Intravitreal injection of clindamycin and dexamethasone appears to be as effective as traditional oral therapy for ocular toxoplasmosis.

**Objective:** To compare the efficacy of intravitreal injection of clindamycin and dexamethasone to classic medical therapy with pyrimethamine, sulfadiazine, and prednisolone for the treatment of active ocular toxoplasmosis.

**Design:** Prospective, randomized masked clinical trial.

**Participants/Methods:** 68 patients with active ocular toxoplasmosis requiring therapy for vision-threatening disease were randomly assigned to 1 of 2 treatment groups. The intravitreal therapy group received an injection of clindamycin 1 mg and dexamethasone 400 µg administered at baseline and at 2 weekly intervals as needed according to response to initial therapy. Classic therapy consisted of oral administration of pyrimethamine, sulfadiazine, prednisolone, and supplemental folinic acid. Patients were monitored on a weekly basis for 6 weeks. At baseline and at each follow-up visit, fundus photographs were taken and an objective image analysis system was used to measure change in lesion size in response to therapy.

**Results:** Mean number of injections in the intravitreal therapy group was 1.6. A statistically significant reduction in lesion size was seen in response to therapy in both groups, but there was no significant difference in the percent reduction at 6 weeks between treatment groups, with a reduction in lesion size of 57.0% in the intravitreal therapy group and 58.4% in the classic therapy group. A significant improvement in visual acuity was also seen in both groups, which did not differ according to treatment.

**Conclusions:** Intravitreal injection of clindamycin and dexamethasone appears to be equally efficacious as classic oral therapy for active ocular toxoplasmosis.

**Reviewer’s Comments:** The motivation for consideration of local therapy with intravitreal drug injections comes from the significant side-effect profile of medications traditionally used for oral therapy of toxoplasmosis. In patients who tolerate these medications poorly, local therapy with intravitreal clindamycin and dexamethasone may be a good alternative. In addition to the findings mentioned above, there was some indication that patients with positive IgM antibodies to toxoplasma actually responded better to intravitreal therapy than to oral therapy. Further investigation is needed to evaluate this question more carefully. (Reviewer-Scott D. Smith, MD, MPH).

**Keywords:** Toxoplasmosis
Objective: To evaluate the efficacy of intraoperative irrigation of the ocular surface with 0.25% povidone-iodine in reducing aqueous bacterial contamination during cataract surgery.

Design: Prospective clinical trial.

Methods: 404 consecutive eyes undergoing cataract surgery at a single institution were studied. The first 202 eyes underwent traditional intraoperative irrigation with balanced salt solution (BSS). The subsequent 202 eyes underwent intraoperative irrigation with 0.25% povidone-iodine in place of BSS for moistening of the ocular surface during surgery. Pre- and postsurgical aqueous samples were obtained for bacterial culture. In addition, ocular surface cultures were obtained at the time and placement of the lid speculum. Measurement of iodine concentration in the anterior chamber was also performed from samples taken at the end of surgery. Pre- and postoperative corneal endothelial cell density was measured using specular microscopy both before surgery and 1 week after surgery.

Results: Bacterial contamination of the ocular surface at the beginning of surgery was equal in the 2 groups, with 5.5% in the BSS group and 6.0% in the povidone-iodine group showing growth. A significant reduction in bacterial growth from aqueous samples after surgery was seen in the povidone-iodine group, with no growth compared to 5.0% growth in the BSS group. An increased iodine concentration in the anterior chamber was seen at the conclusion of surgery in the povidone-iodine group; however, no difference in corneal endothelial cell counts was seen before or after surgery in the 2 groups.

Conclusions: Intraoperative irrigation of the ocular surface with povidone-iodine 0.25% reduces bacterial contamination in the anterior chamber following surgery.

Reviewer’s Comments: This study did not investigate infection rates, which would require a much larger study given the low rate of endophthalmitis following cataract surgery, but the apparent safety of use of topical povidone-iodine 0.25% and elimination of bacterial growth from aqueous samples certainly make this approach a promising one to investigate further. In the meantime, studies have clearly demonstrated the efficacy of topical povidone-iodine 5.0% for sterilization of the ocular surface at the beginning of surgery, which should be performed by all cataract surgeons. In the future, the technique described in the study may become a standard procedure for cataract surgery as well. (Reviewer-Scott D. Smith, MD, MPH).
Phototherapeutic keratectomy can improve visual acuity and has been shown to reduce photophobia caused by chronic corneal opacities following epidemic keratoconjunctivitis.

Objective: To evaluate the efficacy of phototherapeutic keratectomy for the treatment of corneal opacities after epidemic keratoconjunctivitis.

Design: Prospective, interventional clinical case series.

Participants/Methods: Patients with chronic central corneal opacities causing decreased visual acuity and photophobia due to epidemic keratoconjunctivitis were enrolled in this study. Patients underwent phototherapeutic keratectomy with supplemental mitomycin C 0.002% applied for 1 minute. Ablation depth was calculated on the basis of preoperative measurements of corneal opacity thickness using optical coherent tomography, ultrasound biomicroscopy, and Pentacam imaging (Pentacam, Oculus, Inc, Lynnwood, Washington, USA). Follow-up examination through 1 year allowed evaluation of the efficacy of treatment.

Results: 31 eyes of 23 patients were enrolled in the study. Mean patient age was 41.8 years. Duration of disease before treatment was 19.1±14 months. The proportion of patients with photophobia decreased from 100% to 29% after surgery. An improvement of best-corrected visual acuity of at least 2 lines was seen in 78% of patients at 12-month follow-up. Contrast sensitivity also improved under both phototropic and mesopic conditions, but a hyperopic shift of +1.5 diopters was seen on average in treated patients.

