Pharmacological induction of a complete posterior vitreous attachment can be achieved in a significant proportion of patients who receive an intravitreal injection of microplasmin, alleviating the need for surgery in some cases.

**Objective:** To evaluate the safety and efficacy of preoperative intravitreous injection of microplasmin in patients with vitreomacular traction scheduled for pars plana vitrectomy.

**Design:** Phase 2, multicenter, placebo-controlled, double-masked, randomized clinical trial.

**Participants:** 125 patients with macular hole or other diseases of the vitreomacular interface resulting from vitreomacular traction scheduled for pars plana vitrectomy.

**Methods:** A single intravitreal injection of placebo or microplasmin at 1 of 3 doses (25 µg, 75 µg, or 125 µg in 0.1 mL) was given. Evaluation of progression of posterior vitreous detachment (PVD) or documentation of complete PVD prior to vitrectomy was documented by clinical examination and optical coherence tomography of the vitreomacular interface. Outcomes evaluated included proportion of patients with complete PVD at time of surgery, ease of induction of complete PVD in those who did not already have one at time of surgery, and proportion of those who had resolution of their pathology and did not require surgery after pharmacologic induction of a complete detachment.

**Results:** A dose-related increase in proportion of patients with total PVD at time of surgery was noted, with 10% having complete PVD in the placebo group and 14%, 18%, and 31% in the 25-µg, 75-µg, and 125-µg groups, respectively. Resolution of vitreomacular interface abnormalities precluding the need for vitrectomy 1 month after injection was also significantly higher in the microplasmin patients, with 3% of placebo patients and 10%, 15%, and 31% in the microplasmin 25-µg, 75-µg, and 125-µg groups, respectively, not requiring surgery.

**Conclusions:** Intravitreous injection of microplasmin, particularly at a dose of 125 µg, leads to a higher proportion of induction and progression of PVD than placebo injection. A higher proportion of patients receiving microplasmin did not require vitrectomy surgery and had resolution of their vitreomacular traction with pharmacologic induction of a PVD.

**Reviewer's Comments:** This study demonstrates promise for this pharmacologic intervention in the management of vitreomacular interface disease. It certainly warrants continued investigation in Phase 3 clinical trials to verify the safety and efficacy of microplasmin for management of these conditions. (Reviewer-Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: Posterior Vitreous Detachment, Vitrectomy

Print Tag: Refer to original journal article
Objective: To evaluate the safety and efficacy of intravitreal ranibizumab 0.5 mg or triamcinolone 4.0 mg combined with focal/grid laser photocoagulation compared with focal/grid laser alone for the treatment of diabetic macular edema (DME).

Design: Multicenter, randomized clinical trial.

Participants: 854 eyes of 691 diabetic patients with visually significant DME involving the fovea.

Methods: Eligible patients had visual acuity with Snellen equivalent of 20/32 to 20/320. Eyes were randomly assigned to receive either an active drug injection of ranibizumab 0.5 mg or triamcinolone 4.0 mg or a sham vehicle injection. Patients in the ranibizumab group were also randomly assigned to receive either immediate laser photocoagulation to the macula within 10 days after injection or a deferred laser performed 24 weeks after injection. Patients in the control group and those in the triamcinolone group also underwent photocoagulation within 3 to 10 days after injection. Retreatment followed an algorithm that was standardized for the study protocol. Main Outcome Measures: Best-corrected visual acuity and safety of drug administration at 1 year of follow-up.

Results: A significantly greater improvement in mean visual acuity was seen at 1-year follow-up in patients who received ranibizumab with either immediate or deferred laser. A mean improvement of 9 letters on the Early Treatment Diabetic Retinopathy Study visual acuity chart, corresponding to almost 2 lines of improved visual acuity, was seen. In contrast, the triamcinolone group and the laser-only group showed improvement of vision of 4 and 3 letters, respectively. Follow-up evaluation also demonstrated a reduction in mean central subfield foveal thickness by optical coherence tomography in the ranibizumab- and triamcinolone-treated patients, in comparison to those who received laser alone. Three eyes in the ranibizumab group experienced postinjection endophthalmitis. In the intraocular triamcinolone-injection group, additional complications of cataract and elevated intraocular pressure were seen in some patients.

Conclusions: Intravitreal ranibizumab injection performed in conjunction with either prompt or deferred laser treatment is more effective through at least 1 year of follow-up compared to laser alone for the treatment of DME involving the fovea. In contrast, visual acuity improvement is not as evident in patients who receive intraocular triamcinolone combined with laser photocoagulation.

Reviewer's Comments: This important study demonstrates the combined efficacy of 2 common forms of treatment for DME, injection of the vascular endothelial growth factor inhibitor ranibizumab and focal/grid laser photocoagulation. (Reviewer-Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing
Nocturnal hypoxia appears to increase the risk of proliferative retinopathy in patients with type 2 diabetes mellitus.

**Objective:** To investigate the relationship between sleep-disordered breathing and diabetic retinopathy.

**Design:** Cross-sectional, comparative clinical study.

**Participants:** A consecutive series of 68 patients with type 2 diabetes and nonproliferative diabetic retinopathy and 151 patients with proliferative diabetic retinopathy who had undergone ophthalmic surgery in a single institution.

