

Journal Highlights

NEW FINDINGS FROM *OPHTHALMOLOGY*, *AJO* AND *ARCHIVES*

Hormone Replacement Associated With Risk of Cataract Extraction

March's *Ophthalmology*

In a population-based prospective cohort study, Lindblad et al. found a statistically significant positive association between hormone replacement therapy (HRT) and the incidence of cataract extraction. This increased risk was higher in current users of HRT with longer duration of use, compared with women who never used HRT. In addition, current users of HRT consuming more than one alcoholic beverage per day had further increased risk of cataract.

The study included 30,861 postmenopausal women ages 40 to 83 participating in the Swedish Mammography Cohort who completed a self-administered questionnaire in 1997 about hormone status and HRT. They were followed through October 2005. In the multivariate adjusted analysis, previous use of HRT was associated with a 14 percent increased risk of cataract compared with those who never used HRT, and current use was associated with an 18 percent increased risk.

The authors conclude that if these findings are confirmed, an increased rate of cataract extraction may be yet another potential negative outcome associated with HRT.

Endothelial Cell Loss With DSAEK

March's *Ophthalmology*

Price et al. have found that at one year following surgery, the overall graft success rate for Descemet stripping automated endothelial keratoplasty (DSAEK) is comparable to the success rate for penetrating keratoplasty (PK) in patients with a moderate risk condition (principally Fuchs dystrophy or pseudophakic/aphakic corneal edema). However, endothelial cell loss is higher with DSAEK.

In this multicenter, prospective clinical trial, 173 patients undergoing DSAEK were compared with 410 patients undergoing PK from the Specular Microscopy Ancillary Study of the Cornea Donor Study. While the one-year graft rate was comparable, endothelial cell loss in the DSAEK group at six months (34

percent) and 12 months (38 percent) was significantly greater than in the PK group at six months (11 percent) and 12 months (20 percent), a finding the researchers attribute primarily to greater surgical manipulation and trauma to the graft.

The authors call for further data collection on longer-term graft success and cell loss with objective determination of endothelial cell density.



Effects of Simvastatin on Visual Field Progression

March's *Ophthalmology*

In light of the hypothesis that normal-tension glaucoma may be a variant of open-angle glaucoma influenced by vascular factors, Leung et al. investigated whether statins have beneficial effects on normal-tension glaucoma.

They conducted a prospective cohort study looking at the effects of simvastatin on visual field progression in patients with normal-tension glaucoma. In this study, 31 of 256 Chinese patients with normal-tension glaucoma (12.1 percent) were taking simvastatin and 225 (87.9 percent) were not. After adjusting for other risk factors, simvastatin use was associated with a reduced risk of visual field progression in patients with normal-tension glaucoma. Logistic regression showed that a history of disc hemorrhage, history of cerebrovascular accidents and baseline age (10 years and older) represented significant risk factors of visual field progression, while simvastatin use offered a protective effect.

The authors conclude that their data demonstrate the need for a randomized controlled clinical trial that looks at both the association between statins and visual field stabilization in patients with normal-tension glaucoma and the cost-effectiveness of this treatment approach.

Drusenoid Pigment Epithelial Detachment in AMD

March's *Ophthalmology*

Using participants enrolled in the Age-Related Eye Disease Study, Cukras et al. designed a long-term evaluation of the natural history of eyes with drusenoid pigment epithelial detachments (DPED) associated with age-related macular degeneration.

The researchers identified 311 eyes of 255 patients with DPED and followed them for eight years. Of the 282 eyes that did not have advanced AMD at baseline, 119 eyes (42 percent) developed advanced AMD within five years. Researchers detected progressive fundus changes including the development of calcified drusen and pigmentary changes in the 163 eyes that did not develop advanced AMD. About 40 percent of all eyes experienced visual acuity decreases of 15 or more letters at five-year follow-up. Mean visual acuity loss averaged 26 letters for eyes progressing to advanced AMD and eight letters for eyes that did not progress to advanced AMD.

The authors conclude that studies incorporating imaging modalities such as optical coherence tomography and fundus autofluorescence may provide additional information about the pathogenesis of DPED.

