What’s New and Important in Pediatric Ophthalmology and Strabismus for 2015

THE ALL-STARS ABRIDGED HANDOUT

AAPOS Annual Mtg.
New Orleans, LA
Friday, 3/27/15
Workshop E, 2:45-4PM

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**AMBLYOPIA/VISION SCREENING**

**A binocular iPAd treatment for amblyopic children**  
S L Li, R M Jost, S E Morale, D R Stager, L Dao, D Stager and E E Birch  
Eye (2014) 28, 1246–1253

The authors demonstrate the efficacy of using an iPad platform technology to treat children with anisometropic and strabismic amblyopia. Children wear anaglyphic glasses and play binocular games for just 4 hours per week, in this well controlled study. Vision improved and was sustained for 3 months after cessation of therapy. Patching did not add any benefit. This pilot study involving 75 children demonstrates that new technology may finally bring amblyopia therapy into the 21st century.

**The Effect of Amblyopia on Visual-Auditory Speech Perception**  
**Why Mothers May Say “Look At Me When I’m Talking To You”**  
Robert Burgmeier, Rajen U. Desai, Katherine C. Farner, Benjamin Tiano, et.al.  

This is a retrospective observational study to determine if amblyopes have visual auditory processing difficulties. The McGurk phenomenon demonstrates that how you interpret what you hear is influenced by what you see. An examiner will say “ba,ba,ba” which the test subject will hear as “ba,ba,ba”, but if the examiner changes his mouth expressions while saying “ba,ba,ba” the test subject will hear “fa,fa,fa.” The McGurk effect is an example of visual auditory integration. Thirty three children older than age 3 with no hearing or neurologic problems were examined. Twenty four of the children had amblyopia and nine children did not have amblyopia and served as controls. An audio track played the sound “pa” and a video track showed a person verbalizing “ka.” The integrated sound was “ta.” The McGurk effect, that is, the fused sound “ta,” was perceived by 11 of the 24 children with amblyopia (45.8%) and all 9 controls (100%)

The McGurk effect was perceived by 100% of children with amblyopia that was resolved by 5 years of age and by 100% of participants whose onset at amblyopia developed at or after 5 years of age. However, only 18.8% of participants with amblyopia that was unresolved by 5 years of age (n = 16) perceived the McGurk effect. The authors conclude that children with amblyopia have impaired visual auditory speech recognition and the timing of onset and resolution of amblyopia affects this process of integration.
Beyond Screening for Risk Factors Objective Detection of Strabismus and Amblyopia

The authors identify a limitation of commercially available vision screening devices. These devices identify refractive risk factors for amblyopia, not amblyopia or strabismus itself. This study examined the Pediatric Vision Scanner (PVS), a device which relies on retinal birefringence to detect amblyopia, with the Suresight autorefractor.

Primary outcome was sensitivity and specificity of identifying amblyopia and strabismus in a cohort of children age 2-6 years old. Secondary outcomes included positive and negative likelihood ratios of identifying amblyopia and strabismus. A masked complete pediatric ophthalmology exam was the gold standard. Of 300 patients, 188 had strabismus only, amblyopia only, or both and 112 had neither strabismus nor amblyopia. The sensitivity of the PVS to detect strabismus and amblyopia was higher than the Suresight (0.97 vs. 0.74). Specificity was also significantly higher for the PVS than the Suresight (0.87 vs. 0.62). The Suresight autorefractor had 8.8 x as many false negatives and 3.1 times as many false positives as the PVS. The PVS was easy to use with only one child not being able to be screened, compared with 17 children not completing a successful screening with the Suresight. A limitation of the study is that examiners, during the gold standard complete exam, used fixation preference as a surrogate for amblyopia in children too young to cooperate for visual acuity testing. Also, the setting for the study was “enriched” and not the primary care setting, which is the environment a pediatric vision screening device would be most useful.

### NEURO-OPHTHALMOLOGY/NYSTAGMUS

Handheld Optical Coherence Tomography During Sedation in Young Children With Optic Pathway Gliomas

Determining vision loss in young children with optic pathway gliomas can be difficult. The authors postulate that retinal nerve fiber layer (RNFL) thickness may be a surrogate for visual acuity/visual field. OCT measures retinal nerve fiber layer thickness. Study objective includes determining if measurement of circumpapillary RNFL can predict which children had vision loss from optic pathway gliomas. Main outcome measures were area under the curve of the receiving operating characteristic (ROC), sensitivity, specificity, positive and negative predictive values of quadrant specific and total RNFL thickness. Children with a sporadic or neurofibromatosis-related optic pathway glioma
(OPG) at a tertiary hospital who could cooperate for visual acuity testing, but required sedation for MRI, were included. Hand held OCT measurements during sedation were taken. Thirty three children (64 eyes) were included (median age 4.8 years) with OPG and a cohort of children, normally sighted without OPG, were used as controls (median age 8.7 years) In children with vision loss (visual acuity or visual field) all quadrants had reduction of RNFL compared with children with no vision loss (p<0.01). A longitudinal multicenter trial is needed to define the temporal relationship between RNFL loss and vision loss.

