In patients, age <50 or >80 years, African-American race, and an overall poor level of health are important predictors of non-adherence to glaucoma medication use.

**Objective:** To identify factors associated with non-adherence to glaucoma medication use.

**Design:** Prospective, observational cohort study.

**Participants:** 196 patients with primary open angle glaucoma or ocular hypertension were recruited from two academic institutions for participation in this study.

**Methods:** Patients were managed with topical prostaglandin therapy and were instructed at enrollment in usage of the Travatan Dosing Aid, an electronic monitoring device that allows timing and frequency determination when using Travatan eyedrops. Patients were given free medication during the 3-month study. Patients underwent baseline testing, which included clinical examination as well as questionnaires assessing socio-demographic information, mental health status, and overall health status. In addition, patients completed a questionnaire assessing their overall knowledge of glaucoma therapy and its goals. Statistical analysis was performed to determine factors associated with non-adherence to glaucoma medication use. Non-adherence was defined by failure to use their dose within 4 hours of the scheduled dosage time ≥75% of the time.

**Results:** Multivariate statistical analysis allowed identification of independent predictors of non-adherence. These factors included age <50 or >80 years, African-American race, and an overall lower level of health status. A lower level of education and socioeconomic status were also associated with a higher likelihood of non-adherence. Patients who expressed a poor understanding of the goals of glaucoma therapy were more likely to be non-adherent.

**Conclusions:** Age, socioeconomic status, African-American race, and a lower level of overall health status are important risk factors for non-adherence to glaucoma medication use.

**Reviewer's Comments:** It was also found that patients, when asked in a non-confrontational manner, were fairly willing to admit to non-adherence to glaucoma medication use. Having an understanding of risk factors for non-adherence and how to bring up the subject with patients in a manner that will put them at ease and not make them feel embarrassed or ashamed about their failure to completely follow recommended therapy will assist in identifying individuals who need intervention in the form of patient education thus allowing them to gain benefits from glaucoma medication use. (Reviewer-Scott D. Smith, MD, MPH).

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Keywords: Glaucoma, Medical Therapy

Print Tag: Refer to original journal article
A novel biodegradable dexamethasone intravitreal drug delivery system is beneficial in reducing macular edema due to uveitis or Irvine-Gass syndrome.

**Objective:** To evaluate safety and efficacy of a dexamethasone intravitreal drug delivery system in patients with persistent macular edema due to uveitis or Irvine-Gass syndrome.

**Design:** Randomized, prospective, controlled clinical trial.

**Methods:** 315 patients with chronic macular edema (≥90 days in duration) were randomized to receive surgical implantation of a 350 or 700 μg dexamethasone implant, or to observation without treatment. Preoperative and postoperative evaluations took place through 6 months of follow-up, which included measurement of best corrected visual acuity and fluorescein angiography. These tests permitted statistical analysis of the relationship between the dose of steroid implant and improvement in visual acuity and retinal vascular leakage through 6 months of follow-up.

**Results:** At the 90-day follow-up period, a 2-line improvement in visual acuity was seen in 41.7% of patients in the 350 μg implant group, and 53.8% of patients in the 700 μg implant group. In contrast, an improvement of this magnitude was seen in only 14.3% of patients in the observation group (both \( P < 0.05 \)). Improvement in visual acuity continued through the final 6-month follow-up visit. A 3-line improvement of visual acuity was seen in 53.8% of patients in the 700 μg group, which was significantly >7.1% of patients in the observation group who had this amount (\( P = 0.008 \)). In addition, a significantly greater reduction in fluorescein leakage was seen on follow-up fluorescein angiography in patients receiving either steroid implant. Steroid-induced cataract occurred in all phakic patients who received the steroid implant. Intraocular pressure (IOP) elevation was also seen in patients after insertion of the steroid implant, and was reported in 25% of patients in the 350 μg group, and 31% of patients in the 700 μg group. All cases of intraocular pressure elevation were successfully managed with topical glaucoma medications.

**Conclusions:** A biodegradable dexamethasone intravitreal drug delivery system is effective in reducing macular edema and improving visual acuity in patients with macular edema due to chronic uveitis or Irvine-Gass syndrome.

**Reviewer's Comments:** It is hoped that this type of drug delivery system will offer efficacy in improving visual acuity and reducing macular edema without the relatively high rate of steroid-induced glaucoma seen with other intravitreal steroid implants. Longer-term evaluation of this novel drug delivery system will be needed in order to determine whether persistent IOP elevation and medically uncontrolled steroid-induced glaucoma may occur. (Reviewer-Scott D. Smith, MD, MPH).

© 2009, Oakstone Medical Publishing

Keywords: Drug Delivery, Retinal Edema, Uveitis, Irvine-Gass Syndrome

Print Tag: Refer to original journal article
Patients with isolated branch retinal artery occlusion, not associated with giant cell arteritis or retinal vein occlusion, generally have a good visual prognosis with improvement in vision over time.

**Objective:** To report the natural history of untreated branch retinal artery occlusion (BRAO).

**Design:** Observational cohort study.

**Participants:** Consecutive series of 199 untreated patients with BRAO seen at a single academic institution over a 25-year period.

**Methods:** All patients underwent a detailed ophthalmic and medical history, which included measurement of visual acuity and visual field testing with manual Goldmann perimetry. Identical ophthalmic evaluation was repeated on each follow-up visit. Patients were categorized according to the presence of a cilioretinal or other branch retinal artery occlusion. Among those patients with a cilioretinal artery occlusion (CLRAO), further categorization with regard to presence or absence of giant cell arteritis and associated central retinal or hemiretinal vein occlusion was also made.

**Results:** Patients with isolated BRAO were classified according to the presence or absence of observed reperfusion on follow-up examination. In eyes with transient occlusion, uniformly good visual outcome was seen. In those with permanent BRAO, improvement in visual acuity over time was also common, with final visual acuity of 20/40 or better seen in nearly 90% of patients. In patients with CLRAO, clinical outcome was better in the absence of associated giant cell arteritis or retinal vein occlusion. Outcomes of patients with giant cell arteritis depended upon the severity of associated ischemic optic neuropathy. Outcome of those with associated retinal vein occlusion depended upon the severity of ischemia associated with the retinal vein occlusion.