**Methods:** Severity of diabetic retinopathy prior to ophthalmic surgery was documented. Patients were hospitalized overnight following their surgery, during which time nocturnal oxygen saturation was measured by placement of a pulse oximeter on the wrist. Continuous monitoring of the pulse rate and oxygen saturation was done, which allowed measurement of parameters describing the level of hypoxia during sleep. Association between these parameters and presence of proliferative, as opposed to nonproliferative, diabetic retinopathy was evaluated.

**Results:** Number of episodes of nocturnal oxygen desaturation at least 4% below baseline levels was higher in patients with proliferative diabetic retinopathy than in those with nonproliferative retinopathy. In addition, cumulative time spent at a level of 90% oxygen saturation or less was higher in the proliferative diabetic retinopathy group. Multivariate statistical analysis adjusting for differences in age, gender, and other potentially confounding factors confirmed the lowest level of nocturnal oxygen saturation was significantly associated with probability of having proliferative diabetic retinopathy.

**Conclusions:** This study indicates that intermittent nocturnal hypoxia is associated with the presence of proliferative diabetic retinopathy in type 2 diabetic patients.

**Reviewer’s Comments:** It has been hypothesized that intermittent nocturnal hypoxia can lead to persistent autonomic dysfunction that can predispose to inflammatory activation of the vascular endothelium and promote atherosclerosis and microvascular disease. Prospective studies investigating the relationship between nocturnal hypoxia and diabetic retinopathy are needed. In addition, such studies will be able to evaluate whether treatment for sleep-disordered breathing may reduce the risk of progression of diabetic retinopathy. (Reviewer-Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: Diabetic Retinopathy

Print Tag: Refer to original journal article
Intracameral injection of voriconazole appears to be effective and may be less toxic than amphotericin B for treating fungal endophthalmitis resulting from keratitis.

**Objective:** To evaluate the therapeutic efficacy of intracameral voriconazole injection in treating fungal endophthalmitis due to keratitis.

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

**Methods:** Medical records were reviewed of a consecutive series of 10 patients who underwent treatment with intracameral injection of 100 µg of voriconazole in the management of fungal endophthalmitis due to keratitis. All patients had a fungal corneal ulcer with intraocular spread contiguous to the site of the corneal infiltrate. Once-daily injection of intracameral voriconazole was performed until resolution of the intraocular plaque.

**Results:** The most common causative organisms were *Fusarium* and *Aspergillus*. The number of voriconazole injections given intracamerally ranged from 1 to 8. Patients suffering from *Fusarium* or *Acremonium* infection were more likely to require a larger number of repeat injections, but those with *Aspergillus* or *Alternaria* infection required fewer injections. Three eyes required therapeutic penetrating keratoplasty for reduction of fungal corneal load. In all cases, improvement of resolution of the intraocular fungal mass resolved after treatment.

**Conclusions:** Intracameral injection of voriconazole appears to be an effective treatment for fungal endophthalmitis resulting from contiguous spread from a fungal corneal ulcer.

**Reviewer's Comments:** Traditionally, amphotericin B has been the drug of choice for intraocular injection in the management of fungal endophthalmitis. In relatively low concentrations, however, amphotericin B can result in retinal toxicity. In addition, recent reports have suggested increasing resistance of some strains of fungus to this drug. Consequently, intraocular injection of voriconazole has been considered. This study appears to support its use as a treatment in the management of this difficult condition. (Reviewer-Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: Fungal Keratitis, Endophthalmitis

Print Tag: Refer to original journal article
Recurrence of anterior segment neovascularization is seen in nearly 50% of patients, even after treatment with intravitreal bevacizumab and panretinal photocoagulation.

**Objective:** To investigate the clinical factors associated with recurrence of anterior segment neovascularization following intravitreal injection of bevacizumab.

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

**Methods:** Clinical records were reviewed of a consecutive series of 54 patients with anterior segment neovascularization treated with intravitreal bevacizumab injection and panretinal photocoagulation. All patients underwent completion of panretinal photocoagulation within 1 month after intravitreal bevacizumab injection, if it had not already been completed. Statistical analysis was performed to identify baseline clinical and demographic factors associated with risk of recurrence.

**Results:** Recurrence of anterior segment neovascularization occurred in 48% of eyes after treatment. Mean follow-up at which recurrence was noted was 4.7 months (range, 2.0 to 11.0 months) after bevacizumab injection. Multivariate statistical analysis identified bevacizumab injection and trabeculectomy as protective factors against the recurrence of anterior segment neovascularization.

**Conclusions:** Recurrence of anterior segment neovascularization after intravitreal bevacizumab injection is relatively common despite panretinal photocoagulation. Trabeculectomy and repeat intravitreal bevacizumab injection offer protection against such recurrences.

**Reviewer's Comments:** This study is important in that it highlights the need for vigilant surveillance of patients with anterior segment neovascularization for recurrence after treatment. After an initial diagnosis of anterior segment neovascularization is made, prompt treatment with bevacizumab intravitreal injection is useful in inducing rapid regression. Retinal ablation is needed to prevent short-term recurrence; however, long-term recurrences may still occur, necessitating long-term monitoring of these patients. If allowed to progress to a more advanced stage of iris neovascularization, such recurrences may lead to progressive secondary angle closure and neovascular glaucoma as well as other hemorrhagic complications. (Reviewer-Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: Neovascular Glaucoma

Print Tag: Refer to original journal article
Boys More Likely Than Girls to Develop Blindness Due to JIA-Associated Uveitis

Male Gender and Poor Visual Outcome in Uveitis Associated With Juvenile Idiopathic Arthritis.

