What’s New and Important in Pediatric Ophthalmology and Strabismus for 2016
The Complete and Unabridged handout

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Presented by the
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1. AMBLYOPIA

**Newer methods of treatment**

**Binocular iPad treatment for amblyopia in preschool children.**

The authors attempted to determine whether a binocular treatment approach could be effective for home use by amblyopic preschool children ages 3 to <7. Spectacles had to have been worn for at least 3 months prior. Anisometropic amblyopes and small-angle strabismic amblyopes were included. 50 consecutive amblyopic children were enrolled. 5 were assigned to sham iPad, and 45 to the binocular iPad group (dichoptic treatment). The groups played on the iPad 4 hours per week for 4 weeks. Red-green anaglyphic glasses were used. Enrolling physicians were allowed to continue patching therapy as well which seems to confound results (2/3 did in fact also patch). Most patients also had previously patched. Mean visual acuity at enrollment was 0.43 logMAR and most patients (74%) had nil stereoacuity. In the binocular iPad group acuity improved to a mean of 0.34 logMAR and type of amblyopia and presence or absence of stereopsis did not affect the results. Stereoacuity did not improve. The sham group showed no improved acuity (0.40 to 0.38 logMAR). Only 62% of patients reported playing more than 50% of what was prescribed. Improvement of >=0.1 logMAR was seen in 71% of those with >=50% compliance versus 12% with <50% compliance. In the compliant group, results did not seem affected by whether the child patched or not. This study was not randomized, as it was an exploratory cohort. The sham group was very small although data from other sham patients is available from a prior study. Patching treatment introduces another variable. This approach to amblyopia treatment is in its infancy in the ophthalmic community and this paper may serve as a springboard for future studies.

**Binocular iPad Treatment of Amblyopia for Lasting Improvement of Visual Acuity** Simone L. Li, Reed M. Jost, Sarah E. Morale, Angie De La Cruz, et.al. JAMA Ophthalmol 2015;133(4):479-480.

The authors sought to determine the durability of visual acuity gains in a subgroup of children age 4-12, who were enrolled in a larger study of amblyopia treatment with home-based dichoptic games viewed on an iPad. Eligibility for this follow up study included children from that study who demonstrated at least a one line improvement in the amblyopic eye at the conclusion of treatment and no patching was reinstated. A comparison group was recruited of children who also completed the 4-12 weeks of treatment but who resumed patching. Best-corrected visual acuity was obtained at baseline, at end of iPad treatment, and 3months, 6 months and 12 months. Eight children were in the no patch group.
and 10 in the patching group. Both groups achieved improved vision after binocular iPad treatment. Using a post hoc analysis of variance, the authors did not find an effect of patching on maintenance of post treatment visual acuity gains. The authors conclude that best corrected visual acuity is maintained for at least 12 months after cessation of binocular iPad treatment for amblyopia.

Behavioral training as new treatment for adult amblyopia: a meta-analysis and systematic review


Recently, it has been shown that the adult brain is much more plastic than it was once thought to be. New behavioral treatment methods, including dichoptic training, perceptual learning, and video gaming, have been proposed to improve visual function (visual acuity, stereoacuity, and/or contrast sensitivity) in adult amblyopia. In dichoptic training, stimuli are presented dichoptically with the contrast of the image to the fellow eye attenuated in order to encourage binocular combination of the two inputs. Perceptual learning involves extensive training on a task with the fellow eye patched. Video gaming involves playing video games with the fellow eye patched. The authors conducted a meta-analysis of these methods to investigate the factors involved in amblyopia recovery and their clinical significance. Mean and individual participant data meta-analyses were performed on 24 studies using the new behavioral methods in adults. Studies were identified using PubMed, Google Scholar, and published reviews. The authors found that the new methods yielded a mean improvement in visual acuity of 0.17 logMAR with 32% participants achieving gains ≥ 0.2 logMAR, and a mean improvement in stereo sensitivity of 0.01 arcsec\(^{-1}\) with 42% of participants improving ≥2 octaves. The most significant predictor of treatment outcome was visual acuity at the onset of treatment. Participants with more severe amblyopia improved more on visual acuity and less on stereo sensitivity than those with milder amblyopia. Better initial stereo sensitivity was a predictor of greater gains in stereo sensitivity following treatment. Treatment type, amblyopia type, age, and training duration did not have any significant influence on visual and stereo acuity outcomes. Adults with amblyopia may benefit from behavioral training, however clinical trials are required to confirm these findings. Despite the diverse nature of the new behavioral methods, the lack of significant differences in visual and stereo sensitivity outcomes among them suggests that visual attention—a common element among the varied treatment methods—may play an important role in amblyopia recovery. This is a well done, thorough meta-analysis of the currently available literature on behavioral treatments for adult amblyopia and the authors offer suggestions to designing more complete clinical trials comparing the treatment methods.

Eight amblyopic children (ages 4-10) were treated for 2 weeks with dichoptic movie viewing. Three of the children had anisometropic amblyopia, 1 had strabismic amblyopia, and 4 had a combined-mechanism. Mean movie viewing time over the 2 weeks was 9.4 hours. Best-corrected amblyopic eye acuity improved from 0.72 logMAR to 0.52 logMAR (2-lines). Fellow eye acuity did not change significantly. All patients had nil stereoacuity. There was no separate control group. This study shows the efficacy of a potential new amblyopia treatment modality with results obtained through 9.4 hours of treatment over 2 weeks rather than hours of patching daily.

A Randomized Trial of Levodopa as Treatment for Residual Amblyopia in Older Children The Pediatric Eye Disease Investigator Group Ophthalmology May 2015; 122(5) pp.874-881

Many children treated with patching for amblyopia have an incomplete response. For this reason clinicians have looked for alternative options. Levodopa, used for Parkinson’s disease and dystonia, has been tried with variable success for amblyopia. A meta analysis of 4 studies showed efficacy. However, due to many study limitations they were inconclusive. This is a prospective, randomized, placebo-controlled multi-center trial from the Pediatric Eye Disease Investigator Group. 139 children (ages 7-12yrs) with residual amblyopia (VA 20/50-20/400) after patching were enrolled. Patients were assigned to 16 weeks of patching (2hrs daily) along with oral levodopa or placebo. Outcome VA, measured at 18 weeks, in the amblyopic eye improved 5.2 letters in the levodopa group and 3.8 letters in the placebo group. No serious adverse effects from levodopa were reported, however, the levodopa group reported a slightly higher incidence of headaches. For children 7-12 years of age with residual amblyopia after patching therapy, oral levodopa while continuing to patch 2 hours daily does not produce a clinically or statistically meaningful improvement in VA compared with placebo and patching.

What is Next in Amblyopia Treatment (Editorial) Creig Hoyt Ophthalmology May 2015; 122(5) pp. 871-873

Historical overview of amblyopia treatment. Brief discussion of two prior treatments that proved to have no benefit – pleoptics and CAM visual stimulator. Discussion of rationale behind levodopa. Levodopa found to have an important role in retinal function and central visual processing. Dopamine levels in the brain can be enhanced with oral levodopa. However, there is no dopamine deficiency in amblyopic brains. It has been suggested that levodopa treatment might enhance experience-dependant plasticity of the visual cortex, however animal studies have not been supportive of this. There is no convincing evidence
that alterations in the neural retina have any influence on amblyopia. Human studies have shown only small gains in vision, and have been inconclusive due to small sample sizes, short treatment duration, lack of controls, and regression of vision after treatment cessation. Discussion of current PEDIG study which showed no benefit of levodopa in residual amblyopia. Author states it is time to move on as levodopa has no benefit in the treatment of amblyopia. Future studies need to provide better understanding of neural mechanisms in amblyopia and thereby tailor future treatments accordingly.

**Using liquid crystal glasses to treat amblyopia in children.**


Liquid crystal glasses (LCG) were evaluated for their effectiveness in treating slightly older children with monocular amblyopia. 14 consecutive patients were enrolled. Mean age was 7.4 years. 10/14 (71%) had anisometropic amblyopia, 2/14 (14%) had strabismic amblyopia and the remaining 2/14 (14%) had mixed amblyopia. Mean follow-up was 4.0 months. The LCG glasses were used on average 8.2 hours/day. Baseline logMar acuity was 0.6 and it improved to 0.3, T which was statistically significant. No side effects were noted. The problem with this study was the lack of a refractive adaptation period so the improvement may have been secondary to correcting their refractive error rather than actual amblyopia improvement from the LCG glasses. Compliance was based on parental reports. Various new amblyopia treatment methods are entering the literature so pediatric eye care providers need to stay abreast of these novel early studies.

**Traditional Methods of Treatment**

**Time Course and Predictors of Amblyopia Improvement with 2 Hours of Daily Patching**


This study seeks to determine predictors for vision improvement and resolution of amblyopia, as well as the time course of vision improvement in a cohort of children age 3 to 8 who initially were treated just with glasses for 12 weeks, but still had moderate (20/50-20/80) or severe (20/100-20/400) amblyopia at the end of the run-in period. These children were then prescribed 2 hours of patching a day. There were 135 children in the moderate amblyopia group ad 61 in the severe amblyopia group. The median duration of patching until there was no further improvement in vision was 20 weeks. About half the moderate and half the severe amblyopes achieved their best-corrected vision by 12 weeks. Thirty three percent of the moderate amblyopes and 11% of the severe amblyopes achieved visual acuity of 20/25 in the amblyopic eye and was within one line of the nonamblyopic eye. Greater improvement in vision of the amblyopic eye was associated with worse baseline vision and younger age at enrollment, but not
with amblyopia cause. Better vision in the amblyopic eye at enrollment was the only predictor of achieving amblyopia resolution.


This was a randomized trial in 3- to 8-year old children with clinically stable residual amblyopia following prescribed initial treatment with at least 12 weeks of daily or weekend atropine. 73 patients with a mean age of 5.8 years were randomly assigned to continue weekend atropine alone or wearing a plano lens over the fellow eye in addition. Patients were enrolled from 20 sites. All patients completed the study. Atropine compliance and spectacle-wear compliance was excellent overall. Vision testers were masked. At the 10-week primary outcome visit, amblyopic-eye acuity improved 1.1 lines in the plano-lens group and 0.6 lines in the atropine-only group. >=2 lines of improvement was seen in 27% and 21% of patients respectively. For those patients who met criteria for continued treatment, best visual acuity improved 1.9 lines and 0.8 lines respectively. No patient ultimately had decreased vision in the fellow eye. Side effects included light sensitivity (n=7) and dry skin (n=1). Conclusions based on study results are limited based on small sample sizes. This randomized trial evaluates the benefit of attempting to augment atropine treatment of amblyopes by adding a Plano lens.

Ultrastructural Studies


This study aimed to determine whether abnormal macular thickness in myopic anisometropic amblyopia changed after amblyopia treatment. It also investigated whether changes in macular thickness were associated with subject age or improvement in stereoacuity. Seventeen children with a mean age of 9.0 ± 3.0 years (range, 5.7-13.9 years) were treated with 16-week refractive correction, followed by an additional 16-week refractive correction and patching. Mean baseline visual acuity (VA) in the amblyopic eye was 1.0 (Snellen: 20/200) ± 0.3 logMAR and improved to 0.7 (Snellen: 20/100) ± 0.3 after amblyopia treatment (p < 0.0001). This was significantly associated with average foveal thickness (p = 0.040). The average foveal thickness in the amblyopic eye was significantly reduced after amblyopia treatment (p=0.049); no treatment effect was seen in the fellow eyes (p=0.245). This study found that the central macula (fovea) was thicker in myopic anisometropic amblyopic eyes (and peripheral macula thinner)
than in fellow eyes. The foveal thickness in amblyopic eyes decreased following amblyopia treatment with no significant changes in peripheral macular thickness. Subject age was not correlated with the change of macular thickness in amblyopic eyes. Nine subjects had no stereoacuity improvement. Eight had stereoacuity improvement, and although they seemed to experience a larger change in intraocular difference of foveal thickness, this was not found to be statistically significant. This is the first longitudinal study to determine whether macular thickness can change with amblyopia treatment in amblyopic eyes associated with myopic anisometropia.


This meta-analysis included 28 clinical trials involving 408 patients. The primary outcome parameters were foveal minimum thickness (FMT), mean foveal thickness (MFT), mean macular thickness (MMT), and peripapillary retinal nerve fiber layer (pRNFL) thickness.

Results: The FMT, MFT, and MMT in the amblyopic eyes was significantly greater than that of the fellow eyes (SMD = 0.22, 95% CI 0.05-0.39, p = 0.011; SMD = 0.21, 95% CI 0.06-0.36, p = 0.005; SMD = 0.21, 95% CI 0.08-0.35, p = 0.002, respectively). Only FMT was significantly increased in the amblyopia group compared with the normal control group (SMD = 0.38, 95% CI 0.19-0.57, p<0.00001). Analysis showed that pRNFL thickness in the amblyopic eyes was thicker than in the fellow eyes (SMD = 0.13, 95% CI 0.02-0.24, p = 0.016).

Conclusion: A thicker foveola was found in the amblyopic eyes when compared with visually normal control eyes. This suggests that the amblyopic process may involve the macula.

Choroidal thickness of children’s eyes with anisometropic and strabismic amblyopia.

The authors compared choroidal thickness of eyes with amblyopia and with that of fellow eyes and with age-matched controls. This was a cross-sectional comparative study over a six-month period. 120 eyes of 120 subjects (40 anisometropic, 40 strabismic and 40 controls) were included. Subfoveal choroidal thickness measurements between the two investigators were significantly correlated. All measured locations were the same between the groups except for the subfoveal choroid when comparing control eyes and amblyopic and fellow eyes of patients in the anisometropic group. Subfoveal, N500 and N1000 (distance from fovea) showed a difference between control eyes and amblyopic and fellow eyes. There was no difference between the fellow and control eyes.
These differences may reflect changes in choroidal blood supply. The choroid may have a role in emmetropization and refractive error development so this concept requires further study.

**Choroidal And Peripapillary Retinal Nerve Fiber Layer Thickness In Adults With Anisometropic Amblyopia**


High-definition spectral-domain optical coherence tomography (SD-OCT) was used to evaluate choroidal thickness, macular thickness, and peripapillary retinal nerve fiber layer (RNFL) thickness in amblyopic eyes compared to fellow and normal control eyes in 54 adults with anisometropic amblyopia.

**Results**

Mean peripapillary RNFL thickness of the amblyopic, fellow, and control eyes was 107.5 ± 15.5 µm, 109.3 ± 12.7 µm, and 108.8 ± 8.6 µm, respectively (p = 0.343). The average CMT was 231.7 ± 14.7 µm in amblyopic eyes, 232.5 ± 15.7 µm in fellow eyes, and 230.8 ± 14.8 µm in control eyes (p = 0.599). Mean subfoveal choroidal thickness was significantly greater in the amblyopic eyes than in the fellow and control eyes (396.3 ± 104.3 µm, 361.0 ± 103.9 µm, 390.6 ± 91.7 µm). Mean axial measurement in amblyopic eyes was 22.7 ± 1.3 mm (20.5–26.1), in fellow eyes 23.1 ± 0.9 mm (20.9–25.0), and in control eyes 23.3 ± 0.9 mm.

**Conclusion :** In adults with anisometropic amblyopia, subfoveal, temporal, and nasal choroidal thickness of amblyopic eyes are significantly thicker than in fellow eyes. However, no significant differences in peripapillary RNFL thickness or CMT were found between amblyopic and fellow or control eyes.

**Retinal thickness in children with anisohypermetropic amblyopia**


In amblyopic eyes, microstructures of the photoreceptors of are abnormal. The foveal ellipsoidal zone (EZ), aka photoreceptor inner and outer segment (IS/OS) line, is absent more frequently in amblyopic eyes compared to normal eyes. In addition, subtle changes are seen in the outer nuclear layer (ONL). In this study the authors compared the amblyopic eye to the fellow normal eye and to aged-matched controls. In addition microstructural findings on OCT were compared before and after one year of treatment. Twenty-one patients (age 6.0±2.3 years) with anisohypermetropic amblyopia and 25 age-matched controls (5.6±1.9 years) were studied. Spectral-domain optical coherence tomography (SD-OCT) was used to obtain OCT images. The foveal thickness and the thickness of the outer nuclear layer (ONL), photoreceptor inner segment (IS) layer and outer segment
(OS) layer were measured using the embedded OCT software. The length of the OS was significantly greater in the fellow eyes (48.0±6.6 µm) than in the amblyopic eyes (42.4±4.6 µm, p=0.03). One year after the optical treatment of the anisohypermetropia, the best-corrected visual acuity (BCVA) improved and the length of the OS was significantly increased (p=0.0001) in the amblyopic eye. After optical treatment, the OS length was similar between the amblyopic eyes and the fellow eyes (p=0.95). The change of BCVA was significantly correlated with the change of the length of the OS 1 year after the treatment (r=0.52; p=0.0004).

Choroidal and peripapillary retinal nerve fiber layer thickness in adults with anisometropic amblyopia

Fifty-four adults with anisometropic amblyopia were included in this prospective study. Choroidal thickness, central macular thickness, and RNFL thickness were measured by using high-definition spectral-domain optical coherence tomography (SD-OCT). The choroidal thickness was measured at the fovea and at 500 µm intervals from the foveal center in both temporal and nasal directions. In adults with anisometropic amblyopia, choroidal thickness of the amblyopic eyes was significantly thicker than in fellow eyes in the area of the subfoveal, temporal, and nasal choroid. No significant difference in the peripapillary RNFL thickness or central macular thickness was found between amblyopic and fellow or control eyes.

Characteristics of Amblyopia

Prevalence of Amblyopia in School-Aged Children and Variations by Age, Gender, and Ethnicity in a Multi-Country Refractive Error Study
O Xiao, IG Morgan, LB Ellwein, M He, The Refractive Error Study in Children Study Group, Ophthalmology September 2015; 122(9) pp.1924-1931

The purpose of this study was to estimate the age, gender, and ethnicity specific prevalence of amblyopia in children age 5 to 15 yrs using data from the multi-country Refractive Error Study in Children (RESC). The RESC data were obtained from 2 sites in China (urban and semi urban), 2 sites in India (urban and rural), 1 site in Chile (urban), 1 site in Malaysia (urban), 1 site in Nepal (rural), and 1 site in South Africa (semi-urban). 39,551 children had a detailed ocular examination and visual acuity (VA) measurement in 1 or both eyes. Amblyopia was defined as BCVA ≤20/40 in at least 1 eye associated with strabismus, anisometropia of ≥2 D, or hyperopia ≥6 D. The overall prevalence of amblyopia
was 0.74% with significant variation across ethnic groups: 1.43% in Hispanic, 0.93% in Chinese, 0.62% in Indian, 0.52% in Malay, 0.35% in Nepali, and 0.28% in African children. Amblyopia was not associated with age or gender. The most common cause of amblyopia was anisometropia. Most cases were unilateral and developed before 5 years. The prevalence of amblyopia was considerably lower than previous studies. This is likely due to using a very narrow definition of amblyopia. Across all sites, there were 857 children with BCVA ≤20/40 in 1 or both eyes (without fundus or anterior segment abnormalities), but only 290 children met the explicit criteria that require “amblyopia risk factors” (ARFs) in the RESC definitions, leaving 567 children as “unexplained or undetermined cases” of low VA. Modification of the ARFs such as lowering the threshold for anisometropia to 1D, adding myopia ≥6 D, and adding astigmatism ≥1.50 D increased the prevalence of amblyopia significantly in the study population. Also, prevalence likely would have increased further if BCVA >20/40 had been measured and interocular difference (IOD) of ≥ 2 lines had been included in the definition. This indicates that the choice of ARFs for diagnostic purposes is critical and more work is required to develop internationally consistent definitions for amblyopia.


This study reports the incidence of ametropic amblyopia and visual acuity outcomes in a vision screening program in the United Kingdom. Medical records of all children aged 4-5 years referred for a routine vision screening over a 1-year period were retrospectively reviewed. The criteria for ametropic amblyopia are somewhat questionable (spherical equivalent >4.00 D of hyperopia or myopia, or >1.50 D of astigmatism, and acuity <0.200 logMAR after 6-weeks of spectacle wear. Ametropic amblyopia was found to have an incidence of 2.0%. 33 patients met inclusion criteria. Some patients underwent occlusion therapy. Mean visual acuity outcome excluded those requiring patching was 0.12 logMAR. Visual acuity of at least 0.20 logMAR was achieved in 17/33 at 30 weeks and 30/33 at 60 weeks. Final visual acuity was not correlated with age of initial refractive correction (but all patients started in a limited range). Overall acuity did improve, but in 50% of patients did not reach normal visual acuity levels by age 7. This study shows improvement can be expected but may not fully normalize. It also reinforces the need for early screening and detection.