Conclusions: Successful reduction of photophobia and decreased visual acuity was accomplished in the majority of patients who underwent phototherapeutic keratectomy for chronic corneal opacities caused by epidemic keratoconjunctivitis.

Reviewer’s Comments: It must be emphasized that this is not a completely benign procedure and resulted in significant refractive shift; however, in patients with long-standing symptoms not successfully managed with conservative therapy using topical steroids or who have developed recurrence despite this therapy, phototherapeutic keratectomy may be considered as a treatment option. (Reviewer-Scott D. Smith, MD, MPH).

Keywords: Corneal Opacity, Epidemic Keratoconjunctivitis, Excimer Laser

Print Tag: Refer to original journal article
Achievement of uveitis quiescence with methotrexate therapy for at least 2 years reduces the rate of relapse following cessation of systemic immunosuppression in children with juvenile idiopathic arthritis-associated uveitis.

**Objective:** To assess the efficacy of methotrexate in the management of chronic anterior uveitis associated with juvenile idiopathic arthritis (JIA), and to determine the rate of relapse after its discontinuation.

**Design:** Retrospective clinical case series.

**Methods:** Data were reviewed from 22 cases of pediatric JIA treated with methotrexate for active uveitis. Clinical and demographic data were reviewed, as well as period of disease quiescence, duration of methotrexate therapy, and severity of anterior chamber inflammation. Decision for methotrexate use and discontinuation was based on the joint decision of a rheumatologist and ophthalmologist, considering the period of disease quiescence from both an arthritis and uveitis standpoint. All children continued methotrexate therapy for at least 1 year. Statistical analysis allowed the identification of factors associated with relapse after discontinuation of methotrexate.

**Results:** Achievement of disease quiescence was successful in 82% of patients within 3 months of initiation of methotrexate therapy. Successful reduction in use of topical steroids was also achieved in patients who responded to treatment. In patients who discontinued methotrexate therapy, relapse was observed within 1 year after cessation of therapy. Mean time of relapse was 7.5 months after discontinuation. A significantly better relapse-free survival was seen after withdrawal of methotrexate in patients treated with systemic immunosuppression for >3 years, in those who were aged >8 years at the time of methotrexate cessation, and in those who had a period of uveitis inactivity of at least 2 years.

**Conclusions:** Methotrexate is successful in reducing the dependency on topical steroids and improving control of inflammation in children with JIA-associated uveitis. The rate of relapse during the first year after cessation of methotrexate therapy can be high, however, and is decreased with longer duration of methotrexate therapy, older patient age, and longer duration of disease inactivity.

**Reviewer's Comments:** Use of methotrexate for the management of chronic uveitis in patients with JIA-associated ocular inflammation has become commonplace during the past 20 years. This study provides guidance as to the use of this medication and highlights the importance of long-term duration of therapy prior to its withdrawal. (Reviewer-Scott D. Smith, MD, MPH).

**Keywords:** Uveitis, Juvenile Idiopathic Arthritis

**Print Tag:** Refer to original journal article
Is Age a Risk Factor for Cataract Development After DSEK?

Rate and Risk Factors for Cataract Formation and Extraction After Descemet Stripping Endothelial Keratoplasty.

Price MO, Price DA, et al:

Br J Ophthalmol 2010; 94 (November): 1468-1471

Visually significant cataract develops within 3 years in >50% of phakic patients aged >50 years who undergo endothelial keratoplasty.

**Objective:** To estimate the rate of cataract development after Descemet stripping endothelial keratoplasty (DSEK), and to identify risk factors for this complication.

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

**Methods:** Records were reviewed of a consecutive series of 1050 cases of primary DSEK. The first-treated phakic eye of each patient was included in the analysis. Surgery was performed by a single experienced surgeon and included creation of a 5-mm scleral tunnel or clear corneal incision. The graft was elevated against the cornea with an air bubble that completely filled the anterior chamber for 5 to 10 minutes. Enough air was removed to prevent postoperative pupillary block. Primary outcome was time to removal of visually significant cataract.

**Results:** 60 eyes met the criteria for inclusion in the study. Median age of patients was 52 years (range, 32 to 69 years). Cataract extraction was required in 37% of eyes during follow-up. All grafts remained clear following cataract extraction. In patients aged ≤50 years at the time of DSEK, 1-year and 3-year rates of cataract surgery were 0% and 7%. In contrast, older patients had a significantly higher rate of cataract surgery, with 1-year and 3-year rates of 31% and 55%, respectively.

**Conclusions:** Age >50 years is a significant risk factor for the development of visually significant cataract in phakic patients who undergo DSEK.

**Reviewer's Comments:** Since visually significant cataract is common in older patients who are phakic and who undergo DSEK, consideration of initial combined phacoemulsification with DSEK is a reasonable option. Although no graft failures were observed when subsequent phacoemulsification was performed in this study, intraocular surgery is always associated with endothelial cell loss and is certainly not beneficial to a successful graft. When symptomatic, or even relatively asymptomatic, lens opacity is already present, proceeding with combined surgery may be the most prudent approach. (Reviewer-Scott D. Smith, MD, MPH).

Keywords: Keratoplasty, Cataract, Complications of Surgery

Print Tag: Refer to original journal article
Brimonidine does not reduce intraocular pressure during sleep.

**Objective:** To investigate the diurnal effect of brimonidine therapy on intraocular pressure (IOP).

**Design:** Prospective, open-label experimental study.

**Participants/Methods:** 15 patients with newly diagnosed open-angle glaucoma or ocular hypertension between the ages of 46 and 72 years were enrolled in this study. All patients underwent 24-hour IOP measurement under controlled conditions in a sleep laboratory. Measurement of IOP was performed every 2 hours using a pneumatometer in both the sitting and supine body positions, during the 16-hour diurnal/wake period, and in the supine body position during the 8-hour nocturnal/sleep period. After collection of baseline IOP measurements through a 24-hour cycle, patients were treated with brimonidine 0.1% (Alphagan® P, Allergan, Irvine, CA) 3 times daily for 4 weeks. After 4 weeks of treatment, a repeat 24-hour IOP cycle was measured under the same conditions in the sleep laboratory.

