

# News in Review

A LOOK AT TODAY'S IDEAS AND TRENDS

## Phaco May Speed Retinopathy

**A** growing body of literature supports the idea that diabetic retinopathy (DR) progresses more rapidly after phacoemulsification cataract surgery. A recent report describes a clinic-based

cohort study by a team of Australian researchers at Westmead Hospital in Sydney, which found that progression rate of DR doubled in diabetic patients 12 months after surgery compared with nonoperated eyes.<sup>1</sup>

The study was undertaken to determine whether phacoemulsification exacerbated DR, a side effect previously associated with earlier cataract surgical techniques, said Jie Jin Wang, MMed, PhD, an author of the study and associate professor of

EyeNet thanks Susan B. Bressler, MD, for her help with this issue's News in Review.

ophthalmology at University of Sydney, New South Wales, Australia.

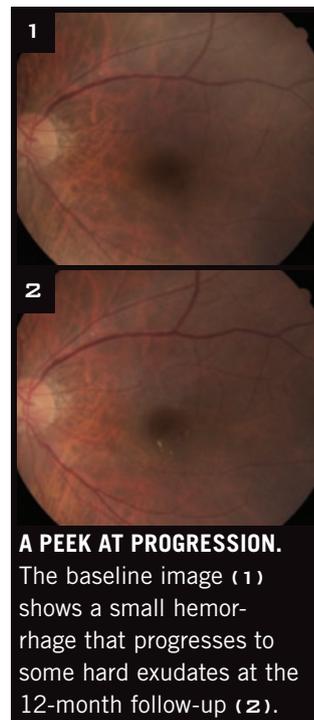
Of the 169 patients followed for 12 months postoperatively, incident DR, or DR newly developed since baseline, occurred in 28.2 percent of operated eyes compared with 13.8 percent of nonoperated eyes. And in a paired-eye comparison of 45 patients who remained unilaterally operated for at least 12 months and who were at risk of DR progression, 35.6 percent of operated eyes exhibited DR progression compared with 20.0 percent of fellow nonoperated eyes.

The authors observed DR progression in 81 eyes (both surgical and nonsurgical) during 12 months of follow-up. Of these, 33 eyes (40.7 percent) progressed by one ETDRS step, 12 (14.8 percent) by two ETDRS steps and 36 (44.4 percent) by three or more ETDRS steps.

The findings were consistent with other studies that looked at the DR progression rate after phacoemulsification. Three earlier studies that compared operated to nonoperated eyes found consistently higher rates of progression in the operated eyes, although the difference was not significant.

While phacoemulsification seemed to contribute to DR development and progression, the effect was less than previously documented with intracapsular and extracapsular surgical techniques.

Why DR progresses after surgery is not clear, said Dr. Wang, though poor glycemic control in diabetic patients has been associated with both cataract and DR. Therefore, the presence of



**A PEEK AT PROGRESSION.** The baseline image (1) shows a small hemorrhage that progresses to some hard exudates at the 12-month follow-up (2).

cataract may be a marker for greater severity of DR or increased likelihood of progression of DR.

In addition to the need for adequate control of blood glucose and blood pressure levels prior to surgery, these patients will require close monitoring after cataract surgery, said Dr. Wang, reminding clinicians that current practice

includes preoperative laser to adequately control active DR features and diabetic macular edema.

“While these findings should not argue against

performing cataract surgery in older people with diabetes, it is important for clinicians to recognize this residual risk and to take appropriate precau-

tions,” said coinvestigator Paul Mitchell, MD, PhD. “Patients with diabetes or diabetic retinopathy should be followed regularly after cataract surgery to monitor

retinopathy development or progression.”

—Miriam Karmel

1 Hong, T. et al. *Ophthalmology* 2009;116(8):1510–1514.

Diabetes News

# Blood Pressure Drugs May Slow Retinopathy

The search for a pharmaceutical “magic bullet” to stop diabetic nephropathy took a surprising turn recently, when a study found that two inhibitors of the renin-angiotensin system instead prevented progression of diabetic retinopathy.