**Conclusions:** The natural history of isolated BRAO or CLRAO tends to be good. Visual outcome in patients with giant cell arteritis or associated retinal vein occlusion depends upon the severity of those associated conditions.

**Reviewer’s Comments:** This study is useful in delineating the natural history of BRAO, which will serve as a standard against which therapeutic interventions must be compared. Since the natural history of isolated BRAO is good, this must be kept in mind when considering the outcome of any potential therapy. It is also important to recognize that patients must be evaluated for possible associated giant cell arteritis, particularly when a CLRAO is seen. Identification and prompt initiation of treatment for this condition is critical to preventing severe, bilateral vision loss. (Reviewer-Scott D. Smith, MD, MPH).

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Keywords: Retinal Artery Occlusion

Print Tag: Refer to original journal article
Periocular triamcinolone acetonide injection can reduce macular edema and improve visual outcome following panretinal photocoagulation for treatment of diabetic retinopathy.

**Objective:** To evaluate efficacy of a single dose of posterior sub-Tenon triamcinolone acetonide (PSTA) before panretinal photocoagulation (PRP) in improving visual outcome and macular thickness.

**Design:** Randomized, controlled clinical trial.

**Participants/Methods:** 41 patients with bilateral severe non-proliferative or proliferative diabetic retinopathy in need of PRP were enrolled in this study. In each patient, 1 eye of was randomly assigned to receive a 20 mg PSTA immediately prior to the performance of PRP. The other eye received PRP without any supplemental therapy. Pre-laser and post-laser evaluations were completed through 6 months of follow-up to allow determination of visual outcome in both groups. In addition, macular thickness was measured by optical coherence tomography (OCT) before and after treatment, and was compared in the groups.

**Results:** Mean patient age was 60.1 years. No significant difference in visual acuity or in presence and severity of macular edema was seen between groups. At the 6-month follow-up time point, best-corrected visual acuity was significantly better in eyes that received the periocular steroid injection. In addition, macular thickness was decreased in eyes from baseline following treatment when a supplemental steroid injection was given. In contrast, macular thickness increased at the 1- and 3-month follow-ups, and gradually returned toward baseline by the 6-month follow-up in eyes that did not receive the steroid injection.

**Conclusions:** A single 20 mg dose of sub-Tenon triamcinolone acetonide improves visual outcome and reduces macular edema following PRP.

**Reviewer's Comments:** PRP has been the cornerstone of therapy for proliferative diabetic retinopathy since it was first shown to be efficacious in inducing regression of posterior segment neovascularization. It has long been known, however, that diabetic macular edema may develop or increase after PRP is performed. This study suggests that a simultaneous injection of triamcinolone acetonide can reduce the severity of this complication, and actually appears to reduce macular thickness from baseline. Subgroup analysis demonstrated similar results in patients whether or not macular edema was present at baseline, suggesting that this may be beneficial therapy for all patients undergoing this procedure. In addition, the relatively small dose of 20 mg may lead to a lower incidence of steroid-related complications, including posterior subcapsular cataract and intraocular pressure elevation. (Reviewer-Scott D. Smith, MD, MPH).

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Keywords: Retinal Photocoagulation, Macular Edema, Drug Therapy, Diabetic Retinopathy

Print Tag: Refer to original journal article
Individualizing Tx for Macular Degeneration Produces Favorable Results

A Variable-Dosing Regimen With Intravitreal Ranibizumab for Neovascular Age-related Macular Degeneration: Year 2 of the PrONTO Study.

Lalwani GA, Rosenfeld PJ, et al:


Individualization of therapy with ranibizumab for treating neovascular age-related macular degeneration results in a need for fewer injections with similar clinical outcomes to those seen in earlier clinical trials.

**Objective:** To evaluate long-term efficacy of a variable-dosing regimen with intravitreal ranibizumab for the treatment of subfoveal neovascular macular degeneration.

**Design:** 2-year, prospective, open label, uncontrolled clinical trial.

**Participants:** 40 patients with subfoveal neovascular age-related macular degeneration were enrolled in the Perspective Optical Coherence Tomography (OCT) Imaging of Patients with Neovascular Age-Related Macular Degeneration Treated with intra-Ocular Ranibizumab Study (PrONTO) study.

**Methods:** For eligibility, patients had to be aged ≥50 years and have visual acuity between 20/40 and 20/400 in the study eye. Only 1 eye was eligible for enrollment in each patient. All patients received a baseline and 2 follow-up monthly injections of intravitreal ranibizumab. Thereafter, standardized criteria from clinical examination and OCT imaging of the retina were used to determine need for follow-up injections. Patients were re-evaluated on a monthly basis. Total number of injections, as well as visual and OCT outcomes were tabulated through 2 years of follow-up.

**Results:** At the two-year follow-up visit, mean visual acuity improved by 11.1 letters on the Early Treatment Diabetic Retinopahty Study visual acuity chart (<0.001). In addition, improvement in OCT central retinal thickness was seen with a decrease of 212 μm (<0.001). Mean number of injections required during the 24 months of follow-ups was 9.9.

**Conclusions:** The PrONTO study demonstrates that variable dosing regimen of intravitreal ranibizumab leads to visual acuity outcome similar to those recorded in previous clinical trials involving monthly injections throughout 24 months.

**Reviewer's Comments:** This study indicates that individualization of therapy according to the clinical response of intravitreal injections can lead to similar clinical outcomes as those seen in previous studies where 24 injections were given on a monthly basis. This approach makes a great deal of sense, both from an economic standpoint given the high cost of the drug, and from a standpoint of minimizing intervention according to the individual patient's response to treatment. It must be acknowledged that this study does not make a direct comparison between the 2 protocols within a single study, and therefore cannot be used to offer a definitive comparison of the clinical outcomes. However, it certainly lends strong support to the concept of individualization of therapy, which has already been adopted by the majority of retinal specialists managing this condition. (Reviewer-Scott D. Smith, MD, MPH).

