News in Review

COMMENTARY AND PERSPECTIVES

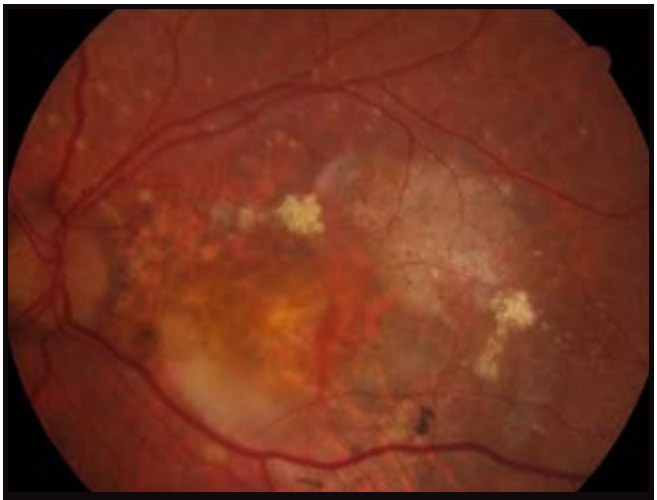
Allergy May Protect Against AMD

The body's immune system has produced another surprise. European researchers found that a personal history of allergy may confer a protective effect against development of age-related macular degeneration (AMD).[1]

"We were interested in nongenetic risk factors for AMD," said lead investigator Sascha Fauser, MD, professor of ophthalmology at the University Hospital of Cologne in Germany. "The involvement of the complement system and inflammation in AMD led us to investigate the association with allergy, as both the complement system and inflammation have connections with allergy."

The study. The researchers evaluated 3,585 individuals who were included in the European Genetic Database (1,878 in Cologne and 1,707 in Nijmegen, the Netherlands). All told, 864 of the German participants and 938 of the Dutch participants had AMD, with a subset of 495 German and 664 Dutch individuals determined as having late AMD (defined as AMD with subfoveal geographic atrophy and/or choroidal neovascularization in at least one eye). The remainder served as controls.

The participants filled out questionnaires that asked about their history of smoking, use of corticosteroids, and history of allergy. The latter was characterized as being triggered by pollen, drugs, specific food items, house dust mites, or other allergens. In addition, blood levels of the complement components C3d and C3 were measured, and the C3d:C3 ratio—a measure of the systemic level of complement activation—was calculated.



WET AMD. One study shows that a history of allergy may protect against the development of age-related macular degeneration.

Using logistic regression analysis, the researchers found that a positive history of allergy showed a strong protective effect against the development of AMD and an even greater effect against the development of late AMD. This effect was detected for all subtypes of allergy, irrespective of the triggering allergen.

On the other hand, individuals with AMD had a higher median C3d:C3 ratio than did those who served as controls. "Allergy itself was not associated with increased complement activation," the authors reported. "These results indicate that increased complement activation may not be the connecting marker between

SASCHA FAUSER, MD

AMD and allergy."

"I was surprised by the magnitude" of the protective effect of allergy against AMD, Dr. Fauser said. "I expected a slight influence, at most. And I guessed wrong about the direction: I thought it would be negative instead of protective."

Future focus. In their discussion of the findings, the researchers note that it is possible that allergy may mediate some of the factors that contribute to AMD. Alternatively, it may be that allergy itself is not protective against AMD; instead, it may be that the susceptibility for allergy and the protection against AMD share a common cause.

A significant limitation of the study is that the association was with a history of allergy, not with allergy itself, as participants self-reported their experience of allergy and did not undergo formal allergy testing.

Nonetheless, the finding is tantalizing enough that Dr. Fauser's team plans to continue following this new trail. "We are currently looking into various cytokines, growth factors, and complement components that may mediate this protective effect," she reported.

—Jean Shaw

1 Ristau T et al. *Invest Ophthalmol Vis Sci.* 2014;55(1):210-214.

***Dr. Fauser** reports no related financial interests.*

Cornea Report

Ganciclovir Gel Treats Zoster Pseudodendrites

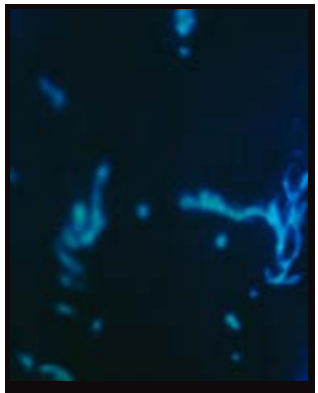
Topical ganciclovir 0.15 percent gel effectively treated epithelial lesions in four immunocompetent patients who failed to respond to antiviral treatment with oral valacyclovir.[1] The patients, diagnosed with herpes zoster ophthalmicus (HZO) epithelial pseudodendrites, were treated at the cornea and refractive surgery service at the Massachusetts Eye and Ear Infirmary between 2011 and 2013.