American Journal of Ophthalmology

Mycophenolate Mofetil for Ocular Inflammation

March's *AJO*

Ocular inflammation is frequently a chronic condition with inadequate response to simple treatments. Daniel et al. evaluated mycophenolate mofetil as a single noncorticosteroid immunosuppressive treatment for noninfectious ocular inflammatory diseases.

Characteristics of patients with noninfectious ocular inflammation treated with mycophenolate mofetil at four subspecialty clinics from 1995 to 2007 were abstracted in a standardized chart review of every eye at every visit.

Main outcomes measured were control of inflammation, corticosteroid sparing effects and discontinuation of mycophenolate mofetil (including the reasons for discontinuation). Survival analysis was used to estimate the incidence of outcomes and to identify risk factors for each.

Among 236 patients (397 eyes) treated with mycophenolate mofetil monotherapy, 20.3 percent, 11.9 percent and 39.8 percent had anterior uveitis, intermediate uveitis and posterior uveitis or panuveitis, respectively; 14 percent had scleritis; 7.6 percent had mucous membrane pemphigoid and 6.4 percent had other ocular inflammatory diseases. By Kaplan-Meier estimation, complete control of inflammation (defined as sustained over consecutive visits spanning at least 28 days) was achieved in 53 percent and 73 percent of patients within six months and one year, respectively. Systemic corticosteroid dosage was reduced to 10 mg of prednisone or less (while maintaining sustained control of inflammation) in 41 percent and 55 percent of patients in six months and one year, respectively. Twelve percent of patients discontinued mycophenolate mofetil within the first year because of side effects of therapy.

The authors conclude that, given sufficient time, mycophenolate mofetil was effective in managing ocular inflammation in approximately half of the treated patients. Treatment-limiting side effects were observed in 12 percent of patients and typically were reversible.

Quality of Life in Keratoconus Patients

March's *AJO*

Yildiz et al. evaluated vision-related quality of life (QoL) as measured with the National Eye Institute Visual Function Questionnaire (NEI-VFQ) in keratoconus patients who underwent penetrating keratoplasty (PK) in one or both eyes. They compared the results of the study to those of historical controls.

This clinic-based, cross-sectional

study included 149 consecutive patients who underwent PK for keratoconus between June 1, 2008, and Dec. 31, 2008. The NEI-VFQ was administered to all 149 patients. The relationship between demographic and clinical factors and NEI-VFQ subscale scores was evaluated.

Eighty-three of 149 patients (55.7 percent) were male. Approximately half of the patients had PK in both eyes. Visual acuity with current correction in the better eye was better than 20/40 in 80 percent of patients. The sample had significantly lower (worse) NEI-VFQ scores than the Collaborative Longitudinal Evaluation of Keratoconus historical control group for the subscales of role difficulties, dependency, driving and peripheral vision. In general, scores of the sample were between scores of patients with age-related macular degeneration categories 3 and 4. Patients with visual acuity better than 20/40 (in the better eye) showed significantly higher scores in all subscales except color vision. There was a significant relationship between minimum graft age and NEI-VFQ overall score better than AMD category 3.

The authors conclude that despite satisfactory results on visual outcome measures obtained after PK, vision-related QoL in keratoconus patients remains impaired.

PDT and Indocyanine Green Angiography Findings

March's *AJO*

Various treatment protocols have been used for central serous chorioretinopathy (CSC). Inoue et al. evaluated the efficacy of photodynamic therapy (PDT) and indocyanine green angiography (ICGA) findings for treating CSC.

In this observational case series, 32 eyes of 27 patients with chronic CSC and symptoms for at least six months were followed for a minimum of one year. The total PDT energy was reduced to about 36 to 42 mJ/cm². The baseline middle-phase ICGA findings were classified as intense, intermediate

or no hyperfluorescence depending on the degree of hyperfluorescence. The resolution of the subretinal fluid and recurrence rates were assessed in relation to each ICGA finding at baseline.

ICGA before PDT showed intense hyperfluorescence in 23 eyes, intermediate hyperfluorescence in six eyes and no hyperfluorescence in three eyes.

The subretinal fluid resolved completely three months after one application of PDT in 23 eyes with intense hyperfluorescence, six eyes with intermediate hyperfluorescence and no eyes with no hyperfluorescence. In the last group, the subretinal fluid did not resolve throughout the follow-up period despite additional applications of PDT. The subretinal fluid recurred in seven of 29 eyes in which the subretinal fluid resolved at three months; recurrence was frequent in eyes with intermediate hyperfluorescence.