**Results:** A significant reduction in IOP was seen at each of the time points measured during waking hours after treatment with brimonidine. In contrast, there was no significant change in IOP after brimonidine therapy during any of the 4 nocturnal time points measured.

**Conclusions:** Brimonidine monotherapy reduces IOP during waking hours but does not reduce IOP during the sleep period.

**Reviewer's Comments:** The results of this study correspond closely to results of a similar study performed with timolol therapy. Timolol and brimonidine both function by modifying the activity of the sympathetic nervous system in the eye. Other studies have demonstrated that sympathetic activity is low during sleep, and blockade of beta-receptors or stimulation of alpha-2 receptors, which both reduce aqueous production while the sympathetic nervous system is active, seem not to have much effect at night. In contrast, carbonic anhydrase inhibitors reduce aqueous production through an entirely different mechanism that functions both day and night. In addition, prostaglandin analogs reduce IOP through increased uveoscleral outflow, which works throughout the 24-hour cycle. It is important for ophthalmologists who manage glaucoma patients to understand the pharmacology of drugs used to treat this condition and to be aware of the 24-hour circadian effects of each of these medications. (Reviewer-Scott D. Smith, MD, MPH).

**Keywords:** Glaucoma, Medical Therapy

**Print Tag:** Refer to original journal article
Optic disc hemorrhages are an indication of lack of stability of glaucoma and are associated with a more rapid decline in the visual field.

**Objective:** To evaluate the rate of visual field progression in eyes with optic disc hemorrhage, and to investigate the effect of reduction of intraocular pressure (IOP) on visual field loss.

**Design:** Observational cohort study.

**Participants/Methods:** 510 eyes of 348 patients with glaucoma who participated in the Diagnostic Innovations in Glaucoma Study were included in this analysis. All patients underwent a baseline clinical examination, which included standard automated perimetry in optic disc photographs. Annual repeat examination was performed and included a repetition of the same tests as were performed at baseline. Mean follow-up was 8.2 years. Presence of optic disc hemorrhage was identified on the basis of masked rating of stereophotographs. Patients who developed optic disc hemorrhage were compared with regard to rate of decline of the visual field index to those who did not have a disc hemorrhage.

**Results:** During follow-up, 19% of eyes developed at least 1 disc hemorrhage. Rate of decline of the visual field index was significantly greater in eyes with disc hemorrhage compared to those without (-0.88% per year vs -0.38% per year; \( P < 0.0001 \)). In addition to demonstrating a more rapid rate of visual field loss, the post-hemorrhage level of IOP was also found to be significantly associated with this rate. In patients who had a significant reduction in IOP, the subsequent rate of visual field loss after a disc hemorrhage was slower. For each 1 mmHg reduction of IOP, a slower rate of progression of 0.31% per year change in the visual field index was seen.

**Conclusions:** Optic disc hemorrhages are associated with more rapid decline in the visual field in patients with glaucoma; however, IOP reduction after the occurrence of disc hemorrhage is associated with a significant reduction in the subsequent rate of visual field loss.

**Reviewer's Comments:** It was found that a subset of patients in the study, despite IOP reduction after disc hemorrhage, continues to develop visual field progression. This suggests that the pathophysiology of glaucoma may differ in some patients, with intraocular pressure playing a less important role in some patients than in others. Further research is needed to clarify whether vascular or other factors may play a role in the pathophysiology of this subset of glaucomatous patients; however, this study clearly indicates the need to identify and respond to the occurrence of optic disc hemorrhages by further reduction of IOP. (Reviewer-Scott D. Smith, MD, MPH).

Keywords: Glaucoma, Visual Field Loss

Print Tag: Refer to original journal article
The ICare rebound tonometer is well tolerated in the majority of infants for measurement of intraocular pressure.

Objective: To evaluate the feasibility of intraocular pressure (IOP) measurement using the ICare rebound tonometer in healthy infants.

Design: Prospective clinical study.

Participants/Methods: 46 infants aged 3 to 18 months were included in the study. IOP measurements were made using the ICare rebound tonometer with a subset of 10 infants undergoing the same measurement by 2 different examiners. Each examiner measured the IOP using the tonometer 3 times, and the process was repeated if variants of >3 mmHg were seen among the measurements. Mean of the 3 measurements was considered to be the final IOP measurement. Statistical comparison of the IOP values measured by each of the examiners was made.

Results: 6 infants (13%) refused to cooperate and were unable to be examined with this instrument. Mean IOP value of the remaining 39 infants was 11.8 mmHg (range, 7.3 mmHg to 17.0 mmHg). In the subset of children who underwent IOP measurement by the 2 examiners, virtually identical results were found with differences between 0 mmHg to 1 mmHg in 90% of cases. Mean difference between IOP measured by the examiners was 0.8 mmHg. The examination was tolerated well by 87% of children who were cooperative, and no child showed any sign of discomfort during or after IOP measurement.

Conclusions: The handheld ICare rebound tonometer appears to be feasible for use in the vast majority of infants.

