

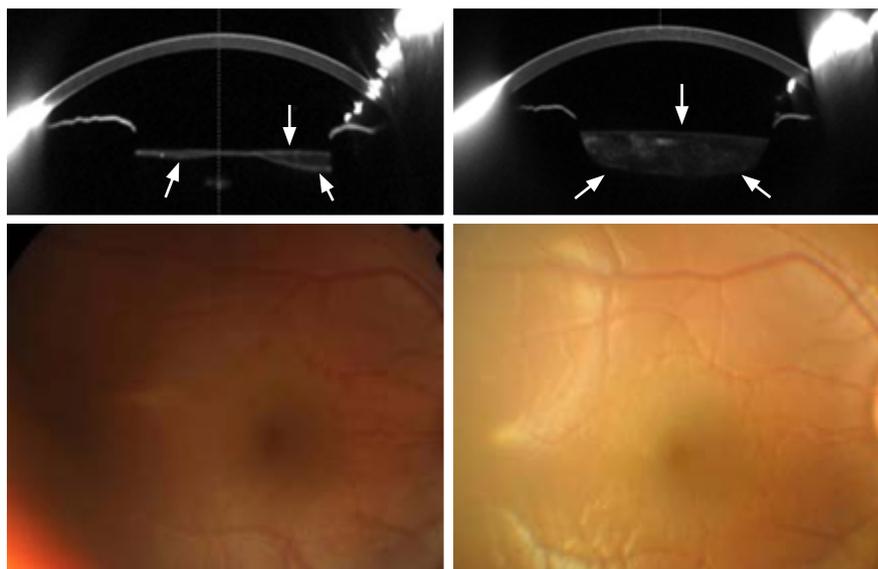
News in Review

COMMENTARY AND PERSPECTIVE

Novel Method for Lens Regeneration

IN A MATTER OF WEEKS, LOWER vertebrates such as lizards and frogs can regenerate a lost limb or tail—fish can regrow an entire eye or even half a heart or brain. Now, U.S. and Chinese researchers have discovered a novel method to harness the regenerative potential of the human lens by using endogenous lens epithelial stem cells (LECs). Their method has been used to regrow a new, functioning lens in 24 eyes of 12 children under age 2 whose congenital cataracts were removed.¹ Because the patient's native LECs are used, this technique theoretically avoids the risks of infection, tumor formation, and immune rejection linked to pluripotent stem cells.

Standard procedures damage LECs. Early clues to this capability emerged from observing the unwanted aberrant lens regeneration that occurs after removal of congenital cataracts, said coauthor Kang Zhang, MD, PhD, chief of ophthalmic genetics at University of California, San Diego, School of Medicine. The standard capsulorrhexis and lensectomy procedure subjects these eyes to insults from large incisions, he said, and removes more than half of the lens stem cells, increasing the risk of scarring and inflammation. "Lacking the proper environment and support," he said, "the remaining LECs randomly regenerate into disorganized lens tissue known as posterior capsular opacity, which requires a laser procedure to



LENS REGROWTH. (Left panels) Treated eye 3 months after surgery. The regenerating lens tissue grew from the periphery of the capsular bag toward the center; the bag was only partially filled and the lens appeared spindle shaped. The fundus was clearly visible on ophthalmoscopy. (Right panels) At 6 months, the capsular bag was filled with regenerated lens tissue and appeared biconvex. The fundus could be seen clearly using an ophthalmoscope with an 18-D lens.

remove it and open the posterior capsule."

New method spares LECs, allows regrowth. Dr. Zhang and colleagues developed and tested a minimally invasive method to remove the cataract while preserving the lens epithelial stem cells, first in rabbits and macaques and then in humans. It involved creating a 1.5-mm self-healing incision in the periphery of the anterior capsule—out of the visual axis—and removing the soft cataractous lens. "This preserved the integrity of the lens capsule and a sufficient number of stem cells to proliferate and differentiate into a new functioning lens, along with the support of growth factors," said Dr. Zhang.

In the study, all 12 human infants regenerated a clear, biconvex, functioning lens at 3 months, and there was no sign of cloudiness or significant complications at 6 months. Refractive

power increased significantly from the first week to 8 months after surgery, at which time the average central thickness of the regenerated lens was comparable to that of a native lens.

In comparison, 25 infants who had a large capsulorrhexis and standard surgery in both eyes experienced a higher incidence of postsurgical inflammation, early-onset ocular hypertension, and increased lens clouding. Moreover, removing the whole lens—a standard procedure for infants under age 2 with congenital cataracts—disrupts ocular development and puts the child in need of frequent refractions and at high risk for complications such as glaucoma.