**Interpretation of Lumbar Puncture Opening Pressure Measurements in Children**

This review of the literature on pediatric idiopathic intracranial hypertension suggests that cerebrospinal fluid opening pressure ≤28 cm H2O is likely normal for children. Sedation, particularly with ketamine, but even with other agents, typically increases opening pressure about 3-4 cm H2O and this likely secondary to induced hypercapnia. Agitation increases opening pressure. Leg position (flexed or extended with patient in the lateral decubitus position) has minimal to no impact on opening pressure. Resolution of headache directly after sedated LP may be secondary to sedative analgesics and is not necessarily diagnostic.


This is a cross-sectional evaluation of 37 children (ages 8-18) diagnosed with a demyelinating disorder, performed at least >6mos after diagnosis, in comparison to healthy controls. Evaluation included high-contrast visual acuity (HCVA), low-contrast visual acuity (LCVA) with Pelli-Robson chart, visual fields, color vision, and OCT of the optic disc and macula. The ganglion cell layer (GCL) was measured using automated software, and thickness was reported. The authors found that the retinal nerve fiber layer (RNFL) was 26μ (25.6%) lower in patients with demyelinating disease (76.2μ) in comparison to controls (102.4μ)[p<0.0001]. Mean GCL thickness was 20% thinner in patients with demyelinating disease [p<0.0001]. 100% of children with a RNFL thickness <87μ (15% less than controls) had abnormal scores on the Pelli-Robson chart. 100% of children with a GCL thickness of <76μ (10% less than controls) had abnormal scores on the Pelli-Robson chart. There was a trend for the RNFL to be thinner among patients with demyelinating disease who suffered optic neuritis, versus those who had not [p=0.08]. The GCL was not affected by the presence or absence of optic neuritis among those with demyelinating disease. RNFL thickness declined in a stepwise manner dependent upon number of optic neuritis episodes (9μ per episode). In contrast to previous studies in adults, the history and number of episodes of optic neuritis was not associated with decrements in GCL thickness.
Further study of the utility of OCT as an objective measure of neuronal damage in the evaluation of pediatric demyelinating disease is needed.

**A Randomized Controlled Trial Comparing Soft Contact Lens and Rigid Gas-Permeable Lens Wearing in Infantile Nystagmus**

Pavitra Jayaramachandran, Frank A. Proudlock, Nita Odedra, Irene Gottlob, *Ophthalmology* September 2014; 121(9):1827-1836

This article comes from the Ophthalmology Group, University of Leicester, Faculty of Medicine & Biological Sciences, Leicester Royal Infirmary, Leicester, United Kingdom. This is a randomized, controlled cross-over trial with an intention-to-treat design. This study is designed to perform the first randomized controlled trial comparing soft contact lens with rigid gas-permeable lens (RGPL) in infantile nystagmus using spectacle wear as a baseline. Twenty-four patients (12 idiopathic, 12 with albinism) were randomized into 1 of 2 treatment arms: A) spectacles with soft contact lens, rigid gas-permeable lens and spectacle wear or B) spectacles, rigid gas-permeable lens, soft contact lens and spectacle wear. The main outcome measure was mean intensity of nystagmus at the null region viewed at 1.2 meters. Secondary outcome measures included the same measurement at 0.4 meters viewing and across the horizontal meridian. There was no significant difference between soft contact lenses and rigid gas-permeable lens wearing for any nystagmus characteristics when compared with spectacle wearing.

Conclusions: Nystagmus was not significantly different between soft contact lens wear and rigid-gas permeable lens wear in infantile nystagmus. Contact lens wearing does not significantly reduce the nystagmus when compared with baseline spectacle wearing. The wearing of soft contact lenses leads to small but statistically significant deterioration in visual function compared with both rigid gas-permeable lenses and spectacle correction at baseline.