Reviewer's Comments: Measurement of IOP in young children suspected of glaucoma can be difficult. This instrument appears to offer a simple method that may be tolerated much better than other handheld devices commonly used for IOP measurement in infants. Studies evaluating its correlation to Goldmann applanation tonometry have shown good correlation within the range of up to 23 mmHg. There may be significant discrepancies between the results of this measurement and Goldmann applanation tonometry when IOP is higher. When IOP elevation is suggested by the rebound tonometer, further evaluation is indicated; however, this may be a very suitable instrument for screening IOP in infants and for measurement of follow-up IOP between examinations under anesthesia where a more detailed examination can be performed.. (Reviewer-Scott D. Smith, MD, MPH).

Keywords: Glaucoma, Intraocular Pressure Measurement

Print Tag: Refer to original journal article
**Glaucoma Increases Risk of Endothelial Decompensation Following PK**

*Effect of Glaucoma on Corneal Graft Survival According to Indication for Penetrating Keratoplasty.*

Stewart RMK, Jones MNA, et al:

Am J Ophthalmol 2011; 151 (February): 257-262

---

Glaucoma is a risk factor for graft failure after penetrating keratoplasty, particularly in patients with a history of primary or secondary endothelial disease as an indication for corneal transplantation.

---

**Objective:** To evaluate risk factors for graft failure in patients following penetrating keratoplasty (PK), and to assess the role of glaucoma in graft survival.

**Design:** Retrospective, comparative clinical study.

**Methods:** Included were patients with data available from the United Kingdom Transplant Registry who underwent an initial PK during a 7-year period and who had at least 1 year of follow-up data. Available data included patient demographics, indication for PK, and history of glaucoma as well as glaucoma medication use. In addition, follow-up data included graft survival information allowing statistical analysis of the association between glaucoma treatment and graft survival to be performed.

**Results:** 6255 transplants were performed in eyes without glaucoma and in 1994 eyes with glaucoma. The overall survival of corneal grafts was 86% in patients without a history of glaucoma and 72% in those with glaucoma ($P = 0.0001$). In patients with medically managed glaucoma, graft survival at 3 years was 73% compared to 63% in those who required glaucoma surgery ($P = 0.07$). The risk of glaucoma-related corneal graft failure was higher in patients with a history of Fuchs dystrophy, with a relative risk of 1.9 associated with topical glaucoma medication use and 3.1 with oral glaucoma medication use. A similar increase, although smaller in magnitude, was seen associating glaucoma and risk of graft failure in patients with pseudophakic bullous keratopathy. Patients with a history of trauma or keratoconus as an indication for PK did not have an increased risk of failure associated with glaucoma therapy.

**Conclusions:** Glaucoma increases the risk of graft failure following PK, particularly in patients with a history of endothelial disease.

**Reviewer's Comments:** The results of this study should remind ophthalmologists who manage patients following PK that control of intraocular pressure is essential not only to optimizing the visual outcome from a glaucoma standpoint but also from a graft survival standpoint. (Reviewer-Scott D. Smith, MD, MPH).

---

Keywords: Glaucoma, Penetrating Keratoplasty

Print Tag: Refer to original journal article
Similar Clinical Outcomes Seen With 1-Site & 2-Site Phacotrabeculectomy

Meta-Analysis of 1- Versus 2-Site Phacotrabeculectomy.

Gdih GA, Yuen D, et al:

Ophthalmology 2011; 118 (January): 71–76

Clinical outcomes are similar with either 1-site or 2-site phacotrabeculectomy.

**Objective:** To compare the efficacy of intraocular pressure (IOP) reduction between 1- versus 2-site phacotrabeculectomy.

**Design:** Meta-analysis.

**Methods:** Literature search of MEDLINE and Cochrane Registry databases allowed the identification of randomized clinical trials comparing 1- versus 2-site phacotrabeculectomy. Studies eligible for inclusion were randomized clinical trials with a minimum of 12 months of follow-up in the English language. Four reviewers independently evaluated each of the articles and judged the quality of the clinical trials. Consensus opinion was used to select the final 10 articles included in the analysis. Primary outcome measure was IOP reduction from baseline, with secondary outcomes including reduction in number of glaucoma medications, visual outcome, complications, and surgical time.

**Results:** No statistically significant difference was seen in the amount of IOP reduction between 1- and 2-site phacotrabeculectomy. During the first year of follow-up, overall IOP control was approximately 1 mmHg better in the 2-site group; however, by 1-year follow-up, the level of IOP control was equivalent in the 2 groups. In addition, there was no statistically significant difference in reduction in use of glaucoma medications between groups. Visual outcomes and development of complications were similar between groups. Mean surgery time, as assessed by 4 of the trials included in the study, was 13 minutes shorter for phacotrabeculectomy performed by 1-site compared to 2-site surgery.

**Conclusions:** The clinical outcomes of 1- and 2-site phacotrabeculectomy are not significantly different.

**Reviewer's Comments:** This study should reassure glaucoma surgeons that their personal preference of 1- or 2-site combined phacotrabeculectomy can provide equivalent long-term clinical outcomes. Other factors, including depth of the patient’s orbit, which can determine the ease of performance of phacoemulsification as well as surgeon comfort and surgery time, can be used to help each individual surgeon make the appropriate choice for the surgical technique in each particular patient. (Reviewer-Scott D. Smith, MD, MPH).

Keywords: Glaucoma Surgery, Cataract Surgery

Print Tag: Refer to original journal article
Xeomin® and BOTOX® appear to have equal efficacy in the treatment of blepharospasm.

**Background:** Patients with benign essential blepharospasm (BEB) experience uncontrollable, excessive blinking of the eyelids. This can render them functionally blind. In the United States, BOTOX® (Allergan, Inc) was the only approved form of botulinum toxin A until recently.