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Keywords: Macular Degeneration, Drug Therapy

Print Tag: Refer to original journal article
Diabetes Slows Corneal Wound Healing

In Vivo Confocal Microscopic Findings of Corneal Wound Healing after Corneal Epithelial Debridement in Diabetic Vitrectomy.
Chen W-L, Lin C-T, et al:

Ophthalmology 2009; 116 (June): 1038-1047

In vivo confocal microscopy demonstrates abnormalities after corneal epithelial debridement for >3 months after surgery and long after corneal epithelial defects have disappeared on slit-lamp examination.

**Objective:** To evaluate the healing of corneal wounds using confocal microscopy in patients following corneal epithelial debridement during pars plana vitrectomy for proliferative diabetic retinopathy.

**Design:** Prospective, interventional clinical case series.

**Participants:** 40 diabetic patients who underwent vitrectomy for proliferative diabetic retinopathy, and in whom intraoperative debridement of the corneal epithelium was performed to improve visualization during surgery.

**Methods:** Slit-lamp examination and in vivo confocal microscopy were used to evaluate the corneal epithelium, stroma, and endothelium before and during 6 months of follow-up after surgery. Multiple linear regression analysis was performed to determine potential risk factors associated with delayed corneal healing.

**Results:** Corneal epithelial defects persisted in 22.8% of eyes 2 weeks following surgery; 5.4% of eyes continued to have a visible epithelial defect 1 month after surgery. Incomplete healing of surface corneal epithelial cells was seen in 81.1% of eyes 1 month after surgery and in 9.1% of eyes 3 months after surgery. Complete epithelial healing was not observed until 6 months after surgery, long after corneal epithelial defects had resolved. Statistical analysis demonstrated that the use of silicone oil and perfluorocarbon gas tamponade were associated with delayed corneal healing by slit-lamp examination. Delayed healing by a confocal microscopy was also seen in association with a more complex diabetic treatment regimen and scleral buckling. These findings suggest that more complicated surgery and greater severity of diabetes are associated with slower wound healing.

**Conclusions:** Healing of corneal epithelial wounds in diabetic eyes appears to be slower than that in non-diabetic individuals.

**Reviewer's Comments:** These results should remind us that ocular complications associated with diabetes extend beyond the retina. It is believed that the effects of diabetes on corneal nerves are responsible for delayed wound healing in these patients. When managing patients with postoperative or traumatic corneal epithelial defects, it is important to remember the potential effects of diabetes on wound healing. (Reviewer-Scott D. Smith, MD, MPH).

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Keywords: Diabetes, Corneal Wound Healing

Print Tag: Refer to original journal article
The ratio of central to superior corneal thickness can be used to estimate the correct intraocular lens power for cataract surgery.

**Objective:** To evaluate a new method which does not require pre-laser keratometry values for adjusting the intraocular lens (IOL) power in eyes that require cataract surgery after previous corneal refractive surgery.

**Design:** Retrospective, non-comparative clinical case series.

**Methods:** Data from 36 eyes of 23 patients who had undergone successful phacoemulsification with posterior chamber IOL implantation after previous excimer laser corneal refractive surgery were evaluated. Central and superior corneal thickness was measured prior to cataract surgery and the ratio of central to superior corneal thickness was used in a regression equation to adjust IOL power calculation from the standard Sanders, Retzlaff, Kraff (SRK/T) formula. This technique was compared to other previously described methods for determining the correct IOL power after corneal refractive surgery.

**Results:** This new pachymetric technique resulted in a low proportion of hyperopic refractive surprises, with 92% of eyes falling within the range of -1.0 to +0.5 diopters, with no overcorrections >0.5 diopters. These results compared well with 4 other previously described methods, which the author now considers to be a group of consensus techniques for calculating IOL power in the absence of historical information.

**Conclusions:** The described pachymetric method for IOL power calculation offers a new approach for determining IOL power in patients who have undergone previous refractive surgery where no historical data are available.

**Reviewer's Comments:** As time passes, a significant number of patients who have undergone prior excimer laser refractive surgery will not have available historical information upon which to base the IOL power calculation. Failure to adjust the power results in a large refractive error, and the most accurate techniques described so far require knowledge of pre-laser keratometry and refractive error. This new technique offers the possibility of achieving satisfactory results without any such historical information, and performs as well as some other techniques previously described. Regardless of the technique used to determine the IOL power, it is important to discuss with patients the fact that power calculations are less certain than under normal circumstances. A discussion with the patient of possible IOL exchange if a refractive surprise occurs can reduce anxiety on the part of the patient, since they have been told in advance that such an IOL exchange can be performed with relative ease in the weeks after surgery. (Reviewer-Scott D. Smith, MD, MPH).

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Keywords: Intraocular Lens Calculation, Refractive Surgery

Print Tag: Refer to original journal article
Because positive temporal artery biopsy specimens demonstrate increased expression of angiotensin II type 1 receptors in giant cell arteritis patients, ACE inhibitors may reduce reliance on corticosteroid treatment.

**Background:** Current treatment for giant cell arteritis (GCA) is long-term, high-dose corticosteroids. This nonspecific therapy is fraught with numerous side effects, therefore target immunotherapy is desired. Angiotensin II is a vasoactive peptide that plays a role in vessel inflammation leading to atherosclerosis.

**Objective:** To determine the number of angiotensin type 1 (AT\(_1\)) and type 2 (AT\(_2\)) receptors in negative and positive temporal artery biopsy specimens.