Ayuso VK, Ten Cate HA, et al:

Am J Ophthalmol 2010; 149 (June): 987-993

Boys are more than 6 times more likely than girls to develop blindness due to juvenile idiopathic arthritis-associated uveitis.

**Objective:** To evaluate the clinical course of uveitis associated with juvenile idiopathic arthritis (JIA), and to identify clinical and demographic factors associated with visual outcomes.

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

**Methods:** Medical records of 65 children diagnosed with JIA-associated uveitis were reviewed. Best-corrected visual acuity at baseline and at 1, 3, and 5 years after diagnosis was used as the clinical outcome. Visual outcomes were analyzed according to gender, age at time of diagnosis of uveitis, and initial manifestation of JIA (either uveitis or arthritis).

**Results:** Median age of onset of uveitis was 4.2 years. Of children in the study cohort, 75% were female. Uveitis was diagnosed prior to arthritis in 23%. Best-corrected visual acuity in boys was significantly worse at both 1- and 3-year follow-up. In addition, multivariate statistical analysis demonstrated male gender to be a significant predictor of blindness (best-corrected visual acuity, <20/200; odds ratio, 6.61). Children with initial onset of uveitis prior to arthritis had a worse visual outcome. No difference in visual outcome was seen between younger-onset or older-onset disease.

**Conclusions:** Male gender is an independent risk factor for poor visual outcome in children with JIA-associated uveitis.

**Reviewer’s Comments:** Although the gender difference in risk of vision loss due to JIA-associated uveitis is not likely to alter the management of any individual patient, it is certainly an association in which all ophthalmologists should be aware. It is crucial to identify uveitis as early as possible in children identified by JIA, because vision-threatening complications, such as band keratopathy, cataracts, and cystoid macular edema, can be avoided in many cases with proper control of inflammation. (Reviewer—Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: Uveitis, Juvenile Idiopathic Arthritis

Print Tag: Refer to original journal article
SSRIs May Increase Rate of Cataract Development

Selective Serotonin Reuptake Inhibitors and the Risk of Cataracts: A Nested Case-Control Study.
Etminan M, Mikelberg FS, et al:

Ophthalmology 2010; 117 (June): 1251-1255

Use of selective serotonin reuptake inhibitors may increase the risk of cataract development.

**Objective:** To investigate the possible association between selective serotonin reuptake inhibitors (SSRIs) and the development of cataracts in a large Canadian population.

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

**Methods:** Linked administrative databases of the health insurance of the province of Quebec, Canada, were used as the source of data for this study. A large cohort of patients who had undergone coronary artery bypass surgery between 1995 and 2004 was identified. Subsequent diagnosis with cataract was also determined, and cases were selected from among this group. Control subjects not diagnosed with cataracts were also selected, and there were 10 age-matched controls for each case. Medication usage data were also available, which allowed identification of individuals using SSRIs. Multivariate logistic regression analysis was performed to determine an independent association between SSRI use and diagnosis of cataract, adjusting for age, gender, and other potentially confounding factors.

**Results:** 18,784 cases and 187,840 controls were included in the study. SSRI use was significantly more common among patients diagnosed with a cataract (adjusted relative risk for cataract, 1.15). The risk of a cataract was highest with use of fluvoxamine, venlafaxine, and paroxetine (relative risks, 1.39, 1.33, and 1.23, respectively).

**Conclusions:** This study suggests that SSRI use is associated with an increased risk of cataract development.

**Reviewer’s Comments:** SSRIs are among the most commonly prescribed medications in the United States, with an estimate of up to 10% of the adult population using a medication in this class. Given the fact that a cataract is the most common cause of vision loss, this study has significant health implications. Future prospective studies are needed to further elucidate the magnitude and mechanism of this risk. The results of such studies will have obvious public health implications. (Reviewer-Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: Antidepressant Medication, Cataracts

Print Tag: Refer to original journal article
Transverse ultrasound, in the latest generation of phacoemulsification instruments, offers improved thermal characteristics over traditional longitudinal ultrasound.

**Objective:** To compare the thermal characteristics of the Signature Ellips (Abbott Medical Optics) and Infiniti OZil (Alcon, Inc.) transverse ultrasound and to compare both with longitudinal ultrasound.

**Design:** Laboratory investigation.

**Methods:** Artificial anterior chambers were created and standardized for measurement of the thermal characteristics of each instrument. Testing conditions were standardized with regard to phacoemulsification needle, size of the artificial chamber, and control of irrigation fluid with a complete water-tight system. Temperature increase over baseline after 60 seconds of continuous transverse ultrasound was measured at positions in 90-degree increments around the sleeve near the proximal needle shaft for both devices. The experiments were also performed with the Signature device in longitudinal ultrasound mode. With each device, temperature measurements were made with aspiration blocked and unblocked.