**Objective:** To compare the efficacy and safety of 2 forms of botulinum toxin A for the treatment of BEB.

**Design:** Prospective, randomized parallel study.

**Participants:** 65 patients with BEB from 3 centers in Germany.

**Methods:** Patients with blepharospasm were included if they had previously received at least 20 units per eye of BOTOX® and had a baseline Jankovic Rating Scale (JRS, a measure of BEB severity) of >2. Exclusion criteria were pregnancy, breastfeeding, atrophy of target muscles, any concurrent condition or medication interfering with study results, history of substance abuse, and inability to give consent. Each patient was randomized to receive either Xeomin® or BOTOX® using the same pattern and dose as the most recent treatment. The patient and injector were masked to treatment. Follow-up occurred at 4, 8, 11, and 14 weeks. Patients could schedule repeat injections if symptoms had returned to baseline between 11 and 13 weeks.

**Primary outcome measure** was change in Blepharospasm Disability Index (BSDI) at week 4. The BSDI measures 6 daily activities from 0 (no impairment) to 4 (not possible due to disease) for a maximum score of 24.

**Results:** 32 patients received BOTOX® and 33 received Xeomin®. One patient from each group did not complete the study. Mean age, percent female, mean dose of botulinum toxin A, and mean BSDI score were similar between groups. There was no difference in mean BSDI score at 4 weeks between groups. In addition, the BSDI and JRS scores were not different between groups at any of the time points. Duration of treatment effect did not differ between groups. After the study was completed, the authors went back and defined “responder” as achieving at least a 4-point improvement in BSDI. Significantly more patients in the BOTOX® group (13 of 19) were responders than in the Xeomin® group (6 of 24). There was no difference in adverse events.

**Conclusions:** No significant differences were observed between Xeomin® and BOTOX® in the treatment of BEB using the JRS and BSDI scores. Significantly more patients improved at least 4 points on the BSDI score in the BOTOX® group.

**Reviewer's Comments:** Xeomin® was approved by the FDA in September of 2010. This study showed that there was no difference in the main treatment outcome for blepharospasm. To me, this suggests equal efficacy and safety for these products. Later they went back and did a posthoc analysis and found more “responders” in the BOTOX® group than the Xeomin® group. This may have been a study design issue or the fact that Allergan, the maker of BOTOX®, provided financial support for this study. (Reviewer-Michael S. Lee, MD).
Rapid glycemic improvement may lead to diabetic papillopathy in type I diabetes.

**Background:** Diabetic papillopathy represents a swollen optic disc from no other cause but diabetes. A couple of case reports have suggested this may result from rapid correction of hyperglycemia.

**Objective:** To investigate the metabolic control of type I diabetics with bilateral diabetic papillopathy.

**Design:** Retrospective review of the records of 2066 type I diabetics from a single center in Denmark.

**Methods:** The authors included only type I diabetes since there is a much clearer time of onset and the long duration of follow-up at their diabetes center. Other criteria included endocrine records for 6+ months, 2 measurements of HbA\textsubscript{1c} within a year, and fundus photographs of the papillopathy. Bilateral cases were chosen to exclude diagnoses other than diabetes. Patients also were tested for malignant hypertension and increased intracranial pressure. Metabolic control was calculated as a rate of HbA\textsubscript{1c} change per 3 months (the shortest period during which HbA\textsubscript{1c} can change).

**Results:** There were 2066 patients with almost 5 years of mean follow-up. There were 7 patients with bilateral optic disc edema. Of these patients, 1 was excluded for lack of neuroimaging and another was diagnosed with thyroid optic neuropathy. The remaining 5 patients experienced a change in HbA\textsubscript{1c} of -2.5% per 3 months compared to the overall rate of -0.04% per 3 months for the entire cohort. There were 77 other patients with a drop in HbA\textsubscript{1c} of >1.5% per 3 months. Before optic disc edema, the cup-to-disc ratio was ≤0.18 in all 10 eyes. Mean duration of optic disc edema was 5 months. Acuity was ≤20/60 in 4 of 10 eyes, and the optic discs were atrophic in 3 of 10 eyes. Four of 5 patients had worsening of diabetic retinopathy during follow-up.

**Conclusions:** Compared to other patients with type I diabetes, those with diabetic papillopathy had a significant reduction of glycemia and a small cup-to-disc ratio.

**Reviewer’s Comments:** At first blush, it seems to be counterintuitive that reducing the HbA\textsubscript{1c} rapidly causes diabetic papillopathy; however, it has been noted that rapid improvement in metabolic control worsens diabetic retinopathy. The authors tried to reverse course and raise the HbA\textsubscript{1c} in 4 of the patients. This did not appear to affect the outcome, but there was no control group with which to compare. (Reviewer-Michael S. Lee, MD).

Keywords: Diabetic, Diabetes, Papillopathy, Disc Edema, Disc Swelling, Treatment, Risk Factor

Print Tag: Refer to original journal article
Following vitrectomy with intraocular gas for macular holes $<400\ \mu m$, avoidance of supine positioning is as effective as facedown positioning.

**Objective:** To compare the efficacy of facedown positioning and simple avoidance of supine positioning following pars plana vitrectomy (PPV) with intraocular gas tamponade for the management of small macular holes.

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

**Participants/Methods:** 69 patients with small macular holes $<400\mu m$ in diameter were enrolled in this study. All patients underwent PPV, peeling of the inner limiting membrane, and placement of 17% perfluoroethane gas. Patients were randomly assigned to adhere to strict facedown positioning or were advised to simply avoid supine positioning for 10 days after surgery. Follow-up evaluation allowed comparison of the rate of successful closure of the macular hole between groups.

**Results:** There was no significant difference between groups in baseline clinical or demographic factors, including size of the macular hole. Rate of successful closure 3 months after surgery was 91% in the facedown positioning group and 94% in the non-supine positioning group. Similar visual outcomes were also achieved in the groups.

**Conclusions:** Strict facedown positioning appears to offer no advantage of simple avoidance of supine positioning following PPV with gas tamponade in patients with small macular holes.