“The magnitude of the effect was striking,” said Ronald Klein, MD, MPH, a senior author on the study.<sup>1</sup> Dr. Klein is professor of ophthalmology and visual sciences at the University of Wisconsin School of Medicine and Public Health.

“This is one of three controlled clinical trials that showed a benefit of lower blood pressure in persons with type 1 diabetes randomized to angiotensin-converting-enzyme (ACE) inhibitors or angiotensin-receptor blockers in reducing the incidence or progression of diabetic retinopathy,” Dr. Klein said. “Ophthalmologists should alert their type 1 diabetic patients and their primary care physicians about this benefit.”

In the latest double-blind, multicenter trial, researchers randomized 223 normotensive, type 1 dia-

betic patients and followed them for five years. One-third of the subjects took the ACE inhibitor enalapril (Vasotec, 20 mg daily); one-third took the angiotensin-receptor blocker losartan (Cozaar, 100 mg daily); and the controls took a placebo.

Stereo color fundus photos taken at the beginning and end of the study were assessed by masked graders and the retinopathy severity was determined based on a modified 15-step ETDRS severity scale. Compared with untreated controls, the patients treated with enalapril were 65 percent less likely and the patients treated with losartan were 70 percent less likely to show two or more steps of progression of their diabetic retinopathy.

The retinal benefits occurred even though all the subjects began the study with normal blood pressure (< 135/85 mmHg), and 91 percent had no retinopathy or only minimal or mild stages of nonproliferative diabetic retinopathy. Their average age was about 30 years, and the average duration of type 1 diabetes was 11 years.

There has been increas-

ing interest recently in the possibility of using antihypertensive drugs, alone or in combination, to prevent long-term organ damage from diabetes by blocking the renin-angiotensin system. Last year, two European-based studies, the Diabetic REtinopathy Candesartan Trials (DIRECT), reported that candesartan, an angiotensin blocker, lowered the incidence of retinopathy in type 1 diabetic patients by about 18 percent ( $p = 0.0508$ ) but did not prevent progression. In persons with type 2 diabetes, the trial showed that candesartan statistically significantly induced regression of diabetic retinopathy but did not reduce progression.<sup>2,3</sup>

The current study research adds support to the emerging idea that ocular renin-angiotensin system plays a role in the development of diabetic retinopathy, independent of systemic blood pressure, Dr. Klein

said.

“When I see diabetic patients in clinic, I measure their blood pressure and discuss both blood pressure and glycemic control with them,” he said. “These data suggest that if they are normotensive with normal renal function, and have type 1 diabetes with no or minimal retinopathy, further discussion of the results of these studies with their primary care physician is indicated to decide whether it would be beneficial to be treated with an ACE inhibitor.”

—Linda Roach

1 Mauer, M. et al. *N Engl J Med* 2009;361(1):40–51.

2 Chaturvedi, N. et al. *Lancet* 2008;372(9647):1394–1402.

3 Sjölie, A. K. et al. *Lancet* 2008;372(9647):1385–1393.

Dr. Klein has served on an external advisory board in the DIRECT trial for which he has received an honorarium from AstraZeneca.

| Effects of Enalapril and Losartan on Retinopathy During the Five-Year Follow-Up Period |  |           |
|--|--|-----------|
| PROGRESSION  | NUMBER OF EVENTS<br><i>no./total no. (%)</i> | P VALUE   |
| <b>By two steps or more</b>  |  |           |
| Placebo  | 28/74 (38)                                   | Reference |
| Enalapril  | 19/77 (25)                                   | 0.02      |
| Losartan   | 15/72 (21)                                   | 0.008     |
| <b>By three steps or more</b>  |  |           |
| Placebo  | 21/74 (28)                                   | Reference |
| Enalapril  | 15/77 (19)                                   | 0.06      |
| Losartan   | 9/72 (12)                                    | 0.005     |

SOURCE: Mauer, M. et al. *N Engl J Med* 2009;361(1):47.

