

News in Review

COMMENTARY AND PERSPECTIVE

IMMUNOLOGY

Immune Privilege in the Lens? Think Again

CONTRARY TO LONG-STANDING ophthalmic dogma, immune privilege in the crystalline lens does not exist, scientists investigating the intraocular response to eye injury have discovered. Instead, the lens and associated structures should be regarded as immune-quiescent.¹

“While the lens is avascular, it’s not an immune-privileged tissue, and this is a huge sea change in the way we think about things. Everyone, including myself, just presumed that because this tissue was avascular there would be no source of immune cells” to protect the lens, said senior author A. Sue Menko, PhD, at Thomas Jefferson University in Philadelphia.

A surveillance response to corneal injury? In their experiments in mice, Dr. Menko and her colleagues found that the ciliary zonules, which contain a reservoir of two likely immune-mediator molecules, MAGP1 and TSP-1, react to corneal injury by recruiting leukocytes to the lens. Scanning electron microscope images showed that the immune cells travel along the zonular fibers, but they can also migrate onto the capsule and sometimes into the lens itself.

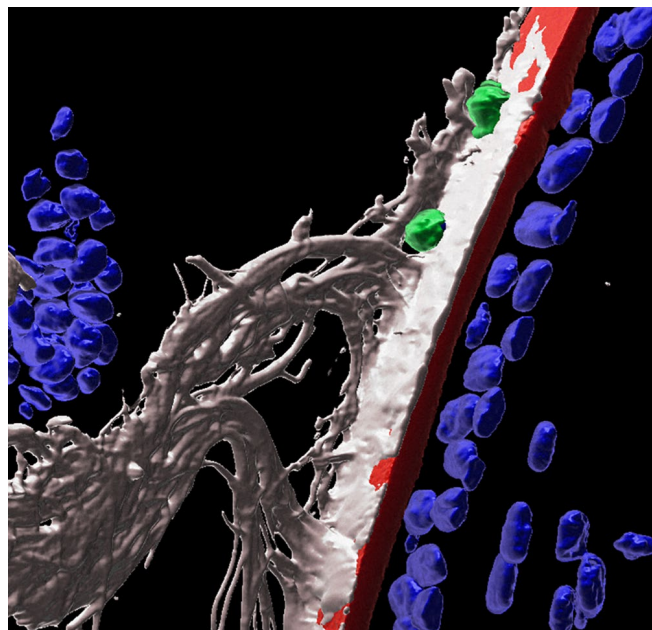
“We imagine what we’re describing is a protective response to the lens, as the cornea is getting repaired. It’s not

an overabundance of immune cells. It looks like a surveillance response,” Dr. Menko said.

Robustness of immune response.

Patient-specific cofactors, such as genetics and concurrent ocular inflammation, appear to influence the robustness of the immune response and its potential to be pathologic, she said.

However, research has shown that some of the recruited immune cells acquire a myofibroblast phenotype and begin producing a fibrotic collagen matrix. Fibrosis triggered by these cells might explain the genesis not only of posterior capsular opacification after cataract surgery but also of anterior subcapsular cataracts associated with corneal wounds, Dr. Menko said. She and coauthor Mary Ann Stepp, PhD, at George Washington University in Washington, D.C., along with Rachel R. Caspi, PhD, of the NEI, are investigating this possibility by studying the movement of autoimmune cells into the lens and resulting cataract formation in patients with inflammatory conditions such as uveitis. They hope to publish their results within the next year, she said.



RESPONSE. At day 1 following corneal wounding, 3D surface structure imaging shows immune cells (CD45+, green) migrating within ciliary fibrils (MAGP1+, white) that extend along the surface of the matrix capsule that surrounds the lens (perlecan+, red). The ciliary zonules (white) are also evident, as are the nuclei (blue).

Obvious in hindsight? The researchers’ paradigm-shifting conclusion that the lens does not have immune privilege might seem surprising at first—but it may appear less startling in retrospect, Dr. Menko said. “In science, sometimes we believe things because they’re dogma, but if you think about it you realize that those things don’t make sense,” she said.

“We began looking for signs of an immune response to the lens because it just seemed against all logic that you’d have a tissue that is so crucial throughout a lifetime, but which evolved in such a way that the body would not try to protect or repair it.” —Linda Roach

1 DeDreu J et al. *FASEB J*. Published online May 25, 2020.

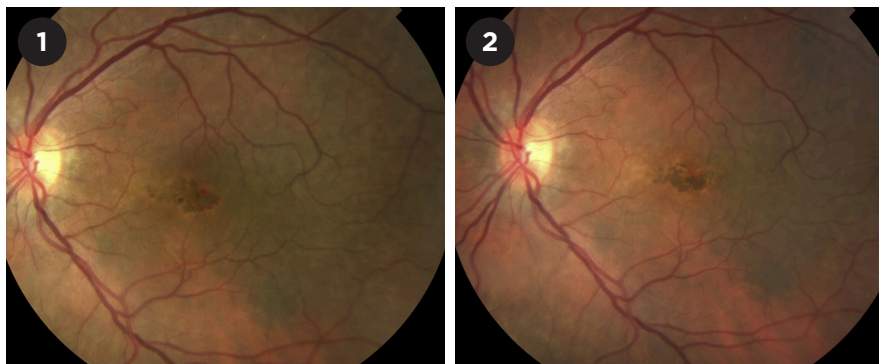
Relevant financial disclosures—Dr. Menko: None.