**Reviewer's Comments:** Facedown positioning following vitrectomy with intraocular gas injection has been advocated by most retinal surgeons to achieve tamponade of the hole during the early postoperative period. This study indicates that in patients with small holes, simple avoidance of supine positioning appears to result in an equally high success rate. (Reviewer-Scott D. Smith, MD, MPH).

Keywords: Macular Hole, Vitrectomy

Print Tag: Refer to original journal article
Objective: To investigate the efficacy of different methods of anesthesia for pain control during intravitreal drug injection.

Design: Randomized, double-masked, controlled clinical trial.

Methods: Patients undergoing intravitreal drug injection were randomly assigned to 1 of 3 treatment groups. Group 1 (n=31) received 2 drops of topical tetracaine 0.5% plus local application of a 4% lidocaine-soaked pledget applied for 10 seconds at the intended injection site. Group 2 (n=31) received 2 drops of topical tetracaine 0.5% alone. Group 3 (n=31) received 2 drops of topical cocaine 4%/epinephrine 1:100,000. Anesthetic administration was performed by a study coordinator. A retina specialist then entered the room and administered the intravitreal drug injection through the pars plana. A standardized system for grading pain was used to quantify patient pain using the visual analog scale (VAS), which rates pain on a scale of 0 to 100. Physician-rated perception of patient pain was also assessed using the Wong-Baker FACES scale, validated for use as an observer's assessment of pain. Pain scores were compared among the groups.

Results: Mean VAS pain scores for groups 1, 2, and 3 were 19, 21, and 21, respectively. There were no statistically significant differences among the groups. No differences were seen among the groups in the Wong-Baker pain scores, with mean scores of 1.9, 2.1, and 2.3 for groups 1, 2, and 3, respectively.

Conclusions: Use of a topical 4% lidocaine-soaked pledget applied at the injection site offers no advantage over topical tetracaine 0.5% alone for pain control during intravitreal drug injection.

Reviewer’s Comments: The administration of intravitreal drugs by pars plana injection has become commonplace with the introduction of vascular endothelial growth factor inhibitors such as bevacizumab (Avastin) and ranibizumab (Lucentis), as well as the expanded use of intravitreal triamcinolone for the management of macular edema. This study demonstrates that the simple application of topical tetracaine 0.5% drops appears to be as effective as topical anesthetic drops with supplemental lidocaine 4% on a pledget. I find topical tetracaine to be very adequate for cataract surgery, and I am not surprised by this finding. Its use offers a simple and effective method of pain control for a variety of ophthalmic surgical procedures. (Reviewer-Scott D. Smith, MD, MPH).

Keywords: Intravitreal Injection Anesthesia

Print Tag: Refer to original journal article
Autorefraction Is Less Accurate Following LASIK

Factors Influencing the Reliability of Autorefractometry After LASIK for Myopia and Myopic Astigmatism.

Mirshahi A, Wesemann W, et al:

Am J Ophthalmol 2010; 150 (December): 774–779

Autorefraction results are less accurate following laser in situ keratomileusis, particularly when the optical zone for excimer laser treatment is small.

**Objective:** To assess the accuracy of autorefraction following laser in situ keratomileusis (LASIK) for myopia and astigmatism, and to identify factors associated with its accuracy.

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

**Methods:** A consecutive series of 250 eyes of 132 patients who underwent LASIK for myopia and/or astigmatism were included in this case series. Medical records were reviewed to determine clinical and demographic factors for each patient. Detailed treatment parameters used during surgery were also recorded. Follow-up evaluation included measurement of refractive error by autorefractor (Topcon RM A-2300, Tokyo, Japan). In addition, all patients underwent cycloplegic refraction before and after surgery to determine the refractive error. Statistical analysis allowed estimation of the accuracy of the postoperative autorefraction. In addition, factors influencing the accuracy of autorefraction were identified.

**Results:** Mean age of patients was 37 years. Mean preoperative spherical equivalent refractive error was -6.6 diopters. The correlation between preoperative autorefraction and subjective refraction was very strong (correlation coefficient r=0.98). In contrast, the correlation between autorefraction and subjective refraction was much weaker following LASIK (r=0.79). The mean difference in spherical equivalent between autorefraction and subjective refraction changed from +0.13 to -0.30 following LASIK. Patients with a smaller optical zone of treatment had a substantially larger mean error of autorefraction, with a mean error of -0.61 for an optical zone of 5.1 to 6.0 mm compared to -0.13 for an optical zone of 6.1 mm to 7.0 mm.

**Conclusions:** Autorefraction is less accurate following LASIK. The problem is particularly great in patients with smaller optical zone.

**Reviewer’s Comments:** Awareness of the fact that the results of autorefraction are less accurate following LASIK and probably following other corneal refractive surgical procedures such as photorefractive keratectomy is important to avoid being misled by these results. There is no substitute for a manifest refraction to accurately measure the refractive error in patients following this procedure. (Reviewer-Scott D. Smith, MD, MPH).

Keywords: LASIK, Autorefractometry

Print Tag: Refer to original journal article
The lack of correlation between postoperative endothelial cell counts and tissue storage time indicates there is no need to make special requests to eye banks for short storage time in the hope of improving the results of endothelial keratoplasty.

Objective: To assess the relationship between tissue storage time and postoperative endothelial cell counts following Descemet's stripping automated endothelial keratoplasty (DSAEK).

Design: Retrospective, interventional clinical case series.

Methods: Medical records were reviewed of a consecutive series of 362 eyes of 265 patients who underwent DSAEK for management of Fuchs' endothelial dystrophy. Follow-up evaluation included measurement of endothelial cell count at regular intervals following surgery. In addition, eye bank records allowed determination of the storage time of tissue used for the surgery. Statistical analysis was performed to identify the relationship between storage time and postoperative endothelial cell loss.