**Results:** The OZil device with unblocked aspiration had a greater temperature rise than the Ellips system (8.1°C vs 5.2°C; \(P<0.0001\)). An even larger difference in temperature rise was noted with blocked aspiration (OZil 29.3°C vs Ellips 12.2°C; \(P<0.0001\)). Greatest temperature rise with the OZil system was noted near the proximal shaft of the phacoemulsification needle. Both devices had significantly less increase in temperature over baseline in comparison to the Signature device in longitudinal ultrasound mode.

**Conclusions:** Temperature rise with transverse ultrasound is less than that with longitudinal ultrasound devices. A clinically relevant increase in temperature in torsional ultrasound of the Infiniti OZil system, however, is seen when aspiration is blocked and when the proximal needle shaft is near the corneal incision.

**Reviewer’s Comments:** Transverse ultrasound leads to rotational rather than translational movement of the phacoemulsification needle and significantly less friction within the corneal incision. This study suggests that variation in temperature along the phacoemulsification needle with the OZil system may still predispose to wound burns with aspiration blocked when the proximal needle is in contact with the cornea. Both devices, however, exhibit significantly improved thermal characteristics in comparison to longitudinal ultrasound. (Reviewer-Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: Phacoemulsification, Complications, Corneal Wound Burn

Print Tag: Refer to original journal article
Vision Rehabilitation of Central Scotoma Via Eccentric Viewing Training

Effective Rehabilitation of Reading by Training in the Technique of Eccentric Viewing: Evaluation of a 4-Year Programme of Service Delivery.

Palmer S, Logan D, et al:

Br J Ophthalmol 2010; 94 (April): 494-497

Formal, eccentric viewing training improves reading in patients with central visual loss.

Background: Central visual loss from age-related macular degeneration (ARMD) is very common. These patients may be able to use eccentric viewing in order to read.

Objective: To determine the effect of eccentric viewing training on reading speed and ability among patients with central visual loss.

Design: Retrospective case series involving 242 patients with ARMD.

Methods: Trainers first determined an optimum eccentric area of visual field for the patient to utilize their preferred retinal locus. Patients were then taught to use steady eye strategy. In this monocular technique, the eye remains steady while text moves in front of the eyes using high magnification and a short reading distance (2.0 cm to 6.5 cm). Trainers were experienced in adult literacy and tutoring. They tried to balance between correction and encouragement to minimize anxiety and promote confidence and motivation. Sessions were one on one for 1 hour. Homework consisted of 20 minutes of reading per day in 2- to 3-minute increments. Outcome measurements included reading speed, font size, reading duration, and comprehension.

Results: Data for 165 women and 77 men with a mean age of 75 years were reviewed. Mean reading speed improved significantly from 48 words per minute (wpm) to 72 wpm. Of the patients, 17% did not improve or worsened. Font size improved significantly from 14.3 to 11.5. Reading duration improved significantly from 1.7 minutes to 15.8 minutes. Reading comprehension improved significantly from 74% to 93%.

Conclusions: Formal, eccentric viewing training improves reading speed, font size, reading duration, and reading comprehension among patients with central visual loss from ARMD.

Reviewer's Comments: This is a paradigm shift from traditional reading in that the material moves instead of the patient's eye or head. Without a control group, it is very difficult to know whether the technique plus training is what drove the improvement. Perhaps improvement would occur just by having a formal coach pushing a patient along. (Reviewer-Michael S. Lee, MD).

© 2010, Oakstone Medical Publishing

Keywords: Reading, Visual Rehabilitation, Macular Degeneration, Central Scotoma

Print Tag: Refer to original journal article
Polymethyl methacrylate implants using the myoconjunctival technique provide excellent prosthesis movement following enucleation.

**Background:** After enucleation, prosthesis movement is extremely important for cosmesis. Nonintegrated implants (eg, polymethyl methacrylate [PMMA]) are 150 times cheaper than porous implants (eg, Medpore, hydroxyapatite). Porous implants have been reported to result in better movement, but no randomized trials have been performed.

**Objective:** To compare prosthesis movement after enucleation using 3 different techniques.

**Design:** Randomized, masked interventional study.

**Participants:** 150 patients undergoing enucleation.

**Methods:** Patients were randomized to 1 of 3 groups: (1) traditional PMMA implant using muscle imbrications; (2) PMMA implant using myoconjunctival technique; (3) porous polyethylene implant. After conventional enucleation, group 1 patients had the lateral rectus sewn to the medial rectus and the superior rectus sewn to the inferior rectus. In the myoconjunctival PMMA group, the rectus muscles were sewn near respective fornices. In group 3, a scleral cap was sewn onto the porous polyethylene implant, and the rectus muscles were sewn into the scleral cap. At 6 weeks after surgery, a masked examiner measured degrees of excursion using slit-lamp mounted rulers in real time and then also on photographs. Total horizontal and vertical movements were calculated and then repeated by a second masked observer. The 2 measurements were averaged. No implants were pegged.

**Results:** Among the 3 groups, there was no significant difference in operating time or size of implant. The myoconjunctival technique with PMMA implant showed significantly greater horizontal (8.0 mm) and vertical (6.8 mm) movement than the traditional PMMA (horizontal, 4.1 mm; vertical, 3.4 mm) and the porous polyethylene (horizontal, 7.4; vertical, 6.3 mm) implants.

**Conclusions:** The myoconjunctival technique with a PMMA implant for enucleation delivers better prosthesis movement than either the traditional PMMA implant or the porous polyethylene implant.