**Design:** Immunohistochemical evaluation of archived tissue.

**Participants:** 10 patients with GCA and 10 controls from a single center in Sweden.

**Methods:** Pathologic specimens from 20 temporal artery biopsies were retrieved from the archives of the pathology department. Each specimen was reviewed and verified as positive or negative based on presence of inflammation and clinical history. More sections were cut from the formalin fixed, paraffin embedded blocks. Immunohistochemical staining for AT\(_1\) and AT\(_2\) receptors was performed on all specimens. The intensity of immunostaining was quantified using ImageJ software.

**Results:** Obvious inflammation was observed in 10 specimens considered positive for GCA. Evidence of atherosclerosis without inflammatory cells was seen among control specimens. Immunohistochemical staining for AT\(_1\) receptors was significantly (\(P<0.05\)) greater for GCA patients (73±28) compared to controls (40±22) in the smooth muscle layer. There was no significant difference in immunostaining in the endothelial cell layer (60±19 in GCA vs 56±20 in control). AT\(_1\) immunostaining was also seen among inflammatory cells. No significant difference in immunostaining for AT\(_2\) receptors occurred in either the endothelial (47±20 in GCA vs 49±17 in control) or the smooth muscle (41±22 in GCA vs 36±18 in control) layers between groups.

**Conclusions:** AT\(_1\) receptors expression is elevated in temporal arteries of GCA patients compared to controls. This suggests that AT\(_1\) may play a role in the pathogenesis of GCA and that ACE inhibitors could conceivably provide an alternative to corticosteroids.

**Reviewer’s Comments:** If you have a GCA patient that also has hypertension, it may be reasonable to suggest to the rheumatologist or internist to switch the patient to an ACE inhibitor. If AT\(_1\) is truly pathogenic it may reduce the duration and dosage of corticosteroid treatment. (Reviewer-Michael S. Lee, MD).

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Keywords: Angiotensin II, Temporal Artery, Giant Cell Arteritis

Print Tag: Refer to original journal article
For Blepharospasm Pts, Tint Can Improve Symptoms

*FL-41 Tint Improves Blink Frequency, Light Sensitivity, and Functional Limitations in Patients with Benign Essential Blepharospasm.*

Blackburn MK, Lamb RD, et al:


The FL-41 tint improves symptoms in patients with blepharospasm.

**Background:** The majority of patients with benign essential blepharospasm (BEB) experience substantial photophobia.

**Objective:** To study the subjective effect of FL-41 tinted lenses among patients with BEB, including evaluation of these lenses on blink frequency, duration and force.

**Design:** Randomized, crossover study.

**Participants:** 26 to 30 patients with BEB and 26 controls from a single center in Utah.

**Methods:** Patients had to have symptoms of BEB for ≥1 year. Patients who had received a prescription for tinted lenses were excluded to avoid bias. If patients wore spectacles, clip on lenses were given. If they didn't wear spectacles, patients wore plano-tinted lenses. Of patients, 30 were randomized to wear FL-41 or grey tinted lenses for 2 weeks, wear nothing for 2 weeks, and then cross over to wear the other tint for 2 weeks. They filled out questionnaires before and after each lens was used. Electromyography (EMG) measurements of blink frequency, duration, and force were performed on 26 BEB patients and 26 controls. In one trial, 13 BEB patients and 13 controls compared FL-41 lenses to a similarly rose-colored lens that did not block the same wavelengths as FL-41. In the absence of a spectrophotometer, one could not distinguish between these lenses. In another trial, 13 BEB patients and 13 controls compared the FL-41 to grey tinted lenses. EMG measurements were taken while reading under a calibrated light.

**Results:** Among the 30 patients in the first trial, there were 20 women and 10 men with a mean age of 66 years. These patients perceived that the FL-41 lenses gave them greater improvement than grey tinted lenses for all activities of daily living, photophobia, and the frequency and severity of their blepharospasm. For various activities of daily living (ADL), the improvement with FL-41 lenses alone was noted by about 15 to 30% of patients compared to 3 to 4% for the grey lenses alone. For the various ADL, 13 to 46% felt that both lenses helped and 33% to 57% did not feel that either was beneficial. For EMG trials, there was no change for any controls using any of the lenses. FL-41 lenses for BEB patients improved blink rate (by 7 blinks/min) and blink force (by 6.7mV) compared to the rose tinted lenses. FL-41 lenses improved the mean blink rate by 6 blinks/min compared to grey tinted lenses. FL-41 did not affect duration of blinks.

**Conclusions:** Patients with blepharospasm enjoy subjective and objective improvements using FL-41 tinted lenses.

**Reviewer's Comments:** This tint can be very helpful for blepharospasm patients. Keep in mind that it does not help all BEB patients. Nor does it make all of their symptoms go away. (Reviewer-Michael S. Lee, MD).

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**Keywords:** FL-41, Photophobia, Blepharospasm, Benign Essential Blepharospasm

**Print Tag:** Refer to original journal article
Memantine Induces Reversible Neurologic Impairment in Patients With MS.
Neurology 2008; 72 (May): 1630-1633

Memantine may cause transient neurologic symptoms among patients with multiple sclerosis.

**Background:** Patients with multiple sclerosis may develop cognitive dysfunction. Memantine is a NMDA receptor inhibitor used in the treatment of patients with Alzheimer disease.

**Objective:** To test the safety and efficacy of memantine for cognitive function among patients with multiple sclerosis (MS).

**Design:** Randomized, double-masked crossover trial.

**Participants:** Patients enrolled in this trial from a single center in Spain.

**Methods:** The study planned to recruit 60 patients with MS aged 18 to 65 years. For inclusion, patients had to score >1.5 standard deviations below controls on standardized cognitive testing. Patients with depression or psychiatric disease, substance abuse, or use of benzodiazepines were excluded. Each patient was to be randomized to either memantine 30 mg a day or placebo for a period of 6 months and then switched to the other group. The dose was initially 10 mg per day for a week, then 20 mg a day for a week, and then 30 mg a day for the rest of the time.