**ROP**


Results of FA in 13 patients at 9 months after treatment comparing intravitreal injection of bevacizumab with fellow eyes treated with laser photocoagulation for zone 1 Type 1 ROP. Among 23 eyes available for FA at 9 months, all bevacizumab eyes had peripheral abnormalities including large avascular areas, abnormal branching and shunts, and hyperfluorescent lesions or abnormalities
of the foveal avascular zone. These abnormalities were not observed in the majority of lasered eyes.
Conclusion – long lasting structural abnormalities appear to be more common in bevacizumab treated eyes than in lasered eyes and the effect on function of these abnormalities must be studied.


Purpose: Evaluate the validity of a telemedicine system to identify infants who have sufficiently severe ROP to require evaluation by an ophthalmologist. 1257 infants with BW<1251 enrolled in 13 North American Centers from May 2011- Oct 2013. Trained non-physician retinal imagers obtained images and submitted them for grading by non-physician readers. Primary outcome was comparison of grading results for referral warranted ROP (zone I ROP, stage 3 or worse ROP, and/or plus disease) with the results of diagnostic examination by the ophthalmologist. Sensitivity for detection of RW-ROP was 90% and specificity of 87% for a single exam for an infant.
These results support the validity of remote evaluation by trained non-physician readers of digital images obtained by trained non-physician imagers for at risk infants.

STRABISMUS/STRABISMUS SURGERY

Incidence, Types, and Lifetime Risk of Adult-Onset Strabismus
J M. Martinez-Thompson, N N. Diehl, J M. Holmes, B G. Mohney, Ophthalmology April 2014; 121:877-882

This is a retrospective reviewed population-based cohort designed to describe the incidence and types of adult-onset strabismus in a geographically defined population, mainly Olmsted County, Minnesota.
Participants: Residents, 19 years of age and older who were newly diagnosed with some form of strabismus from January 1, 1985, to December 31, 2004, were included in this study.
Methods: The medical records of all potential cases identified by the resources of the Rochester Epidemiology Project were reviewed.
Main Outcome Measures: Incidence rates for adult-onset strabismus and its different types.
Results: 753 cases of new onset adult strabismus were identified during a 20 year period. The average annual age and gender adjusted incidence rate was 54.1 cases per 100,000 individuals 19 years of age and older. The foremost common types of new onset strabismus were paralytic strabismus 44.2, convergence insufficiency 15.7, small angle hypertropia 13.3 and divergence insufficiency 10.6.

Conclusions: Paralytic strabismus was the most common subtype of new onset adult strabismus in this population based cohort (limited to Olmsted County, Minnesota). All of the most common forms of adult onset strabismus increased with age especially after the sixth decade of life.


This is an important paper that should be read by all strabismologists. In this retrospective study the authors investigate the "cure" rate for exotropia comparing those who had surgery to those who did not. After seven year followup the cure rate for the surgical group was 30% and for the non surgical group 12%, not a statistical difference. More important than the numbers is the authors discussion of the challenges of studying this challenging condition. They are commended for presenting long term results, as such data is rare in our literature.

A Randomized Trial Comparing Part-Time Patching with Observation for Children 3 to 10 Years of Age with Intermittent Exotropia


This is a multicenter, randomized clinical trial of 358 children 3 to less than 11 years of age. The purpose is to determine the effectiveness of prescribed part-time patching for treating intermittent exotropia in children.

Results: Of the 324 participants (91%) completing the 6-month primary outcome examination. Main Outcome Measures: Deterioration occurred in 6.1% in the observation group and 0.6% in the part-time patching group.

Conclusions: Deterioration of previously untreated childhood intermittent exotropia over a 6-month period is uncommon with or without patching. There is a slightly lower deterioration rate with patching. Both management approaches are reasonable for treating children 3 to 10 years of age with intermittent exotropia.
Superior Rectus Transposition vs Medial Rectus Recession for Treatment of Esotropic Duane Syndrome

The authors compared the effectiveness of superior rectus transposition (SRT) +/- ipsilateral medial rectus recession (MRrc) with unilateral or bilateral MRrc in the treatment of esotropic Duane’s syndrome. This was a retrospective review which identified 36 patients who had 37 procedures (18 in the SRT group and 19 in the non-SRT group). Main outcomes included binocular alignment, ocular ductions, head position, stereopsis, and fundus torsion measured pre-operatively and at the 2-month and final postoperative visits. The authors conclude that SRT was more effective in improving abduction than MRrc alone. No vertical or torsional complications were noted. In 24 patients followed for greater than 6 months mean esotropia decreased from 8.2 to 6.1 PD in SRT group and increased in MRrc group from 7.2 to 10.9PD.


