, Dr. Schwartz presented the results of a multi-center phase 2 clinical trial evaluating the safety and efficacy of a drug, recombinant microplasmin, in creating a posterior vitreous detachment (PVD) with a single injected dose. The study, facilitated in large part by the Clinical Research Center, yielded surprising results – including macular hole closure without surgery and release of vitreomacular traction by pharmacotherapeutic means. Based on



Recurrent inflammation adjacent to a pre-existing scar in a patient infected with *T. gondii*

these findings, the U.S. Food and Drug Administration has sanctioned pivotal clinical trials at JSEI that may lead to new drug approval.

Among the other presentations at the prestigious meeting:

- Allen Y. Hu, MD, a member of JSEI's senior resident class, presented research in which he reviewed more than 3,000 medical records, collated data, and with the help of Clinical Research Center statistician Fei Yu, PhD, was able to demonstrate that JSEI's infection prevention protocol reduces the risk of 25-gauge vitreous surgery to the same level as that for 20-gauge surgery.
- Pradeep P. Prasad, MD, another senior resident, presented his research demonstrating that new imaging technology available at JSEI can detect retinal neovascularization, retinal capillary non-perfusion and other causes of vision loss with a much greater precision and accuracy than ever before.
- Scott C. Oliver, MD, a recent graduate of the retina fellowship at JSEI and now a faculty member at the University of Colorado in Denver, presented his fellowship research project on Wide Field Angiographic Findings in Diabetic Retinopathy – work with the potential to alter the way diabetic retinopathy is evaluated and managed.

New Faculty Colin A. McCannel, MD



Colin A. McCannel, MD, has been appointed associate professor of Ophthalmology in the Retinal Disorders and Ophthalmic Genetics Division at UCLA's Jules Stein Eye Institute, effective October 15, 2008.

Dr. McCannel received his medical training from the Mayo Medical School in Rochester, Minnesota. He completed his ophthalmology residency training, and two-year vitreoretinal surgery fellowship at the Jules Stein Eye Institute, David Geffen School of Medicine at UCLA.

His fellowship was followed by more than 10 years of service as a consultant and staff vitreoretinal surgeon in the Department of Ophthalmology at the Mayo Clinic. Prior to his recruitment to UCLA, he held the academic title of associate professor of ophthalmology at the Mayo Medical School.

During his time at the Mayo Clinic, Dr. McCannel developed a reputation as a leader in the field of vitreoretinal surgery, and was a choice referral destination for patients with complex vitreoretinal problems. His clinical focus includes the management of vitreoretinal surgical conditions, particularly complex retinal detachments, complications of diabetic retinopathy, macular holes and epimacular membranes (puckers), and age-related macular degeneration.

Dr. McCannel has written more than 40 peer-reviewed articles, served as president of the Minnesota Academy of

Ophthalmology, and is the recipient of several honors, most recently the "Innovation in Education" award from the Mayo School of Continuing Medical Education and the Achievement Award from the American Academy of Ophthalmology.

At the Jules Stein Eye Institute, he will be leading an initiative to implement surgical simulation technology to improve the surgical training of ophthalmology residents and vitreoretinal surgery fellows. As part of this teaching commitment, he will be chief of retina at Harbor-UCLA Medical Center. His other research interests include surgical techniques, epidemiologic studies and outcomes research.

Please join us in welcoming Dr. McCannel back to the Jules Stein Eye Institute.

Patient Appointments and Referrals: (310) 794-9922,
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