An eye movement recording system was used to evaluate reading grade-appropriate paragraphs of text silently. Seventy-three children met comprehension and tracking criteria (29 amblyopes, 23 strabismus patients with no amblyopia and 21 normal controls. Nine children were excluded from evaluation for poor comprehension or poor tracking reliability. Amblyopic children read significantly more slowly than strabismic children and normals. Amblyopic children made significantly more forward saccades. Regressive saccades and mean fixation duration did not differ between the groups. Amblyopic eye acuity did not correlate with reading rate, or saccade number. Amblyopic type subgroups did not show any differences. This data is interesting and should be explored in a larger study. We may need to advise the schools of amblyopic children to allow extra reading time and reading help as a standard for children with an amblyopic eye.

The repeatability of the Sbisa bar for testing density of suppression

L. Crawford, H. Griffiths Br Ir Orthopt J 2015; 12:35-40

The aim of this study was to assess the repeatability of the Sbisa bar to measure density of suppression by the same and different observers. The author conducted a prospective repeated measures study performed on participants aged 5–16 years. Participants with constant suppression due to strabismus had the Sbisa bar test performed twice by one observer and once by a second observer with a period of 15 minutes between each test. Thirty participants were recruited with a mean age 7.3 years. Median filter value for the first, second and third tests were 15, 15 and 14, respectively. Interclass correlation coefficient was 0.70 for the same observer and 0.73 for different observers. Inter-rater repeatability coefficient, k, was 0.32. There was no correlation between the median filter value from the first observer’s tests with age (R = 0.08), visual acuity in the amblyopic eye (R = 0.01) or visual acuity difference (R = 0.01). The authors conclude that in patients with suppression > filter 10 the Sbisa bar is repeatable within one to three filters when assessed by the same or different observers. There is no correlation between density of suppression and visual acuity or age.

Comment: The basis for testing suppression in patients with amblyopia using a tool such as the Sbisa bar was to avoid the risk of developing intractable diplopia due to disruption of suppression through amblyopia treatment. In my personal experience (now 13 years following fellowship), I have never had a patient develop diplopia with amblyopia treatment so I am not sure if this is a theoretical risk or a real possibility. This study looks only at the reproducibility in measuring suppression but not applicability to practice.
Prehension of a flanked target in individuals with amblyopia

Reduced binocularity is a prominent feature of amblyopia and binocular cues are thought to be important for prehension (the act of grasping). Previous studies have shown deficits in prehension in both amblyopes and individuals with strabismus without amblyopia. However, no previous studies looked at prehension when the target-object was flanked (rather than isolated), which is more representative of what individuals would encounter in everyday life. The purpose of the study was to examine prehension in individuals with amblyopia when the target-object was flanked, mimicking everyday prehension. Twenty amblyopes and 20 visually-normal controls reached forward, grasped, and lifted a cylindrical target-object that was flanked with objects either side of the target, or in front and behind it in depth. Only 6 of the amblyopes had measureable stereoacuity. Trials were completed in binocular and monocular viewing, using the better eye in amblyopic participants. Compared with visual normal, amblyopes displayed a longer overall movement time, lower average reach velocity, smaller maximum aperture, longer duration between object contact and lift. Not surprisingly, differences between groups were more apparent when flankers were in front and behind rather than on either side, suggesting that amblyopic deficits are greatest when binocular cues are richest. Both amblyopes and controls demonstrated significant (and similar) binocular advantage. This suggests that there is considerable residual binocularity in amblyopes, or that they are able to make very good use of whatever binocularity they do have. This supports the idea that we should be aiming therapy at recovering binocularity in individuals with amblyopia.

2. VISION SCREENING

Outcomes of an Inner-City Vision Outreach Program

The authors identify a healthcare gap, more pronounced in children in low socioeconomic groups. Although vision screening has increased, there have not been declines in visual impairment. The study provides a snapshot of insurance status, visual care needs and demographics of 924 children (age 0-18 years) who attended a one day program in Philadelphia, Pennsylvania which combined vision screening and immediate vision care if required. Twenty seven percent were not insured and 35% of families did not realize their insurance provided vision coverage. Sixty one percent were given glasses, 10% required continuous eye care, most commonly for amblyopia, and 10 children required surgery for nasolacrimal duct obstruction, cataract, strabismus, ptosis, or nystagmus. A
social worker is instrumental in promoting follow up after such a screening, increasing show rates for follow up care from 2% to 59%. Barriers to eye care include language other than English, low socioeconomic status, no health insurance, and knowledge gap about what the family’s insurance covers. To overcome these barriers, a patient navigator, such as a social worker, is critical to close the gap between identifying vision disorders through screening and gaining access to the treatment of vision disorders in children.

**Efficient Referral Thresholds in Autorefraction- Based Preschool Screening** Lowry E, Campomanes A. AJO: 159 (6); June 2015; pg. 1180.

This retrospective study was an economic evaluation of screening protocol for vision in preschools using auto-refraction. Preschoolers from 2 cities underwent Retinomax screening and comprehensive exams if necessary. AAPOS criteria for amblyopia risk factors was used. Costs were obtained from a third party payer. In one city, 3974 children were screened, 631 referred, and 412 examined. 48% of referred children met criteria. In the other city, 2359 children were screened, 269 examined. The modeled referral criteria were applied to the second group, and cost per case was $258. The original referral cost was $424 and $371. So the modelled referral criteria had lower cost. Perhaps a more stringent referral criteria should be applied to screenings to help with costs.

**Normative data for three tests of visuocognitive function in primary school children: cross-sectional study** C Williams, ID Gilchrist, S Fraser, HM McCarthy, et al. Br J Ophthalmol June, 2015;99:752-756

This is work by Lea Hylvarinen. Her goal is to develop tests that can be easily performed in clinic to assess visuocognitive ability, which can be selectively impaired in children with neurogenetic disorder such as Down syndrome, cerebral palsy, or prematurity. In this study she described three tests of visuocognitive function: (1) postbox task assessing orientation recognition and adaptive movement, (2) rectangles task assessing object recognition and (3) contour task assessing spatial integration. She examined 214 normal children with normal visual acuity and stereovision who attended primary school. Children ranged in age from <5 to 11 years old. The majority of children were able to do the postbox task easily. The rectangles task was challenging for children younger than 6 years old. The contour task was also challenging for younger children but after age 8, 99% of the children were able to perform the task. Repeatability was tested in 19 children. Agreement between the graders was fair for the postbox, and fair to poor for the two rectangles tasks. The authors have revised the rectangles test since interobserver variability was high. In conclusion this study describes the normative data for children using three different tests. However, these tests will need further development and field
testing in normal children and in children with visuocognitive impairment.

**The usefulness of the Retinomax autorefractor for childhood screening validated against a Danish preterm cohort examined at the age of 4 years** H C Fledelius, R Bangsgaard, C Slidsborg and M laCour  
Eye 29: 742-747; March 2015;

This study conducted in Denmark, the authors report that the results of a nation-wide study of vision screening of pre-term infants using the retinomax autorefractor. In this study, children with a history of gestational age greater than 28 weeks were examined at 4 years corrected age using the retinomax instruments. 178 pre-term infants and 56 controls were included in this study. Measurements were taken before and after installation with cyclopentoll 1% and all recording were performed by senior pediatric ophthalmologists. The authors found that there is high testability of retinomax, however there are many false positive and false negative results. They also found that there is a wide and unsystematic variation in equipment induced myopia in children who are not cyclopleged. The authors advocate the use of multiple tests be considered when screening children at risk for refractive error.


This paper investigated whether vision screening rates in a community-based multispecialty group practice were altered by adopting use of a PlusOptix S08 vision screener. Reliability rates, referral rates and positive predictive values in 3-year olds were evaluated. This was a retrospective review. Children were aged 33-39 months. 593 children attended well-child visits pre-PlusOptix and 958 after the introduction of the PlusOptix. The later group was slightly older (0.14 months) and included more Asian children. Vision screening was performed in 59 children in period 1 (10%) and 766 in period 2 (80%). This increase was statistically significant. PlusOptix screening was attempted in 871 children and was successful in 766 (88%). 2.39 attempts were needed to achieve a reliable result on average. 74/766 were referred. 35/74 received a complete eye exam. 18/35 met criteria for an amblyopia-causing risk factor. Positive predictive value was 51% for amblyopia risk factors and 41% for potential amblyopia. Bias could have occurred because of the lack of blinding screening results. Photoscreening can have a positive impact on the rates of vision screening in younger children.

The authors evaluated the sensitivity and specificity of VisionForKids.org, a web-based vision screening test, when administered by an untrained layperson. This was a prospective, randomized study enrolling patients and accompanying siblings between the ages of 3 and 12, over a 4-month period. The test requires less than 10 minutes. 203 study participants were included. The false negative rate was 9.3%. Sensitivity was 8.7% and specificity was 89.4%. The correlation coefficient between the web-based testing and EVA testing by a trained ophthalmic professional was 0.89. The error rate for laypersons was 26.1% with the most frequent errors: patching the wrong eye, incorrectly measuring the distance from the computer to the chair, and confusion with calibration. Testing was performed under ideal circumstances with supervision of a trained eye care professional. Also this population had a higher prevalence of ocular pathology than the general pediatric population. This cost-effective vision screening test could be employed by laypersons, and increase pediatric access to vision screening.


The Jaeb Visual Acuity Screener (JVAS) is a computerized vision screening program that uses optotype testing and published age-referenced normal visual acuity thresholds. This is a pilot study of 3-7 year old children using this test. Testing was performed by an ophthalmic technician. Data from 175 subjects was analyzed. No subjects were excluded for being unable to perform testing. Median subject age was 6 years and mean elapsed screening time was 84 seconds. 37% of those screened failed a gold-standard ophthalmic examination. Sensitivity of JVAS was 88-91% depending on how many failure criteria were used in determination. Specificity was 73-86%. Positive predictive value was 66-79% and NPV was 92-93%. JVAS can be downloaded at no cost. This is an enriched cohort so the PPV and NPV are not representative of a general population. The JVAS is an acuity test and most of the failed gold-standard examinations were secondary to reduced visual acuity (as opposed to alignment issues). Therefore this would increase sensitivity and specificity results. This vision screener is easily implementable in the school or office setting and could be used to standardize screening practices.

This study evaluated the accuracy of the Spot and the Plusoptix S12 in detecting astigmatism meeting AAPOS referral criteria. Participants were from the Tohono O’odham reservation. 116/209 students screened (55%) with a mean age of 11.89 years had a refractive error that met referral criteria. 105/116 met the referral criteria for astigmatism. Only 1 student was identified with constant strabismus. Screening results were obtained in 97% with the Spot and 54% with the Plusoptix. The Spot had better specificity and PPV, the Plusoptix had better sensitivity and NPV. This group of children has a high rate of astigmatism compared to other groups which contributed to the Plusoptix screening success. This study group was much older on average than most study groups. No comment can be made on strabismus detection. The results cannot be applied to other study populations because of the very high astigmatism rates in this group. This study highlights the need to assess photoscreeners with specific groups as results may not be applicable generally.


The Spot screening and a pediatric ophthalmology exam were compared to determine the sensitivity and the specificity of the Spot screener in detecting amblyopia risk factors according to 2013 AAPOS guidelines. This was a prospective study of patients, ages 2-9 years of age over a 4-month period. Of the 219 children included, 98% were Hispanic with an average age of 60 months. The youngest group (31-48 months) was excluded from analysis because of a small sample size. The Spot referred 19.6% of children with a sensitivity of 92.6% and a specificity of 90.6%. PPV was 58.1% and NPV was 98.9%. No cases of astigmatism meeting referral criteria were missed by the Spot screening. The study results are based on a very homogeneous ethnic population and may not be applicable to all ethnicities.


This study evaluated the ability of the Spot Vision Screener to detect AAPOS guideline strabismus. This was a prospective study of patients aged 1-16 years over a 16-month period. Four hundred and forty-four children were included with an average age of 6 years. On ophthalmology exam 20.9% of patients were found to have strabismus. Sensitivity was 77.17%, specificity was 93.73%, PPV
was 76.34% and NPV was 94.0%. These numbers are skewed because the rate of strabismus in this population is higher than the general population. The Spot detected 55/67 esotropes, 13/21 exotropes and 3/3 hypertropes. It is estimated that 1 in 3 children referred by the Spot for strabismus in a general screening setting would be found to have strabismus-related amblyopia risk on examination. The device is not designed to detect smaller degrees of horizontal strabismus so monofixation syndrome would not be detected.


Most screening devices screen for risk factors for amblyopia, rather than amblyopia and strabismus directly. The Pediatric Vision Scanner uses retinal birefringence to analyze binocular scans to detect amblyopia and/or strabismus. This study looked at the specificity of this test in a pediatric primary care office. Consecutive well-child visits ages 2-6 years were enrolled (n=293). Of these, 102 completed a gold-standard eye examination at an average age of 3.6 years within an average of 100 days after the Vision Scanner. Only 1 child was found to have anisometropic amblyopia. Both the Pediatric Vision Scanner and a Suresight detected the anisometropic individual. The authors discuss sensitivity and specificity rates but this data has to be viewed with extreme caution since there was only one patient with a positive exam. Further studies are needed to make any meaningful comments on the use of this device, possibly in a pediatric population with greater levels of pathology.

**A Comparison on Pre-school Versus School-age Orthoptic Screening Programmes in the North-East of England**


The authors performed a retrospective chart review of visual outcomes of children who failed a vision screening. Vision screening was voluntary and was performed either at age 3.5 years (Group A or “pre-school” group) or at age 4-5 years (Group B or “school entry” group). Of the 4567 pre-school children solicited for screening, 2742 were screened and 168 (Group A) failed. Of the 6082 school age children solicited, 5842 were screened and 711 (Group A) failed. Visual acuity data were available for only 40 Group A patients and for 130 Group B patients. For Group A, initial mean visual acuity (VA) was 0.516 logMAR (Snellen equivalent 20/66) and mean final VA was 0.195 logMAR (20/31) with p<0.0001. For Group B, mean initial VA was 0.514 logMAR (20/65) and mean final VA was 0.209 logMAR (20/32) with p<0.0001. Mean treatment duration was 25.24 months and 9.01 months for Groups A and B, respectively. The authors conclude that children in group B (school age) achieved the same visual outcome as group
A (pre-school) in a shorter episode length and with a larger proportion of the target group screened.

Comment: The idea that screening at an older age could yield equivalent results in less time is interesting. However, in this paper, the statistical analysis presented only compared Group A initial visual acuity to Group A final visual acuity. Statistical analysis comparing Group A acuities to Group B acuities was not included in this paper; however the authors indicate that similar improvements in acuity were found in both groups. Although duration of treatment was reported, there was no statistical analysis comparing this property of each treatment group. Although a large number of children failed screening, only a small number could be included in this study.

**Primary vision screening: outcomes from referrals unrelated to visual acuity** K. Taylor, H. Whibley *Br Ir Orthopt J* 2015; 12: 26-8

The authors performed a chart review of children referred from Orthoptic School Screening Services academic year 2009 to 2010. Referrals were based on our local vision screening protocol. Children were eligible for inclusion if they passed the visual acuity assessment but had abnormal eye movements, strabismus, or any ocular pathology. Of the 7600 children screened, 94 (1%) were referred because of an abnormality other than reduced acuity. Of these, 77 attended an outpatient appointment and were included in the study. Fifty-six had strabismus. Twenty-two of 56 received treatment for strabismus and the remaining 34 were only observed or discharged. Ten of the 22 treated were given treatment to improve binocular vision and 12 were treated to improve cosmesis. The authors conclude that the use of cover testing in the primary screening setting is important in combination with vision screening.


The authors performed a retrospective analysis of children who underwent vision screening from 2005 and 2006. Screening included visual acuity, cover test, motility, and stereo-acuity. All children referred had their hospital case notes reviewed and data on final corrected visual acuity, refractive error and followup period collected. Of the 2468 children offered vision screening 2240 were tested (90.8% coverage), 309 (13.8%) children were referred, and 264 (85.4%) patients attended of whom 33 (12.5%) were false positive referrals. The vision screening program had a positive predictive value of 87.5%. Corrected visual acuity was 0.200 logMAR (20/32) or better in each eye in 89.1% of patients, 64.0% required only optimum refractive correction as their sole treatment and 10.2% required a
period of occlusion therapy. The authors conclude that orthoptic-based screening programs provide an efficient vision screening mechanism, achieving high coverage, and low re-test and false positive levels.
Comment: Vision screening tests used in this study were Crowded Kay’s Picture test and Keeler Crowded logMAR which are not as commonly used in the US.

Comparing Visual Acuity Measured by Lea Symbols and Patti Pics  
E. Singman, N. Matta, J. Tian, D. Silbert  

The authors of this prospective observational study of 52 subjects aged 3-88 years (mean 58 years) compared visual acuities test by two methods: Lea symbols and Patti Pics. Both were ETDRS-style charts. Visual acuities were found to be not significantly different when analyzed as a whole group, when grouped by age (children, adults) and when grouped by visual acuity (better than 20/30, 20/30-20/50, worse than 20/50). The authors conclude that Patti Pics have reliability similar to Lea symbols and continued use of Patti Pics is warranted.

3. **REFRACTIVE ERROR**

*Prevalence and Risk Factors*

Secular Trends of Reduced Visual Acuity From 1985 to 2010 and Disease Burden Projection for 2020 and 2030 Among Primary and Secondary School Students in China  
Hong-Peng Sun, Ang Li, Yong Xu, Chen-Wei Pan  

This study compiles cross sectional data obtained by National Health surveys conducted in China every 5 years since 1985 to look for secular trends in myopia prevalence. The authors used unaided visual acuity as a proxy for myopia which was measured in a cohort of children between age 7 and 18. The sample size numbered in the hundreds of thousands and there appears to be a significant increase in myopia over the last 3 decades in China. The design of the study does not allow for determining the etiologic factors for this trend. But the authors conjectured that population shifts to urban areas, more time spent in school, and less time spent outdoors may be contributing factors to the rising prevalence of myopia. The authors cite the utility of their epidemiologic methods to assess for disease burden and the utility of such methods to aid public health initiatives and government planning for allocation of resources to help meet the needs of patients with myopia.
**Prediction of Juvenile-Onset Myopia**

Findings from the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) study are presented. The authors looked at a number of risk factors for incident myopia, which they defined as -0.75D or greater, and developed a prediction model. Near work, having myopic parents, and time spent outdoors were not predictive in the model they studied. They conclude that future myopia can be predicted by determining the refractive error by a single cycloplegic refraction. Children in grade 1 with a cycloplegic refraction of 0.75D of hyperopia or less are at high risk for developing incident myopia.

**Risk Factors for Progressive Myopia in the Atropine Therapy for Myopia Study**
Loh K, Lu Q, Tan D, Chia A. AJO April 2015; vol 159 (5); pg 947.

This retrospective cohort study looked at variables associated with myopic progression even though patients were treated with atropine. The ATOM 1 study was a prospective, randomized double masked, placebo controlled trial of 400 children between 6-12 years of age with low to moderate myopia. Only the children from the atropine group were used for this study.

200 children were randomized to get 1% atropine in one randomized eye and methylcellulose in the other eye. Children were followed every 4 months over 2 years. 182 of the initial 200 were still in the study at 1 year. Children who progressed by more than .50 diopters, were considered progressors. 12% (22 eyes) progressed on atropine therapy with a mean myopic progression of -.92 diopters in the atropine eye compared to the -1.06 for the untreated eye. Non-progressors had a mean hyperopic shift of +.16 at 1 year compared to the untreated eye with -.73 diopters. Over 2 years, there was -1.25 diopters of increase in myopia in the progressor group vs -.15 in the non-progressor group. Patients qualifying as progressors tended to have higher myopia at baseline (-3.6 vs. -2.8 diopters), younger age (8.5 years vs. 9.3 years), and 2 myopic parents (73.8% vs. 48.1%). No significant differences were found for time spent outdoors or with various near activities.

Non-progressors had less myopia in the atropine treated eye but the progressors had similar progression. It was found, the lower the myopia at baseline and the older the child, the better they responded to atropine.

This study analyzed the relationship between age at menarche and myopia in Korean adult females. A total of 8398 women of at least 19 years of age, who participated in the Korean National Health and Nutrition Examination Survey from 2008 to 2012, underwent a refractive examination using an autorefractor. The association between age at menarche and the severity of myopia was evaluated using a four-level multinomial logistic regression analysis. The prevalence of myopia was 61.77% (95% confidence interval [CI], 60.46–63.08), including 40.02% with low, 15.46% with moderate, and 6.29% with high myopia. The mean age at menarche was 14.09 ± 0.03 years (with a range of 8-26 years). Age at menarche was inversely associated with the severity of myopia. In fully adjusted models, older age at menarche decreased the risk of moderate myopia (odds ratio [OR], 0.93; 95% CI, 0.86–0.99; P = 0.0261), and high myopia (OR, 0.85; 95% CI, 0.77–0.95; P = 0.0012). This is the first study to analyze the relationship between age at menarche and the severity of myopia after adjusting for various confounding factors of myopia. The effects of female sex hormones on ocular structures and growth spurts may mediate this relationship between age at menarche and myopia. Although this study is limited by its cross-sectional design and lack of causality assessment, it provides significant “food for thought” to further evaluate this association.