The authors describe a novel surgical technique to improve eye alignment in patients with third nerve palsy. The surgeon needs to extensively split the lateral rectus (LR) anteriorly to posteriorly and secure the split LR each with a Vicryl suture. Then the split muscle is threaded beneath the vertical rectus and oblique muscles on its way to the medical rectus. The two portions of the LR are ultimately secured at the poles of the medial rectus with an adjustable noose knot suture. The study describes the pre-op characteristics and postoperative course of 6 patients who had the procedure. Three out of 6 patients achieved orthotropia. Mean pre-op deviation was 68 PD of exotropia. Two patients with vertical misalignment improved because of the ability to adjust one pole of the LR versus the other. One patient had undercorrection and transient choroidal effusion. MRI imaging post-operatively identified the split lateral rectus to be posterior to the globe in all cases except in the one patient who was undercorrected and had a choroidal effusion. In this patient, the split lateral rectus followed a course in apposition to the globe. Case selection is important since prior surgery on the lateral rectus could render the muscle stiff and scarred and not amenable for the long course it needs to take to be secured to the medial rectus.
Muscle belly union associated with simultaneous medial rectus recession for treatment of myopic myopathy: results in 33 eyes
M Fresina, A Finzi, P Versura and E C Campos Eye (2014) 28, 557–561;

This is the largest clinical series describing the treatment of esotropia and hypotropia associated with high myopia. The authors described 26 patients with high myopia (spherical equivalent -22.0D +/- 9) who underwent union of ½ width lateral rectus muscle to ½ width superior rectus muscle with non absorbable suture 12-15 mm from original insertions. All had simultaneous medial rectus recession. Scleral fixation was not performed. There was marked improvement in alignment (45 ET preop to 7 ET postop) and few complications. Such patients should receive orbital MRI preop to confirm presence of inferior displacement of the lateral rectus and medial displacement of the superior rectus.


The purpose of this study is to assess the extent of standardization of reported outcomes in studies of surgery for IXT. A systematic literature review was conducted of outcomes of surgery for IXT published in the last 10 years. The databases used were Medline and EMBASE. Fifty-six studies met the inclusion criteria (thirty-two retrospective and twenty-four prospective). Results showed that outcome measures varied widely between studies and variously included ocular alignment, stereopsis, visual acuity, re-operation rate, and postoperative drift. Even for ocular alignment, there was no agreed definition of postoperative success. The authors suggest redefining the criteria for success in IXT surgery based on which outcomes, and what level of outcome, translate into noticeable benefit to patients, rather than what matters to surgeons or researchers. They suggest 4 core outcomes for all future studies: alignment, near stereoacuity, control score, and quality of life score.

CATARACT SURGERY

Comparison of Contact Lens and Intraocular Lens Correction of Monocular Aphakia During Infancy A Randomized Clinical Trial of HOTV Optotype Acuity at Age 4.5 Years and Clinical Findings at Age 5 Years The Infant Aphakia Treatment Study Group JAMA Ophthalmol. 2014;132(6):676-682.

This study provides data on visual acuity and clinical course, at age 4.5 years and 5 years, respectively, for the cohort of children who were enrolled in the
Infant Aphakia Treatment Study. One hundred thirteen patients with visually significant cataracts identified and operated between age 1 and 6 months of life were randomized to aphakia correction with a contact lens or intraocular lens (Acrysof SN60AT or MA60AC). The authors conclude that there was no significant difference in visual acuity between the 2 groups (median visual acuity 0.9 logMar or 20/159) and half of patients in each group had visual acuity of 20/200 or less. The group who received an IOL had more complications and required additional surgeries. Seventy two percent required at least one additional surgery in the IOL group compared with 21% in the contact lens group (p<0.001). Most common complications were lens reproliferation into the visual axis, pupillary membranes and corectopia. Glaucoma/glaucoma suspect developed in 28% of patients with IOL and 35% with contact lens. Most patients developed strabismus. The authors conclude there is no visual benefit from implanting an IOL in an infant less than 7 months of age.