**Results:** After 19 patients had been recruited into the study, 9 developed neurological symptoms including blurred vision, cognitive decline, increased weakness, severe headache, reduced ability to walk and severe fatigue. These adverse events were reported to the Institutional Review Board (IRB) and investigators were told to unmask the data. Of 9 patients in the memantine group, 7 had symptoms. Of patients, cognitive decline of 1 was considered due to disease progression. Of 10 patients in the placebo group only 2 had symptoms and both were considered due to changes in their disease modifying therapy. All patients described remission of their symptoms within 1 to 2 days of stopping memantine. The clinical trial was halted early.

**Conclusions:** Memantine at 30 mg per day may induce reversible neurologic symptoms among patients with moderately severe MS.

**Reviewer’s Comments:** The typical dose of memantine for Alzheimer disease patient is 20 mg a day. No patient developed symptoms at 10 or 20 mg of memantine. It may be that 30 mg a day was too high for this group of patients. The medicine appears to exacerbate neurologic symptoms but does not actually cause a relapse to occur. Symptom resolution within 48 hours of stopping memantine argues against another demyelinating event. (Reviewer-Michael S. Lee, MD).

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Keywords: Memantine, Multiple Sclerosis, Namenda

Print Tag: Refer to original journal article
White matter lesions on a brain MRI increase the risk of multiple sclerosis among children with optic neuritis.

**Background:** Among adults, an abnormal brain MRI in a patient with an initial attack of optic neuritis is a strong predictor for the development of multiple sclerosis (MS).

**Objective:** To identify the predictive value of brain MRI among pediatric patients after an isolated attack of optic neuritis.

**Design:** Retrospective, consecutive, observational case series.

**Participants:** 18 children from a single center in Philadelphia.

**Methods:** Patients with a diagnosis of optic neuritis from 1993 to 2004 were identified from a computerized database and billing records. Patients with any of the following disorders were excluded: neoplastic, inflammatory, infectious, demyelinating, or rheumatologic. For inclusion, patients had to be aged <18 years at diagnosis, suffer a first time attack, and have a brain MRI. Patients received a clinical diagnosis based on evidence of an optic neuropathy and presence of eye pain. Establishment of MS was based on accepted criteria at the time of diagnosis. Neuromyelitis optica antibody was neither routinely performed nor available for all patients.

**Results:** 46 patients were diagnosed with optic neuritis. Workup revealed a systemic disorder in 17 and these were excluded. Of the remaining 29, nearly all were girls with a mean age of 10 years. The optic neuritis was bilateral and simultaneous in more than half. The optic disc was swollen in nearly 70% of affected eyes. Almost 40% of patients had white matter lesions on brain MRI. Of patients, 18 had ≥24 months follow-up and 11 had ≥60 months follow-up. Of these patients, 11 had a normal brain MRI and did not develop MS, 7 had an abnormal brain MRI, and 3 developed clinically definite MS. Of the 3 patients who developed MS, 1 had bilateral and 2 had unilateral optic neuritis. Almost one-third of the 29 patients developed a recurrence of optic neuritis.

**Conclusions:** An abnormal brain MRI at the time of the first attack of optic neuritis increases the risk of MS among children.

**Reviewer's Comments:** While many have traditionally believed that optic neuritis among children is likely viral in etiology, it appears that the predictive value of the brain MRI in adults holds true for children as well. A child with optic neuritis deserves a brain MRI for predictive purposes. (Reviewer-Michael S. Lee, MD).

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Keywords: Pediatrics, Optic Neuritis, Multiple Sclerosis, MRI

Print Tag: Refer to original journal article
Computerized Version of Amsler Grid Hits the Web

The Amsler Grid in Modern Clothes.

Frisén L:

Br J Ophthalmol 2009; 93 (June): 714-716

The author has created a virtual Amsler grid that utilizes a dynamic presentation and quantifiable results.

Background: The Amsler grid is used by patients who take Plaquenil® or have received a diagnosis of macular degeneration to identify subtle paracentral scotomas or metamorphopsia. A computerized version may allow quantitative assessment of any changes.

Objective: To evaluate a computerized version of the Amsler grid among normal and abnormal eyes.

Design: Prospective observational study.

Participants: 1 patient with metamorphopsia and 3 normal individuals.

Methods: A grey grid on a white background was displayed on a personal computer liquid-crystal display screen. The grid covered 20° of visual field at 0.25 meter distance. Gridlines were 1 pixel in width and separated by 1°. The grid moved across the screen at 1° per second. Subjects were tested monocularly with appropriate near correction. For normal subjects, simulated scotomas were inserted into the grid by deleting randomly selected line segments. Squares were also bent to simulate metamorphopsia. Computer screen contrast was set to either 0.25 or 0.50.

Results: Normal subjects varied in their ability to detect a scotoma. Of subjects, 1 could reliably detect a 0.5° scotoma on the high contrast chart. All normal individuals could reliably observe a scotoma ≥2°. There were no false positive errors. The smallest grid deformation was detected centrally, but needed to be up to 5 times larger at the edge of the grid. The patient with metamorphopsia "nullled" the grid by adjusting it so that he viewed it as normal. On 5 trials, the axis of deformation was very similar.

Conclusions: The "MacuFlow" test, a computerized version of the Amsler grid, reliably detected small scotomas. It was able to quantify metamorphopsia. It is available on the internet and results can be transmitted electronically.

Reviewer's Comments: This is a neat concept because it allows a patient to monitor change quantitatively. It appears to identify small, paracentral scotomas. It requires more rigorous study, but is a great idea. It is available at the following website: http://www.oft.gu.se/webdiagnos and is listed under diagnostic aids and MacuFlow. (Reviewer-Michael S. Lee, MD).

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Keywords: Amsler Grid, Macular Degeneration, Computerized Monitoring

Print Tag: Refer to original journal article
Patients who underwent endothelial keratoplasty by experienced corneal surgeons or by cornea fellows had similarly good visual outcomes and corneal endothelial cell loss.

**Objective:** To compare clinical outcomes of patients undergoing Descemet stripping automated endothelial keratoplasty (DSAEK) by an experienced corneal surgeon and inexperienced corneal fellows using a standardized surgical technique.