Caveats and challenges. Dr. Zhang cautions that this preliminary research needs independent replication with larger numbers of patients and longer follow-up. In addition, he cannot exclude the possibility that the regener-

ated lens may become cloudy again. “If the cataract is caused by an inherited mutation, we have not solved the root problem,” he said.

Earlier research by Dr. Zhang and colleagues found that an endogenous molecule called lanosterol may prevent protein aggregation.² He is optimistic that lanosterol might prove useful in the regenerated lens. “Regardless, keeping the lens clear for even a year or two buys an infant precious time for visual development,” he said, “and gives the ophthalmologist a chance to later insert an intraocular lens, if needed, during a preferable time.”

Future areas of research. The investigators are also turning their attention to age-related cataracts, looking for ways to overcome the reduced regenerative capacity in older adults, as well as to minimize damage to lens stem cells by using smaller incisions and lower-energy removal of cataracts.

—Annie Stuart

1 Lin H et al. *Nature*. 2016;531(7594):323-328.

2 Zhao L et al. *Nature*. 2015;523(7562):607-611.

Relevant financial disclosures: Dr. Zhang—None.

ETHNICITY & EPIDEMIOLOGY

Chinese American Eye Study

WHEN IT COMES TO THE PREVALENCE

of age-related macular degeneration (AMD) and diabetic retinopathy (DR), all people are not created equal.

More evidence for this truism of ophthalmic epidemiology emerged recently when investigators in the Chinese American Eye Study (CHES) reported the results of extensive clinical examinations and retinal photography in more than 4,000 participants aged 50 and older.^{1,2} The CHES is the largest-ever ophthalmic study in Americans of Chinese ancestry, the authors wrote.

Participants were drawn from Monterey Park, Calif., a Los Angeles–area community with a sizable and stable population of Chinese Americans. A large majority of them were first-generation immigrants, primarily from mainland China.

Following are some key findings from this population-based cross-sectional study, which was funded by the National Eye Institute.

AMD results. The study detected 320 cases of any type of AMD, for an overall age-adjusted prevalence of 8.1% (95% CI, 7.2%-9.0%). Estimates of the disease prevalence in Chinese individuals living in urban and rural China and urban Taiwan range from 3.0% to 9.2%, suggesting that environmental or behavioral factors could be influencing AMD risk in Chinese Americans, said Rohit Varma, MD, PhD, chief investigator for CHES.

Early disease. In 306 of the cases, the disease was classified as early AMD, for an age-adjusted prevalence of 7.8% (95% CI, 6.9%-8.7%).

Advanced AMD. There were 14 cases of advanced AMD, for an age-adjusted prevalence of 0.4% (95% CI, 0.2%-0.6%). This is similar to the levels found in people of African descent by the Barbados and Baltimore eye studies and lower than what has been reported among Latinos and non-Hispanic white people, the researchers noted. Of the 14 advanced cases in CHES, 86% had neovascular AMD and 14% had geographic atrophy.

The influence of age. In an analysis of the data by 10-year age groups, the

REFRACTIVE RESEARCH

Phakic IOL: 10-Year Safety Data

During the 10 years after phakic intraocular lens (PIOL) implantation, visually significant cataracts developed in 18.3% of the high myopes implanted with the device, a long-term outcomes study has found.¹

The Swiss researchers analyzed the refractive and safety outcomes from 133 consecutive surgeries (1998-2004) in which the V4 version of the Visian ICL (Implantable Collamer Lens; Staar Surgical) was implanted. This lens is the only sulcus-supported PIOL approved by the U.S. Food and Drug Administration.

What to watch for. Although the PIOL's long-term safety and refractive results were generally good, with stable endothelial cell counts, the data also showed that patients should be warned about 2 potential complications: cataract and ocular hypertension, the authors reported. The analysis found that after 10 years of follow-up:

- Lens opacities were present in 54.8% of the eyes (95% CI, 44.7%-63.0%).

- Phacoemulsification to remove visually significant cataracts was required in 18.3% of the eyes (95% CI, 10.1%-25.8%). This compared to 4.9% at year 5.
- Although no cases of elevated intraocular pressure had been observed at the 5-year follow-up, at 10 years, 12 eyes (12.9%; 95% CI, 5.6%-19.6%) had developed ocular hypertension requiring medication.

Long-term follow-up required. “Phakic lenses are the best refractive surgical option today to correct high ametropia. But our study shows that these patients must have careful follow-up forever,” said coauthor François Majo, MD, PhD, professor and head of refractive surgery at the Jules-Gonin Eye Hospital at the University of Lausanne.

Dr. Majo said the study's findings will enable refractive surgeons to better inform PIOL candidates about the potential risks. “This is important information to give to the patient before the surgery. But, surprisingly, in my experience it does not change their decision,” he said.