The authors conclude that PDT success rate in eyes with chronic CSC depends on the degree of hyperpermeability on ICGA. PDT is not effective or the recurrence rate is predicted to be high in eyes without intense hyperfluorescence.

Archives of Ophthalmology

Cost Analysis of Povidone-Iodine for Ophthalmia Neonatorum Prophylaxis

January's Archives

In August 2009, the Centers for Disease Control and Prevention reported a shortage of erythromycin ophthalmic ointment in the United States. Keenan et al. compared the costs of topical azithromycin and povidone-iodine as suitable replacements for erythromycin as a prophylaxis of ophthalmia neonatorum.

The cost of erythromycin ointment 0.5 percent was \$1.94 per tube, and the cost of topical azithromycin 1 percent was \$72.12 per bottle, according to the average wholesale price in the 2009 *Red Book*. The authors calculated the costs for a hospital pharmacy to formulate 1-ml doses of povidone-iodine 2.5 percent in sterile syringes. Assuming that 10 doses were made in each batch,

the total cost per dose of povidone-iodine was \$7.77. Assuming an average of 354,000 births per month in the United States, universal prophylaxis of ophthalmia neonatorum with erythromycin would cost \$0.7 million, with topical azithromycin would cost \$25.5 million and with povidone-iodine would cost \$2.8 million.

Given the potential cost savings of povidone-iodine, the demonstration of its efficacy for ophthalmia neonatorum prophylaxis in a large clinical trial, and the absence of efficacy data for topical azithromycin, the authors suggest that povidone-iodine would be a suitable and perhaps preferable alternative to topical azithromycin for ophthalmia neonatorum prophylaxis.

High Caloric/Sodium Intakes and Retinopathy

January's Archives

Roy et al. examined baseline dietary nutrient intakes in relation to six-year progression of diabetic retinopathy in 469 African-Americans with type 1 diabetes.

At both baseline and six-year follow-up examinations, participants completed a food frequency questionnaire, had a complete eye examination, underwent blood and urine testing, and had masked grading of retinal photographs taken to determine progression of diabetic retinopathy.

Patients with the highest caloric intake at baseline were more likely to develop vision-threatening retinopathy—either proliferative diabetic retinopathy or macular edema—at the six-year follow-up and/or severe hard exudates after adjusting for clinical risk factors for retinopathy progression. Patients with the highest sodium intake at baseline were more likely to develop macular edema at the six-year follow-up.

The authors conclude that in African-Americans with type 1 diabetes, high caloric and sodium intakes are significant and independent risk factors for severe forms of diabetic retinopathy. These results suggest that low caloric and sodium intakes in African-

Americans with type 1 diabetes may have a beneficial effect on the progression of diabetic retinopathy and thus might be part of dietary recommendations for this population.

Effect of Bifocal and Prismatic Bifocal Spectacles on Myopia

January's Archives

Cheng et al. investigated whether bifocal and prismatic bifocal spectacles could control myopia in children with high rates of myopia progression. One hundred and thirty-five myopic Chinese-Canadian children with myopic progression of at least 0.5 D in the preceding year were randomly assigned to one of three treatment groups: 41 wore single-vision lenses, 48 wore standard executive bifocals (add +1.5 D) and 46 wore executive bifocals with a three-prism diopters base-in prism in the near segment of each lens. Refractive error was measured by an automated refractor under cycloplegia, and axial length was measured by ultrasonography at six-month intervals for 24 months.

Of the 135 children, 131 (97 percent) completed the 24-month study. Progression of myopia was slowest among children who wore prismatic bifocals—with a 55 percent difference in the rate of progression compared with children wearing single vision lenses. There was a 38 percent difference in the rate of progression between users of regular bifocals and single vision lenses. Both prismatic and standard bifocals prevented 34 percent of the axial elongation.

The authors conclude that bifocal spectacles could be considered for children with progressive myopia. However, the modest myopia control benefit should be weighed against factors such as the increased cost of the lenses and poor cosmetic appearance.

Ophthalmology summaries are written by Lori Baker Schena and edited by John Kerison, MD. American Journal of Ophthalmology summaries are edited by Thomas J. Liesegang, MD. Archives of Ophthalmology summaries are written by the lead authors.