GENETICS


When testing for disease association in common, complex diseases most widely used tests assume an additive risk model. One hypothesis is that variants may influence disease susceptibility in a nonadditive, recessive fashion. The power of the additive model to detect recessive alleles is greatly diminished at lower frequencies. Therefore, conventional association tests may miss rare variants associated with common, complex diseases. The authors describe a statistical methodology, termed recessive-allele-frequency-based test (RAFT), designed to detect rare recessive variants in complex diseases. RAFT does not directly compare homozygous counts in case and control subjects. Instead, it evaluates the likelihood of observing the number of homozygotes in the cases \( N_{\text{case}} \) compared to the expected number of homozygotes and normalizes this by the same statistic for observing \( N_{\text{controls}} \), the number of homozygotes in the controls compared to the expected number of homozygotes. RAFT was applied to 1,791 Finnish individuals with type 2 diabetes (T2D) and 2,657 matched control subjects. A rare variant (c.1189A>G) in Bardet-Biedl syndrome 10 (BBS10) was detected that confers significant risk of T2D in a recessive manner. It was determined that this rare variant would be missed by Fisher’s exact test, a conventional method. The variant was tested in an in vivo zebrafish model and confirmed to be pathogenic. When compared to standard additive tests, RAFT provides significantly more power to detect lower-frequency recessive variants (allele frequency ≤ 5%). The evidence provided in this study suggests that targeted methods, such as RAFT, may prove to be crucial in identifying rare recessive variants associated with complex diseases.
Vitritis in Pediatric Genetic Retinal Disorders
Maria Stunkel, Sajag Bhattacharai, Andrew Kemerley, Edwin M. Stone,
Ophthalmology January 2015; 122(1):192-199

This is a retrospective, observational study in humans designed to determine which types of pediatric retinal degeneration are associated with inflammatory cells in the anterior vitreous.

Main Outcome Measures: Cell counts in slit lamp examination of anterior vitreous (SLAV) and clinical and molecular genetic diagnoses were documented. Anterior vitreous cells were graded clinically with SLAV from rare cells 1+ 5-9, 2+ 10-30 and 3+ greater than 30 cells.

Results: The most frequent diagnosis of cells included Bardet-Biedl syndrome (BBS), Leber's congenital amaurosis (LCA) and retinitis pigmentosa. The most frequent diagnosis without cells included congenital stationary nightblindness, Stargardt's disease and blue cone monochromacy.

Discussion: A nonrandom subset of pediatric retinal degenerations exhibit vitritis. Cells were present in 5 of 5 Bardet-Biedl patients, whereas cells were not detected in any of the 12 patients with congenital stationary nightblindness.

Conclusions: Studying vitritis in pediatric retinal degenerations may reveal whether inflammation accompanies progressive vision loss in certain subtypes. Potentially, inflammation could be treated. In addition, slit-lamp examination of anterior vitreous may aid in a clinical diagnosis.


Stargardt disease (STGD), the most common juvenile macular degeneration, displays a large amount of phenotypic and genotypic variability. This retrospective case series describes characteristics of childhood-onset STGD and compares them to that of adult-onset STGD. Forty-two patients < 17 years of age with molecularly confirmed STGD were examined at Moorfields Eye Hospital. The median age of onset was 8.5 years, whereas the median age of baseline examination was 12.0 years. The median baseline logMAR VA was 0.74. Thirty-nine patients had baseline color fundus photos. The most common fundus appearance was macular atrophy with macular/peripheral flecks (67%), followed by macular atrophy without flecks (28%), and numerous flecks without macular atrophy (2.5%). A normal fundus appearance was observed in 2.5% of patients. At baseline, central atrophy was present in 95% of patients and flecks were not observed in 31% of patients. Thirty-two patients obtained baseline fundus autofluorescence (FAF). The most common fundus FAF pattern (69%) was described as a localized low macular AF signal surrounded by a heterogeneous background with widespread high or low AF foci extending anterior to the
vascular arcades. Foveal outer retinal disruption was detected in all patients who received a baseline SD-OCT. Twenty-five patients underwent electrophysiological testing at baseline. Macular and generalized cone and rod dysfunction, the most prevalent ERG phenotype observed, occurred in 60%. Retinal dysfunction confined to the macula was seen in 36%. Forty-six $\text{ABCA4}$ variants were identified, of which 13 were novel variants. In 90% of patients at least one disease-causing $\text{ABCA4}$ variant was identified. Two or more variants were confirmed in 81% of patients. The childhood-onset STGD group was compared to 64 adult-onset STGD patients harboring $\geq 2$ disease-causing $\text{ABCA4}$ variants. The childhood-onset group had less retinal pigmentation, more deleterious variants, and thinner central fovea thickness compared to the adult-onset group. Two deleterious variants were identified in 18% patients with childhood-onset STGD, while only 5% of adult-onset STGD patients harbored this amount. This study supports that childhood-onset STGD is associated with foveal structural changes and severe vision loss early in the disease process. Though most children in the study displayed the classic fundus appearance of STGD, one-third in fact did not have visible flecks at presentation. When compared to the adult-onset disease, childhood-onset STGD is more likely to be associated with generalized retinal dysfunction. The higher proportion of deleterious $\text{ABCA4}$ variants in childhood-onset STGD suggests that the earlier disease onset and more severe phenotype in this patient population may be attributed to more severe variants in $\text{ABCA4}$.