**Reviewer's Comments:** Great study. I have always been taught that the porous implant with the muscles imbricated to the implant provides better movement. This study was randomized and used masked observers to evaluate movement. They showed that the much cheaper PMMA implant using the myoconjunctival technique provides not only comparable but superior prosthesis movement. As health care becomes more cost conscious, this may be an important study. With only 6 weeks of follow-up, however, we do not know the extrusion rate of the implants. (Reviewer-Michael S. Lee, MD).

© 2010, Oakstone Medical Publishing

Keywords: Enucleation, Prosthesis, PMMA, Hydroxyapatite, Porous Implant

Print Tag: Refer to original journal article
Chronic cerebrospinal venous insufficiency has been associated with multiple sclerosis.

**Background:** The cause of multiple sclerosis (MS) is unknown. Recently, it has been noted that poor venous drainage from the extracranial veins is strongly associated with MS.

**Objective:** To review the literature on and to discuss future application of chronic cerebrospinal venous insufficiency (CCSVI) and its relationship to MS.

**Design/Methods:** Critical literature review.

**Results:** Zamboni and colleagues used an imaging technique called transcranial color-coded Doppler sonography to evaluate blood flow in intracranial vessels. They found a strong association between MS and reflux in the internal jugular vein (IJV), vertebral veins, and deep cerebral veins. They also found narrowing of the IJV and poor postural control of venous outflow. They reported 100% sensitivity, 100% specificity, 100% positive predictive value, and 100% negative predictive value for the diagnosis of MS. Using selective catheterization, this group found 90% of MS patients had IJV or azygous vein (AV) stenoses. Follow-up for 18 months after angioplasty showed improved clinical outcomes. Almost 50% experienced restenosis; therefore, the authors suggested stenting of the IJV or AV. How can poor venous outflow cause MS? Proponents hypothesize that iron overload occurs within the brain. The authors argue that there are many discrepancies between what is known about MS and this theory. Venous outflow should worsen with time, but MS incidence does not rise with age. Parkinson’s disease and Alzheimer’s disease are thought to be related to iron deposition, but CCSVI was not seen in the “other neurologic disease” controls. Increased intracranial pressure is not a feature of MS. CCSVI does not explain the spinal cord involvement in MS. The jugular veins are removed in radical neck dissections, but these patients do not routinely develop MS.

**Conclusions:** The numbers are amazing between CCSVI and MS, but it is very unclear how this could cause MS. The authors strongly discourage endovascular angioplasty and stenting until further conclusive justification is provided.

**Reviewer’s Comments:** It doesn’t make much sense how poor venous outflow could cause MS. There has been a huge stir within the MS community among providers and patients alike. It seems that there will be a randomized clinical trial coming for the treatment of MS. (Reviewer-Michael S. Lee, MD).

© 2010, Oakstone Medical Publishing

Keywords: Chronic Cerebrospinal Venous Insufficiency, Multiple Sclerosis

Print Tag: Refer to original journal article
Factors other than documented tumor growth more commonly prompt surgical excision of conjunctival nevi.

**Objective:** To evaluate the epidemiology and clinical outcomes of conjunctival nevi.

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

**Participants:** 255 patients with conjunctival nevi.

**Methods:** Mean period of observation was 5.3 years (range, 1.0 to 11.0 years). Factors associated with need for surgical excision were evaluated.

**Results:** Of 255 patients enrolled in the study, operative excision was performed in 75 (29%). Decision to remove the nevi was made by the surgeon in 17% of cases and by the patient in 83% of cases. Surgeon-recommended excision was based on concern of possible malignant transformation based on suspicious clinical features (13%) or documented tumor growth (4%) on serial photography. Subjective concern about cancer prompted patient-initiated excision in 45% of cases, cosmetic concerns in 12% of cases, and ocular surface irritation due to irregularity of the lesion contour in 25% of cases. Factors associated with excision included older patient age, larger basal lesion diameter, presence of clear cysts, prominence of feeder vessels, and corneal involvement.

**Conclusions:** Documented tumor growth is a relatively uncommon cause for surgical excision of conjunctival nevi. Older patient age, prominent intrinsic vasculature and feeder vessels, and corneal involvement are important factors leading to patient- or surgeon-initiated surgical excision.

**Reviewer’s Comments:** Acquired conjunctival nevi generally appear in the first 2 decades of life. Although malignant transformation to melanoma is rare, the clinical features described in this study should prompt the clinician to recommend surgical excision. Otherwise, in the absence of patient concerns or symptoms, they may be monitored with serial photographic documentation to confirm absence of growth or development of worrisome features. (Reviewer—Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: Conjunctiva, Nevi

Print Tag: Refer to original journal article
Floppy eyelid syndrome is commonly associated with obstructive sleep apnea.

**Objective:** To evaluate the clinical and demographic characteristics of floppy eyelid syndrome (FES) and to assess its associations with keratoconus and obstructive sleep apnea-hypopnea syndrome (OSAHS).

**Design:** Case-control study.

**Participants/Methods:** 102 patients diagnosed with FES were identified. A control group of 102 patients without FES was recruited from a diabetic retinopathy clinic and matched to cases by age, gender, and body mass index. A complete medical and ophthalmic history was obtained for each subject. In addition, a complete ocular examination was conducted, including assessment of eyelid laxity and levator function of the upper eyelid. Pentacam imaging was performed to evaluate corneal topography, which was graded in a standardized fashion to assess keratoconus. Screening for OSAHS was completed using the Epworth daytime somnolence score.