Results: Mean storage time was 99.0±33.0 hours (range, 20.6 to 186.0 hours). Mean proportional loss of endothelial cells from baseline was 29%±16% at 6 months, 31%±16% at 1 year, and 32%±20% at 2 years after surgery. There was no significant correlation between storage time and amount of endothelial cell loss seen at any time point through 2 years of follow-up. Stratification of patients based on storage time showed essentially identical magnitude of endothelial cell loss over time.

Conclusions: Tissue storage time is not associated with the amount of endothelial cell loss seen following DSAEK.

Reviewer's Comments: This study evaluated the outcome following endothelial keratoplasty in eyes receiving donor tissue stored for up to 8 days. No conclusions can be drawn, therefore, about tissue stored for longer periods. Within the 8-day storage time evaluated in this study, DSAEK surgeons should be comfortable using tissue regardless of the time of tissue procurement. (Reviewer-Scott D. Smith, MD, MPH).

Keywords: DSAEK, Tissue Storage

Print Tag: Refer to original journal article
Topical ciclosporin A 2% does not improve the efficacy of treatment of corneal graft rejection in comparison to topical steroid therapy alone.

**Objective:** To investigate the efficacy of topical ciclosporin A 2% as adjunctive therapy in the treatment of graft rejection following penetrating keratoplasty (PK) in patients with a history of graft rejection.

**Design:** Prospective, randomized masked clinical trial.

**Participants/Methods:** 43 patients with a prior episode of subepithelial or endothelial graft rejection following PK who presented with a subsequent episode were enrolled in this clinical trial. All patients received topical betamethasone 0.1% hourly during waking hours. Patients with endothelial graft rejection also received oral prednisolone 1 mg/kg body weight for 2 weeks. Patients were randomly assigned to receive supplemental therapy with topical ciclosporin A 2% or placebo 4 times daily for 6 months. Topical steroids were tapered according to clinical response. Duration of steroid therapy required to control inflammation, recurrence of graft rejection, and graft survival were compared between groups.

**Results:** There were 22 eyes assigned to the ciclosporin A group and 21 eyes assigned to the placebo group. No differences in clinical or demographic features were present between groups. There were no differences in time to resolution of rejection episode between groups (both groups, 26 vs 33 days; P =0.22). Graft survival rates were also similar between groups at 34.8% versus 31.7% at 20 months (P =0.9).

**Conclusions:** Topical ciclosporin A is not effective in improving the results of treatment of epithelial or endothelial graft rejection following PK.

**Reviewer's Comments:** The concentration of topical ciclosporin A used in this study is 4 times stronger than that of ciclosporin A commercially available in the United States (Restasis). The findings of this study indicate that there is no benefit in adding topical ciclosporin A to the treatment regimen of patients suffering an episode of graft rejection who had a history of a similar episode. Although not specifically evaluated in this study, these results are not encouraging for use of this drug in primary graft rejection either. Rather, aggressive treatment with topical steroids has been and should remain the mainstay of treatment for this complication following keratoplasty. (Reviewer-Scott D. Smith, MD, MPH).

**Keywords:** Graft Rejection, Topical Ciclosporin A
Objective: To evaluate the efficacy of oral propranolol in reducing the size of periocular capillary hemangioma for the management of astigmatism in infants.

Design: Retrospective, interventional clinical case series.

Methods: 3 healthy infants with periocular capillary hemangioma causing astigmatic refractive error were treated with oral propranolol 2 mg/kg per day. At time of initiation of therapy, the infants were monitored for changes in heart rate, blood pressure, and stability of blood glucose level. Clinical follow-up included repeat measurement of cycloplegic refractive error to assess the efficacy of treatment in improving the quality of the retinal image.

Results: Mean age of infants included in the study was 6 months (range, 3 to 8 months). A rapid treatment effect was noted with respect to size and color of the lesion in all cases. The mean astigmatic refractive error decreased from 2.8 diopters to 1.3 diopters 1 month after treatment. The drug was well tolerated in all cases with no significant adverse effects.

Conclusions: Oral propranolol can rapidly reduce the size of periocular capillary hemangiomas and can thus reduce their compressive effect on the eye with secondary astigmatism.

Reviewer's Comments: Anisometropic amblyopia affects the majority of infants with orbital capillary hemangioma due to the mass effect of the tumor indenting the sclera and/or cornea. When this type of tumor interferes with formation of a proper retinal image, treatment is indicated. Side effects from traditional therapy with systemic corticosteroids are common, which prompted this study investigating the potential effect of systemic beta blockers on this vascular lesion. Although the mechanism of action of propranolol is not fully understood in the reduction of size of capillary hemangiomas, this may offer some advantages over traditional therapy. (Reviewer-Scott D. Smith, MD, MPH).

Keywords: Capillary Hemangioma, Amblyopia, Propranolol

Print Tag: Refer to original journal article
Accommodation May Contribute to Iris Concavity in Pigment Dispersion Syndrome

The Concave Iris in Pigment Dispersion Syndrome.
Liu L, Ong EL, et al:

Ophthalmology 2011; 118 (January): 66–70

The iris concavity that leads to pigment dispersion in predisposed eyes may be related to accommodation.

Objective: To investigate changes in the iris contour in eyes with pigment dispersion syndrome.
Design: Observational, clinical case series.