Early-onset Stargardt disease lies within a spectrum of retinal phenotypes associated with mutations in the $\text{ABCA4}$ gene. Due to its wide clinical variability, Stargardt disease can be challenging to diagnose at a young age. This retrospective cohort study described the phenotype and genotype of 51 early-onset Stargardt patients (defined by $\leq 10$ years). Genetic screening of 44 patients revealed $\geq 2$ $\text{ABCA4}$ mutations in 37 patients (84%) and single heterozygous mutations in seven (16%). The mean age at onset was 7.2 years (range, 1-10). The median times to develop BCVA of 20/32, 20/80, 20/200, and 20/500 were 3, 5, 12, and 23 years, respectively. Initial ophthalmoscopy revealed no abnormalities in 24.4% of patients (10/41). Foveal retinal pigment epithelium (RPE) changes were observed in 22% (9/41). The remaining 53.7% (22/41) of patients had foveal atrophy, atrophic RPE lesions, and/or irregular yellow-white fundus flecks. Foveal atrophy occurred before flecks developed in 28% of patients (14/50). A “dark choroid” was seen in 21 out of 29 patients (72.4%) on fluorescein angiography (FA). On fundus autofluorescence (FAF), disseminated atrophic spots underwent centrifugal expansion with progression to eventual profound chorioretinal atrophy. Spectral-domain optical coherence tomography (SD-OCT) revealed early photoreceptor damage followed by atrophy of the outer
retina, RPE, and choroid. On full-field electroretinography (ffERG), 57.7% (15/26) of patients had normal amplitudes, while 42.3% (11/26) had reduced photopic and/or scotopic amplitudes at their first visit. Thirteen out of 25 (52%) patients had progressive ffERG abnormalities. However, no correlation between ffERG abnormalities and the rate of vision loss was found. The findings in this study indicate that early-onset Stargardt disease can be considered a distinct severe subtype characterized by early foveal abnormalities and rapid loss of visual function. In contrast, foveal sparing is common and visual acuity is often preserved to a relatively advanced age in late-onset Stargardt disease. The study also advocates for the utilization of FAF and SD-OCT in patients suspected of having early-onset Stargardt disease, particularly when no or mild foveal abnormalities are present in a child with unexplained central vision loss.

**Macular Function and Morphologic Features in Juvenile Stargardt Disease: Longitudinal Study.**


Autosomal recessive Stargardt disease (STGD1) is caused by mutations in the photoreceptor-specific ATP-binding cassette transporter (ABCA4) gene. This longitudinal cohort study evaluated disease progression in patients with a clinical and genetic diagnosis of STGD1. The study was designed to incorporate patients who satisfy the inclusions criteria required in gene therapy clinical trials, such as the StarGen study (clinicaltrials.gov; identifier NCT01367444), which enrolled patients with at least two mutations in ABCA4. A total of 56 patients with early-onset STGD1 were followed for a median length of two years. The patients had a mean age at disease onset of 15.3 years (range, 3-28 years), mean disease duration of 12.1 years, and mean age at baseline of 27.4 years. The median BCVA was 20/200 in both eyes. Optical coherence tomography (OCT), which was not obtained in seven patients due to poor signal quality, revealed a mean retinal pigment epithelium (RPE) lesion area of 2.6 mm², preserved foveal inner segment/outer segment (IS/OS) junction in 4.1% of patients, foveal IS/OS junction loss in 59.2% of patients, and extensive macular IS/OS junction loss in 36.7% of patients. Microperimetry (MP) showed reduced macular sensitivity (mean, 10 decibels [dB]) and an unstable fixation in half of the patients. The longitudinal analysis showed a significant progressive reduction in BCVA and macular sensitivity (at an estimated rate of 0.04 decimals and 1.19 dB/year, respectively) with a significant associated RPE lesion area enlargement (0.282 mm²/year). There were no significant changes in ophthalmoscopic findings and electroretinographic responses detected. The literature supports that visual acuity data alone were not able to detect Stargardt disease progression, particularly in the short-term (< 5 years). This highlights the importance of monitoring retinal function by MP and OCT in order to accurately define disease progression in STGD1 during a short-term follow-up. Previous studies investigated MP parameters in heterogeneous cohorts of patients with macular diseases including only small subgroups of STGD1. In addition, few data
regarding OCT lesion area have previously been available since the algorithm was only recently introduced. This study suggests that MP and OCT should be included as outcome measures in the design of future gene therapy clinical trials.