**Results:** Significant associations were noted between FES and OSAHS ($P = 0.0008$) and keratoconus ($P < 0.0001$). Other clinical findings associated with FES included dermatochalasis, lash ptosis, and medial canthal laxity.

**Conclusions:** Important associations with FES include both keratoconus and OSAHS.

**Reviewer's Comments:** It has been hypothesized that mechanical stress on the eyelids and on the cornea can lead to the co-existing occurrence of both FES and keratoconus. The strength of these associations in this and other studies lends support to this hypothesis. The association between OSAHS and FES has been hypothesized to relate to decreased arousability to noxious stimuli, allowing patients to tolerate greater mechanical stress to the upper eyelid during sleep that would normally cause an unaffected individual to wake and alter his sleep position. (Reviewer-Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: Floppy Eyelid Syndrome, Keratoconus

Print Tag: Refer to original journal article
Reduced contrast sensitivity in patients with AIDS is often indicative of retinal and systemic microvascular disease and is correlated with a higher rate of mortality.

**Objective:** To study the relationship between contrast sensitivity (CS) and mortality in patients with acquired immunodeficiency syndrome (AIDS).

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

**Participants/Methods:** Data for this study were derived from the Longitudinal Study of the Complications of AIDS (1998 to 2008). Eligible subjects were free from ocular opportunistic infections and were evaluated every 6 months. Examinations included measurement of best-corrected visual acuity, determination of CS using the method of Pelli-Robson, visual field testing, slit-lamp examination, and dilated fundus examination. Data were analyzed to evaluate the relationship between CS and mortality during follow-up.

**Results:** Abnormal CS (logCS <1.5, representing the lowest 2.5th percentile for a normal population) was observed at baseline in 16.8% of subjects. A significant association was seen between abnormal CS at baseline and mortality during follow-up (relative risk, 2.0; \(P <0.0001\)). Other associations between abnormal CS included cardiovascular disease, stroke, and renal disease.

**Conclusions:** Abnormal CS is associated with increased mortality in patients with AIDS.

**Reviewer's Comments:** The results of this study strongly suggest that abnormal CS in patients with AIDS is an indicator of microvascular disease of the retina and that this is, in turn, associated with systemic microvascular disease in the heart, brain, and kidneys. This systemic microvascular disease is likely to underlie the observation of an increased rate of mortality in AIDS patients with reduced CS. This was the underlying hypothesis that the investigators wished to test in performing the study, and their results supported their hypothesis. This suggests that measurement of CS may provide a useful marker of the presence of systemic microvascular abnormalities and of the global risk of death in AIDS patients, and it may lead to better methods of monitoring these individuals. (Reviewer-Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: AIDS, Vision

Print Tag: Refer to original journal article
Male Gender Associated With More Complications of JIA-Associated Uveitis

Male Gender as a Risk Factor for Complications in Uveitis Associated With Juvenile Idiopathic Arthritis.
Ayuso VK, Ten Cate HA, et al:
Am J Ophthalmol 2010; 149 (June): 994-999

Cystoid macular edema, papillitis, and cataract occur more frequently in boys than in girls affected by juvenile idiopathic arthritis-associated uveitis.

Objective: To evaluate factors predictive of secondary complications of uveitis in children with juvenile idiopathic arthritis (JIA).

Design: Retrospective, interventional clinical case series.

Methods: Medical records were reviewed of a consecutive series of 65 children (117 eyes) affected by JIA-associated uveitis. Development of secondary complications of uveitis was evaluated by gender, age of onset of uveitis (<7 years or >7 years), and initial manifestation of JIA (uveitis or arthritis).

Results: 75% of patients were female. Follow-up after diagnosis ranged from 1.1 to 27.5 years (median, 7.6 years). Median time between onset of arthritis and uveitis was shorter in boys than in girls (0.3 vs 1.0 years, respectively; \( P = 0.01 \)). At 5 years of follow-up, boys were more likely than girls to suffer complications of cystoid macular edema and papillitis; they were also more likely to require cataract surgery.

Conclusions: Male gender is associated with a more complicated course of JIA-associated uveitis with more frequent development of cystoid macular edema, papillitis, and cataracts.

Reviewer’s Comments: This study complements the findings in the companion article discussed in this month’s program that demonstrated a significantly worse visual outcome in boys than in girls affected by JIA-associated uveitis. Although these findings do not imply that boys should be monitored more closely than girls, as all children affected by JIA require similar surveillance, it does highlight the importance of proper anti-inflammatory therapy to prevent the vision-threatening complications of this disease. Management of these children in collaboration with a pediatric rheumatologist is important to ensure that proper topical and systemic therapy is provided to control inflammation and minimize the risk of vision loss. (Reviewer-Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: Juvenile Idiopathic Arthritis

Print Tag: Refer to original journal article
Older age, male gender, elevated intraocular pressure, and sun exposure are associated with reduced endothelial cell counts in older adults.

Objective: To determine the distribution of corneal endothelial cell counts in an adult population in Japan, and to identify factors associated with lower endothelial cell counts.