This is a meta-analysis of 33 population-based, cross-sectional studies from the European Eye Epidemiology Consortium. The purpose was to investigate whether myopia is becoming more common across Europe and explore whether increasing education levels, an important risk factor for myopia, might explain this trend. There was a significant cohort effect for increasing myopia prevalence across more recent birth decades. Age-standardized myopia prevalence increased from 17.8% for those born between 1910-1939 compared to 23% for birth year between 1940-1979. Education was significantly associated with myopia and prevalence was 25.4% for those completing primary levels, 29.1% for secondary levels, and 36.6% with completion of higher education. Higher education seems to be an additive rather than an explanatory factor.
Role of Educational Exposure in the Association Between Myopia and Birth Order
Guggenheim J, Williams C, for the UK Biobank Eye and Vision Consortium

This study seeks to determine if birth order is related to the development of myopia. The authors make 2 assumptions, based on the literature, that first born children are 10% more likely to develop myopia and high myopia. The second assumption is that the intensity of education is greatest for the first born and decreases with subsequent siblings. Study design is cross sectional of white participants in the UK Biobank (n=89120) from age 40-69 recruited in 2006-2010 with no other eye disorder other than myopia defined as -0.75 D or less and high myopia defined as -6.0D or less. Main outcome measures were odds ratios for myopia and high myopia by birth order, using logistic regression and adjusting for age and sex or age, sex, and highest educational qualification. In the model with no adjustment for education, birth order was associated with myopia and high myopia. The odds ratios for myopia and high myopia, comparing first born with second born subjects, respectively were 1.12 and 1.15. When educational attainment was accounted for in the model, the effect size of birth order on myopia was attenuated by about 25% and the dose response effect of birth order on myopia was abolished. The authors conclude that their study confirms other studies that first born adults are 10% more likely to be myopic or highly myopic and that less parental pressure on siblings resulting in less educational attainment may be partly responsible for the finding of reduced incidence of myopia in siblings.

Importance: This study, with almost 90,000 subjects, was able to detect increased odds of a first born to develop myopia or high myopia compared with siblings with a p value that was so small that the authors expressed it as a natural log to a negative power! Certainly, their findings are highly statistically significant! However, the average magnitude of that difference between siblings was about -0.25D of myopia, so the clinical significance is less apparent.


This study prospectively investigated the associations of near work, outdoor activity, and anthropometric risk factors with early-onset myopia in Singaporean preschool children. Parents of 572 children completed questionnaires on parental myopia, near work, outdoor activities when their child was 2 years old. Cycloplegic autorefraction and axial length were obtained in 3-year-old children. Height and weight were measured in the children at various time points from birth to 3 years of age. Thirty-five (6.1%) of the children studied had early-onset myopia. In multivariable regression models, compared to children whose parents
were not myopic, those with two myopic parents were more likely to have a more myopic spherical equivalent and longer axial length and more likely to have myopia. Neither near work nor outdoor activity was associated with myopia. Taller children were found to have longer axial lengths at each year of life, but this was not found to be associated with spherical equivalent. The lack of association with near work may be due to lower amount of near work reported among 2 years olds in this study compared to preschoolers in Hong Kong (though that study looked at 2- to 6-year-olds). Similarly, the protective effect of time spent outdoors had been seen in previous studies in children spending more than 14 hours per week outdoors, whereas in this study, children on average spent 9.8 hours per week outdoors, so they may not have reached the threshold amount required for an effect to be observed. Regardless, this study suggests that genetic factors may have a greater contribution to early (by 3 years of age) development of myopic refractive error compared to environmental factors, which had not been previously well-studied.


There is growing evidence from both human and animal studies of refractive error showing that ambient light exposure is an important environmental factor involved in the regulation of eye growth. Documented seasonal variations in eye growth and refractive error progression in childhood (with slower eye growth seen in summer months and faster rates of eye growth in winter months) support a potential role for ambient light exposure in the control of human eye growth. Although it has been postulated that the association between less myopia and more time outdoors is due to increased light exposure when outdoors, most studies examining the relationship between outdoor activity and myopia have used questionnaires to estimate outdoor activity. To date there have been no longitudinal studies examining the influence of objectively measured light exposure upon eye growth in humans. The authors examined the relationship between ambient light exposure and axial eye growth in childhood. A total of 101 children (41 myopes and 60 nonmyopes), 10 to 15 years of age participated in this prospective longitudinal observational study. Axial eye growth was determined from measurements of ocular optical biometry collected at four study visits over an 18-month period. Each child's mean daily light exposure was derived from two periods (each 14 days long) of objective light exposure measurements from a wrist-worn light sensor. Over the 18-month study period, a modest but statistically significant association between greater average daily light exposure and slower axial eye growth was observed (P = 0.047). Other significant predictors of axial eye growth in this population included children’s refractive error group (P < 0.001), sex (P < 0.01), and age (P < 0.001). Categorized according to their objectively measured average daily light exposure and adjusting for potential confounders (age, sex, baseline axial length, parental
myopia, nearwork, and physical activity), children experiencing low average daily light exposure exhibited significantly greater eye growth than children experiencing moderate, and high average daily light exposure levels (P = 0.01). In this population of children, greater daily light exposure was associated with less axial eye growth over an 18-month period. These findings support the role of light exposure in the documented association between time spent outdoors and childhood myopia. In conclusion, this study provides the first evidence of a modest but statistically significant relationship between objectively measured daily ambient light exposure and eye growth in children, consistent with more light exposure resulting in slower axial growth of the eye. These findings support the role of light exposure in the documented association between time spent outdoors and childhood myopia and support interventions aimed at increasing daily light exposure to slow childhood myopia progression.

**Higher-order aberrations and best-corrected visual acuity in Native American children with a high prevalence of astigmatism.**
Miller JM, Harvey EM and Schwiegerling J. J AAPOS 2015;19:352-357.

This study compared higher order aberrations (HOA) in children from a Native American population with a prevalence of high astigmatism to population norms. HOAs may limit final acuity with spectacles. Children were 5-9 years of age who participated in a longitudinal study of visual development. HOAs were measured with the Pediatric Wavefront Evaluator. Children with a pupil diameter <4mm were excluded. 218 children were included with a mean age of 6.6 years. Adult normative data was used. In the Native American children, HOAs were elevated compared to population norms. With-the-rule astigmatism is significantly related to higher order HOAs. Spherical aberration and higher with-the-rule astigmatism are associated with decreased best-corrected visual acuity. Observations were made without cycloplegia, which can cause inconsistency and adult normative data was used as opposed to pediatric normative data. This study is complex and extremely difficult to read, using terminology that is not widely used.

**Reducing the Progression of Myopia**


This was a 1-year study of the effect of daily atropine on the progression of myopia in low myopic children. Patients were enrolled over 10 months and the entry myopia was -0.50D to -2.00D. Patients were randomized to daily 1% atropine versus vehicle eyedrops. The 1-year study was completed by 132 patients. Mean myopia at outcome was -0.91 D in the treated group (initial was -1.23 D) and -2.00 D in the control group (initial was -1.15 D). Mean axial length
at one-year was 23.71mm (unchanged from initial) in the treated group and 24.05 in the control group (0.32mm growth). No side effects were reported. The study was not double-masked and long term efficacy or side effects cannot be determined. Confounding factors (parent myopia, outdoor time, near work time) were not evaluated. This treatment modality is promising and further studies are critical for this rapidly increasing world-health problem.

Five-Year Clinical Trial on Atropine for the Treatment of Myopia

2: Myopia Control with Atropine 0.01% Eyedrops

A Chia, Q Lu, D Tan

Ophthalmology February 2016; 123:391-399

This study, a randomized double-masked clinical trial, looks at the safety and efficacy of different concentrations of atropine eyedrops in controlling myopia progression over 5 years. A total of 400 children (aged 6-12 yrs) with myopia ≥ −2.0D were originally randomized to receive atropine 0.5%, 0.1%, or 0.01% once daily in both eyes in a 2:2:1 ratio.

Children received atropine for 24 months (phase 1), after which medication was stopped for 12 months (phase 2). Children who had myopia progression (≥−0.50 diopters [D] in at least 1 eye) during phase 2 were restarted on atropine 0.01% for a further 24 months (phase 3). Change in spherical equivalent and axial length over 5 years were measured. There was a dose-related response in phase 1 with a greater effect in higher doses, but an inverse dose-related increase in myopia during phase 2 (rebound during the washout), resulting in atropine 0.01% being most effective in reducing myopia progression (50% reduction) at 3 years. 24% of children originally in the atropine 0.01% group, 59% from the 0.1% group and 68% of children in the 0.5% group, progressed in phase 2 and were restarted on atropine 0.01%. Younger children and those with greater myopic progression in year 1 were more likely to require re-treatment. The lower myopia progression in the 0.01% group persisted during phase 3, with overall myopia progression and change in axial elongation at the end of 5 years being lowest in this group (−1.38±0.98 D; 0.75±0.48 mm) compared with the 0.1% (−1.83±1.16 D; 0.85±0.53 mm) and 0.5% (−1.98±1.10 D; 0.87±0.49 mm) groups. Atropine 0.01% also caused minimal pupil dilation (0.8 mm, compared with 2.25mm and 3.11 mm in the 0.1% and 0.5% groups respectively), minimal loss of accommodation (2–3 D, compared with 10.1D and 11.8D in the 0.1% and 0.5% groups respectively), and no loss of near visual acuity compared with higher doses. Over 5 years, atropine 0.01% eyedrops were more effective in slowing myopia progression with less visual side effects compared with higher doses of atropine. The percentages of high myopia (≥6.0D) were 44%, 49%, and 50% and the percentages of very high myopia (≥8D) were 7%, 9%, and 17% in the atropine 0.01%, 0.1%, and 0.5% groups respectively. The study shows that atropine eyedrops, especially 0.01%, are promising for the treatment of myopia progression in children. However, the study has several limitations. There is no control group and the population was comprised entirely of east Asian children.
Additional studies are needed with these factors taken into consideration along with longer follow up. The mechanism of action of atropine in slowing myopia progression remains unknown and is not simply due to inhibition of accommodation.

**Myopia Control during Orthokeratology Lens Wear in Children Using a Novel Study Design**

H Swarbrick, A Alharbi, K Watt, E Linn et al
Ophthalmology March 2015;122(3)pp.620-630

This was a prospective, randomized study of 26 myopic children (ages 10.8-17 yrs) of East Asian ethnicity conducted over a 1 year period without any long term follow-up. Subjects were fitted with a rigid contact lens with special design for overnight wear (OK lens) for 6 months. The fellow eye was fitted with a conventional rigid gas permeable lens (GP lens) for daytime wear. After 6 months the eyes were reversed and the process repeated. After 6 months of lens wear the GP eye axial length increased by a mean of .04mm and the OK lens eye showed no change in axial length. The subsequent 6 month period showed a similar pattern. When translating this to refractive error: the OK eyes showed a regression of myopia of about 0.25 D and the GP eyes showed a progression of myopia of about 0.25D from baseline. This study is very poorly designed and provides no evidence regarding the usefulness of orthokeratology for halting the progression of myopia. The logic for switching eyes after 6 months eluded me. The sample size is too small, the study duration very short and there is no long term follow-up. The authors claim it is randomized, but actually isn’t as there is no control group and the study is not blind. There is no discussion of complications from overnight lens wear- either potential or in this study. Corneal topography showed flattening of the cornea in the OK eyes and was a significant factor in axial length differences.

**Miscellaneous**

**Population Prevalence of Need for Spectacles and Spectacle Ownership Among Urban Migrant Children in Eastern China**

Half of the 13 million children worldwide who have impaired vision due to lack of spectacles live in China. A particularly vulnerable population includes migrants to urban areas. To address this huge public health problem, this study determined the population prevalence of a cross section of children in 5th grade who owned spectacles and those who needed them. This study identified children who failed a vision test (≤ 6/12) during a 2-week period in 94 randomly selected primary
schools in migrant communities. Twenty five percent of migrant children needed spectacles but only 15% owned them. This rate of ownership is significantly lower than conventional Chinese urban schools (66%) with populations which have better access to health care.

**Importance:** Healthcare disparities exist in China based on socioeconomic factors such as being a migrant to an urban area.

**Choroidal Thickness Profiles in Myopic EYEs of Young Adults in the Correction of Myopia Evaluation Trial Cohort**

Harb E, Hyman L, Gwiazda J, et al. AJO; 160(1); July 2015; pg. 62.

This cross sectional multicenter study examined the relationship of choroidal thickness with axial length and myopia in young adults in the group Correction of Myopia Evaluation Trial (COMET) cohort.

346 young myopic adults aged 20-27.5 years at their final visit 14 years after baseline. As part of the COMET study, refractive error, axial length were measured. OCT images were performed starting in the 11th study year. At the final visit, 6 mm line scan was taken of the fovea in each eye. Patients had a mean myopia of -5.3 diopters and mean AL of 25.5 mm.

Overall choroidal thickness was at the fovea, and thinnest nasally. There was a nasal-temporal asymmetry in the COMET cohort. This asymmetry is more pronounced in myopic eyes and may suggest that the nasal choroid is more vulnerable to further thinning and degeneration with increased AL. There was significantly thinner choroids in eyes with more myopia, crescents and longer AL. Thickness did vary by ethnicity but only in the furthest nasal locations, with Asians having the thinnest and African Americans the thickest. Suggestion was made that this finding may be why Asians have a higher prevalence of pathological myopia.

4. **VISION IMPAIRMENT**


This study assessed the performance of visually impaired students in braille reading accuracy and examined potential correlations among error categories on the basis of gender, age at vision loss, and level of education. Twenty-one visually impaired Greek children ranging from the 4th through the 12th grade completed a subset of a standardized test that evaluates reading accuracy in
Greek. Eleven participants were congenitally visually impaired; the remainder had acquired visual disability. In total, female participants, students who were adventitiously rather than congenitally blind and elementary rather than secondary school students made more errors in all test subscales. Prevalent patterns in error type (“repetition” vs “replacement” vs “subtraction” type errors) were also noted. The authors conclude that analyzing braille reading errors systematically might reveal error patterns that teachers could use to differentiate their instruction.


Previous studies have described the communication of persons with deafblindness, including comprehension, gesture development, communication actions and purposes, and verbal skills. This study also used the Communication Matrix, a nonstandardized assessment for identifying prelinguistic actions and intentionality, and described communication repair skills that enable a person to take corrective actions when a communication partner misunderstands the person’s initial message. They studied 7 subjects and found that all had sign language skills, 5 had speech, 6 had communication repair abilities, and Communication Matrix scores were at level V – VI, concrete to abstract symbols (range: 1 for preintentional behavior to VII for language). The youngest participants had the fewest signs, and children with CHARGE syndrome used the most sign language. Interestingly, in this study sign language and speech were not related: children who used more or less sign language were not the same children who used more or less speech. Although the number of participants was small, this study confirms diverse prelinguistic and early communication abilities among children with congenital deafblindness, and demonstrates communication repair strategies that are similar to individuals with severe disabilities who are not deafblind. Communication repair skills may also be related to independent ambulation.


Compared to peers without visual impairments, school-aged children with visual impairments report less physical activity and are therefore at greater risk for developing health-related conditions. Pedometers have been shown to objectively and cost-effectively measure physical activity. The purpose of this study was to determine the validity of a commercially available talking pedometer for adolescents with visual impairments in free-living (non-clinical) conditions. Seven adolescents recruited from a Midwestern school for blind students
simultaneously wore the Centrios talking pedometer and the Digiwalker SW200 criterion pedometer over two 210-minute sessions. Twelve data points were obtained as 2 participants wore the pedometers for only one session. Analysis of step counts from the 2 pedometers indicated that the Centrios overestimated step counts in all sessions by an average of 6.1%. Pearson bivariate correlation on actual step counts determined that the pedometers were highly correlated. Although the number of data points in this study was small, the results were highly correlated and indicate that the talking pedometer may be a useful tool for tracking physical activity patterns in adolescents with visual impairments.

Executive Function and Behavioral Problems in Students with Visual Impairments at Mainstream and Special Schools V Heyl, M Hintermair. Journal of Visual Impairment & Blindness, July-Aug 2015: 251. Noting the often atypical development of children with visual impairments, this study sought to investigate whether differences in executive function exist between visually impaired students and a normative sample of sighted children, and whether executive function differs between visually impaired students at mainstream schools and those at specialty schools. The study also explored whether relationships exist between executive function, communicative competencies, and behavioral problems. Questionnaires were sent to teachers of visually impaired students at mainstream and specialty schools in several German states. 226 total surveys were completed and returned. There were highly significant differences in all domains of executive function, with the visually impaired students performing more poorly. There were also considerable within-group differences, with visually impaired students at mainstream schools showing better executive function than those at specialty schools. The within-group differences disappeared when students with additional disabilities were excluded from the analysis, possibly because they are overrepresented at specialty schools. The visually impaired students with lower executive function had more behavioral problems and showed fewer communicative competencies. A major limitation of this study is that the information regarding executive function came from the teachers, not from the children themselves. Also, the degree of visual impairment was not precisely reported, nor was detail regarding additional disabilities. Finally, some behaviors exhibited by visually impaired children might be due to their lack of vision and might not necessarily be indicators of executive or behavioral problems. Nevertheless, this study highlights that a wide range of executive function domains that are significant for socioemotional development are not sufficiently developed in many visually impaired students, and may guide educational focus.

This study reviews the epidemiological characteristics of children referred to a major low vision center in Brazil. Medical records of children aged 0-7 over a five-year period were reviewed retrospectively. 229 patients were included with a mean age of 39.4 months. The most prevalent disorders were congenital cataract (14%), toxoplasmosis (14%), and congenital cataract (13%). 142 (64%) had preventable causes including illnesses (36%), congenital toxoplasmosis (14%), and ROP (11%). It is important to know the most common causes of childhood visual impairment in various countries so resources can be best allocated.


Israel is one of three countries in the world that maintains a nationwide blindness registry. Incidence and causes of childhood blindness in Israel from 1999 to 2013 were described. From 1999 to 2013, newly registered blindness in children declined by 60% with an average annual decline of 5.6%. The leading causes of childhood blindness were optic atrophy and retinitis pigmentosa. Annual incidence of optic atrophy, RP, ROP and albinism all declined. CVI was added as a diagnosis in 2009. There was in increase in cases of CVI, but this may have been due to misclassification as optic atrophy previously (this would also explain the decline in optic atrophy cases once CVI was added as a diagnosis). Consanguineous marriages are on the decline, which may affect incidence rates. Underreporting may have occurred since registration is not legally required in Israel.


Many students with adventitious or progressive vision loss need to transition from print to braille as a primary literacy medium. In this study, constant time delay was used to teach literary braille contractions (2 students) and Nemeth Code for Mathematics and Science Notation (1 student) to 3 adolescent learners who were making the transition from print to braille. The two students each learned 40 short-form literary braille contractions, and the other student learned 28 Nemeth Code symbols throughout the study, and students maintained learning throughout the study at high levels. The authors emphasize the usefulness and
efficiency of the constant time delay method in braille education, and postulate that the efficiency itself may increase students' confidence and motivation to learn braille.

Although the number of subjects was small, this study expanded earlier work that showed that constant time delay was effective and efficient to teach automatic word recognition to young braille learners. This study demonstrated that constant time delay could also be useful to teach unknown contractions to older students making the transition from print to braille who needed to learn the code quickly to access written materials in other subject areas. The students in this study already knew at least one quarter of the braille code, and it is not known how students with little or no braille skills would respond.

Use of an Accessible iPad App and Supplemental Graphics to Build Mathematics Skills: Feasibility Study Results


Mathematics is often especially difficult for students with visual impairments, and algebra in particular has been identified as a critical course. This study evaluated the feasibility of using an iPad application (AnimalWatch Vi Suite) for algebra-readiness mathematics, with accompanying braille materials and accessible graphics. 29 students with visual impairments in grades 4 – 11 used the materials under the direction of their teachers of students with visual impairments. Students completed 984 word problems and solved 80% correctly within 3 attempts. Students and teachers provided feedback about the feasibility of using the app with the supplemental materials and made suggestions for improvements. The project was successful: teachers were able to introduce the app and materials to their students, and students quickly learned to navigate the app using a brief training unit and were then able to solve many of the word problems successfully. The students in this study were already familiar with iDevices and the teachers had participated in a professional development program, so the results might be different for users unfamiliar with an iPad.