ROUNDUP OF OTHER JOURNALS

Adverse Ocular Effects of Oral Moxifloxacin

Eye

2009;23:2260–2262

Oral moxifloxacin, 8-methoxyquinolone, is used to treat acute cases of chronic bronchitis, pneumonia and acute bacterial sinusitis. Prescriptions for this synthetic broad-spectrum antibacterial medication have been increasing in the Netherlands and Belgium. In this case series report, **Bettink-Remeijer et al.** present five patients who experienced iris transillumination and persistent mydriasis three to four weeks after taking oral moxifloxacin.

These otherwise healthy patients all experienced a uveitis-like episode with painful eyes after using oral moxifloxacin. Ten to 14 days later, the patients developed severe photophobia that impeded outdoor activities. Slit-lamp examination showed almost complete iris transillumination with only a few pigmented cells and persistent mydriasis of the pupil with no reaction to light and no near reflex. In one patient, a three-year follow-up exam showed no change in symptoms.

While there may be multiple factors that caused these symptoms, the authors conclude that the use of oral moxifloxacin is one of these factors.

Comparing 24-Hour Sitting vs. Supine Untreated IOP

Eye

Published online Dec. 4, 2009

Is IOP higher in the daytime or nighttime? Not an easy question to answer considering that patients must be in the sitting position to be examined by Goldmann tonometry. To address this problem, **Quaranta et al.** used a Perkins handheld applanation tonometer to measure IOP in untreated patients with glaucoma or ocular hypertension while in a supine position.

The investigators conducted a 16-month study of 100 patients, comparing supine nighttime IOP measurements with Perkins applanation tonometry to 24-hour sitting IOP measurements with Goldmann applanation tonometry. Findings showed that the mean of the sitting IOP measurements recorded at 10 a.m., 10 p.m., 2 a.m. and 6 a.m. was significantly lower than that measured in the supine position. Examination of data at specific time points revealed that the pressure was significantly higher in the supine than sitting position at 10 a.m., 10 p.m. and 2 a.m. In addition, the majority of patients demonstrated their sitting peak pressure in the daytime and trough pressure at night.

The authors call for further research to determine which topical medications may be better for patients in the supine position.

Handheld Intraoperative Spectral Domain OCT

Retina

2009;29:1457–1468

A portable spectral domain-optical coherence tomography (SD-OCT) unit (Bioptigen) previously has been used to image uncooperative pediatric patients, patients with limited mobility or hospitalized patients that cannot be moved. In this study, **Dayani et al.** took the device into the operating room and described its use in macular surgery.

This observational case series involved four patients with macular holes, three patients with epiretinal membranes and one patient with vitreomacular traction. The researchers found that the handheld SD-OCT unit provided unique information regarding the location of persisting internal limiting membrane or epiretinal membrane. In addition, a comparison of images taken prior to the incision and intraoperatively showed distinct changes in retinal contour and macu-

lar hole configuration. The device also identified additional membranes in two patients.

The investigators conclude that the SD-OCT unit is an efficient method of obtaining intraoperative macular pathology images and has the potential to confirm or identify findings during macular surgical procedures.

Gene Therapy for Leber Congenital Amaurosis

The Lancet

2009;374:1597–1605

According to a study by **Maguire et al.**, the efficacy of treating inherited retinal disease with gene therapy can be improved if treatment is delivered prior to retinal degeneration. The researchers conducted a phase 1 trial to assess retinal and visual function in 12 patients ages eight to 44 with RPE65-associated Leber congenital amaurosis. They received one subretinal injection of adeno-associated virus (AAV) containing a gene encoding a protein needed for the isomerohydrolase activity of the retinal pigment epithelium. This injection was given in the worst eye at low, medium or high doses for up to two years.

All patients showed improvement in retinal function—an effect that remained stable during the follow-up period. The greatest improvement was detected in children, all of whom gained ambulatory vision. The most striking finding was the ability of children to navigate an obstacle course independently and accurately even in dim light.

In addition, objective tests resulted in quantitative evidence showing improved retinal function and sensitivity in study patients. Patients also had at least a 2 log unit increase in pupillary light responses.

Roundup of Other Journals is written by *Lori Baker Schena* and edited by *Deepak P. Edward, MD*.