Design: Cross-sectional, population-based study.

Methods: All residents of Kumejima Island, Japan, aged ≥40 years were asked to undergo a comprehensive ocular examination and complete a questionnaire. Home visits were conducted for participants who were unable to go to the study center. Examination included measurement of endothelial cell counts by specular microscopy. Statistical analysis was performed to identify factors associated with reduced endothelial cell counts.

Results: Of 4632 residents of the island, 3762 participated in the study (representing 81.2% of the total population). Mean endothelial cell counts were slightly, but statistically significantly, lower in men than in women (2927 vs 2959, respectively; P = 0.001). Other factors associated with lower endothelial cell counts included older age, higher intraocular pressure (IOP), and a history of outdoor work. For each year of older age, the mean change in endothelial cell count was 0.25%. For each mm Hg of higher IOP, the mean endothelial cell count decreased by 0.33%.

Conclusions: Male gender, older age, higher IOP, and a history of outdoor work are associated with reduced endothelial cell density in the adult population.

Reviewer's Comments: Although the exact mechanism by which outdoor work could result in a reduction of endothelial cell density is not known, it seems plausible that the relevant factor leading to this association is ultraviolet exposure from the sun. This finding suggests that the use of ultraviolet filtering sunglasses may offer protection not only for the lens against cataract and for the retina against age-related macular degeneration but for the cornea against endothelial cell loss. (Reviewer-Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: Corneal Endothelium, Cell Density

Print Tag: Refer to original journal article
The preservative-free topical NSAID diclofenac causes less ocular discomfort and conjunctival redness than the preserved version of this and similar medications.

**Objective:** To compare the efficacy and tolerability of preservative-free diclofenac 0.1% with the preserved version of this drug and with preserved ketorolac 0.5% in patients after cataract surgery.

**Design:** Prospective, investigator-masked, randomized, comparative clinical trial.

**Participants/Methods:** 102 patients who underwent phacoemulsification cataract surgery were randomly assigned to 1 of 3 postoperative regimens of topical nonsteroidal anti-inflammatory drug (NSAID) therapy given 4 times daily in the operated eye. They received either preservative-free diclofenac sodium 0.1%, preserved diclofenac sodium 0.1%, or ketorolac tromethamine 0.5%. Both preserved drugs contain the preservative benzalkonium chloride. During 1 month of follow-up, objective indicators of inflammation were evaluated and included anterior chamber cell and flare and macular thickness. Patients also responded to a questionnaire evaluating ocular discomfort.

**Results:** No differences were observed between treatment groups with regard to anterior chamber cell or flare or macular thickness. Patients who received preservative-free diclofenac reported significantly better tolerability, including reduced ocular discomfort and faster resolution of conjunctival hyperemia, than those using either of the preserved drugs.

**Conclusions:** The efficacy of preserved and preservative-free NSAIDs tested was comparable. Preservative-free diclofenac offered improved subjective patient tolerability when compared with preserved NSAIDs.

**Reviewer’s Comments:** Use of topical NSAIDs for reduction of ocular inflammation and treatment of postoperative macular edema has become widespread. Numerous studies have demonstrated the potential benefits of this treatment in patients predisposed to cystoid macular edema. This study suggests that elimination of preservatives allows retention of the desirable properties of diclofenac while reducing the ocular discomfort that can be associated with its use. (Reviewer-Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: Nonsteroidal Anti-Inflammatory Drugs

Print Tag: Refer to original journal article
Capsular staining with trypan blue causes lens epithelial cell death and may reduce the development of posterior capsule opacity associated with lens epithelial cell proliferation following cataract surgery.

**Objective:** To evaluate the effect of staining of the lens capsule with trypan blue on the ultrastructural characteristics and viability of lens epithelial cells.

**Design:** Laboratory evaluation of specimens obtained during human cataract surgery.

**Participants:** 30 patients undergoing routine cataract surgery were enrolled in the study.

**Methods:** The same experienced cataract surgeon performed all procedures. Patients were equally divided into a treatment group that underwent staining of the lens capsule with trypan blue at the beginning of surgery and a control group, in which no capsular stain was used. The anterior capsular flap was evaluated in the laboratory with optical microscopy and immunohistochemistry for specific markers of lens epithelial cell viability.

**Results:** Death of lens epithelial cells by autophagy was noted in treated, but not in control, eyes. Morphometric analysis of capsular specimens showed significant differences in epithelial cell morphology between groups, including longest nuclear axis length and ratio between total nuclear perimeter and total cell area. No difference was seen between groups in lens capsule thickness.

**Conclusions:** Staining of the lens capsule with trypan blue induces lens epithelial cell death.

**Reviewer's Comments:** Proliferation of lens epithelial cells across the scaffold created by the posterior capsule results in posterior capsule opacification. The findings described in this study of reduced viability of lens epithelial cells following capsular staining with trypan blue suggests that it may protect against posterior capsule opacification. Further investigation will be required to determine whether a clinically significant effect is achieved. (Reviewer-Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: Laser Capsulotomy

Print Tag: Refer to original journal article
There is evidence that patients with retinitis pigmentosa receiving vitamin A supplementation may benefit further from additional supplementation with lutein.

**Objective:** To determine if lutein supplementation slows the decline in visual function in patients with retinitis pigmentosa (RP) who are receiving vitamin A.