RETINA/RETINOBLASTOMA

Vigabatrin retinal toxicity in children with infantile spasms

This is an observational cohort study to evaluate risk factors for, and time to induce retinal damage from vigabatrin (VGB) in children with infantile spasms. The authors included 146 patients who had baseline electroretinogram (ERG) before, or within 4 weeks of initiating VBG therapy, and defined VGB induced retinal damage as a significant reduction in amplitude on 30-Hz ERG flicker. Follow-up ERG was performed every three months. They found that 30 (21%) of patients developed VBG induced retinal damage (5.3% within six months, and 13.3% within 12 months). ERG amplitude was significantly correlated with duration of therapy. They found no recovery following cessation of therapy. Age, sex and cumulative dosage were not associated with the development of VBG induced retinal damage. The authors recommend limiting exposure to VBG to six months to decrease the prevalence of VBG induced retinal damage.

Diversity of Retinal Vascular Anomalies in Patients with Familial Exudative Vitreoretinopathy

This article comes from William Beaumont Hospital, Department of Ophthalmology, Royal Oak, Michigan. A total of 174 eyes of 87 subjects were studied. A retrospective chart review was conducted of patients with a diagnosis of FEVR between January 2011 and January 2013. Data was collected from patient charts including sex, gestational age, age at presentation and referring diagnosis. Clinical and angiographic findings were assessed/evaluated. Results: A total of 87 subjects were studied. A broad spectrum of clinical and angiographic findings was associated with familial exudative vitreoretinopathy (FEVR) on wide-field angiography study. Anatomic and functional changes were evaluated. Conclusions: Familial exudative vitreoretinopathy has a wide range of under-recognized clinical and angiographic findings that are easily identified using wide-field fluorescein angiogram technique. These findings have led to an update of the original FEVR classification scheme. These new findings were more completely characterized of early stages of familial exudative vitreoretinopathy.
Comment: The William Beaumont group has published a familial exudative vitreoretinopathy on a regular basis for the past 10 years. This latest study looks at the familial exudative vitreoretinopathy classification scheme and modifies it according to the findings of the wide-field fluorescein angiography. This can best be seen on Table 3 where the authors describe a revised familial exudative vitreoretinopathy clinical staging system based on the angiographic findings. Stage 1 is defined with and without exudative stages. Stage 2 is defined with and without exudative leakage; likewise, stage 3, stage 4 and stage 5.


The authors emphasize the importance of accurately diagnosing retinoblastoma (RB) as over 25 conditions can simulate RB. Treatment of RB is complex and may include chemotherapy, enucleation, laser photoacoagulation, thermotherapy and cryotherapy. Chemotherapy administration is based on the type of mutation present (germline or nongermline), laterality and stage of disease. Chemotherapy delivery may be intravenous (IV), intra-arterial, periocular and intravitreal. IV chemotherapy is the first line of therapy for bilateral (germline) RB to control intraocular disease, prevent metastasis, and reduce the prevalence of pineoblastoma and second malignant neoplasms. Bilateral groups D and E receive additional periocular chemotherapy with carboplatin or topotecan boost for improved local control. Treatment with intra-arterial chemotherapy for unilateral (nongermline) RB or for salvage after chemoreduction failure should be considered. Intravitreal chemotherapy is reserved for recurrent vitreous seeds following other therapies.

This article is important because it reviews ocular conditions that can be misdiagnosed as retinoblastoma, RB classification, and indications for enucleation and chemotherapy. The treatment strategy for RB is complex but this article helps to break down the decision making process.

UVEITIS/PRACTICE MANAGEMENT/HEALTH CARE SYSTEM


This retrospective cohort study analyzed the predictors for development of uveitis in JRA patients. 147 patients were diagnosed with chronic anterior uveitis (41%). Young age of onset, +ANA, increased ESR were predictive factors. After
adjusting for other relevant factors, elevated ESR appears to be a predictor of uveitis in patients with JIA.


This study investigates the long-term efficacy and tolerability of tumor necrosis factor α (TNFα) inhibitors in the therapy of children with refractar antinuclear antibody (ANA) – associated chronic anterior uveitis. The study is a retrospective review of 31 children with ANA-associated uveitis treated with TNFα inhibitors with a minimum follow-up period of 2 years. The indication for treatment had to be anterior uveitis and not control of arthritis to be included in the study. The authors evaluated control of inflammation, corticosteroid-sparing potential, and side effects. 74% were treated with adalimumab, 16% with infliximab, and 10% with etanercept. Control of uveitis was defined as 0 anterior chamber cells while on < 2 drops/day of topical corticosteroids. This was achieved in 22 of 31 patients (71%) after 1 year and 22 of 31 patients after 2 years of treatment. Control was observed in 78% of children treated with adalimumab and 40% of those treated with infliximab. Control of uveitis was not observed in any of the children treated with etanercept. 71% of children were able to discontinue systemic corticosteroids and 55% were able to stop topical corticosteroids. The authors conclude that adalimumab and infliximab have beneficial effects in the therapy of severe ANA-associated anterior uveitis in children. They do note that the results should be interpreted cautiously given the small number of patients receiving infliximab and etanercept.