—Linda Roach

1 Guber I et al. *JAMA Ophthalmol*. Published online March 3, 2016. doi:10.1001/jamaophthalmol.2016.0078.

Relevant financial disclosures: Dr. Majo—None.

investigators found a direct correlation between older age and greater AMD prevalence. In all age groups, however, men had a higher rate of AMD than women. AMD prevalence ranged from 5.8% in subjects 50 to 59 years old to 17.6% in those 80 years or older. For the same 2 age groups, respectively, the prevalence rates were 9.8% and 32.4% for large drusen, 27.6% and 58.6% for soft drusen, and 4.1% and 7.2% for retinal pigment abnormalities.

Diabetes and retinopathy. Blood testing revealed that 736 participants (16.1%) had type 2 diabetes; 35.8% of this subgroup had DR (95% CI, 32.1%-39.6%). This compares to a 46% rate of DR previously reported among Chinese with type 2 diabetes in rural China, and 48% in Latinos living in Los Angeles, the CHES investigators wrote.

Participants with diabetes were 3 times more likely (6.7% vs. 2.2%; $p < .001$) than those without diabetes to have significant visual impairment, defined as best-corrected visual acuity worse than 20/40 in the better-seeing eye. The causes of the impaired vision were cataracts and macular edema.

Takeaway messages. “This study sounds a clarion call for all eye care providers to be aware of the higher relative prevalence of wet AMD compared with dry AMD in those of Chinese ancestry and to provide the available treatments such as anti-VEGF injections and laser therapies,” said Dr. Varma, director of the University of Southern California Roski Eye Institute. “And while [diabetic eye disease is] not as prevalent as we see in the Latino community, we also need to be aware of addressing those Chinese Americans with diabetes to prevent diabetic retinopathy and the onset of significant visual impairment.” —*Linda Roach*

1 Varma R et al. *JAMA Ophthalmol*. Published online April 7, 2016. doi:10.1001/jamaophthalmol.2016.0588.

2 Varma R et al. *JAMA Ophthalmol*. Published online April 7, 2016. doi:10.1001/jamaophthalmol.2016.0445.

Relevant financial disclosures: Dr. Varma—National Eye Institute: S.

RECURRENCE & CHRONICITY

HZO: A Painful Problem

HERPES ZOSTER OPHTHALMICUS (HZO) may not be the monophasic illness that ophthalmologists learned about in medical school. A hospital-based epidemiology study supports more recent data showing that recurrent and chronic HZO are much more common than previously thought.¹

Study details. The researchers performed a retrospective medical record review of data in the Broward and Miami Veterans Affairs Healthcare System from 2010 through 2014 and studied 90 patients who had a clinically documented episode of HZO, consisting of vesicular rash and pain in the dermatome of the ophthalmic division of cranial nerve V (V1). Within that group, 62 patients had HZO with eye involvement, as diagnosed by an ophthalmologist.

Recurrence rates for HZO with either rash or eye disease were 8% at 1 year, 17% at 3 years, and 25% at 5 years. The presence of ocular hypertension or uveitis, which often occurred together, increased the risk of recurrent and chronic HZO. In addition, those with active eye disease for more than 90 days after initial presentation were more likely to experience recurrence. Immune status, gender, age, and vaccination status were not significant risk factors for recurrence or chronicity.

More questions. Although methodologies differed, the Florida study had findings similar to those of an Italian study,² which included a population that more equally represented both sexes compared with the predomi-

nantly male VA group, said Anat Galor, MD, MSPH. “Seeing VZV as no longer a monophasic illness, however, creates more questions than it answers: Is there a role for chronic antiviral therapy similar to that used with herpes simplex virus? Would this reduce the frequency of complications? Would increased VZV vaccination after onset of HZO change the frequency of recurrence and chronic disease?”

Rethinking roles. The study was not designed to answer these questions, she said, so it is too soon to recommend changes in clinical practice. However,



HZO. Eye involvement in herpes zoster can be a serious problem, especially when recurrent or chronic.

given the study findings, as well as the fact that 10% of patients have herpes zoster affecting the V1 distribution, she recommended that ophthalmologists play a more assertive role. “We can educate patients about the potential value of the vaccine as well as the potential risks of recurrence and chronic disease.”

This is particularly critical, she said, given the disease’s high morbidity, including the complication of postherpetic neuralgia, which is a leading cause of suicide in patients older than 70 with chronic pain. —*Annie Stuart*

1 Tran KD et al. *Ophthalmology*. Published online April 8, 2016. doi:10.1016/j.ophtha.2016.03.005.

2 Miserocchi E et al. *Cornea*. 2014;33(6):565-570.

Relevant financial disclosures: Dr. Galor—None.

See the financial disclosure key, page 10. For full disclosures, including category descriptions, view this News in Review at www.aao.org/eyenet.