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

**Participants:** 225 patients with RP between ages 18 and 60 years. Smokers were excluded from participation.

**Methods:** All patients received supplementation of 15,000 IU/day of vitamin A. Patients were randomly assigned to receive additional supplementation of lutein 12 mg/day or a daily placebo tablet. Follow-up evaluation during a period of 4 years included visual field testing to quantify the rate of progression of visual field loss. Primary outcome was the rate of change in 30° automated perimetry results. Secondary outcomes were designated as the rate of change in 60° visual fields, 30-Hz electroretinogram (ERG) amplitude, and visual acuity.

**Results:** No significant effect of lutein supplementation was seen on rate of decline in peripheral retinal sensitivity on 30° visual field testing; however, there was a slower rate of decline of retinal sensitivity on 60° visual field testing. No difference was seen between groups in rate of decline of ERG amplitude.

**Conclusions:** In patients with RP using vitamin A supplements, additional supplementation with lutein may reduce the rate of decline in extreme peripheral vision.

**Reviewer's Comments:** It is important to note that the study was not primarily designed to evaluate the rate of decline of the 60° visual field. As such, one must interpret the results with some caution. Risks of lutein supplementation, however, are by most standards negligible, suggesting that lutein supplementation could be a reasonable recommendation for patients with RP. (Reviewer-Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: Retinitis Pigmentation, Lutein Supplementation

Print Tag: Refer to original journal article
The success of scleral buckling surgery appears to be unaffected by a patient's refractive error and by their lens status as either phakic, aphakic, or pseudophakic.

Objective: To evaluate the success rate of scleral buckling surgery in the management of rhegmatogenous retinal detachment (RRD), and to determine factors that influence its success.

Design: Retrospective, interventional clinical case series.

Methods: This study was based on data collected over a 20-year period at an academic center in Germany involving 4325 patients with RRD. Patient demographic and clinical information were recorded, including spherical equivalent refractive error and lens status at time of surgery (phakic, aphakic, or pseudophakic). In addition, for patients who were aphakic or pseudophakic, interval between cataract surgery and RRD was recorded. All patients underwent scleral buckling for repair of RRD. Data collected included persistence or recurrence of RRD after surgery and any associated complications.

Results: Mean patient age was 55 years. Trauma was the etiology of RRD in 8.5% of cases. Anatomic success in reattaching the retina without further surgery was achieved in 84.0% of patients. No significant difference was seen in the probability of achieving anatomic success as a function of patient age, lens status, or level of refractive error.

Conclusions: Scleral buckling surgery has a high rate of success in the management of RRD.

Reviewer's Comments: Many vitreoretinal surgeons prefer primary pars plana vitrectomy for the management of certain patients with RRD, such as in cases of vitreoretinal traction or when localization of all retinal breaks is uncertain. In cases of uncomplicated RRD, however, scleral buckling surgery offers a high probability of success and avoids the risk of proliferative vitreoretinopathy that may follow vitrectomy surgery. (Reviewer-Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: Retinal Buckling Surgery

Print Tag: Refer to original journal article
Clinical Outcomes of ARN Are Often Poor

Treatment of Acute Retinal Necrosis.
Tibbetts MD, Shah CP, et al:
Ophthalmology 2010; 117 (April): 818-824

Visual outcome in eyes with acute retinal necrosis is generally poor, even with treatment aimed at controlling the underlying viral infection.

Objective: To evaluate clinical outcomes and effect of different treatment strategies in patients with acute retinal necrosis (ARN).

Design: Multicenter, retrospective, interventional clinical case series.

Methods: Medical records were reviewed of a series of 58 patients diagnosed with ARN managed at 1 of 4 different tertiary referral centers between 1981 and 2008. Patients were categorized according to the period in which they developed ARN: patients treated during the acyclovir-only era and those treated more recently when newer antiviral therapies were available, including valacyclovir, famciclovir, valganciclovir, ganciclovir, and foscarnet. Some patients were also managed with oral steroids and/or prophylactic laser retinopexy. Outcome measures analyzed included visual acuity, development of retinal detachment, and occurrence of ARN in the fellow eye.

Results: A wide variety of antiviral therapies are currently employed in managing ARN. Despite use of newer antiviral therapies, visual outcome was similar to that of the acyclovir-only era. In both groups, the incidence of a decline in visual acuity to 20/200 or worse was 24% per year. In addition, a similarly high prevalence of retinal detachment was seen in both groups (acyclovir only, 47%; newer antiviral therapy, 55%; P = 0.6). Prophylactic laser retinopexy did not alter the rate of development of retinal detachment. Development of ARN in the fellow eye occurred in 3.4% of patients.

Conclusions: Despite use of a variety of newer antiviral therapies, clinical outcomes of ARN are often poor.

Reviewer's Comments: ARN is an infectious retinitis caused by members of the herpes virus family. The investigators did not find evidence to support any particular therapeutic approach to this disease and found similarly poor outcomes despite use of newer antiviral medications. Worse visual acuity at time of presentation and development of retinal detachment are strong predictors of a worse final visual outcome. (Reviewer-Scott D. Smith, MD, MPH).

© 2010, Oakstone Medical Publishing

Keywords: Acute Retinal Necrosis

Print Tag: Refer to original journal article