A Comparison of Handwriting Abilities of Secondary Students with Visual Impairments and Those of Sighted Students


This study sought to determine if there is a significant difference in the handwriting performance of people with visual impairments compared to that of sighted individuals, and if there is evidence supporting the use of a test of visual-motor integration as an indicator of handwriting performance in individuals with visual impairments. 21 subjects with vision worse than 20/60, age 12 – 18 years, who used handwriting as the main mode of completing school work, were age- and gender-matched with a sighted control group. Participants completed the DASH assessment (Detailed Assessment of Speed of Handwriting), as well as the Beery VMI to assess visual-motor integration. Results showed that the
students with visual impairment completed fewer legible words per minute and had more large-scale drawings and writing, a larger diversity in writing size, an inability to write within the constraints of lines, and irregularity maintaining spacing between letters and words. The study also determined that people with visual impairments had lower visual-motor integration abilities than sighted people. However, no correlation was found between performance on the Beery VMI and DASH, indicating that lower visual-motor integration abilities do not necessarily result in a corresponding difficulty in handwriting performance.

This study was limited by small sample size. Also, outcomes may be affected by the increase in the use of technology in society and in schools, reflecting a decrease in handwriting use and abilities. Nevertheless, the results can inform parents and teachers to determine if a student with visual impairments who is struggling may require accommodations such as an increased time allowance when completing handwriting tasks.


Although digital-based learning is increasingly being used, students with visual impairments face greater challenges in accessing digital learning, especially in the field of mathematics. These authors sought to understand the experiences and perceptions of 5 visually impaired high school students who were accessing algebra via a digital textbook. For all but one student, there was a clear preference for using a traditional textbook rather than the digital textbook. Although the students acknowledged benefits of the digital textbook, they expressed the need to look at or touch things such as numbers or graphics within a physical textbook. The authors conclude that educators should proceed with caution when implementing digital textbooks since student preference, including willingness to use digital textbooks, is an important aspect of assistive technology considerations for students with visual impairments.

5. NEURO-OPHTHALMOLOGY

Idiopathic Intracranial Hypertension

The Idiopathic Intracranial Hypertension Treatment Trial (IIHTT) was a multicenter, randomized, double-blind, placebo-controlled trial of patients ages 18-60 designed to determine if weight reduction and a low sodium diet plus acetazolamide was more effective than the same diet plus a placebo in reducing vision loss from IIH. The study demonstrated that participants treated with acetazolamide rather than placebo (both plus diet) had significantly improved visual field function, papilledema grade, quality of life measures, and ICP. This paper is a sub study within the IIHTT designed to look at whether worsening visual fields (SITA 24-2) correlated with worsening visual function as opposed to performance failure (inattentiveness to the task of performing a visual field). Performance failure was defined as visual field loss that was transient (visual field returned to baseline by the next interval examination) and associated with stability in all other parameters of visual function. 2950 visual fields of 165 participants were reviewed. True treatment failure was documented in 7/165 (4%) whereas performance failure occurred in 21% of participants. 87% of those with performance failure had fields with false negative/ false positive and fixation losses within the range typically thought to indicate “good” performance. Take-home message: If visual field decline does not seem in keeping with other clinical data, repeat the test, as it is 5 x more likely to represent performance failure than actual decline in visual function.

**Overdiagnosis of Idiopathic Intracranial Hypertension**

Idiopathic intracranial hypertension (IIH) is mistakenly diagnosed in many patients who are referred to neuro-ophthalmology clinics. Most frequently these are obese young women with headaches. In this retrospective chart review, the authors examine records to determine at what point patients were misdiagnosed with IIH using the Diagnosis Error Evaluation in Research tool. Approximately 40% of all patients referred to their practice carrying the diagnosis of IIH were misdiagnosed. As a result 34% underwent unnecessary testing, and 31% underwent unnecessary invasive procedures. The authors found that misdiagnosis occurred most frequently as a result of inadequately or misinterpreting the optic nerve examination, followed by failure to order the appropriate test or misinterpretation of the performed test. Physicians including ophthalmologists, neurologists, and optometrists may misinterpret physical findings due to subconscious biases pushing care providers into cognitive errors, leading to misdiagnosis. Additionally, lack of training in evaluating the optic disk leads to inability to properly diagnose papilledema for non-ophthalmic providers. Knowledge of biases and how misdiagnoses are made, improving clinical skills, and early referrals may be the best way to avoid costly diagnostic tests, invasive procedures, and overdiagnosis of IIH.

This study sought to determine whether the bedside assessment of the optic nerve sheath diameter could identify elevated intracranial pressure in individuals with suspected idiopathic intracranial hypertension. This was a single-center, prospective, rater-blinded study performed in a freestanding pediatric teaching hospital. Patients aged 12 to 18 years scheduled for an elective lumbar puncture with the suspicion of idiopathic intracranial hypertension were eligible to participate. Optic nerve sheath diameter was measured via ultrasonography before performing a sedated lumbar puncture for measuring cerebrospinal fluid opening pressure. Abnormal measurements were predefined as optic nerve sheath diameter ≥4.5 mm and a cerebrospinal fluid opening pressure greater than 20 cmH2O. Thirteen patients participated in the study, 10 of whom had elevated intracranial pressure. Optic nerve sheath diameter was able to predict or rule out elevated intracranial pressure in all patients. The authors concluded that noninvasive assessment of the optic nerve sheath diameter could help to identify patients with elevated intracranial pressure when idiopathic intracranial hypertension is suspected.


Neuroimaging features associated with longstanding IIH include: empty sella, flattening of the posterior globes, optic nerve head protrusion, distention of optic nerve sheaths, tortuosity of the optic nerve, cerebellar tonsillar herniation, meningocele, CSF leak, and transverse venous sinus stenosis. The presence of these findings is not required for diagnosis of IIH. Incidental discovery on brain imaging should not prompt invasive procedures, unless other signs of IIH, such as papilledema are present. The role of transverse venous sinus stenosis should not be overlooked in this population.


This is an analysis of data created as part of the Idiopathic Intracranial Hypertension Treatment Trial (IIHTT), a randomized placebo-controlled trial of acetazolamide for IIH in patients with mild vision loss. This analysis looked at risk factors for treatment failure as defined by the study. Of the 165 patients enrolled in the study, seven of the 151 with sufficient follow-up experienced
treatment failure. Treatment failure was defined as a 3dB reduction in perimetric mean deviation from baseline. Grade III to V papilledema, male sex, number of transient visual obscurations per months, and lower visual acuity in the study eye were all associated with treatment failure. These characteristics may help to identify patients with IIH and mild vision loss who are at high risk for further vision loss.


This is a cross-sectional evaluation of quality of life (QOL) patients enrolling at the onset of the idiopathic intracranial hypertension treatment trial (IIHTT) who had mild vision loss. Both vision specific and overall QOL were evaluated. 165 patients who met the inclusion criteria for the IIHTT were included. The most common symptoms were headache (84%) and transient visual obscurations (68%). Headache burden was associated with worse vision related QOL. Worse visual field perimetric mean deviation was associated with worse vision related QOL. Both vision related and health related QOL scores were worse than those reported for disease free controls. This study will lead to further evaluation of how treatment affects QOL in IIH. While not addressing a pediatric population, this study may lead to further evaluation of pediatric quality of life in IIH.


This study evaluated CSF protein levels in prepubertal (n=23) and pubertal children (n=16) with IIH as well as in healthy children (n=12). Medical records from a 10-year period were reviewed retrospectively. Headaches on presentation were reported in 94% of pubertal children but only 48% of prepubertal children (50% of controls also reported headaches). Opening pressures were 32.4 cm H2O for prepubertal IIH patients, 38.8 cm H2O for pubertal IIH patients and 23.7 cm H2O for controls. CSF protein levels were significantly lower in prepubertal IIH patients (17.3 mg/dL) versus pubertal IIH patients (23.4 mg/dL) and healthy controls (23.5 mg/dL). 9 of 23 prepubertal IIH patients had abnormally low CSF protein levels compared to zero patients in the other two groups. There was no difference in CSF glucose. Acetazolamide increased CSF protein levels in 14/14 patients who underwent repeat lumbar puncture. CSF protein levels are inversely proportional to CSF outflow and the authors feel prepubertal IIH is a result of CSF overproduction in contradistinction to low flow/obstructive states in pubertal IIH patients. This is an interesting studies which sheds light on some of the differences between prepubertal and pubertal IIH patients.

This study evaluated accuracy of those proposed markers of increased intracranial hypertension, including increased nerve tortuosity, flattening in posterior aspect of globe, intraocular protrusion of the optic nerve, and enlarged optic nerve sheath on magnetic resonance imaging in children with increased intracranial hypertension. Eleven patients between 3 and 15 years of age with intracranial hypertension were selected for re-evaluation of magnetic resonance imaging that had been previously described as normal to determine the presence of: (1) increased tortuosity and elongation of the optic nerve; (2) enlargement of the optic nerve sheath on axial and coronal T2 so called by us “target sign” and postcontrast T1 sequences; (3) flattening in posterior aspect of the globe; and (4) intraocular protrusion of the optic nerve head. Of the 11 patients, tortuosity of the optic nerve (10/11, 90.9%) and enlarged optic nerve sheath—target sign (7/11, 63.6%)—were the most common findings. Flattening in the posterior aspect of globe (5/11, 45.5%) and intraocular protrusion (3/11, 27.3%) were also detected as a novel magnetic resonance imaging findings. The authors concluded that magnetic resonance imaging findings of the optic nerve and sheath include valuable signs of intracranial hypertension not only in adults but also in children. This is the first detailed analysis of the magnetic resonance imaging findings in children with increased intracranial hypertension.

**Asymmetric Papilledema in Idiopathic Intracranial Hypertension**

Significant asymmetry in the degree of papilledema seen in a small number of patients with IIH (and other disorders associated with elevated intracranial pressure) is poorly understood. A retrospective review of 559 adult patients with IIH identified 20 with significant asymmetry in papilledema. Investigators found that patients with asymmetry were, on average, slightly older (39 versus 30 years at presentation) and were more likely to be headache free (27% versus 3%). Visual fields were worse for the eye with greater papilledema. The most notable finding was the association smaller optic canals on the side with less papilledema. This finding was present in all (8) patients in whom imaging was sufficient for reliable measurements. This finding supports the notion that optic canal architecture plays a significant role (perhaps by controlling transmission of CSF) and that a smaller optic canal may, in fact, modulate the impact of elevated ICP. It is unclear whether the anatomical differences in canal size are congenital or acquired.
Papilledema


The authors evaluated the prevalence of true papilledema versus pseudopapilledema among patients referred. This was a prospective, cross-sectional, descriptive analysis of consecutive patients <18 years old referred for a concern of possible papilledema over a 22-month period. 34 patients with a mean age of 9.9 years were referred. 26/34 were referred by Optometrists. Six patients had healthy normal optic nerves. Twenty patients had pseudopapilledema (19 drusen, 1 anomalous disk). Two patients had papilledema (one of which also had optic disk drusen). Three patients never had a definitive diagnosis of pseudo- versus true papilledema. One patient had bilateral optic neuritis, one had a retinal dystrophy and one had a vascular anomaly. Of the 10 asymptomatic patients, none had papilledema. Headaches were a nonspecific complaint, but headaches with features associated with elevated ICP were rarely seen in patients without papilledema. This study is limited by the lack of a gold standard to diagnose optic disk drusen and the small number of patients with papilledema. This study helps with some general guidelines, but a larger study would be needed to make firm recommendations.


As OCT NFL measurements are not typically reliable for detection of optic atrophy in the presence of papilledema, the authors studied SD-OCT macula parameters as an alternative method for monitoring optic atrophy in this population. 43 of 94 patients with IIH met the following inclusion criteria for this retrospective study: papilledema Frisen grade ≤2; absence of other ophthalmic pathology that might alter SD-OCT such as glaucoma, drusen, myopia or hyperopia >5 diopters or astigmatism>3 diopters; and available SD-OCT. Automated SD-OCT segmentation was performed on patients with non-atrophic and atrophic papilledema and controls. Patients with non-atrophic papilledema were defined as those with best corrected acuity ≥20/40, no visual field abnormality beyond enlarged blind spot and a mean deviation of <-3.0 and no visible optic atrophy on examination. Patients with atrophic papilledema had significantly thinner RNFL both for inner and outer macula ring than controls and 2/3 had retinal structural changes. Perhaps more important was the finding that total macula and inner macula thickness was significantly less in non-atrophic papilledema than for controls. SD-OCT revealed thinning of the fovea, inner macula ring and outer macula ring of the outer plexiform and nuclear layers in these patients who did not demonstrate clinical signs of optic atrophy.
**Perimetry**

**Study of Optimal Perimetric Testing in Children (OPTIC) – Normative Visual Field Values in Children**  
D Patel, P Cumberland, B Walters, I Russel-Eggitt et al  
Ophthalmology August 2015; 122(8) pp.1711-1717

This study provides normative data on visual field values in children. It is a prospective, observational study. 154 children (ages 5-15 yrs) with normal ophthalmic exams underwent perimetric assessments in a randomized order using Goldmann and Octopus kinetic perimetry, and Humphrey static perimetry using standardized clinical protocols. Visual field size and sensitivity increase with age in patterns that are specific to the perimetric approach used. These developmental changes should be accounted for when interpreting perimetric test results in children, particularly when monitoring change over time. For example, when monitoring progressive VF loss longitudinally in young children, a failure to demonstrate larger/more sensitive VFs over a number of years may indicate loss of VF function or arrested development, rather than stability. Further studies are needed to assess the utility of perimetry in children with glaucoma and neuro-ophthalmic disease.

**Perimetry in Young and Neurologically Impaired Children**  
The Behavioral Visual Field (BEFIE) Screening Test Revisited  

Visual field determination is difficult to obtain in young or neurologically impaired children because of poor cooperation or impaired understanding of the test. The authors studied the utility of the Behavioral Visual Field Screening Test( BEFIE) in young and neurologically impaired children. The device is a modified arc perimeter which allows kinetic determination of the visual field in about 5 minutes. The authors emphasize the utility of this test as a way of preventing diagnostic delays in diseases of the optic pathways. The test had high positive predictive value and specificity in children who were able to perform both BEFIE and standard conventional perimetry examinations. However, informational bias may degrade the validity of the study since the pediatric neuroophthalmologist who performed all BEFIE tests was aware of the child’s clinical background and suspected pathology.
**Optic Nerve Imaging**

**Peripapillary Retinal Nerve Fiber Layer Thickness Correlates to Drusen Location and Extent of Visual Field Defects in Superficial and Buried Optic Disc Drusen**


This retrospective study compares peripapillary RNFL thickness to extent and location of visual field defects in patients with superficial and buried optic nerve head drusen. The cohort studied was 18 years and older. Of 149 eyes, 109 had superficial optic disc drusen and 40 had buried drusen. Peripapillary RNFL thinning was seen in 83.6% of eyes, where optical coherence tomography was performed (n = 61). Eyes with superficial ODD had greater mean peripapillary RNFL thinning (P = 0.0001) and visual field defects (P = 0.002) than eyes with buried drusen. Visual field abnormalities were most typically arcuate and more typically nasal in location. The authors postulate that buried drusen might represent an earlier stage in drusen evolution. They suggest that the actual migration from buried, to superficial, may itself cause NFL damage. This paper confirms the RNFL thinning previously reported in some patients with drusen yet is distinct from the *many* other studies which associate optic nerve head drusen with *increased* RNFL thickness and a cause of pseudopapilledema. Perhaps characteristics like location of drusen, and diameter of the optic nerve head may have an impact on RNFL thickness. Age or conditions like chronic papilledema may play a role as well. In a recent study (Gospe SM, et al. Br J Ophthalmol 2015; 0:1–5.) on pediatric patients with IIH and papilledema, nearly 50% of patients with true papilledema (that resolved with treatment) had buried ONHD as well resulting in elevation in RNFL thickness. They postulated that chronic stasis of axoplasmic flow might itself result in drusen formation. Take home: Drusen, both buried and superficial, can have a variable impact on RNFL thickness depending on etiology of drusen, age, size of optic nerve head and scleral opening, and co-existent pathology.

**High-Resolution Imaging of the Optic Nerve and Retina in Optic Nerve Hypoplasia**


The aim of this study was to characterize the optic nerve and macular morphology in patients with various degrees of optic nerve hypoplasia (ONH) using high-resolution spectral domain ocular coherence tomography (SDOCT). 16 patients with ONH (10 female, 6 male, mean age 17.2 years) and 32 matched healthy controls were examined with SDOCT. Patients with ONH had significantly smaller discs, horizontal cup diameter, and cup depth. In the macula affected patients showed thinner RNFL, ganglion cell layer (GCL), inner plexiform...
layer (IPL), outer plexiform layer (OPL), and inner segment layers. More than 80% patients with ONH demonstrated foveal hypoplasia with thicker GCL, IPL, and OPL in the central retinal area. SDOCT showed high sensitivity and specificity for detecting ONH demonstrating its usefulness for clinical diagnosis.

Characterization of abnormal optic nerve head morphology in albinism using optical coherence tomography

In this study, spectral-domain OCT (SD-OCT) was used to obtain three-dimensional images from 56 people with albinism (PWA) and 60 age- and sex-matched control subjects. B-scans were corrected for nystagmus associated motion artefacts. Disc, cup, and rim ONH dimensions and peripapillary retinal nerve fiber layer (ppRNFL) thickness were calculated using Copernicus and ImageJ software. Median optic disc areas were similar in PWA (median = 1.65 mm²) and controls (1.71 mm², P = 0.128), although discs were significantly elongated horizontally in PWA (P < 0.001). In contrast, median optic cup area in PWA (0.088 mm²) was 23.7% of that in controls (0.373 mm², P < 0.001), with 39.4% of eyes in PWA not demonstrating a measurable optic cup. This led to significantly smaller cup to disc ratios in PWA (P < 0.001). Median rim volume in PWA (0.273 mm³) was 136.6% of that in controls (0.200 mm³). The ppRNFL was significantly thinner in PWA compared with controls (P < 0.001), especially in the temporal quadrant. In PWA, ppRNFL thickness was correlated to ganglion cell thickness at the central fovea (P = 0.007). Several optic nerve head (ONH) abnormalities, such as cup to disc ratio, were related to higher refractive errors in PWA. In PWA, ocular maldevelopment is not just limited to the retina but also involves the ONH. Reduced ppRNFL thickness is consistent with previous reports of reduced ganglion cell numbers in PWA. However, best-corrected visual acuity was not correlated to the pattern of thinning of the temporal ppRNFL observed in albinism, an area typically containing the fibers of the papillomacular bundle. In contrast to ppRNFL, best-corrected visual acuity was correlated to optic disc area with smaller disc sizes associated with worse visual acuity, although the reason for this correlation remains unclear. The thicker rim volumes may be a result of incomplete maturation of the ONH. Although treatments for ocular albinism are currently limited, this study provides an important reference point for assessing structural abnormalities of the ONH in albinism using OCT imaging.

Optical Imaging of the Optic Nerve: Beyond Demonstration of Retinal Nerve Fiber Layer Loss
MJ Kupersmith J Neuro-Ophthalmol
June 2015;(35):210-219
In this annual Hoyt Lecture at NANOS the author delivered an inspired summary of the utility, and limitations of SD OCT and SLP (scanning laser polarimetry). A helpful set of images provide guidance for monitoring the architecture of the optic nerve in the presence of progressive papilledema and its resolution for a patient with a robust RNFL and for a patient with severe optic atrophy (mean RNFL 43 microns). He demonstrates the importance of evaluating the neural canal border. The retinal pigment epithelium/Bruch membrane (RPE/BM) border bows upward in the presence of papilledema, and will return to neutral or may even deflect slightly outward with effective treatment. This is a nice clinical pearl.


Quantitative differences in macular thickness in all retinal layers was evaluated using SD-OCT in eyes with unilateral optic nerve hypoplasia versus normal contralateral eyes. This was a retrospective review of patients seen over an 18-month period. Patient age ranged from 8-12 years. (n=5). The contralateral eye had normal thickness of all layers. ONH eyes showed decreased thickness and hypoplasia of all retinal layers, including the outer retinal layers. Inner retinal layers were thinner in all three macular regions and outer retinal thickness was thinner in 2 of the 3 regions. There was strong agreement between the three graders. This study helps define anatomic abnormalities associated with ONH and this may shed light on pathogenesis.

Myasthenia Gravis


Myasthenia gravis is a disease causing fatiguability of skeletal muscle with the locus of pathology at the neuromuscular junction. Testing for myasthenia gravis can include serum antibody testing, Tensilon testing, ice test, rest test, repetitive nerve stimulation, and electromyography. Testing may be normal or equivocal, especially in patients with ocular myasthenia gravis. This is a prospective case-control study evaluating a novel method of testing for myasthenia gravis in which ocular vestibular evoked myogenic potentials of the inferior oblique muscle were measured in response to vibratory stimuli in patients with myasthenia gravis and control patients. Ocular vestibular evoked myogenic potentials are based on the vestibulo-ocular reflex. It has been previously demonstrated to be useful in primary vestibular disorders and inflammatory or neurodegenerative central nervous system disorders. The authors found a significant decrease in ocular vestibular evoked myogenic potentials for both ocular and generalized
myasthenia gravis patients in comparison to controls at a vibration frequency of 20Hz. The test was found to be 89% sensitive and 64% specific for myasthenia gravis. This suggests that this test could be a useful non-invasive test to evaluate for myasthenia gravis. Further evaluation of this technique is necessary.