## Glaucoma Update

# Open-Angle Glaucoma May Predict Stroke

Taiwanese researchers found that open-angle glaucoma (OAG) may be a major predictor of stroke.<sup>1</sup> The longitudinal study of 4,032 OAG patients and 20,160 control subjects retrospectively reviewed data from the Taiwan National Health Insurance Research Database, a collection of information from more than a million random subjects among the nation's 23 million residents.

Checking for five-year stroke-free survival rates and adjusting for factors that might confound results such as demographics and comorbid conditions, the researchers found that patients with OAG had a 1.52-fold higher risk of stroke than the comparison cohort. Stroke developed in 14.9 percent of OAG patients and 9.5 percent of the comparison group.

"The results of this study are significant, as they potentially indicate a shared pathogenetic link between OAG and stroke," said Dexter Yu-Lung Leung, MD, clinical assistant professor of ophthalmology and visual sciences at the Chinese University of Hong Kong. Dr. Leung was principal investigator for a related recent study regarding silent cerebral infarcts and normal-tension glaucoma.<sup>2</sup>

"We are not entirely sure whether stroke and glaucoma have any mutual cause-

and-effect relationship," he said, "or whether there is a yet unknown third factor—a common link between the two. In this study, it is interesting to note that the risk of stroke was still significantly elevated in OAG patients without systemic hypertension and diabetes."

Determining the types of stroke involved—whether hemorrhagic or ischemic, for example—might prove illuminating, said Dr.

Leung. Also, strokes in Asians tend to result more commonly from intracranial vessel occlusion than in Caucasians. It remains to be seen whether the results of this study will generalize to other ethnic groups.

Although elevated IOP is still the single most important risk for glaucoma development and progression, said Dr. Leung, further research is needed to delineate the connections between glaucoma and stroke and to determine how big a role vascular risk factors play in this eye disease. "It is possible that IOP and vascular factors are not truly independent pathways of damage but may potentially interact with each other across

the entire range of IOP in producing glaucoma."

The implications of this study for clinicians? "Ophthalmologists may need to pay more attention to the various vascular risk factors in their OAG patients," said Dr. Leung, adding that collaboration with neurologists and other physicians to lower or detect these risks may prove beneficial to many glaucoma patients.

—Annie Stuart

1 Ho, J. D. et al. *Stroke* 2009; 40(8):2685–2690.

2 Leung, D. Y. et al. *Ophthalmology* 2009;116(7):1250–1256.

*Dr. Leung reports no financial interests related to this story or his related study.*

## RETINA: Diabetes & Wet AMD

Results from the population-based EUREYE study show a positive association between a self-reported history of diabetes and neovascular age-related macular degeneration.<sup>1</sup> However, no association was found between diabetes and geographic atrophy or early AMD.

EUREYE was a cross-sectional study with seven European centers. The centers were located in disparate geographical regions, which meant study participants had different diets and levels of sunlight exposure. All participants were aged 65 or older.

In the study, 2,117 participants without AMD served as control subjects; 2,182 individuals had early AMD, 49 had geographic atrophy and 101 had wet AMD. Of the participants, 13.1 percent self-reported a history of diabetes.

The authors noted that the results were adjusted for demographic, behavioral, dietary and medical history confounders. But, said lead author Fotis Topouzis, assistant professor of ophthalmology at Aristotle University in Thessaloniki, Greece, "The information for past laser treatment was not available. Since choroidal neovascularization has been reported as a rare complication of diabetic laser treatment, we believe that it is unlikely the association of diabetes with neovascular AMD is mediated from past laser treatment."

In the study, the authors conclude that further research is needed. Dr. Topouzis said, EUREYE is a cross-sectional study and as such has limitations; longitudinal studies are likely to provide more robust information in the future. In the meantime, Dr. Topouzis recommended that ophthalmologists provide their older diabetic patients with information concerning the possible association of diabetes with neovascular AMD.

—Lori Baker Schena

1 Topouzis, F. et al. *Br J Ophthalmol* 2009;93:1037–1041.



**COUNSEL.** Some patients may want to know that there's a possible association between diabetes and wet AMD.