**Design:** Retrospective, comparative interventional clinical case series.

**Methods:** A consecutive series of 327 cases of DSAEK performed at a single institution was included in this study. Medical records were reviewed to determine postoperative best corrected visual acuity, endothelial cell density, and occurrence of postoperative complications in each case. A comparison of these outcomes was made between patients who were operated by a single experienced corneal surgeon and by 3 inexperienced corneal fellows working at the same institution. The corneal fellows used the identical surgical technique employed by the attending surgeon.

**Results:** A significant improvement in best corrected visual acuity was seen in patients in both groups. When evaluated 6 months after surgery, those operated by the attending surgeon had a mean Snellen equivalent acuity of 20/37 compared to 20/36 in those patients operated by a fellow. In addition, there was no statistically significant difference in the mean corneal endothelial cell loss between groups (32% vs 35%). With regard to dislocation of the corneal graft following surgery, this complication was rare in both groups, occurring in only 2% of cases operated by the attending surgeon, and 1% of those operated by fellows.

**Conclusions:** There is no difference in clinical outcomes of patients undergoing DSAEK by an experienced corneal surgeon or by inexperienced surgical fellows. Results of supervised novice surgeons can result in excellent clinical outcomes.

**Reviewer's Comments:** This study should be encouraging to those who have not yet begun performing this relatively new procedure, confirming that good clinical outcomes can be achieved even when the beginning surgeon is still working his or her way up the learning curve. The more rapid visual recovery, reduction in post-keratoplasty astigmatism, and superior structural integrity of the globe are all reasons why patients with corneal endothelial disease benefit from this procedure in comparison to penetrating keratoplasty, and why anterior segment surgeons should perform DSAEK in appropriate candidates. (Reviewer-Scott D. Smith, MD, MPH).

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Keywords: Endothelial Keratoplasty, Complications

Print Tag: Refer to original journal article
Inflammatory markers are present in increased levels in the tears of patients with keratoconus, indicating that chronic low-grade inflammation may play a role in the pathogenesis of this condition.

**Objective:** To determine levels of markers of inflammation in the tears of patients with keratoconus (KC).

**Design:** Prospective, observational clinical case series.

**Methods:** Tear samples were obtained from both eyes of a consecutive series of 30 patients with unilateral KC and from a control group of 10 healthy subjects without KC. Samples were processed to measure the concentration of 3 markers of chronic inflammation, interleukin-6 (IL-6), tumor necrosis factor α (TNF-α), matrix metalloproteinase-9 (MMP-9). Concentration was compared between eyes with KC, contralateral eyes with subclinical KC, and eyes of normal control subjects.

**Results:** Mean concentrations of IL-6 were similar between eyes with KC and subclinical KC, each of which were greater than in normal controls ($P <0.00001$). Levels of TNF-α were greatest in KC eyes, lowest in control eyes, and intermediate in eyes with subclinical KC. Concentration of MMP-9 was elevated only in eyes with manifest KC.

**Conclusions:** Increased expression of TNF-α and IL-6 is seen in eyes with KC and subclinical KC. Elevated levels of MMP-9 are seen only in eyes with KC. These findings suggest that KC is associated with chronic inflammation.

**Reviewer's Comments:** Traditionally, KC has been considered a non-inflammatory type of corneal degeneration. The findings of this study, that various markers of inflammation are expressed in higher concentration of eyes with KC and subclinical KC, indicates that chronic, low-grade inflammation appears to be present in this condition. Although further study will be required to elucidate the role that inflammation plays in the development of KC, this study indicates that this condition cannot be defined as a non-inflammatory disease, and that chronic inflammation may play a role in its pathogenesis. (Reviewer-Scott D. Smith, MD, MPH).

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Keywords: Keratoconus, Tears, Inflammation

Print Tag: Refer to original journal article
Objective: To evaluate feasibility and clinical outcomes of performing arcuate keratotomy with the femtosecond laser for the management of postoperative astigmatism following penetrating keratoplasty (PK) or deep lamellar keratoplasty.

Design: Prospective, non-comparative, interventional clinical case series.

Methods: All procedures were performed with the Femtosecond Laser Arcuate Keratotomy for the Correction of High Astigmatism After Keratoplasty.


Arcuate keratotomy performed with the femtosecond laser can effectively reduce astigmatism following penetrating or deep lamellar keratoplasty.

Results: Patients were followed 6 months after treatment. A significant improvement in both uncorrected and best corrected visual acuity was seen at final follow-up in comparison to baseline. A significant reduction in astigmatism measured by subjective refraction decreased from 7.2 diopters to 2.2 diopters by 1 month after treatment (P =0.002) and remained stable throughout the follow-up period. Anterior segment optical coherence imaging of the laser keratotomy incisions confirmed the incision depth and location to be consistent with the preoperative surgical plan.

Conclusions: Arcuate keratotomies performed with the femtosecond laser are effective in managing patients with high astigmatism following penetrating or deep lamellar keratoplasty.

Reviewer's Comments: The performance of an arcuate keratotomy with the femtosecond laser represents another application of this laser in corneal refractive surgery. While originally developed to create lamellar corneal flaps during LASIK surgery, it can also be programmed to make corneal incisions in a large variety of configurations, with applications in the performance of penetrating keratoplasty, as well as the management of post-keratoplasty astigmatism as described in this study. (Reviewer-Scott D. Smith, MD, MPH).

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Keywords: Refractive Keratotomy, High Astigmatism

Print Tag: Refer to original journal article
Residual refractive error compromising the clinical outcome after implantation of a multifocal IOL can be effectively managed by LASIK.

**Objective:** To evaluate the safety and efficacy of laser in situ keratomileusis (LASIK) for management of residual refractive error following phacoemulsification with implantation of an apodized diffractive multifocal intraocular lens (IOL).