The study provides detailed analysis of a prior publication of EHR. Productivity, efficiency, and work hours are evaluated in an academic pediatric ophthalmology practice. Data from four providers with varied volume of patients were evaluated. Overall patient volume declined by 11% when comparing pre-EHR to post-EHR (allowing for the assumed slow ramp up time for a few months during transition). However data was widely distributed with one provider actually seeing more patients and one provider unchanged. Chart completion also varied widely and seemed most affected by the practice style of the specific clinician. Overall 56% of charts were completed during normal business hours. The authors comment that the volume decrease in patients seen was greater than that of the ophthalmology department as a whole, and that Pediatric Ophthalmologists may be more burdened and negatively affected by currently available EHR systems. The volume of patients seen by each provider was dramatically different and the
The Care of the Patient: Field Notes from a Veteran

Dr. Kushner shares with us 10 points of wisdom, which he gained from his 40 years of practice as an academic pediatric ophthalmologist. During this time, he taught many medical students, fellows and ophthalmology residents. Dr. Kushner delivered the keynote address at the graduation of the Wisconsin Department of Ophthalmology 2014 graduation.
The theme of Dr. Kushner’s presentation was “What would be meaningful to these about-to-become colleagues who were just beginning their careers.”

Recommendation #1: On talking to patients with wisdom derived from Mark Twain. “The difference between the almost right word and the right word is really a large matter---“tis the difference between the lightning-bug and the lightning.”

Dr. Kushner recommended using the words “relax” rather than “paralyze” for their pupil. “Relaxation” has good energy; “paralysis” sounds ominous. After dilation, tell patients they may “sensitive to light, rather than bothered by light.”

Recommendation #2: Listening to patients with words from a Zen Master. 1) Listen for the facts, 2) Listen to the emotions, 3) the body language, 4) how the conversation is affecting you and 5) what is not being said.

Recommendation #3: Talking in front of patients with advice from a former mentor. Every word we utter in the patients’ presence will be chewed upon, mulled over and repeated. When doctors talk to one another in front of patients, the patient may not understand the meaning and importance of what we are discussing. Physicians need to recognize that we speak a different language than patients. Dr. Kushner counsels that whenever things are discussed between residents and fellows in front of the patient that the attending physician turns to the patient and says “excuse us while we talk shop for a minute and then I will translate for you what we have said.”

Recommendation #4: The importance of offering hope with reference to the drinking glass. Always emphasize the positive. Be truthful to the patients. Don’t mislead them with false hope, but on the other hand, don’t dwell only on the negative findings.

Recommendation #5: Understanding the patients’ needs and wants with humor and a clinical pearl from Art Jampolsky, MD. When doing a refraction instead of saying, which is better 1 or 2? You ask, “Pick the worst choice.” The patient can always pick the worst choice because they love playing out the negative.

Recommendation #6: Expand your own horizons with words about Descartes’ Error. Descartes was famous for the statement, “I think therefore I am.” Descartes’ Error was reframed by Rousseau by declaring, “I feel, therefore I am.” To enhance the “feeling for the patient”, Dr. Kushner recommended reading fiction and poetry. Dr. Kushner felt that fiction was the best way to understand peoples’ plights, situations and make us more empathetic. He recommended the books The Heart Is a Lonely Hunter by Carson McCullers’, Tunnel Visions by

**Recommendation #7:** Take care of your heart and soul with intervention from a son of the Goddess Aphrodite. Dr. Kushner recommends being more heartfelt or compassionate and you will understandably make a more caring doctor.

**Recommendation #8:** Get to know your patients as people. Take the time to find out your patients’ job, family members, accomplishments, hobbies, etc.

**Recommendation #9:** The ultimate secret about caring for patients with teachings from renowned physician. “The secret of the care of the patient is to care for the patient.”

Comment: This is an extraordinarily fine article in summary from one of our greatest mentors, Dr. Burton Kushner. I personally have started reading poetry and fiction (2 areas that I have eschewed). I now use the words dilating drops will “relax your eyes” and that with dilated pupils you may be “slightly bothered by the light.”