Initial presentation of myasthenia gravis is limited to pure ocular symptoms in 50-60% of cases (ocular myasthenia gravis or OMG). Conversion rates to generalized myasthenia gravis (GMG) from previous studies are accepted to be 50-65% with 90% converting within 2 years. This is a retrospective chart review of 158 patients who were diagnosed with OMG. Patients were divided into 2 groups – immunosuppressive treatment group (76 patients), and nonimmunosuppressive treatment group (82 patients). The overall conversion rate of OMG to GMG was 20.9%, which is much lower than previous reports. Of the patients who converted, 30% converted within 1 year, 70% within 2 years, and 30% after 2 years of symptom onset. At 2 years, GMG developed in 8/76 in the immunosuppressive treatment group (median time 20 months), and 15/82 in the nonimmunotherapy group (median time 24 months). The fact that conversion occurred after 2 years in 30% of patients indicates that close monitoring should be continued. No predictive factors for GMG conversion were found.


The objective of this study was to describe the clinical characteristics, outcome and factors that may affect the outcome of childhood-onset myasthenia gravis (CMG) patients in China. The authors have followed up 424 patients with CMG for at least 5 years at Tongji Hospital. At the end of follow-up, the outcome of all the patients was measured according to MGFA Post-intervention Status. In this study, the patients had been followed up for 9.8 ± 5.4 years. The mean onset age was 5.4 ± 3.6 years. Ocular myasthenia gravis (OMG) was the major type of CMG within 2 years after onset (95%). Thymic hyperplasia was found in 116 patients, and thymoma was confirmed in 6 patients. Acetylcholine receptor antibodies were elevated in 69.5% of the patients. All the patients were routinely treated. Thymectomy was performed in 34 patients (8.0%). At the end of follow-up, seventy-one patients (16.7%) were significantly improved, 66 patients (15.6%) remained unchanged, 53 patients (12.5%) were worsened, and 234 patients (55.2%) were exacerbated. Importantly, fifty OMG patients (12.4%) had transformed into generalized myasthenia gravis (GMG) over 2 years after onset.
Thymectomy did not effectively reduce the transformation from OMG to GMG. However, GMG cases significantly benefited from the surgery. This study indicated that the cases with autoimmune CMG account for over 50% in Chinese MG population. The long-term follow-up discloses that CMG patients have a low percentage of improvement, and a high percentage of worsening and exacerbation. The treatment should not be withdrawn too early after the patients obtain complete stable remission. More studies are needed to gain better control of CMG symptoms.

**Optic Neuritis**


The purpose of this study was to compare the clinical features, laboratory findings, and visual outcomes of optic neuritis between prepubertal children and postpubertal adolescents and evaluate the conversion rate of optic neuritis to multiple sclerosis in Korean children. This study was a retrospective analysis of children less than 18 years of age presenting with optic neuritis at Pusan National University Hospital between January 2002 and December 2013. Outcomes and clinical, ophthalmologic, magnetic resonance imaging, and laboratory findings were reviewed. Twenty-six children (male:female, 1:1.2) were included. Follow-up duration was 16.3 ± 27.5 months in the prepubertal children (≤10 years, n = 13) and 8.2 ± 9.2 months in postpubertal adolescent (>10 years, n = 13) (P = 0.32). There was no significant difference between the prepubertal group and postpubertal group in clinical, ophthalmologic, magnetic resonance imaging, or laboratory findings. Of two patients (7.7%) with abnormal brain magnetic resonance images, one developed multiple sclerosis and the other developed acute disseminated encephalomyelitis. Of three patients (11.5%) with relapsing optic neuritis, two developed systemic lupus erythematosus and one developed multiple sclerosis. The authors concluded that the risk of developing multiple sclerosis after pediatric optic neuritis was low (7.7%). Abnormal brain magnetic resonance imaging and relapsing optic neuritis should alert the clinician to systemic or neurological disorders.

**Clinical features of neuromyelitis optica in children**


This prospective review of a clinical database evaluated children diagnosed with multiple sclerosis, acute disseminated encephalomyelitis (ADEM), neuromyelitis optica (NMO), and other demyelinating diseases. Of the 37 patients diagnosed with NMO, 36 met the recently proposed criteria for diagnosis proposed by the
International Panel on NMO Diagnosis NMO-SD 2014. Children with NMO were more frequently non-white. NMO IgG antibodies were present in serum in 60% of patients, and in CSF in 50% of patients. The cerebellum and brainstem were the most common site of disease involvement (72%), followed by optic nerve (65%), spinal cord (55%), and cerebrum (32%). Constitutional symptoms were present in 66%, followed by vision symptoms in 62%, and motor symptoms in 53%. More than half of the patients with pediatric NMO were diagnosed prior to age 11, while only 20% of those diagnosed with MS were under 11 years old. Sex ratios were increasingly female for both MS and NMO with increasing age, suggesting an effect of puberty. No demographic, feature, or CSF abnormality aside from positive NMO IgG distinguished NMO from MS or ADEM. Diagnosis of NMO was delayed compared to MS, and this may have contributed to higher disability due to effects on vision. Further research regarding biomarkers and treatment of pediatric NMO is necessary.


Severe, recurrent or bilateral optic neuritis (ON) often falls within the neuromyelitis optica spectrum disorders (NMOSD), but the diagnosis can be particularly challenging and has important treatment implications. The authors report the features, course and outcomes of patients presenting with atypical ON when isolated at onset. They retrospectively analyzed 69 sequential patients referred to a single UK NMO center with isolated ON at onset. Aquaporin-4 antibody (AQP4-Ab) assessment was performed in all patients and IgG1 myelin-oligodendrocyte glycoprotein (MOG-Ab) in AQP4-Ab neg patients. 37 AQP4-Ab positive (AQP4-Abpos) and 32 AQP4-Ab negative (AQP4-Ab neg) patients (8 with MOG-Ab) were identified. The AQP4-Abneg group included heterogeneous diagnoses: multiple sclerosis (MS), NMO, relapsing isolated ON (RION), monophasic isolated ON and relapsing acute disseminated encephalomyelitis (ADEM)-like syndromes. Compared to AQP4-Abneg patients, AQP4-Abpos patients had a worse residual visual outcome from first attack (median VFSS 4 vs. 0, p = 0.010) and at last assessment (median VFSS 5 versus 2, p = 0.005). However, AQP4-Abneg patients with RION also had poor visual outcome. Up to 35 % of AQP4-Abneg patients developed a LETM and two developed low positivity for AQP4-Ab over time. Eight AQP4-Abneg patients (25 %) were MOG-Ab positive, covering a range of phenotypes excluding MS; the first ON attack was often bilateral and most had relapsing disease with a poor final visual outcome [VFSS 4, range (0–6)]. The authors concluded that AQP4-Ab positivity is confirmed as a predictor of poor visual outcome but AQP4-Abneg RION also had a poor visual outcome. Of those without AQP4-Ab, 25 % had MOG-Ab and another 25 % developed MS; thus, MOG-Ab is associated with AQP4-Abneg non-MS ON.

AQP4 mediated inflammation has been linked to fetal demise. This international retrospective cohort study evaluated the effect of neuromyelitis optica spectrum disease (NMOSD) on pregnancy in 60 women. 85 pregnancies in 40 women were included in the multivariate regression analysis. Miscarriages occurred in 12.9% of pregnancies overall, and in 42.9% of pregnancies following the onset of NMOSD, compared to 7% of pregnancies prior to the onset of NMOSD. Univariate logistic regression analysis found maternal age, timing of NMOSD onset with respect to pregnancy, most recent pregnancy ending in miscarriage, and obstetric history of only miscarriages to be associated with increased risk of miscarriage. Timing of NMOSD onset was found to be the strongest predictor of miscarriage in multivariate regression analysis. Preeclampsia was not associated with NMOSD. Pregnancies after NMOSD onset that ended in miscarriage were more likely to be associated with higher preconception and intrapregnancy disease activity, and were receiving more treatment. These findings suggest that AQP4-IgG may lead to miscarriage. Disease activity before and during pregnancy should be minimized to prevent miscarriage. Further studies are necessary to give evidence based guidelines for treating patients with NMOSD who are or wish to become pregnant.


These authors report their experience for the use of Alemtuzumab in neuromyelitis optica (NMO) spectrum disorders. A retrospective case review of patients treated with alemtuzumab in Cambridge, UK, was conducted to identify those who fulfil the criteria for NMO spectrum disorder. Three cases were identified. Case 1, 9-year-old female, presented with transverse myelitis and bilateral optic neuritis, with one lower medullary and several longitudinally extensive cord lesions. Despite immunosuppression including two courses of alemtuzumab, she continued to relapse, was wheelchair bound and registered blind by age 12, and died at age 18. Case 2, 41-year-old female, presented with bilateral optic neuritis and transverse myelitis with longitudinally extensive cervical cord lesions. Despite three courses of alemtuzumab, she had five relapses with visual impairment and new cord lesions. She later developed tumefactive white matter lesions and died aged 51. Case 3, 31-year-old female, presented with transverse myelitis with longitudinally extensive cervical cord lesions and positive aquaporin-4 antibody. After one course of alemtuzumab, she relapsed with 4 episodes of myelitis with new enhancing lesions and accumulating disability. She became relapse free after rituximab and mycophenolate mofetil. From this case series, the authors concluded that
Alemteuzumab failed to prevent disabling relapses and poor outcome in NMO. They hypothesized that rituximab is more effective, as in case 3, because it causes much more prolonged B lymphocyte depletion than alemteuzumab. They therefore caution against the use of alemteuzumab in NMO.


The detection of anti-aquaporin-4 autoantibody (AQP-4 Ab) is crucial to detect patients who will develop neuromyelitis optica (NMO); however, there are few studies on the AQP-4 Ab serostatus of patients with neuromyelitis optica spectrum ON. These authors analyzed the clinical and paraclinical features of neuromyelitis optica spectrum ON patients in China according to the patients’ AQP4-Ab serostatus. 125 patients with recurrent and bilateral ON with simultaneous attacks were divided into AQP-4 Ab-seropositive and -seronegative groups. Demographic, clinical, serum autoantibody data, connective tissue disorders (CTDs), visual performance were compared. A Visual Acuity (VA) of less than 0.1 during acute ON attacks occurred more frequently in the seropositive group ($p = 0.023$); however, there was not a significant difference between groups on VA recovery after the first attack. The seropositive group experienced the worst outcome during the last attack ($p = 0.017$). Other co-existing autoimmunity antibodies ($p < 0.001$) and CTDs ($p < 0.001$) were more prevalent in seropositive patients. There were no significant differences on VA recovery and RNFLT combined with other autoantibodies or CTDs. The two groups did not differ significantly with regard to time to relapse, annualized relapse rates, time of diagnosis NMO, or RNFL. There were no significant differences on VA recovery and RNFLT combined with other autoantibodies or CTDs. RNFLT was thinner in NMO seropositive patients. Although AQP-4 Ab expression predicted poor visual outcome, positive patients were usually associated with mild symptoms at first onset. Anti-SSA/SSB antibody or Sjögren syndrome may be associated with AQP-4 Ab in neuromyelitis optica spectrum ON.


This is an evidence based consensus paper from an international panel regarding criteria necessary for the diagnosis of neuromyelitis optica spectrum disorders (NMOSD). Distinguishing NMO from multiple sclerosis has important prognostic and treatment implications. Previously NMO required transverse myelitis and bilateral optic neuritis. Criteria were relaxed to allow unilateral optic neuritis, and to include positive aquaporin-4 antibody (AQP4-IgG) serologies.
The current consensus criteria allow for aquaporin-4 antibody negativity, and identify core clinical characteristics including optic neuritis, acute myelitis, area postrema syndrome, acute brainstem syndrome, symptomatic narcolepsy or acute diencephalic syndrome with NMOSD-typical MRI lesions, and symptomatic cerebral syndrome with NMOSD-typical brain lesions. Further MRI criteria are described in this article in Table 1. Diagnosis of NMOSD with AQP4-IgG positivity requires at least one core clinical characteristic. Diagnosis of NMOSD without AQP4-IgG positivity requires at least optic neuritis, acute myelitis, or area postrema syndrome, at least two different core clinical characteristics, and must fulfill MRI requirements while excluding alternative diagnoses. Further description of findings which would be atypical for NMOSD, and MRI findings characteristic of NMOSD are described. This paper is important as it further clarifies exactly what constitutes the NMOSD.


This is an update summarizing the characteristic findings on neuroimaging in patients with neuromyelitis optica spectrum disorder (NMOSD). The discovery of aquaporin 4 antibody positivity in patients with this disorder has made it easier to distinguish NMOSD from multiple sclerosis. It has also expanded the definition of neuromyelitis optica to include patients who do not have classic myelitis and optic neuritis but do have antibody positivity as having NMOSD. Lesions in the dorsal brainstem adjacent to the fourth ventricle are one of the most specific abnormalities. Other brain findings include hemispheric tumefactive lesions, involvement of the corticospinal tracts, and areas of "cloud-like" enhancement. The most distinct spinal cord lesions in NMOSD are longitudinally extensive transverse myelitis (spanning more than 3 vertebral segments) predominantly involving central gray matter. Optic nerve involvement tends to demonstrate T2-hyperintensity and enhancement of the optic nerves, with a trend toward more posterior involvement and simultaneous bilateral disease. This summary also compares imaging finding in MS to those in NMOSD. Characterizing and distinguishing these diseases have important prognostic and treatment consequences.

**Other**


The purpose of this study was to examine ophthalmic disorders associated with neurological disorders in children with cerebral palsy. Children clinically diagnosed as cerebral palsy with supportive abnormal magnetic resonance
imaging results were included in this prospective study. All participants were recommended to have comprehensive ophthalmic exams. To assess motor function, the Gross Motor Function Classification System and the Gross Motor Function Measure were used. To assess motor and cognitive function, the Bayley Scales of Infant Development-II was used. Forty-seven children completed all the evaluations and the data were analyzed. Ametropia was seen in 78.7% and strabismus was seen in 44.7% of the 47 children. When subjects were divided into severely impaired and mildly impaired groups based on Gross Motor Function Classification System level, ametropia was more prevalent in the severely impaired than the mildly impaired (95.8% versus 60.9%, \( P < 0.05 \)). According to quantitative analysis, the severity of gross motor impairment correlated with the degree of refractive error in the subjects older than 36 months \((r = -0.65\) for the Bayley Scales of Infant Development-II motor scale, \( P < 0.05 \)).

Based on these findings, the authors purport that children with cerebral palsy with poor gross motor function have a high possibility of severe refractive disorder that becomes evident from 36 months after birth. These results suggest that brain injury and impaired motor development negatively affect ophthalmic development. Hence, an ophthalmic examination is recommended for young children with cerebral palsy to start early management.

**Pediatric cavernous sinus thrombosis: A case series and review of the literature**


This is a case series and literature review of cavernous sinus thrombosis (CST) in the pediatric population. The authors contribute 12 cases and identify another 40 in the English literature. Among patients at the institution, initial imaging was noncontrast head CT in three patients which did not identify the CST, and contrast enhanced head CT in seven patients which identified the CST in all of these patients. An MRV performed in eight of the patients did not identify CST. MRA detected internal carotid artery stenosis in 10/12 patients. All patients had CST identified on gadolinium enhanced MRI. Superior ophthalmic vein thrombosis was identified in 25%. All of the patients at their institution survived. Three had neurologic deficits at final follow-up. Underlying etiology was suspected to be sinusitis in 11/12 patients. Literature review in aggregate revealed an 8% mortality rate. The remaining patients had a 25% rate of suffering long neurologic morbidity. This is an important evaluation and review of a rare potentially fatal disease which may present initially to the pediatric ophthalmologist.

**Sensorimotor Characteristics of Neuro-Ophthalmology and Oculo-Plastics Patients**

The author performed a retrospective review of 575 cases referred to his orthoptic clinic by neuro-ophthalmologists and oculoplastics surgeons over a 9 year period with chief complaint of diplopia or blurred vision. The diagnoses and clinical findings were described in detail. Cranial nerve palsy was the most common diagnosis and of these, CN 6 palsy was most common followed by CN 4 and finally CN 3 palsy. In the group of patients with CN 3 palsy, 40% did not have pupil involvement, which is approximately double the percentage in other studies. Less common diagnoses in this population were thyroid eye disease, Parkinson’s disease, malignancy (especially breast cancer) not involving the head and neck, myasthenia, skew deviation, restrictive strabismus and adult hydrocephalus. There was no statistical difference between unilateral and bilateral ptosis in myasthenia cases. In addition, there was no statistical difference in the number of patients with esotropia and those with exotropia in the subgroup with thyroid eye disease. Half of the patients in this cohort underwent treatment with prisms or surgery. Only 10% underwent surgery. Fresnel prism was used about twice as often as ground-in prism.

Comment: This study provides insight into the array of adult strabismus cases one would expect to see referred by neuro-ophthalmologists and oculoplastics surgeons. The percentages for each diagnosis type may be influence by individual referral patterns and may not be generalizable.

A Case Report: Consecutive Cranial Neuropathies Following the Use of Phosphodiesterase-5 Inhibitors S. van Landingham, E. Singman

Phosphodiesterase-5 Inhibitors are provided as treatment for erectile dysfunction in men. Multiple vascular events have been reported in association with use of these medications. In this single case report, the authors present a patient with partial CN 3 palsy occurring after use of sildenafil (Viagra). The patient experienced exotropia and left hypotropia with left adduction and elevation deficits. Imaging and other studies were performed but did not reveal another etiology for CN 3 palsy. The palsy and symptoms resolved spontaneously within 2 months. The patient was advised to not use sildenafil. The following year the patient presented with right CN 6 palsy following the use of tadalafil (Cialis). Within 3 months the CN 6 palsy and symptoms resolved. The patient was advised to avoid all phosphodiesterase-5 inhibitors.

Comment: This case report suggests that CN palsy may be associated with use of phosphodiesterase-5 inhibitors which is reasonable in that other vascular events have been reported with these medications.
Residual Strabismus in Children Following Improvement of Cranial Nerve Palsies Affecting Ocular Ductions
M. Bratton, M. Hoehn, B. Morris, T. Merchant et al.
Am Orthopt J. August 2015;65:87-93.

The authors perform a retrospective review of 104 children with 3rd, 4th and/or 6th nerve palsies treated for intracranial neoplasms. The number of children with resolution and improvement in duction deficit were 27 and 18, respectively. Of the group of 27 children, 1/3 also had resolution of strabismus. Of the 18 with improved duction, only 3 had resolution of strabismus. Children under age 8 years were more likely to remain strabismic even if duction deficit improved or resolved. Tumor type was not correlated with persistence of duction deficit or strabismus.

A geographic cluster of progressive supranuclear palsy patients in northern France
Caparros-Lefebvre D, Golbe L, Deramecourt V, et al.

This is a retrospective chart review and epidemiological study of 92 patients who presented with progressive supranuclear palsy (PSP) to a single hospital in France. This particular location had 4.95 expected number of PSP cases over the observation period (8 years) but found 12.3 times that number of cases. Thirteen patients underwent autopsy, and satisfied criteria for definite PSP. Cases clustered in the towns of Wattrelos and Leers, which were areas of slag heaps from metal extraction plants. The soil in those areas has been found to be contaminated with toxins. A genetic founder effect is being considered. Further studies will be performed to evaluate for a causative factor, whether genetic or environmental, for the PSP cluster.

Wernicke Encephalopathy
P. Jenkins

Thiamine (vitamin B1) deficiency is the cause of Wernicke encephalopathy that can be seen in cases of poor nutrition such as alcoholism, AIDS, prolonged vomiting, infectious diseases and chemotherapy. The author of this paper describes an example case of Wernicke encephalopathy in a 30-year-old woman after gastric bypass surgery. The author provides a good review of Wernicke encephalopathy symptoms (horizontal oscillopsia, diplopia, headache, irritability, fatigue, lethargy, apathy, confusion, psychosis, coma) and signs (ataxia, loss of deep tendon reflexes, nystagmus, 6th nerve palsy, skew deviation, anisocoria, miosis, light/near dissociation, retinal hemorrhage, papilledema, optic neuropathy, central scotoma, horizontal gaze palsy, Miller-Fischer symptoms) as well as images of MRI findings which includes reversible cytotoxic edema that
most often occur in the medial thalami and periventricular region of the third ventricle. These areas of edema resolve following thiamine replacement treatment. The author suggests an increase in cases of Wernicke encephalopathy due to the increase in gastric bypass surgeries.