**Design:** Retrospective, interventional clinical case series.

**Methods:** Medical records were reviewed of a consecutive series of patients who underwent LASIK for the management of residual refractive error following implantation of an AcrySof ReSTOR multifocal IOL (Alcon Laboratories). The procedure was performed using the IntraLase F60 femtosecond laser for creation of the corneal flap, and with the Visx Star S4 excimer laser. Patients were evaluated after LASIK to compare the refractive error and uncorrected visual acuity before and after the procedure.

**Results:** 85 eyes of 59 patients were included in the study. Myopic correction was performed in 42.3% of eyes, hyperopic correction was performed in 16.5%, and correction for mixed astigmatism was performed in 41.2%. Postoperative YAG capsulotomy was performed in 52.9% of eyes. Uncorrected distance visual acuity of 20/25 or better was achieved 6 months after LASIK in 91.8% of eyes. Uncorrected near visual acuity of J1 or better was seen in 92.8% of patients at this time point. Of eyes, 99% had a final refractive error within 1 diopter of emmetropia.

**Conclusions:** LASIK is a safe, effective, and predictable procedure for the management of residual refractive error following cataract extraction with implantation of an apodized diffractive IOL.

**Reviewer's Comments:** Achievement of minimal residual refractive error is essential in achieving high levels of patient satisfaction with multifocal intraocular lenses. Accurate biometry and good surgical technique are critical elements of accomplishing this objective. In spite of this, however, occasional errors in IOL power calculation can occur, resulting in residual refractive error that compromises the benefits of the multifocal IOL. In this setting, management of residual refractive error can be accomplished with LASIK, yielding good outcomes, as described in this study. (Reviewer-Scott D. Smith, MD, MPH).

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Keywords: Refractive Surgery, Refractive Errors, Lens Implantation

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Ocular Surface Normalizes After Limbal Stem Cell Transplantation

Characterization of the Corneal Surface in Limbal Stem Cell Deficiency and After Transplantation of Cultivated Limbal Epithelium.

Paulkin M, Steuhl K-P, Meller D:

Ophthalmology 2009; 116 (June): 1048-1056

Transplantation of cultured limbal epithelial cells restores a normal corneal architecture in patients with limbal stem cell deficiency.

Objective: To evaluate changes in the cornea in patients with limbal stem cell deficiency (LSCD) and the effects of transplantation of in vitro-cultivated limbal epithelial cells to the ocular surface in these patients.

Design: Experimental study.

Methods: Tissue specimens were obtained at the time of transplantation of cultured limbal epithelium. Transplantation of these cells was performed by growing the cells on the surface of amniotic membrane, which was transferred to bare sclera after removal of pannus tissue from the cornea and sclera. Excised tissue specimens were evaluated of 17 patients with LSCD to characterize changes in the cornea in this condition. Expression of epithelial lineage markers, markers of inflammation, and of vascular endothelial growth factor were analyzed using real-time polymerase chain reaction, Western blotting, and immunofluorescence in each of the samples of corneal pannus tissue obtained from these patients. Corneal buttons were also obtained from 5 patients who underwent penetrating keratoplasty ≥5 months after transplantation of cultivated limbal epithelium. Evaluation of the same markers was performed from these specimens to evaluate the effect of limbal epithelial cell transplantation. Additionally, 6 control samples were obtained and analyzed of healthy central cornea and bulbar conjunctiva from patients who underwent enucleation for posterior segment tumors.

Results: The expression of cell lineage markers from cornea in patients with LSCD was similar to conjunctiva, but not to healthy cornea. In addition, markers of active inflammation were also present in pannus tissue compared to healthy cornea and conjunctiva. After limbal epithelial cell transplantation, the corneal surface returned to a normal phenotype, and there was a significant reduction in the expression of inflammatory markers.

Conclusions: Ingrowth of abnormal, inflamed tissue occurs in the setting of LSCD, with a phenotype similar to conjunctiva. After transplantation of cultured limbal epithelial cells, the cornea returns to a normal phenotype with marked reduction in the expression of inflammatory markers.

Reviewer's Comments: Transplantation of in vitro-cultivated limbal epithelium allows sufficient donor tissue to be generated from a small 1 by 1mm specimen of donor limbal tissue. This reduces the risk of LSCD in the donor eye. Cells can be grown on the surface of amniotic membrane, which is transferred to the ocular surface at the time of surgery. (Reviewer-Scott D. Smith, MD, MPH).

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Keywords: Limbal Stem Cell Deficiency, Transplantation

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Chronic use of contact lenses may predispose to the development of conjunctivochalasis.

**Objective:** To investigate the association between contact lens (CL) wear and development of conjunctivochalasis.

**Design:** Prospective, non-randomized, comparative clinical study.

**Methods:** 600 CL wearers (94 hard CL and 506 soft CL) were prospectively enrolled in this study. In addition, a control group of 579 non-CL wearers were also enrolled. Patients with a history of chronic dry eye requiring punctal occlusion, as well as those with a history of ocular surface or eyelid abnormalities such as entropion, ectropion, and trichiasis were excluded. Each subject underwent a clinical examination which included the grading of conjunctivochalasis in the nasal, middle, and temporal regions using a standardized grading system. Severity of conjunctivochalasis was analyzed with regard to age and use of hard or soft CLs.

**Results:** A significant increase in the prevalence of conjunctivochalasis was seen with age in both wearers and non-wearers of CLs ($P < 0.00001$). In addition, mean grade of conjunctivochalasis was significantly greater in wearers of CLs than in non-wearers ($P < 0.00001$). In addition, mean severity grade was larger in hard CL wearers than those who wore soft CLs ($P = 0.00003$). Gaze dependent conjunctivochalasis was also greater in those who wore CLs than in control subjects.

**Conclusions:** This study strongly suggests that chronic CL wear increases the risk of development of conjunctivochalasis, and that the risk is greater with hard CL than with soft CL use.