Beware Burn Risk With Dual-Mode Laser Systems

DESPITE WARNINGS, INJURIES WITH dual-mode laser capsulotomy/selective laser trabeculoplasty (SLT) laser systems continue to occur. A team of retina subspecialists recently presented a case of a 65-year-old woman whose left macula was scarred when capsulotomy was attempted using the system's SLT mode.¹

This is not the first publication to warn of the potential for serious injury when dual-mode capsulotomy/SLT systems are operated in the wrong mode.² However, published reports of misuse have been scarce. Moreover, gag rules imposed in malpractice settlements prohibit publication of cases, including two other current cases known to the authors.¹

Lack of awareness. “Many clinicians are unaware of and often surprised to



INJURY. (1) Baseline fundus photograph shows foveal retinal pigment epithelium (RPE) mottling from multiple laser lesions. (2) Three months later, traumatic RPE hyperplasia is more prominent, while surrounding hemorrhages have resolved.

learn of this serious recurrent injury,” said coauthor Martin A. Mainster, PhD, MD, at the University of Kansas School of Medicine in Kansas City. “The SLT mode of a capsulotomy-SLT laser system can cause devastating, permanent foveal damage when it’s used erroneously in an attempted capsulotomy.”

Current case report. Dr. Mainster and his colleagues described the case of a woman who underwent cataract surgery—and then, a year later, required

capsulotomy for each eye. Although the treatment of her right eye was successful, the capsulotomy of her left eye failed, and she reported severe vision loss in that eye one week later.

She was referred to the authors, and imaging revealed permanent macular and extramacular photothermal and photomechanical damage. The best-corrected visual acuity (BCVA) in her left eye declined from 20/30 to 20/400. Within three months, the BCVA in that

ONCOLOGY

How to Monitor Adult Retinoblastoma Survivors

IMPROVEMENTS IN THE TREATMENT AND CARE OF retinoblastoma (RB) have resulted in a growing population of adult survivors of the disease. But how should they be managed, particularly given their increased risk of developing additional cancers in adulthood?

An international interdisciplinary panel was convened to review the science and generate recommendations for long-term follow-up for adult survivors of heritable RB, which is associated with mutations in the *RB1* gene. “After abstract and full-text review of 139 papers, we chose 37 papers for detailed data abstraction to quantify risk and evidence regarding surveillance,” said coauthor Emily S. Tonorezos, MD, MPH, at Memorial Sloan-Kettering and Weill Cornell Medical College in New York City.

Risk of subsequent cancers. Adult RB survivors are at risk of developing additional neoplasms, particularly bone and soft tissue sarcomas, melanoma, and uterine leiomyosarcoma.

In addition, the panel noted, those with a history of radiotherapy are at increased risk of brain and central nervous system tumors.

Recommendations for surveillance. The panel, which included ocular oncologists, issued the following recommendations for follow-up:

Strong. An annual skin examination, especially among those with dysplastic nevi, is strongly recommended.

Moderate. The panel issued a moderate recommendation in favor of the following: 1) an annual history and physical exam with attention to bony structures; and 2) prompt evaluation of signs and symptoms that involve the head and neck, such as persistent sinusitis, pain, or skeletal tenderness.

Avoid. The panel advised against the following: 1) routine surveillance for uterine leiomyosarcoma; 2) an annual thyroid ultrasound to screen for thyroid cancer; and 3) additional surveillance (beyond what is recommended based on local guidelines) for bone, brain, breast, colorectal, hematologic, or lung cancers, “where risk is uncertain or benefit cannot be anticipated.”

Uncertain. The panel also noted that “Consideration should be given in favor of surveillance modalities that do not include ionizing radiation, although evidence for or against this recommendation in heritable RB survivors is lacking.”

—Arthur Stone

1 Tonorezos ES et al. *Ophthalmology*. Published online May 15, 2020.

Relevant financial disclosures—Dr. Tonorezos: None.

eye was count fingers at 4 feet, and she was informed of her poor visual prognosis. The diagnosis: laser maculopathy. “SLT mode laser pulses passing through a patient’s pupil reach and destroy retinal tissue,” Dr. Mainster said.

How these accidents occur. These incidents occur when the laser system is inadvertently turned on in its SLT mode or left on after an SLT procedure for others to use, Dr. Mainster said. He explained, “A clinician performing a capsulotomy might confuse the SLT mode’s single-spot capsular reflection with the in-focus fusion of the capsulotomy mode’s multiple-spot-aiming interface.”