Ganciclovir, which inhibits viral DNA replication, was approved by the FDA in 2009 for acute herpetic disease including herpes simplex, herpes zoster, cytomegalovirus, and other herpetic conditions. It had not previously been used to treat HZO infectious lesions, said Deborah Pavan-Langston, MD, FACS, professor of ophthalmology, Harvard Medical School. She specializes in diagnosis and management of herpetic disease.

Origin. The retrospective interventional case series of four patients was inspired by Dr. Pavan-Langston's earlier success with ganciclovir gel to treat a case of cytomegalovirus hypertensive uveitis that had failed to respond to repeated systemic antiviral therapies.[2] On the heels of that success, she elected to use the gel to treat a 61-year-old female patient with multiple zoster dendritic ulcers who had failed to respond to full-dose oral valacyclovir therapy. At the one-week exam, the infection was completely healed.

Over time, three similar zoster dendrite patients responded successfully to topical ganciclovir gel, after failing current or very recent systemic antiviral treatment. Though one patient relapsed several months after initial success, a second round of topical ganciclovir gel eradicated that recurrence.

Treatment. The regimen involved application of topical ganciclovir 0.15 percent gel, five times a day until the lesions healed (in about seven to 10 days). As a precaution, treatment was continued at twice daily for two to four weeks.



DENDRITES. Herpes zoster ophthalmicus epithelial pseudodendrites.

DEBORAH PAVAN-LANGSTON, MD, FACS

Dr. Pavan-Langston said that there has been no consensus on best treatment of zoster dendritic ulcers because therapeutic response is so variable and unpredictable. But in the paper reporting their successes, the study authors noted that ganciclovir gel appeared more effective than oral antivirals in eradicating corneal HZO infectious lesions.

Trifluridine. The authors added that ganciclovir gel is preferable to trifluridine (TFT), the other topical antiviral used for herpetic eye diseases in the United States. They said TFT's use is limited by ocular toxicity, allergic reaction to the preservative thimerosal, and low corneal penetration. "Ganciclovir," they said, "acts only on infected cells and thus has low toxicity and better efficacy."

Because of the rapid and reliable response in her four patients, ganciclovir is now Dr. Pavan-Langston's treatment of choice in recurrent dendrites. However, in the case of an initial attack of HZO, with or without dendrites, she still uses oral famciclovir or valacyclovir. "These almost invariably resolve with systemic treatment," she said.

The authors may eventually publish a longer term and larger study. In the meantime, Dr. Pavan-Langston said, "We recommend the use of ganciclovir gel as therapy for recurrent zoster dendrites or those resistant to systemic therapy during an initial attack of shingles."

—Miriam Karmel

1 Aggarwal S et al. *Cornea.* 2014;33(2):109-113.
2 Pavan-Langston D et al. *Ophthalmology.* 2012;119(11):2411.

***Dr. Pavan-Langston** reports no related financial interests.*

Technology Update

A More Portable OCT

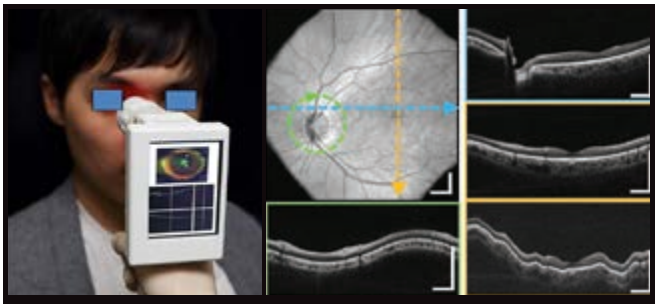
A team of researchers has developed the first handheld OCT that captures widefield 3-D volumetric images of the retina.[1] The instrument generates OCT fundus images and extracts cross-sectional images that are precisely registered to fundus features. Volumetric data also enable screening applications such as automated detection of diabetic retinopathy or glaucoma.

The design combines swept source OCT with novel laser and motion correction technology to achieve the goal of volumetric OCT, said study coauthor James G. Fujimoto, PhD, Elihu Thomson Professor of Electrical Engineering and Computer Science, MIT. He reports that the compact device images 10 times faster than commercially available handheld instruments.

But this promising advance has several hurdles to overcome before moving from bench to clinic. Commercial feasibility will depend on finding a market large enough to compensate for the high cost of engineering development, clinical validation, and regulatory approval, according to Dr. Fujimoto.

Still, he looks forward to a future when these screening technologies are in widespread use. "The ultimate goal is to enable clinical specialists or even primary care physicians to have access to OCT," he said. "OCT screening could reduce unnecessary loss of vision and improve the quality of life for major sectors of the population."