In this retrospective case–control study the authors analyzed the neuro-ophthalmological examination reports of 400 adult patients who presented at the German Center for Vertigo and Balance Disorders to determine an association between ocular misalignment and cerebellar dysfunction. Patients with cerebellar signs (i.e., cerebellar ataxia and/or cerebellar ocular motor signs) had a 4.49 (95 % CI [1.60; 13.78]) times higher frequency of ocular misalignment and specifically a 13.3 (95 % CI [3.80; 55.73]) times increased frequency of esophoria/esotropia (ESO) during distant gaze than patients without cerebellar dysfunction. ESO when looking into the distance was associated with saccadic smooth pursuit, dysmetria of saccades, and downbeat nystagmus (DBN) ($\chi^2$ test, $p < 0.0001$ for all associations). Patients with cerebellar dysfunction also showed mildly impaired eye abduction ($\chi^2$ test, left eye and right eye: $p < 0.0001$), associated with horizontal gaze-evoked nystagmus ($\chi^2$ test, $p < 0.0001$). The association of ESO and DBN implicates a pathophysiological involvement of the cerebellar flocculus, while the association with dysmetric saccades suggests involvement of the oculomotor vermis. This is compatible with animal studies showing that the pathways of the flocculus/posterior interposed nucleus and vermis/nucleus fastigii are both involved in vergence movements and static binocular alignment. From a clinical point of view, a newly diagnosed esophoria/esotropia only during distant gaze may be a sign of a cerebellar disease.


This is a self-controlled claims database analysis evaluating the risk of cardiovascular disease in association with retinal vein occlusion (RVO). The index date was the date of diagnosis, a control period was defined as 180-365 days prior to the index event. Time periods from 180 days leading up to the event and from the event to 365 days after were divided into risk periods. 43,801 patients were diagnosed with a RVO over a two year period, 1,176 of whom had a cardiovascular event over the study period. The authors found that patients with a RVO had a higher incidence of cardiovascular events following RVO, with the highest risk (up to 5 times higher) in the few weeks immediately after the
event. Patients with RVO may require immediate cardiovascular risk analysis and treatment of those risk factors.

**Is there treatment for Leber hereditary optic neuropathy?**

Leber hereditary optic neuropathy (LHON) is an inherited bilateral optic neuropathy caused by mitochondrial DNA mutations. This review article describes LHON treatment modalities and findings of clinical trials that are underway or are in the planning stages. Early treatment of LHON with Idebenone or EPI-743, agents that reduce free radical production, have been reported to preserve retinal ganglion cells. Treatment of LHON with various gene therapy techniques are under investigation. Adeno-virus Associated Virus (AAV) vector therapy inserts normal exogenous DNA into the cell nucleus to enable normal protein production to replace the abnormal mitochondrial respiratory chain protein. Oocyte nuclear transfer is a form of gene therapy where the nucleus from an oocyte with the LHON mitochondrial mutation is transferred to an unaffected enucleated oocyte for subsequent in-vitro fertilization. Idebenone, EPI-743 and gene therapy are not FDA approved for the treatment of LHON. Genetic counseling and low-vision aides remain the mainstay of treatment for LHON. This article provides a succinct summary of ongoing research on LHON treatment and provides the Ophthalmologist with the information necessary to counsel their patients with LHON appropriately.

**Clinical Color Vision Testing and Correlation with Visual Function**
Zhao J, Dave S, Wang J, Subramanian P. AJO September 2015; 160 (3); pg. 547.

This study evaluated the HRR and Ishihara testing in evaluating accuracy of color vision and acquired visual dysfunction. 22 subjects were compared to 18 controls. Individuals with vision worse than 20/200 or with congenital color blindness were excluded. it was found that HRR and Ishihara assess color identification in patients with optic neuropathy. Both tests correlated with contrast sensitivity. These tests may be useful clinical surrogates for contrast sensitivity.

**Ocular fundus photography of patients with focal neurologic deficits in an emergency department**

This is a cross-sectional pilot study in which patients presenting to an emergency room with focal neurologic deficits suspicious for transient ischemic attack (TIA)
or stroke underwent nonmydriatic fundus photography. These patients were part of a larger cohort who underwent fundus photography as part of the FOTO-ED study. Of 257 patients included, 81 were diagnosed with cerebrovascular disease, 27% of whom had a stroke, and 73% of whom were diagnosed with TIA. In patients with focal neurologic deficits 56% had abnormalities of the retinal microvascular. The odds ratio of cerebrovascular disease when controlled for ABCD² score was five times higher in the presence of focal arteriolar narrowing, and three times higher in the presence of generalized narrowing. TIA was associated with these retinal vascular findings. This study further emphasized the importance of examination of the fundus in neurologic disease, and nonmydriatic fundus photography in an emergency department setting can facilitate examination.


This review summarizes topical papers from the fields of neuro-ophthalmology and neuro-otology published from August 2013 to February 2015. The main findings are: (1) diagnostic criteria for pseudotumor cerebri have been updated, and the Idiopathic Intracranial Hypertension Treatment Trial evaluated the efficacy of acetazolamide in patients with mild vision loss, (2) categorization of vestibular disorders through history and ocular motor examination is particularly important in the acute vestibular syndrome, where timely distinction between a central or peripheral localization is essential, (3) the newly described “sagging eye syndrome” provides a mechanical explanation for an isolated esodeviation that increases at distance in the aging population and (4) eye movement recordings better define how cerebellar dysfunction and/or sixth nerve palsy may play a role in other patients with esodeviations that increase at distance.

### 6. NYSTAGMUS

**Effect of Photorefractive Keratectomy on Nystagmus and Visual Functions in Myopic Patients with Infantile Nystagmus Syndrome** Bagheri, H. Abbasi, M. Tavakoli, et al. *AJO* Feb 2016: vol 162; pg. 167. This prospective interventional case series looked at the effect of PRK on involuntary eye movements, VA, and contrast sensitivity in myopic patients with infantile nystagmus syndrome. Patients who had infantile nystagmus and myopia of greater than 100 was included in the study. Contrast sensitivity was measured prior to surgery using the YANG projector, the nystagmus was recorded as well. 24 eyes of 12 patients with a mean age of 23 years. 7 patients had motor nystagmus while 5 had sensory nystagmus. Mean refractive error was 2.16. After PRK, both monocular and binocular vision improved with 20/42 before surgery
and 20/32 after surgery. In addition, contrast improved at 3 frequencies. There was no correlation between the amount of myopia corrected and the improvement in the nystagmus. PRK may be a reasonable option for patients with nystagmus and refractive error.

**Visual processing in infantile nystagmus is not slow**

Treatments for infantile nystagmus (IN) sometimes elicit subjective reports of improved visual function, yet quantifiable improvements in visual acuity, if any, are often negligible. One possibility is that these subjective “improvements” may relate to temporal, rather than spatial, visual function. This study aimed to ascertain the extent to which “time to see” might be increased in nystagmats, as compared to normally sighted controls. By assessing both eye movement and response time data, it was possible to determine whether delays in “time to see” were due solely to the eye movements, or to an underlying deficit in visual processing. The time taken to respond to the orientation of centrally and peripherally presented gratings was measured in subjects with IN and normally sighted controls (both groups: n= 11). For each vertically displaced grating, the time until the target-acquiring saccade was determined, as was the time from the saccade until the subject’s response. Nystagmats took approximately 60 ms longer than controls to execute target-acquiring saccades to vertically displaced targets (P = 0.010). However, the time from the end of the saccade until subjects responded was not significantly different between groups (P = 0.37). Despite this, nystagmats took longer to respond to gratings presented at fixation. This suggests that the centrally presented targets were not always instantly resolvable, presumably owing to the eyes being off-target at the time of presentation, and the inherent variation in photoreceptor density between the foveal and extrafoveal retina. This study demonstrates that increased saccadic latency rather than conscious visual processing accounts for visual timing delays in IN. Studies on the impact of treatments on perception in IN may therefore be more accurately assessed with methods that involve a measure of temporal visual function, such as measuring saccadic latency or using time-restricted visual acuity.

**Eye muscle surgery for recurrent nystagmus related to head tilt after prior torsional surgery.** Kushner BJ and Gamm DM. J AAPoS 2015;19:211-216

This study reports anterior and nasal transposition of the inferior oblique to treat severe overelevation in adduction with exyclotropia. Consecutive patients over a twelve-year period were evaluated retrospectively. Three patients are presented
as case reports. Two of the three had no light perception vision in the operated eye and the other had poor acuity. Head tilt opposite the fixing eye was corrected, but it did not necessarily result in a torsional shift. The authors cannot confidently recommend the surgery for patients with good binocular vision. Nystagmus tracings were not performed. This procedure has a limited role.


The authors previously reported on how oral carbonic anhydrase inhibitors (CAI) improved nystagmus waveform in a single case report. Here, the authors described the effect of using topical CAI, brinzolamide, in 5 patients with idiopathic nystagmus who are at least 18 years of age. Study subjects served as their own controls. They were tested on no drops, placebo drops, and azopt for 1 week used TID. Outcomes measures included visual acuity measured in ETDRS, eye movement recording of foveation period, and nystagmus acuity function (NAFX). Mean visual acuity AFX, and foveation period significantly improved with use of brinzolamide compared to using placebo and no drops. Patient 4 did not show any improvement in vision but this patient started with excellent vision. This is a nice introduction of a new treatment modality for nystagmus.

**Head oscillations in infantile nystagmus syndrome.** Ghasia FF and Shaikh AG. *J AAPos* 2015;19:38-41.

Two types of head oscillations observed in 10 idiopathic nystagmus patients are described. The first type had low oscillation frequency in the 1-3 Hz range. This type is primarily in the horizontal plane with a small vertical component. It is present during the entire recording. The second novel subtype which was noted in 7 of the 10 patients, displayed high-frequency oscillations in the 5-8 Hz range. This type is in prominent in the vertical axis and occurred as a burst of brief episodes superimposed on the low-frequency head oscillations seen in all subjects. Patients were evaluated over a 17-month period. Mean age was 30.2 years. The difference in median frequencies, distribution of trajectories and median amplitude between the two types of oscillations was statistically significant. The authors concluded that the high-frequency head oscillations were not an adaptive mechanism but rather a coexisting pathological process. The authors attempt to elucidate the types and causes of head oscillations in INS.
7. PREMATURITY

Ophthalmic Features of Premature Infants

Eye growth in term- and preterm-born eyes modeled from magnetic resonance images

The authors generated a model of eye growth and tested it against an eye known to develop abnormally, one with a history of retinopathy of prematurity (ROP). They reviewed extant magnetic resonance images (MRIs) from term and preterm born patients for suitable images (n=129). They binned subjects for analysis based upon postmenstrual age at birth and ROP history (“Term” ≥ 37 weeks, “Premature” ≤ 32 weeks with no ROP, “ROP” ≤ 32 weeks with ROP). They used MRIs collected cross-sectionally at preterm through young-adult ages, to chart the development of the eye, and then mathematical modeling to estimate the growth of the eye (including the cornea and posterior segment) throughout development. This is the first model ever to indicate where and when the eye grows as it matures. Relative to Term, development of anterior chamber depth, posterior segment depth, axial length, and corneal and lenticular curvatures was delayed in ROP eyes, but not premature eyes. In addition, lenticular thickness was higher in ROP eyes, corneas were steeper and lens anterior and posterior curvature was steeper—all consistent with short, myopic eyes in ROP. The authors noted that the variability in the ROP group was, in general, higher than in the Term group. Thus, the models are more likely to describe the development of any given “normal” eye than they are to describe the development of any given eye with a history of ROP. Also, the representativeness of the Term sample must be treated as somewhat equivocal, since these children were receiving head MRIs and thus were likely not a perfectly normally developing population. However, there is good agreement with the existing literature. This study adds to the overwhelming body of knowledge that indicates that ROP is a disease of the whole eye, with persistent effects that last well after the clinical disease is resolved. This is the first mathematically-based model of eye growth.

Cup-to-disc and arteriole-to-venule ratios in preterm birth
J Kim, D Y Choi, K-A Park and S Y Oh Eye 29: 1167-1172 June 2015;

The authors were interested in the differences in the appearances in the optic disc in pre-term vs. full-term infants. They compared two groups of children, the first group being 42 pre-term infants with a mean gestational age of 27 weeks and 42 full-term infants. The mean age of the patients when examined was 8 years of age. When comparing the cup to disc ratio using fundus photography, they found the pre-term infant had a larger cup to disc ratio compared to the full term infants. None of these pre-term infants had associated neurologic disease
such as periventricular leukomalacia or intraventricular hemorrhage or hydrocephalus. They also compared retinal vascular appearance and found that the infants in the pre-term had a smaller arterial to venous ratio. The authors conclude that a premature birth can be associated with increased cup to disc ratio without concurrent long term neurologic injury.


This paper reports IOP and CCT data from a large series of premature infants, who were prospectively enrolled over a 10-month period. Infants with significant IOP or CCT asymmetry between the two eyes were excluded. 470 eyes of 470 infants were included. The mean IOP value was 16.86 mm Hg and the mean CCT was 590 um. When patients were split into four subgroups based on post-conceptual age (PCA), the intergroup difference between IOPs and the intergroup difference between CCTs were statistically significant. There was a negative linear relationship between PCA and IOP and between PCA and CCT. There was a strong positive linear correlation between IOP and CCT. CCT showed a dramatic decline up to the 40th week, and then it stabilized. Prior studies were small and conflicting so this study provides normative data in premature infants.

Strabismus and Prematurity

Convergence and accommodation development is preprogrammed in premature infants AM Horwood, SS Toor, and PM Riddell. Invest Ophthalmol Vis Sci. August 2015;56:5370–5380.

This study investigated whether vergence and accommodation development in preterm infants is preprogrammed or is driven by experience. Thirty-two healthy infants, born at mean 34 weeks gestation (range, 31.2–36 weeks), were compared with 45 healthy full-term infants (mean 40.0 weeks gestation) over a 6-month period, starting at 4 to 6 weeks postnatally. Simultaneous accommodation and convergence to a detailed target were measured using a Plusoptix PowerRefll infrared photorefractor as a target moved between 0.33 and 2 m. Stimulus/response gains and responses at 0.33 and 2 m were compared by both corrected (gestational) age and chronological (postnatal) age. When compared by their corrected age, preterm and full-term infants showed few significant differences in vergence and accommodation responses after 6 to 7 weeks of age. However, when compared by chronological age, preterm infants' responses were more variable, with significantly reduced vergence gains, reduced vergence response at 0.33 m, reduced accommodation gain, and increased accommodation at 2 m compared to full-term infants between 8 and 13 weeks after birth. This study suggests that vergence and accommodation in preterm infants follow a maturational developmental trajectory and that responses are not
accelerated by the additional visual experience of earlier birth. A previous study showed an experience-dependent development of sensory binocularity, where the additional visual experience in preterm infants resulted in earlier development. Thus, a mismatch in the time course between the development of oculomotor and sensory binocularity might contribute to the increased risk of Strabismus in children born preterm. This study contributes to our understanding of visual development in preterm infants.

Prematurity and Outcomes


The author review literature published from 2013 to 2015 on the subject of periventricular leukomalacia emphasizing association with cerebral visual impairment (CVI), strabismus, visual field defects and visuoperceptual anomalies. The severity and extent of PVL is proportional to both the likelihood of having an vision/ocular abnormality and the severity of the abnormality. There have been reports of strabismus as the presenting sign of PVL. MRI is the best imaging modality to detect PVL grades I – IV. Ultrasound has sensitivity and specificity above 90% for grade III and IV PVL but sensitivity for grades I and II is only 20%. Ultrasound has the advantage of being performed in the NICU when a patient is not stable enough for transport to MRI scanner. PVL damage is retro-chiasmal with optic radiations most commonly affected with extension to the visual cortex in severe cases. Strabismus associated with PVL may be esotropia, exotropia and less commonly vertical deviations. There is no specific PVL anatomical location that is predictive of strabismus. The severity of CVI is correlated with severity of PVL. Damage involving the visual cortices is high predictive of poor visual outcome. Visuoperceptual deficits associated with PVL are: simultanagnosia (difficulty perceiving more than one object at a time), prosopagnosia (difficulty with recognition of familiar faces), global motion processing deficits (difficulty surrounding visual detection of the speed and direction of a moving object) and difficulty with hand-eye coordination. There is an exacerbation of the crowding effect upon acuity testing. PVL is the most common cause of cerebral palsy.


This multicenter trial from Australia and the United Kingdom studied death and disability at age two years among premature infants born at less than 28 weeks who were randomized to either a lower (85 to 89%) or a higher (91 to 95%)
oxygen saturation range. Disability was defined by a low score on a cognitive or language assessment, legal blindness, severe cerebral palsy, or deafness.

After 1135 infants in Australia and 973 infants in the United Kingdom had been enrolled in the trial, an interim analysis showed increased mortality in the lower oxygen group at a corrected gestational age of 36 weeks, and enrollment was stopped. The final outcome, death or disability at age two years, occurred in 492 of 1022 infants (48.1%) in the lower-target group versus 437 of 1013 infants (43.1%) in the higher-target group (relative risk, 1.11; 95% CI, 1.01 to 1.23; P=0.02), and death occurred in 222 of 1045 infants (21.2%) in the lower-target group versus 185 of 1045 infants (17.7%) in the higher-target group (relative risk, 1.20; 95% CI, 1.01 to 1.43; P=0.04). The data did not reach statistical significance for each country independently, though the trends were in the same direction.

The lower oxygen group infants were less likely to require ROP treatment than the higher oxygen group infants. However, rates of severe vision loss/legal blindness were low, and the rates were similar for the lower and higher oxygen saturation groups (0.7 and 0.4%, respectively, in Australia, and 3.1 and 3.5%, respectively, in the United Kingdom). The authors recommend that oxygen saturation be maintained at 91-95% for premature infants born at less than 28 weeks. Reducing oxygen saturation to 85-89% increases death and disability, and it does not reduce the rate of severe vision loss/blindness.

8. ROP

ROP and Telemedicine


To address the shortage of providers who can perform screening eye exams on infants at risk for retinopathy of prematurity, telemedicine techniques provide a possible solution. Thus it is important to develop a reliable model to identify referral warranted (RW) ROP which ideally incorporates predictors which may lessen the need to have serial exams in these vulnerable infants, exams which are invariably stressful on these babies. Study design is a multicenter observational cohort study which included secondary analysis of data from the Telemedicine Approaches to Evaluating Acute-Phase Retinopathy of Prematurity Study. Infants included in the study had a birth weight less than 1251 g. Outcomes which were measured and analyzed included incidence of referral warranted-ROP and associations with predictive factors. Referral warranted ROP
is defined as the presence of plus disease, zone I ROP, or ROP stage 3 or greater in either eye. Of 979 infants without RW-ROP at initial exam and who underwent at least 2 eye exams, 15.2% developed RW-ROP. Using a multivariate model, significant predictors for developing RW-ROP include male sex, non-black race, low birth weight (less than or equal to 500 g), younger gestational age (less then or equal to 24 weeks), number of clock hours of pre-plus, Zone 2 disease, retinal hemorrhage, need for respiratory support and slow weight gain. When prematurity and low birth weight are controlled for in the analysis, the presence of preplus disease, stage 2 ROP, retinal hemorrhage, and the need for ventilation at time of first study-related eye examination were strong independent predictors for developing RW-ROP.

**Validated System for Centralized Grading of Retinopathy of Prematurity Telemedicine Approaches to Evaluating Acute-Phase Retinopathy of Prematurity (e-ROP) Study**


The need for screening at-risk premature infants for potentially sight threatening retinopathy of prematurity is great. The eROP study provides evidence that telemedicine techniques are possible to address the shortage of screeners. This study examines the efficacy of a training program to certify non-physician reviewers of fundus images from infants with ROP. Specifically, training, certification, operational workflow, and quality assurance in an ROP reading center that supported the e-ROP Study are described. This study details the results from 4 trained readers who assessed 5520 images and graded them to determine if they met criteria for RW-ROP. The authors conclude that under the supervision of a reading center director, trained non-physician readers reliably detected potentially serious ROP with good intragrader and intergrader consistency and minimal temporal drift.

**Evaluation of Screening for Retinopathy of Prematurity by ROPtool or a Lay Reader**


Previously published studies have shown that telemedicine can be used safely and effectively in the screening of infants with retinopathy of prematurity (ROP). Recent studies show that nonphysician readers can perform ROP screening and assess the need for bedside examination with good accuracy. The ROPtool (developed at the University of North Carolina) is a computer program that traces vessels in retinal photographs to generate a numerical value for dilation and tortuosity. The authors of this study assessed whether the presence of vascular abnormalities could be determined effectively by a lay reader or by using the ROPtool. 335 fundus images of premature infants were obtained by neonatal intensive care nurses. A panel of 3 ROP experts graded 84 images showing
vascular dilatation, tortuosity, or both and 251 images showing no evidence of vascular abnormalities. These images were sent electronically to an experienced lay reader who independently graded them for vascular abnormalities. The images also were analyzed using the ROPtool, which assigns a numerical value to the level of vascular abnormality and tortuosity present in each of 4 quadrants or sectors. The ROPtool measurements of vascular abnormalities were graded and compared with expert panel grades with a receiver operating characteristic (ROC) curve. Grades between human readers were cross-tabulated. The area under the ROC curve was calculated for the ROPtool, and sensitivity and specificity were computed for the lay reader. The ROC curve for ROPtool's tortuosity assessment had an area under the ROC curve of 0.917. Using a threshold value of 4.97 for the second most tortuous quadrant, ROPtool's sensitivity was 91% and its specificity was 82%. Lay reader sensitivity and specificity were 99% and 73%, respectively, and had high reliability (κ, 0.87) in repeated measurements. ROPtool had very good accuracy for detection of vascular abnormalities suggestive of plus disease when compared with expert physician graders. The lay reader's results showed excellent sensitivity and good specificity when compared with those of the expert graders. These options for remote reading of images to detect vascular abnormalities show promise and would allow the use of telemedicine with remote reading for efficient delivery of high-quality care and to detect infants requiring bedside examination.