**Reviewer's Comments:** The presence of redundant folds of the conjunctiva, or conjunctivochalasis has been associated with dry eye symptoms. This study suggests that chronic, low-grade inflammation and/or mechanical factors associated with CL use may predispose to this condition. (Reviewer-Scott D. Smith, MD, MPH).

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**Keywords:** contact lens, conjunctivochalasis

**Print Tag:** Refer to original journal article
Patients with non-arteritic ischemic optic neuropathy have smaller optic cups and cup/disk ratios than other individuals.

**Objective**: To compare optic disk parameters in patients with non-arteritic ischemic optic neuropathy (NAION) to control subjects without this condition.

**Design**: Case-control study.

**Methods**: A consecutive series of both eyes of 22 patients who had been previously diagnosed with NAION were included. Diagnosis was made on the basis of a history of acute, painless vision loss accompanied by optic disk swelling and other clinical indicators of an optic neuropathy, in the absence of laboratory or clinical evidence of giant cell arteritis. Optic disk parameters were measured using the Heidelberg Retinal Tomograph III (HRT). Optical coherence tomography (OCT) retinal nerve fiber layer imaging and visual field testing were also performed. A control group was selected of 52 subjects who had undergone similar testing with normal results.

**Results**: The optic disk area tended to be smaller in affected and fellow eyes of NAION patients than of controls, but the difference was not statistically significant. Optic cup size and cup/disk area ratio of both eyes of NAION patients were significantly smaller than those of control subjects. As expected, retinal nerve fiber layer thickness was decreased in eyes affected by NAION, both in comparison to fellow eyes and those of normal control subjects.

**Conclusions**: The optic cup size and cup/disk ratio are small in patients with NAION.

**Reviewer's Comments**: This study supports prior observations that the optic disk of a patient with NAION is "crowded" with a small cup/disk ratio and less unoccupied space in the optic disk than other individuals. It has been postulated that these crowded disks are at greater risk for the development of NAION due to a compressive effect on the neurons within the optic nerve head, subjecting them to ischemia. (Reviewer-Scott D. Smith, MD, MPH).

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Keywords: Ischemic Optic Neuropathy, Coherence Tomography, Ophthalmoscopy

Print Tag: Refer to original journal article
A single dose of oral diclofenac is effective in reducing pain during panretinal photoagulation.

Objective: To evaluate efficacy of oral and topical diclofenac for preventing pain during panretinal photoagulation (PRP).

Design: Prospective, double-masked, placebo-controlled, randomized clinical trial.

Participants/Methods: 90 patients who required initial PRP for the treatment of proliferative diabetic retinopathy were enrolled in this study. Patients were randomly assigned into 1 of 3 study groups. Patients in group 1 received oral diclofenac 50mg 1 hour prior to laser treatment. In addition, they received placebo eye drops 1 hour and 10 minutes prior to treatment. Patients in group 2 received an oral placebo and diclofenac topical eye drops according to the same dosing schedule. Patients in group 3 received both oral and topical placebo medications. Laser treatment was conducted using a standardized regimen, with a maximum of 600 laser applications performed in each case. A standardized instrument designed to assess pain was used to evaluate intraoperative pain in each patient. Patients underwent a second session of PRP at a later date without any administration of study medication. Pain scores in the 3 groups were compared to determine the efficacy of each medication regimen and between the first and second laser sessions.

Results: A clinically and statistically significant difference was seen in pain scores between the oral diclofenac and placebo groups (25.7 vs 41.3, \( P = 0.02 \)). No clinically significant difference in pain scores was seen between the topical diclofenac and placebo groups. Pain scores were higher in both the oral and topical diclofenac groups on the second laser session.

Conclusions: A single oral dose of diclofenac is effective in reducing intraoperative pain during PRP.

Reviewer's Comments: PRP is effective in managing conditions that lead to proliferative retinopathy. However, many patients experience mild to moderate pain during the procedure. Based upon their results, the authors now offer oral analgesia with diclofenac to all of their patients undergoing PRP. (Reviewer-Scott D. Smith, MD, MPH).

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Keywords: Retinal Photocoagulation, Complications

Print Tag: Refer to original journal article
Retinal Vein Occlusion Does Not Predict MI

Retinal Vein Occlusion and the Risk of Acute Myocardial Infarction: A 3-Year Follow-Up Study.
Hu C-C, Ho J-D, Lin H-C:
Br J Ophthalmol 2009; 93 (June): 717-720

After accounting for age and gender, having a history of retinal vein occlusion is not associated with an increased risk of myocardial infarction.

Objective: To investigate the association between retinal vein occlusion (RVO) and the risk of acute myocardial infarction (MI).

Design: Prospective, observational cohort study.

Methods: The Taiwan National Health Research Institute database was used to identify a cohort of individuals who were diagnosed with RVO during a 3-year period. A control group of individuals who were not diagnosed with RVO was also randomly selected from the same database. Subjects were tracked prospectively for 3 years to determine the number of new cases of acute MI in the groups. Statistical analysis was performed to determine whether having had a prior RVO was an independent predictor of the future development of MI.

Results: RVO patients had a significantly greater probability of having an acute MI during the follow-up period (1.86% vs 0.78%, \( P = 0.03 \)). However, after adjusting for patient age, gender, and the presence of other comorbid conditions such as diabetes, hypertension, and renal disease, there was no significant association between RVO and risk of MI.

Conclusions: A history of RVO is not an independent predictor of acute MI.

Reviewer's Comments: This study does not imply that individuals who experience RVO have the same risk as everyone else in the population of having cardiovascular disease. What it does imply is that other risk factors that may have resulted in the RVO are the reason that the risk of cardiovascular disease is present. Having an RVO does not indicate that the risk of cardiovascular disease is increased any further than the risk associated with the underlying conditions such as diabetes or hypertension that resulted in the RVO. If a patient presents with RVO and is unaware of any possible underlying medical conditions, a medical evaluation should be conducted to ensure that no such conditions are present. (Reviewer-Scott D. Smith, MD, MPH).

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Keywords: Retinal Vein Occlusion, Myocardial Infarction

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