How to prevent further incidents. To prevent similar iatrogenic injuries, the authors recommend taking the following steps:

- Have clinicians—not technicians—select the laser delivery mode.
- Double-check the laser mode before treating.
- Enhance engineering controls, such as different-colored backgrounds for each laser mode on a touch screen.
- Require entry of a personal identification number by clinicians—not technicians—to acknowledge a warning before the SLT mode can be used.
- Affix a conspicuous note to every machine warning users never to attempt capsulotomy when the device is in SLT mode.

Ounce of prevention. Administrative and engineering controls could have prevented the woman’s injury, but such controls were either absent or ignored, the authors wrote.

With regard to treatment, Dr. Mainster said that treatments such as anti-inflammatory and neuroprotective drugs are usually ineffective for severe macular injuries. As he noted, “The best way to treat a laser injury is to prevent it.”
—Miriam Karmel

1 Ledesma-Gil G et al. *Ophthalmology*. Published online May 17, 2020.

2 Liyanage SE et al. *Br J Ophthalmol*. 2014;98(1):141-142.

Relevant financial disclosures—Dr. Mainster: Ocular Instruments: C.

RETINA

Topical Tx for Macular Holes?

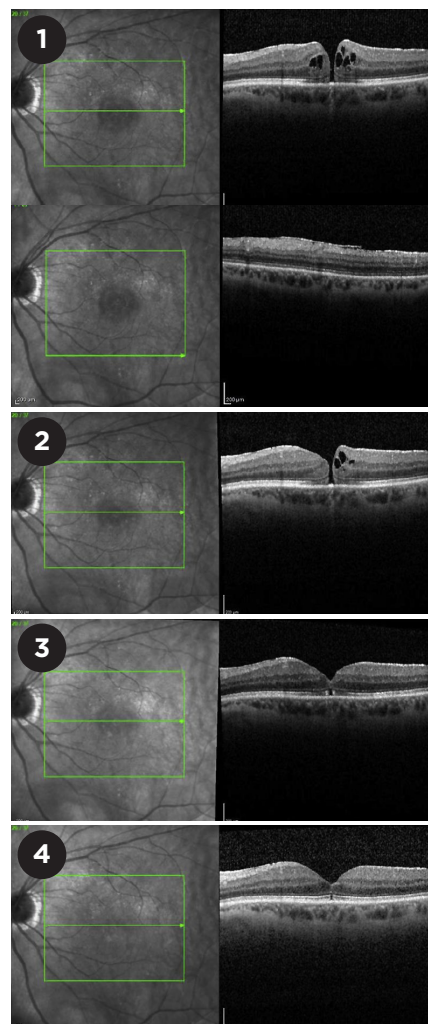
TOPICAL THERAPY MAY BE ABLE TO close small secondary macular holes and potentially eliminate the need for surgery.¹

Study specifics. This retrospective analysis involved nine cases of topically treated, secondary full-thickness macular holes (FTMH). Eight of the eyes (89%) had successful hole closure and resolution of their associated cystoid macular edema. The hole in the ninth eye, in a patient with topically treated bilateral holes, did not close after six weeks of topical therapy, and the patient was then lost to follow-up.

All patients received corticosteroid drops (difluprednate ophthalmic emulsion 0.05%). Six eyes also received a topical carbonic anhydrase inhibitor (dorzolamide 2% or brinzolamide 1%), and two eyes received a nonsteroidal anti-inflammatory drug (bromfenac 0.07%). The average initial hole diameter was 79.6 μm (range, 44 to 132 μm), and the average time until closure was six weeks (range, two to 19 weeks).

A paradigm shift? “The standard of care for primary macular holes caused by vitreomacular traction is vitreoretinal surgery,” said coauthor John Niffenegger, MD, at Retina Associates of Sarasota, Florida. “In cases of small holes (<250 μm) that are secondary to something other than vitreomacular traction, patients often would like to avoid surgery, and interest in addressing their problem with topical therapy has been increasing.”

The outcomes of this study support a role for comprehensive ophthalmologists to consider medical therapy for patients who have small, secondary macular holes, Dr. Niffenegger said. “With spectral-domain optical coherence tomography fairly available now, it’s easier for a comprehensive ophthalmologist to determine the hole’s size and etiology,” he said. “So, in the absence of vitreoretinal traction, it would be reasonable for them to consider a



OCT SEQUENCE. (1) Cystoid macular edema, high retinal surface reflectivity from epiretinal membrane, and a FTMH. The patient was started on difluprednate three times daily. (2) At four weeks, the hole is closed, and the drops are reduced to twice daily. (3) At 22 weeks, the hole remains closed, the outer retinal break is decreased, and treatment is discontinued. (4) At 81 weeks, the hole remains closed without drops.

trial of topical therapy as they refer the patient for vitreoretinal consultation or await scheduling for macular hole surgery. You might be able to spare these patients the expense and possible complications of surgery.”
—Linda Roach

1 Niffenegger JH et al. *Ophthalmol Retina*. Published online Jan 28, 2020.

Relevant financial disclosures—Dr. Niffenegger: None.

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