**SUNDROP: six years of screening for retinopathy of prematurity with telemedicine**

SK. Wang, NF. Callaway, MB. Wallenstein, MT. Henderson et al.

*CAN J OPHTHALMOL VOL. 50 (2) APRIL 2015:101-106*

The Stanford University Network for Diagnosis of Retinopathy of Prematurity (SUNDROP) is an ongoing telemedicine-based community initiative for in-hospital screening of high-risk infants for treatment-warranted ROP. Patients are screened using RetCam II images, which are subsequently sent to the Stanford University Byers Eye Institute reading centre for remote interpretation by an ROP specialist. Photos were captured as necessary until they were deemed to be of sufficient quality as determined by the image interpreter. Later an iris image in each eye was also added to the protocol. Over the 6-year study period, 608 preterm infants (1216 eyes) were screened for ROP with telemedicine. Twenty-two (3.6%) infants of the 608 total screened met criteria for Treatment warranted (TW)-ROP. The 6-year results for the SUNDROP telemedicine initiative were highly favorable, exhibiting a sensitivity of 100%, specificity of 99.8%, PPV of 95.5%, and NPV of 100% compared with bedside BIO examination. Of the 608 infants enrolled in the SUNDROP program over 72 months, not a single case of TW-ROP went undetected as confirmed by bedside BIO, reinforcing the safety and efficacy of telemedicine screening in the identification of clinically significant ROP.
**ROP and Fluorescein Angiography**

Influence of Fluorescein Angiography on the Diagnosis and Management of Retinopathy of Prematurity

M Klufas, S Patel, M Ryan, MPatel Gupta et al Ophthalmology August 2015; 122(8) pp.1601-1608

Fluorescein Angiography (FA) has been found to be safe in children, including neonates with ROP. In eyes with ROP, FA may demonstrate changes in the peripheral retina not visible on clinical examination. Bedside fundus imaging for ROP is becoming more common, and bedside FA is now more accessible and may provide useful information. This is a prospective study of 16 eyes with ROP. Digital fundus photography and FA were performed and images were independently interpreted by 9 ROP experts (3 pediatric ophthalmologists, 6 retina specialists). The addition of FA to color fundus photography resulted in significant improvement in sensitivity for diagnosis of stage 3 or worse ROP (39.8% vs 74.1%), type 2 or worse ROP (69.4% vs 86.8%), and pre-plus or worse disease (50.5% vs 62.6%). Intergrader agreement improved significantly for ROP requiring treatment, but not for diagnosis of stage, zone, or plus disease. FA may lead to misinterpretation of Stage 2 as Stage 3, since vascular shunts in Stage 2 often show leakage on FA and hence mimic neovascularization. While the role of FA in the diagnosis of ROP remains unclear, further studies and standardization of FA images are needed to determine the usefulness of FA in the screening, diagnosis, and management of ROP.

**ROP and Anti-Vascular Endothelial Growth Factor Treatment**

Serum Levels of Vascular Endothelial Growth Factor and Related Factors After Intravitreous Bevacizumab Injection for Retinopathy of Prematurity


Concern exists for the possible systemic side effects from bevacizumab, a humanized recombinant monoclonal antibody against vascular endothelial growth factor (VEGF), which is effective in suppressing neovascularization of the retina and has been found useful in the treatment of advanced ROP. Possible effects of bevacizumab includes impact on neurodevelopment, so it is important to measure the systemic absorption of bevacizumab and determine how long it persists in the circulation. This was a prospective cohort study of 8 infants who developed Type 1 ROP and were treated with intravitreal bevacizumab. Serum levels of bevacizumab, VEGF and other growth factors such as erythropoietin, transforming growth factor, insulinlike growth factor 1, human angioptoin 1, human angioptoin 2, human angioptoinlike 3, and human angioptoin 4 were measured. The authors found a negative correlation between
serum levels of bevacizumab and VEGF which persisted even out to 8 weeks after injection. Study limitations include small sample size and serum determinations of these factors were not consistent across the cohort. An example is only one patient’s serum out of 8 patients in the study was evaluated at 8 weeks. Persistent levels of bevacizumab or suppressed VEGF could be possible beyond 8 weeks, but the study’ time period did not extend beyond 8 weeks so this question remains unanswered.

**Efficacy of Intravitreal Injection of Anti-Vascular Endothelial Growth Factor Agents for Stage 4 Retinopathy of Prematurity**


Established treatments for Stage 4 ROP include scleral buckling and vitrectomy, which interrupt vitreous traction but are associated with significant risks and adverse events. Intravitreal bevacizumab and ranibizumab have shown positive treatment effect for Stage 3+ ROP. This study investigated the efficacy of intravitreal injection of anti-VEGF agents for Stage 4 ROP. The retrospective case series included 13 eyes of 7 patients with Stage 4 ROP who received intravitreal bevacizumab (9 eyes of 5 patients) or ranibizumab (4 eyes of 2 patients, parents’ request). Two eyes of one patient had developed retinal detachment despite laser treatment elsewhere, and one patient required repeat injections because of persistent ROP in one eye and recurrent ROP in the other eye 21 weeks after the initial injection. The active neovascularization regressed and the final anatomical outcomes were ultimately favorable in all patients. Mean follow-up duration was 37.8 months (range 11.0-67.5 months). Three eyes had residual retinal fibrosis at peripheral Zone II or III at the end of follow-up, but all eyes attained retinal reattachment and full vascularization without additional vitreoretinal surgery. Macular contour was normal, and no apparent ocular or systemic adverse effects were noted. Although this study lacked a traditional vitreoretinal surgery comparison group, the authors conclude that anti-VEGF agent injection may be a possible alternative treatment option for these patients. However, attention must be paid to progressive fibrous contraction and late recurrence.

**Intravitreal Anti-Vascular Endothelial Growth Factor Treatment for Retinopathy of Prematurity: Comparison Between Ranibizumab and Bevacizumab**


Bevacizumab was the first anti-VEGF agent used for the treatment of ROP. Ranibizumab was later used for this purpose, with the aim of improved safety due to less systemic VEGF suppression. This retrospective study investigated the effect on disease regression, ROP recurrence, necessity of subsequent ablative procedures, and refractive status at 1 year of corrected age in eyes
treated with bevacizumab versus ranibizumab. 72 eyes of 37 patients had intravitreal injections of either agent as primary treatment for Type 1 ROP. The authors do not state how the particular agent was chosen. They report no differences in gestational age, birth weight, or postmenstrual age at the time of injection between the two groups, and no difference in the stage of disease, presence of plus disease, or rubeosis iridis. The ranibizumab group had a higher proportion of Zone 1 disease (26 vs 5%). All but 1 eye in the bevacizumab group had neovascularization and plus disease regression after intravitreal anti-VEGF treatment. This eye received laser treatment 3 weeks after the bevacizumab injection. At the end of the study period, all eyes in both groups had ROP regression and attached retinas, and no recurrence occurred in either group if the patient initially responded to anti-VEGF treatment. There was no difference in axial length, spherical equivalent, or astigmatism between the two groups. Most patients in both groups had minimal refractive error, but 6 eyes (14.6%) in the bevacizumab group and none in the ranibizumab group developed high myopia >-5.0D. The authors hypothesize that the sustained VEGF inhibition of bevacizumab may induce more apoptosis in the peripheral retina with subsequent dysregulation of emmetropization. A larger, randomized study with longer follow-up is needed to elucidate any differences in treatment outcomes between these two medications. Anterior segment biometry would be useful to determine the cause of myopia in some of these patients.

Reactivation of Retinopathy of Prematurity after Ranibizumab Treatment


This retrospective chart review identified 10 eyes of 6 patients that were treated with anti-VEGF therapy over a 2 year period at a single institution. Intravitreal anti-VEGF was offered in Zone 1 or posterior Zone 2 cases. Infants treated earlier during the course of the study received bevacizumab (4 eyes), and infants treated later received ranibizumab (6 eyes). The decision to switch to ranibizumab was due to its potentially lower systemic toxicity. All 10 eyes demonstrated initial regression of ROP. However, ROP reactivation occurred in 5/6 (83%) eyes treated with ranibizumab (mean treatment to reactivation interval = 5.9 weeks), whereas none of the 4 eyes treated with bevacizumab exhibited ROP reactivation. Due to a cardiopulmonary complication, one infant in the study received a ranibizumab injection in one eye only, but subsequent follow-up revealed symmetric regression of ROP in both eyes, suggesting a potential bilateral effect. This study is limited by its very small sample size and retrospective nature, but suggests that ranibizumab’s shorter half-life, while theoretically reducing systemic absorption, may also increase the chance of reactivation necessitating more frequent and longer follow-up.
Plasma Concentrations of Vascular Endothelial Growth Factor in Retinopathy of Prematurity After Intravitreal Bevacizumab Injection

Yoo Rha Hong, Young Ho Kim, Soo Young Kim, Gi Yup Nam et al. Retina 2015 Sept; 35:1772-1777.

Noting that VEGF is a key molecule involved in organ development in infants, especially during vasculogenesis, and also with processes of neurogenesis, these investigators sought to investigate the changes in plasma concentrations of VEGF, IGF-1, erythropoietin, pigment epithelium-derived growth factor, and IgG1 after intravitreal bevacizumab injection in infants with ROP. They enrolled 11 eyes from 6 patients who received intravitreal bevacizumab. 0.5 mL of blood was collected from each infant at preinjection and postinjection 1, 2, 3, 4, 5, 6, 7, and 8 weeks. The mean plasma VEGF concentration dropped precipitously by 1 week postinjection and did not return to the original level in any of the samples until 8 weeks postinjection. Mean plasma IgG1, erythropoietin, IGF, and PEDF concentrations did not change significantly during the interval between preinjection and any other follow-up time point. This period of plasma VEGF suppression is longer than that previously reported for one infant who received ranibizumab: VEGF concentration was lowest 3 weeks after injection but recovered to preinjection levels by week 4. These authors conclude that the reduction of plasma VEGF over a 7-week period could have negative developmental side effects, and anti-VEGF therapy should be considered with great caution for treatment of ROP in infants.


This study looked at structural outcomes, visual function, refraction, and frequency of follow-up visits for infants with type 1 ROP in zone I or zone II posterior treated with intravitreal bevacizumab (IVB) versus laser. Medical records over a 4.5 year period were reviewed retrospectively. The treatment groups were not randomized but were based on parental decision. IVB treatment occurred in 23 eyes of 13 infants and laser treatment was chosen in 22 eyes of 12 infants. No infants developed unfavorable structural outcomes. Monocular visual acuity was measurable in 15/23 IVB infants and showed a mean of 0.99 logMAR. 18/22 infants in the laser group had measurable monocular acuity and the mean was 0.71 logMAR. Of the eyes with measurable monocular acuity, favorable outcome was seen in 80% of the IVB and 100% of the laser treated infants. Mean myopia was -3.57 D for IVB and -6.39 D for laser treatment, and prevalence of myopia was 61% and 95% respectively. Average number of eye exams was 16 in the IVB group and 6 in the laser group. Although not randomized, this study points out some differences in results and follow-up between laser-treated and IVB patients.
Involution patterns of retinopathy of prematurity after treatment with intravitreal bevacizumab: implications for follow-up
M Isaac, N Tehrani and K Mireskandari
Eye 30: March 2016: 333-341

The authors conducted a retrospective review of 28 eyes of infants with type 1 ROP treated with bevacizumab 0.625 mg intravitreally at a single center over a 4 year time period. The patterns of ROP regression were described. 100% of plus disease had regressed by day 8 following treatment and 100% regression of both plus disease and stage 3 ROP had occurred by week 4 following treatment. Within the first 3 months of follow-up, 17 of 28 eyes demonstrated recurrence of stage one or two, but none required retreatment and none developed unfavorable structural outcome. At 24 months follow-up, 39% of the eyes were not fully vascularized into zone 3. The study confirms the need to follow these patients closely for long periods of time.

Intravitreal bevacizumab for retinopathy of prematurity: Considerations for informed consent
K Mireskandari, ME. Collins,
CAN J OPHTHALMOL VOL. 50( 6), DECEMBER 2015:409-412.

Beginning in 2007, results of a newer treatment modality involving the use of anti-vascular endothelial growth factor (VEGF) agents have been published. The introduction of any new treatment modality in the clinical setting can be done as part of routine clinical care. No treatment is expected to be perfectly safe and effective before being implemented. The risks and benefits of a new treatment should be at least comparable to the current gold standard. The BEAT-ROP study is compelling enough to state that, at least in the short term, Intravitreal Bevacizumab (IVB) results in better outcomes compared with laser and therefore should be considered part of routine clinical care in selected patients with zone I disease. Off-label use should be disclosed to families but cannot be considered exclusionary criteria for the use of IVB.

The following topics related to IVB during detailed consent process with parents of babies with ROP requiring treatment should include:
(1) Pathophysiology of ROP is explained to parents.
(2) The initial effect of IVB and laser on a baby is described.
(3) The results of ET-ROP and BEAT-ROP are reviewed.
(4) Local adverse events described.
(5) Data suggesting systemic absorption from IVB injection are shared.
(6) Because of the risk for late disease reactivation, patients receiving IVB must undergo dilated fundoscopy with scleral depression for a significantly longer period than neonates who receive conventional laser treatment for ROP.
(7) Limited data are available on long-term visual outcomes for ROP patients treated with IVB.
(8) No data is available on long-term systemic effects in patients treated with IVB.
(9) Bevacizumab is not approved for use in ROP by Health Canada or the US Food and Drug Administration.

ROP Epidemiology and Outcomes

Visual impairment due to retinopathy of prematurity (ROP) in New Zealand: a 22-year review
Z Tan, C Chong, B Darlow, S Dai
Br J Ophthalmol June, 2015;99:801-806

This is a retrospective review of medical records of children with moderate to severe visual impairment registered with the Blind and Low Vision Education Network New Zealand from 1991 to 2012. The purpose of the study was to evaluate the incidence of retinopathy of prematurity (ROP)-related visual impairment in New Zealand children. Two time periods were analyzed separately (1991–2004; 2005–2012) based on when the ETROP recommendations were implemented. Mean gestational age and mean birth weight were comparable between the two study periods. Over the study period, the annual incidence of new cases of visual impairment from ROP declined from 271.6 infants/100,000 (period 1) to 146.1 live very preterm births (period 2). As anticipated, improved medical management of these children between the two study periods was associated with a reduction in the incidence of infants with significant visual impairment from ROP in New Zealand. The study also concluded that the current ROP screening criteria, <31 weeks' gestation or <1250 g, is appropriate.

Long-term Outcomes on Lens Clarity after Lens-Sparing Vitrectomy for Retinopathy of Prematurity
E Nudleman, J Robinson, P Rao, K Drenser et al
Ophthalmology April 2015;122(4)pp.755-759

Retrospective chart review at a single tertiary referral pediatric vitreoretinal practice. 496 eyes from 351 patients with diagnosis of ROP stage 4A, 4B, and 5 who underwent lens-sparing vitrectomy (LSV) between 1992-2013 were included. LSV is performed to relieve vitreoretinal traction associated with advanced ROP. This has the advantage of reducing the risk of aphakic deprivation amblyopia or anisometropic amblyopia. The reattachment rate after a single LSV surgery was 82.1% for stage 4A, 69.5% for stage 4B, and 42.6% for stage 5. Subsequent retinal surgeries were required in 19.8% of eyes, with 88.7% of these including lensectomy. Among eyes requiring a lensectomy, 75% occurred within the first year after LSV surgery. Lens opacities were present in 26.6% of eyes at the time of lensectomy. Of all eyes in this series, 5.9% required lensectomy because of lens opacity. This study demonstrates that LSV for ROP

The authors report the ROP incidence in preterm babies during a 10-year period. Incidence was compared over two consecutive 5-year periods. 1565 babies met inclusion criteria. Overall incidence of any stage of ROP was 43.1% (35.3% 2004-2008 and 48.2% from 2009-2013). Stage 4 and 5 ROP decreased from 0.6% to 0.2%. There was no statistical difference between the periods for treatment needs. ROP data vary from country to country and this paper provides information of trends in Turkey with ROP incidence.


A twelve-year medical record review was performed. 137/4304 premature infants were treated for ROP. Mean gestational age was 25.9 weeks and mean birth weight was 776.5 grams. 44% had some degree of IVH. Treatment-requiring ROP increased from 1.05% in 2000 to 5.78% in 2011. Overall, for all live born infants <32 weeks there is a 1 in 25 probability of requiring treatment for ROP. This increases to 1 in 10 for gestational age <28 weeks. Of the 132 treated at one facility, 96% survived to discharge and 96% of treated eyes had a favorable outcome. More infants survived past 42 weeks gestational age, which was a factor in the increased treatment-requiring ROP. Also treatment guidelines changed during the study period. Small for gestational age infants were more likely to develop any stage of ROP.


This study compared single versus 2-session laser photoablation for flat neovascularization in cases with Zone 1 aggressive posterior ROP (APROP). Twenty-nine Asian Indian infants with APROP were randomized, and each eye
received 1 of 2 methods. Group A underwent single session laser to the avascular retina underlying the flat neovascularization by direct laser over the fronds. Group B underwent laser in 2 sessions: first, laser to the avascular periphery up to the flat neovascularization and 7 days later to the avascular bed exposed by the retraction of the fronds. Mean birthweight was 1,276 g and mean gestational age was 30.1 weeks. All eyes showed favorable outcome at a minimum 12-month follow-up. However, hemorrhages after laser were more common in Group A (41.4% vs. 17.2%), and large hemorrhages (>1 DD) seen in Group A took longer than 8 weeks to resolve and developed focal fibrosis. In many other studies the percentage of successful outcomes after laser in Zone 1 ROP is lower than the 100% favorable outcome in this study. The authors speculate several reasons for this difference, and also discuss the differing mean age and birthweight of their cohort compared to those reported in Western literature. Although patient populations may differ worldwide, this study compares 2 laser techniques for APROP using a head-to-head comparison of the two eyes in each infant randomized. Although both methods are successful, fewer hemorrhages, less fibrotic change, and faster resolution may be advantages of a staged laser treatment protocol.

**ROP - Other Topics**


Neutrophil-to-lymphocyte ratio (NLR) is a prognostic tool in numerous systemic inflammatory responses. The authors investigated serum NLR levels in ROP patients. This was a 2-year retrospective review of consecutive patients screened for ROP. 100 patients met inclusion criteria. Babies without ROP had a mean birth weight of 1442 g and a mean gestational age (GA) of 29.65 weeks. ROP babies had a mean birth weight of 1099 g and GA of 27.74 weeks. Clearly these two groups do not have the same baseline characteristics so the results of this study must be questioned since this could have caused the differences reported between the groups. NLR values were 0.67 in the ROP group and 0.32 in the non-ROP group. This difference was significant. Lymphocyte count was significantly lower in the ROP group 4.01 than in the non-ROP group 5.69. NLR values were no different between non-ROP, ROP with no laser and ROP with laser. However lymphocyte counts were lower in the two ROP groups when compared with the non-ROP group. The problem with this study is that we don’t know how NLR values and lymphocyte values change based on GA, regardless of ROP status. All that has been shown is a relationship not a causality. The authors claim that lymphocyte count measured in the first 24 hours of life may be an important predictor of ROP development is unproven as it may be the GA and birth weight which are actually the predictors.
Retinal nerve fiber layer thickness in prematurity is correlated with stage of retinopathy of prematurity K-A Park and S Y Oh
Eye 29: December 2015:1594-1602

The authors performed SD-OCT on 50 premature children and 58 full term normal controls. Exams were performed when the children were on average 7 years old when tested. The authors carefully controlled for age at exam and refractive error. When examining retinal nerve fiber layer (RNFL) thickness, the authors found that the stage of ROP showed a positive correlation with temporal RNFL thickness and an inverse correlation with nasal RNFL thickness. The authors suggest that there needs to be study to determine if function correlates to these structural findings.