—Miriam Karmel



HOW IT WORKS. The patient looks at a fixation light and the operator aligns the instrument using a built-in iris camera and real-time OCT aiming scans. The instrument acquires multiple OCT raster scans, which are motion corrected and merged to generate a 3-D volumetric OCT data set. The axial scan rate is 350 kHz.

1 Lu CD et al. *Biomedical Optics Express.* 2014;5(1):293-311.

***Dr Fujimoto** receives royalties from intellectual property owned by MIT and licensed to Carl Zeiss Meditec and Optovue, and he has a financial interest in Optovue.*

Pediatric News

Bevacizumab by IV for Optic Pathway Gliomas

A case series has shown that intravenous administration of bevacizumab restored vision in four children with optic pathway gliomas (OPGs).[1] The antiangiogenic agent targets vascular endothelial growth factor (VEGF) in these low-grade tumors.

Robert A. Avery, DO, MSCE, principal investigator, said that children at his institution typically undergo standard chemotherapy and some second-line chemotherapy before bevacizumab is considered. The duration of the frontline chemotherapy is typically 12 to 18 months but can vary depending on treatment response.

"Some physicians may use bevacizumab earlier if a child is demonstrating progressive vision loss during their current chemotherapy," said Dr. Avery, assistant professor of neurology, ophthalmology, and pediatrics at Children's National Medical Center, Washington, D.C. "Progressive vision loss after failing first- and sometimes second-line chemotherapy may also be an indication to try bevacizumab." Radiographic and clinical responses can be seen as early as six to 12 weeks.

The four young patients in the study received bevacizumab 10 mg/kg per dose every two to three weeks for several months. All have remained stable for more than one year.

Dr. Avery noted that although three patients experienced adverse effects that required dose-interval modifications (extending treatment from every two to every three weeks), retreatment has been successful.

He added that proteinuria and hypertension are relatively minor and typically reversible side effects of bevacizumab treatment. More serious adverse events that may occur mainly, but not exclusively, in adults include intracranial hemorrhage and thromboembolism. None of these more serious complications were encountered in this study, he said.

"We need to be cautious in our use of bevacizumab in children with OPGs, given the uncertainty about potential long-term side effects," Dr. Avery said. "The standard of care/first-line treatment should remain a carboplatin-based regimen until additional clinical trials can establish the appropriate timing and safety of bevacizumab."

—Marianne Doran

1 Avery RA et al. *JAMA Ophthalmol.* 2014;132(1):111-114.

***Dr. Avery** reports no related financial interests.*

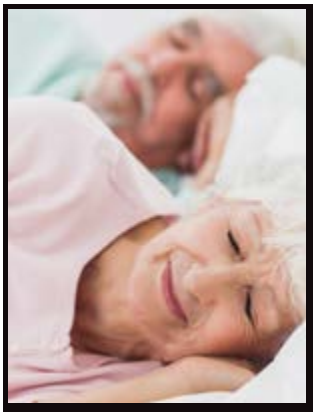
BIOMEDICAL OPTICS EXPRESS. 2014;5(1):293-311.

Sleep Position Linked to Visual Field Loss in OAG

Can sleeping position affect disease progression in patients with open-angle glaucoma (OAG)? Since people spend about one-third of their lives asleep, it's an important question, said Ki Ho Park, MD, PhD, of Seoul National University Hospital, South Korea. Intraocular pressure (IOP) varies with body position; the fact that IOP is generally lower when a person is upright than when reclining suggests that glaucoma progression may occur during sleep.

Dr. Park and his colleagues conducted a retrospective study to assess sleeping position in relation to asymmetric visual field (VF) loss.[1] They looked at two groups: 510 patients with normal-tension glaucoma (NTG; IOP at or below 21 mmHg), and 182 with high-tension glaucoma (IOP above 21 mmHg). Asymmetric VF loss was defined as a difference in mean deviation of at least 2 dB between the eyes. Patients received VF examinations every three to six months.

All patients completed a questionnaire about their preferred sleeping position. Earlier studies found that the most common positions are supine and on the side, and that side sleepers spend more time on one side than the other. As people age, they tend to sleep longer on their preferred side.[2]



MECHANISM. Ophthalmic arterial pressure may be increased by side sleeping, since the eye is lower in relation to the heart than in the supine position, said Dr. Park.

Of the 430 patients (309 NTG, 121 high-tension) who had asymmetric VF loss, nearly two-thirds reported preferring to sleep on the side with the worse eye rather than on the side with the better eye.

"We suspect that the preferred sleeping position, especially side sleeping, is a factor in asymmetric VF progression in NTG patients," said Dr. Park. "The effects of sleeping position may be different in high-tension glaucoma."

—Mary Wade

1 Kim KN et al. *Am J Ophthalmol.* 2014;157(3):739-745.
2 De Koninck J et al. *Sleep.* 1992; 15(2):143-149.

Dr. Park reports no related financial interests.