Participants/Methods: 33 eyes of 20 patients diagnosed with pigment dispersion syndrome underwent imaging with anterior segment optical coherence tomography (AS-OCT). Eyes were imaged along the horizontal meridian. Images were collected under baseline resting conditions and again after 5 minutes of fixation on an internal fixation target, after forced blinking, after maintaining accommodation of 3 diopters and 6 diopters, and after instillation of pilocarpine 2%. Amount of iris concavity was measured from images obtained under each of these conditions by measuring the maximum posterior position of the iris pigment epithelium relative to a line drawn between the iris root and the pupillary margin. Statistical analysis was performed to compare the amount of iris concavity under different conditions.

Results: After 5 minutes of fixation with relaxed accommodation, the iris changed from a concave configuration at baseline to a planar configuration. The planar configuration remained after forced blinking; however, after induction of accommodation with either a -3 diopter or -6 diopter lens, the concave iris configuration returned. Pilocarpine resulted in a planar iris configuration in all eyes.

Conclusions: Accommodation, rather than blinking, appears to play a role in the development of iris concavity in patients with pigment dispersion syndrome.

Reviewer's Comments: Iris concavity is a prominent feature of eyes that are undergoing active pigment dispersion. This iris concavity leads to rubbing of the peripheral iris on the lens zonules, liberating pigment that leads to trabecular obstruction and elevation of intraocular pressure. It has been hypothesized that predisposed eyes develop intermittent iris concavity as a result of sudden aqueous movement from the posterior to the anterior chamber as a result of blinking. This study that used real-time imaging with AS-OCT suggests that accommodation may be more involved in the development of iris concavity than blinking. This may also help to explain why the active phase of pigment dispersion with iris concavity occurs primarily in younger adults. (Reviewer-Scott D. Smith, MD, MPH).

Keywords: Pigment Dispersion

Print Tag: Refer to original journal article
In adults, acute changes in the optic nerve appearance due to intraocular pressure elevation occur due to compression of prelaminar tissue, not displacement of the lamina cribrosa.

**Objective:** To determine changes in the configuration of optic nerve in response to acute elevation of the intraocular pressure (IOP).

**Design:** Prospective case-control study.

**Participants/Methods:** 36 subjects were recruited to participate in this study. A total of 12 subjects had open angle glaucoma, which was diagnosed by standardized criteria. An additional 12 subjects without glaucoma were also recruited as age-matched normal controls, and another 12 subjects served as young controls. Mean age of glaucoma patients and age-matched controls was 68 and 67 years, respectively. Young controls had a mean age of 36 years. Each subject underwent optic nerve imaging by spectral-domain optical coherence tomography. Cross-sectional imaging took place at baseline and again following acute elevation of IOP with an ophthalmodynamometer held against the globe through the lower eyelid. Comparison of images taken with and without IOP elevation in each group allowed the determination of the effect on optic nerve configuration.

**Results:** Mean IOP elevation was 12.4 mmHg and was similar in all 3 groups. None of the groups showed a significant displacement in the position of the lamina cribrosa with IOP elevation. In contrast, small but statistically significant posterior displacement of pre-laminar tissues was seen in each group. The magnitude of pre-laminar tissue displacement was correlated with degree of IOP elevation.

**Conclusions:** In adults, laminar displacement does not occur with moderate acute IOP elevation. Under these conditions, changes in the optic nerve configuration result from compression of pre-laminar tissues.

**Reviewer's Comments:** In young children, the sclera and connective tissues supporting the optic nerve are more elastic. Acute IOP elevation can, in such cases, result in temporary and reversible cupping of the optic nerve. In adults, this study demonstrates that acute IOP elevation does not result in posterior displacement of the lamina cribrosa but rather can lead to compression of the prelaminar tissues. (Reviewer-Scott D. Smith, MD, MPH).

Keywords: Glaucoma

Print Tag: Refer to original journal article
Nerve Fiber Layer Thickness Measurements Differ Among OCT Instruments

Agreement Among Spectral-Domain Optical Coherence Tomography Instruments for Assessing Retinal Nerve Fiber Layer Thickness.

Leite MT, Rao HL, et al:


Although highly correlated, differences between spectral-domain optical coherence tomography measurements of the retinal nerve fiber layer thickness indicate that these measurements are not interchangeable.

Objective: To evaluate agreement among spectral-domain optical coherence tomography (SD-OCT) instruments in measuring retinal nerve fiber layer (RNFL) thickness.

Design: Cross-sectional, observational clinical study.

Methods: Data for this study were derived from the Diagnostic Innovations in Glaucoma Study (DIGS), a longitudinal study in which glaucoma patients, glaucoma suspects, and normal control subjects were enrolled. SD-OCT imaging of the RNFL was measured using 3 different instruments. Comparison of RNFL thickness measurements between the instruments allowed identification of factors associated with difference in measured values.

Results: RNFL thickness measurements were highly correlated among the instruments tested (Cirrus, Spectralis, and RTVue). Factors that affected the level of agreement among the instruments included patient age, spherical equivalent refractive error, axial length, and severity of glaucomatous optic nerve damage. Race and disc area did not influence agreement.

Conclusions: Although strong correlations exist among RNFL thickness measurements among SD-OCT instruments, systematic differences in the measurement process result in a difference in the absolute RNFL thickness measured.

Reviewer’s Comments: Optic nerve imaging has emerged as an important method for the detection and monitoring of glaucomatous optic nerve damage. Technological advances have resulted in improvement in repeatability of RNFL thickness measurements, particularly with the introduction of SD-OCT instruments; however, there are several instruments available on the market that may or may not provide comparable results. This study indicates that the same instrument should be used over time when possible to monitor RNFL thickness as an indicator of glaucoma stability. Although the results among instruments are highly correlated, systematic differences in the conversion of image data into actual thickness measurements exist. Consequently, their results cannot be considered to be interchangeable. (Reviewer-Scott D. Smith, MD, MPH).

Keywords: Optic Nerve Imaging

Print Tag: Refer to original journal article