Human Milk Feeding as a Protective Factor for Retinopathy of Prematurity: A Meta-analysis Zhou J, Shukla V, John D, Chen C
Pediatrics Dec 2015; 136: (6) e1576-e1586;

The aim of this meta-analysis was to pool currently available data on incidence of ROP in infants fed human milk versus formula published through February 2015. RESULTS: Five studies with 2208 preterm infants were included. Searches including various proportions of human milk versus formula, any-stage ROP, and severe ROP were defined to pool data for analyses. For any-stage ROP, the ORs (95% confidence intervals [CIs]) were as follows: exclusive human milk versus any formula, 0.29 (0.12 to 0.72); mainly human milk versus mainly formula, 0.51 (0.26 to 1.03); any human milk versus exclusive formula, 0.54 (0.15 to 1.96); and exclusive human milk versus exclusive formula, 0.25 (0.13 to 0.49). For severe ROP, they were 0.11 (0.04 to 0.30), 0.16 (0.06 to 0.43), 0.42 (0.08 to 2.18), and 0.10 (0.04 to 0.29), respectively. CONCLUSIONS: In very preterm newborns, human milk feeding potentially plays a protective role in preventing any-stage ROP and severe ROP.


A hypothetical model comparing digital imaging–based ROP detection strategies and serial ROP examinations. A hypothetical cohort of 650 infants with gestational age from 23 to 30 weeks were evaluated beginning at 32 weeks’ postmenstrual age (PMA) and continuing to discharge, transfer, or 40 weeks’ PMA. This study compares digital imaging–based ROP detection strategies versus serial ROP examinations. Although digital imaging decreased the number of ROP examinations per infant (#1065.5 vs. 1745.7), there was an increase in
the total number of interventions (ie, ROP examinations and imaging sessions: 1065.5 + 1786.2). Providing an ROP examination at the time of NICU discharge can significantly reduce the number of infants who require follow-up.

9. STRABISMUS

Quality of life and psychosocial issues surrounding strabismus

Reprint of: Social Phobia and Other Psychiatric Problems in Children with Strabismus

Community-based studies report the prevalence rate of strabismus at ~4% in Western countries and 1% in Japan and Israel. Social phobia prevalence estimates in the range of 0.5%-2.5% have been found in mixed samples of children and adolescents. These patients may have trouble with social anxiety, self-image, and interpersonal relationships. Children >6 years of age almost uniformly give a negative description of strabismic dolls and hesitate to play with them. The study group consisted of 42 patients followed-up for strabismus in the Eye Outpatient Clinic of Inönü University, Turgut Ozal Medical Center. The strabismus group consisted of children with constant comitant esotropia or exotropia, with a deviation at distance >30Δ. In addition, any patient in the strabismus group that had decreased visual acuity as the result of amblyopia or any other reason was allowed in the study. Sixteen (38.09%) patients had exodeviation and 26 (61.01%) had esodeviation. Exclusion criteria were the current use of any medication due to a psychiatric disorder, and the presence of any organic disorder or mental retardation that might affect the psychiatric assessment. The Children's Depression Inventory (CDI), which was completed by the child, was used to rate symptoms of depression. The CDI is a self-rating scale that consists of 27 items scored on a 3-point scale (0, absent; 1, moderate; 2, severe) reflecting growing severity of symptoms. Large angle strabismus is perceived as a negative characteristic and that the presence of strabismus could have a potentially detrimental impact on the school lives of children. They found a significantly higher social phobia score in child strabismus patients than in sex- and age-matched control subjects. Satterfield et al. reported that depression and anxiety were higher in children with strabismus than the control group. The levels of depression and anxiety were high in strabismic children in their study (especially for social phobia, school phobia, and separation anxiety). The negative influence of these children’s appearance on others, their externalization from social environments by their friends because of their appearance, and the neglect they suffer increase the child’s anxiety and psychiatric problems while reinforcing social fears.
Evaluation of the Intermittent Exotropia Questionnaire Using Rasch Analysis

Quality of life questionnaires are useful instruments to assess the impact of disease on a patient’s quality of life. The authors reassess a previously developed and validated instrument, the intermittent exotropia quality of life questionnaire, using a psychometric technique called Rasch analysis. This model analyzes categorical data based on the following assumptions: that responses on the questionnaire reflect a trade off of the respondents’ personality traits, abilities and attitudes against the difficulty of the items on the questionnaire. The authors administered the questionnaire to 575 patients and their parents with intermittent exotropia. Based on Rasch analysis, the authors eliminated a few items from the 12 item questionnaire based on frequency of responding at floor (a lot or almost always) versus ceiling (not at all or almost never). The authors encourage readers to download the questionnaire from http://pedig.jaeb.org

Quality of Life in Adults With Strabismus

This article assessed the quality of life in patients living with strabismus. This was a retrospective cohort study, which asked 42 strabismus patients over the age of 50 the 25 questions on the National Eye Institute Visual Functioning questionnaire (which contains 25 questions). These patients were compared to patients with diabetes, ARMD, glaucoma, cataract and CMV. The strabismus patients had a median binocular vision of 20/20. The other groups all had median vision of 20/40 or better except AMD (20/63) and low vision (20/252). Strabismus patients performed the same or worse than all of these categories except low vision patients. Interestingly, on the peripheral vision subscale, strabismic patients performed similar to glaucoma patients. Decreased quality of life in strabismic patients may be related to both functional and psychological factors. 81% of strabismic patients had diplopia; diplopia has been associated with decreased quality of life using the NEI VFQ-25 and Adult-strabismus-20 scales. This study provides important information about the functional deficits associated with strabismus in adults, and that repair of strabismus is not cosmetic.
Effectiveness of Strabismic Surgery on the Health-Related Quality of Life Assessment of Children with Intermittent Exotropia and their Parents: a Randomized Clinical Trial

This study evaluates whether corrective strabismus surgery could improve health-related quality of life in children with intermittent exotropia 8-17 years of age and their parents. This was a prospective, parallel-arm, open-label, randomized, controlled clinical trial, which recruited patients over a 3-year period. Children and parents completed the intermittent exotropia questionnaire (IXTQ). They were randomized to surgery or monitoring. 130 patients were enrolled and randomized into equal sized groups. The study was completed by 63 of the surgical patients and 57 of the monitoring patients. Surgery improved IXTQ scores for the child, parental proxy, and parent at 3-months postop. In the monitoring group, child IXTQ scores remained unchanged, but parent proxy and parent scores declined. Improvements were found in the function, psychosocial and surgery subscale scores. Interestingly surgical success or failure did not alter the improvement in IXTQ scores. It appears that the decision to pursue surgery has important quality of life effects, regardless of the actual motor surgical result. Some of this may be because even those who failed from a motor standpoint had improved deviations but some may be the assumption of an improved state. Conversely, the lack of treatment has negative effects on the parent. Other factors might have included a subconscious desire to justify the decision to have the child undergo surgery and the need for this choice to have been beneficial, and also the child and parent may have felt obligated to report improvement to the member of the treating team who administered the questionnaire. The results of this study are fascinating, less from the standpoint of surgical results, but more from the standpoint of child and parent expectations. What makes a family happy may not be the same as what a clinician considers success.

Prevalence of Mental Health Illness among Patients with Adult-Onset Strabismus
Hassan MB, Hodge DO, Mohney BG. Strabismus September 2015;23(3):105-110

This is a retrospective chart review of patients diagnosed as adults with convergence insufficiency (CI) \((n = 118)\), divergence insufficiency (DI) \((n = 80)\), and small angle hypertropia (HT) \((n = 99)\) in Olmsted County, Minnesota. Each case was compared with a sex- and birth date-matched non-strabismic control. The medical records were reviewed for mental health diagnoses. Adults with DI were found to have a higher number of psychiatric-related hospitalizations and psychotropic medication use (both number and length of time), and were also diagnosed with unspecified anxiety disorder more than their controls in this population-based study. Adults with HT had a higher rate of generalized anxiety disorder, while adults with CI had no increased risk of mental health illnesses compared to controls.
The authors conclude that adults with DI and HT appear to have an increased risk of mental illness.

**Detection of Strabismus by Non–Health Care Professionals in an Ethnically Diverse Set of Images**

This paper wanted to discover the threshold at which strabismus becomes detectable to the lay observer, and whether this threshold is different in study subjects of various ethnicities. Twelve healthy subjects (black, white and Asian) with no strabismus had their photos taken, and then the photos were digitally altered to reflect different magnitudes of strabismus, from 21 prism diopters of esotropia to 21 prism diopters of exotropia. One hundred twenty adult non-healthcare volunteers were asked to state if the person in the image had strabismus. The main outcome measure was 70% positive detection rate. The authors found that exotropia was easier to detect than esotropia. Many orthotropic Asian models were thought to be esotropic.

**Importance:** This interesting paper identifies disparities in the identification of strabismus based on race. Understanding different perceptions of strabismus based on one’s race will help inform the surgeon’s discussion with the patient about the impact of their misalignment. Patient satisfaction after surgical alignment may also be nuanced by his/her race, and needs to be considered in quality and outcome measures of strabismus surgery.

**Strabismus – double vision, binocular vision and visual perception**

**Space Perception of Strabismic Observers in the Real World environment**

Space perception beyond the near distance range (>2 m) is important for target localization, and for directing and guiding a variety of daily activities, including driving and walking. However, it is unclear whether the absolute localization of a single target in the intermediate distance range requires binocular vision, and if so, whether having subnormal stereopsis in strabismus impairs one’s ability to localize the target. The authors investigated this by measuring the perceived absolute location of a target by observers with normal binocular vision (n = 8; mean age, 24.5 years) and observers with strabismus (n = 8; mean age, 24.9 years) under monocular and binocular conditions. The observers used the blind walking-gesturing task to indicate the judged location of a target located at various viewing distances (2.73-6.93 m) and heights (0, 30, and 90 cm) above
the floor. In this procedure, the observer is asked to judge the target distance and to respond by walking briskly in blindfold to where he/she judged (remembers) the target to be located. Blindfolding prevents visual feedback and walking briskly minimizes introspection, thus, providing a measure of visually-directed response. This study added the extra action of judging the height of the target. Near stereopsis was assessed with the Randot Stereotest. Both groups of observers accurately judged the absolute distance of the target on the ground (height = 0 cm) either with monocular or binocular viewing. However, when the target was suspended in midair, the normal observers accurately judged target location with binocular viewing, but not with monocular viewing (mean slant angle, 0.8° ± 0.5° vs. 7.4° ± 1.4°; P < 0.001, with a slant angle of 0° representing accurate localization). In contrast, the strabismic observers with poorer stereo acuity made larger errors in target localization in both viewing conditions, though with fewer errors during binocular viewing (mean slant angle, 2.7° ± 0.4° vs. 9.2° ± 1.3°; P < 0.0025). The authors concluded that monocular depth information is sufficient for locating a single target on the ground, but binocular depth information is required when the target is suspended in midair. Since the absolute binocular disparity information of the single target is weak beyond 2 m, they suggest the visual system localizes the single target using the relative binocular disparity information between the midair target and the visible ground surface. Consequently, strabismic observers with residual stereopsis localize a target more accurately than their counterparts without stereo ability. Some drawbacks to the study include that some of the patients’ stereoacuity was only tested at near, while the study looked at localization at intermediate distances. Also, it is possible some of the patients may have been previously treated for amblyopia and this prior amblyopia could have some effect on the study results. However, this study is the first to demonstrate that strabismic patients with subnormal stereopsis have impaired localization of midair targets at intermediate distances.

Asthenopia, Associated Phoria, and Self-Selected Prism

A commonly held view is that heterophorias can cause asthenopia or “eye strain” and prisms may be a remedy. In this prospective study, the authors evaluated the correlation between heterophorias and discomfort on reading. Forty subjects were included: 20 who reported strain on prolonged reading (“asthenopes”) and 20 who did not (“non-asthenopes”). Associated phoria (AP) was determined by asking subjects to align monocular markers in the Mallett Near Vision Unit. Subjects also adjusted Risley prisms so that viewing appeared most relaxing while looking at fusionable pictures (self-selected prism = SSP). Both AP and SSP were determined at near. Each subject participated in 6 sessions. Before each session, the subjects read for 30 minutes and indicated on a visual analogue scale the discomfort they had experienced. Results showed that
neither AP nor SSP were significantly larger in the asthenopes than in the non-
asthenopes, and the magnitude of discomfort was not significantly correlated to
AP or SSP. Asthenopes who rated their discomfort higher did not have a larger
heterophoria. The authors concluded that the lack of significant correlation
between discomfort and heterophoria (determined as AP or SSP), especially
intra-individually among repeated measurements, does not support a causal
relationship. However, their data does not determine whether some asthenopes
may benefit from prismatic correction.

The Scotogenic Contact Lens: a Novel Device for Treating
Binocular Diplopia
99: 1022-1024

The authors have devised a novel soft contact lens for diplopia that occludes
centrally and degrades vision gradually in a manner that correlates with the low
spatial sensitivity in the peripheral field. In effect, this contact lens allows for
occlusion without reducing peripheral vision. In this study, the investigators
compared 12 healthy adults and 12 adults with binocular diplopia. Healthy
volunteers were induced to have diplopia by wearing Fresnel prism over one eye.
The study participants were then asked to either wear the scotogenic contact
lens or a patch. The outcomes of the study were assessed through a
questionnaire and using Estermann perimetry. The results show that diplopia
was effectively abolished in both groups. Peripheral vision was preserved in the
contact lens group. Satisfaction was also higher in the contact lens group. This
may be a nice tool in dealing with diplopia especially in patients who do not wear
glasses or have torsional diplopia.

Torsional Diplopia A. Miller Am Orthopt J. August 2015;65:21-5.

The author reviews etiologies of torsional diplopia including excyclotorsion
associated with superior oblique palsy, incyclotorsion associate with thyroid
orbitopathy with or without previous orbital decompression or strabismus surgery,
excyclotorsion associate with skew deviation and others. Assessment of torsion
by fundus examination and by using dissociative and non-dissociative modalities
such as double Maddox rods, Lancaster red-green test, Hess screen,
ambyloscope and Bagolini lenses are briefly described. Some surgical and non-
surgical management strategies are described.
Evaluation of Sensory Dominance Using Binocular Rivalry as Related to Ocular Deviations  M. Ito, K. Shimizu, T. Handa  

This prospective observational cohort study aimed to evaluate sensory dominance in 63 patients with strabismus. Ocular dominance is most simply tested by having a patient view a distant object through an aperture small enough to permit only monocular viewing of the object and determining which eye the patient choses to view the object. Sensory dominance testing aims to determine ocular dominance during simultaneous binocular viewing of 2 different stimuli. Sensory dominance may have correlation with monocular suppression in patients with strabismus. The authors used an experimental device to measure sensory dominance in patients with exophoria, intermittent exotropia and constant exotropia. All patients had 20/20 visual acuity in each eye. Patients with X(T) and XT had strong sensory dominance and those with exophoria had weak sensory dominancy. Future work may include comparing this method of assessment with methods that have been used to detect suppression in other studies. The authors conclude by hypothesizing that the new device may, in the future, be an objective method of quantitating the degree of suppression in patients with strabismus.

Comment: This is not an exhaustive discussion on torsional diplopia but there are several clinical pearls in this paper such as: 1) consider the technique that is used to measure torsion since the greater the test disassociation, the less cyclo-fusion plays a part and the greater the torsion that will be measured, 2) inferior oblique palsy and skew deviation may look similar except for the torsion which is incyclotorsion and excyclotorsion, respectively, 3) in thyroid disease, incyclotorsion may occur with superior oblique muscle involvement, following disinsertion of the inferior oblique during orbital decompression or following recession of a restricted inferior rectus.

Clinical Assessment of Stereoacuity and 3-D Stereoscopic Entertainment  
Tidbury LP, Black RH, O’Connor AR. Strabismus December 2015;23(4):164-169

Clinicians are frequently asked what the results of a stereoacuity test mean in relation to 3-D entertainment. In an attempt to answer this question, the authors vary the amount of stereopsis in 57 subjects (aged 16–62 years), and assess their perception of depth. Monocular blur was used to vary interocular VA difference, creating 4 levels of measurable binocular deficit from normal stereoaucuity to suppression. Stereoacuity was assessed at each level using the TNO, Preschool Randot®, Frisby, the FD2, and Distance Randot®. Subjects also completed an object depth identification task using the Nintendo 3DS, a static 3DTV stereoacuity test, and a 3-D perception rating task of 6 video clips.
As interocular VA differences increased, stereoacuity decreased (eg, 110", 280", 340", and suppression). The ability to correctly identify depth on the Nintendo 3DS remained at 100% until suppression of one eye occurred. The perception of a compelling 3-D effect when viewing the video clips was rated high until suppression of one eye occurred. These data suggest that if there is any measurable stereoacuity, the perception of 3-D when viewing stereoscopic entertainment will be present. The presence of motion in stereoscopic video appears to provide cues to depth, where static cues are not sufficient. The authors indicate the need to develop a dynamic test of stereoacuity, to allow full assessment of patients with binocular vision problems.

**Improvement in Binocular Summation After Strabismus Surgery**


Binocular summation (BiS) refers to improved visual function measured with both eyes open, compared with the visual function of testing the better seeing eye alone. There are normative values for BiS and this value decreases with age and reduced visual acuity. Testing for BiS with low versus high contrast sensitivity letters also impacts a subject’s score. Binocular inhibition refers to impaired binocular summation and is postulated to be the cause of complaints among patients with strabismus such as occasional preference to close 1 eye, despite a lack of diplopia. The authors seek to determine in a cohort of strabismus patients if binocular summation improves after strabismus surgery. Ninety patients with strabismus of a variety of etiologies were enrolled. The mean age was 35 years old. Seventy-five of the 90 patients met criteria for surgical success. BiS improved overall for low contrast letters postoperatively. At the lowest contrast level, mean BiS improved from a negative value, signifying binocular inhibition to a positive score, suggesting there may be functional benefits to strabismus surgery beyond improved stereopsis, visual field normalization, and psychosocial concerns.

**Preoperative Factors Affecting Stereopsis after Surgical Alignment of Acquired Partly Accommodative Esotropia**

Iordanous Y, Mao A, Makar I. *Strabismus* December 2015; 23(4):151-158

Despite successful ocular realignment, many strabismus patients never develop stereopsis. This retrospective review of 57 patients who underwent successful surgery for acquired partially accommodative esotropia (APAET) compared preoperative factors between patients achieving postoperative stereopsis of ≥100 seconds of arc versus <100 seconds of arc. Twenty-four (42%) had a final stereopsis of ≥100 seconds of arc. The mean age of onset of esodeviation for patients attaining stereopsis of ≥100 seconds of arc was 31.8 months, versus 23.9 months (p = 0.012) for patients with <100 seconds of arc. Duration of constant misalignment was not significantly different between the two groups.
(30.1 months for ≥100 seconds of arc versus 27.3 months; \( p = 0.57 \)). A multivariate regression analysis found older age of onset to be the only predictive factor for achieving better postoperative stereopsis (odds ratio 1.065, 95% CI: 1.014–1.118).

The authors conclude that older age of onset appears to be the strongest predictor for developing postoperative stereopsis in APAET. Patients with an age of onset >36 months tend to have better outcomes. Duration of misalignment and age at surgery did not have a significant impact on postoperative stereopsis. This information may be helpful when counseling patients regarding the potential for functional improvement following surgery.

**Factors Affecting Improvement of Stereopsis Following Successful Surgical Correction of Childhood Strabismus in Adults**
Andalib D, Nabie R, Poormohammad B. *Strabismus*. July 2015; 23(2): 80–84

This prospective study evaluated the factors affecting improvement of stereopsis following successful surgical correction of childhood strabismus in adults. Thirty-four patients (20 exotropes and 14 esotropes) with childhood-onset, comitant, horizontal, constant strabismus; absent stereopsis in TNO; and with postoperative alignment within 10 prism diopters of orthotropia were enrolled. The mean age at the time of surgery was 26.08 ± 10.53 years. Stereopsis testing using the TNO stereo was improved in 8 of 34 patients (23.5%). 38.1% of patients who had orthotropia gained stereopsis, whereas none of patients who had horizontal heterotropia (esotropia or exotropia) of 10 PD or less gained stereopsis. Misalignment of 10 years’ duration or longer did not preclude the development of postoperative stereoacuity. There was a statistically insignificant increase in improvement of stereopsis in nonamblyopic group (30.4%) compared with amblyopic group (9.1%) \( (p = 0.22) \). Also, there was a statistically insignificant increase in improvement of stereopsis in exotropes (35%) compared with esotropes (7.1%) \( (p = 0.1) \). The angle of preoperative deviation had no influence on improvement of stereopsis. The authors concluded that postoperative correction of orthotropia was the only predictive factor for improvement of stereopsis in adults with childhood strabismus. The main limitation of the study is the lack of follow-up beyond 3 months.

**Extraocular muscle anatomy**


Compartmentalization has been recognized as a feature of extraocular muscles. Recently Le and Assoc suggested the same theme of compartmentalization to
the SO muscle. The trochlear nerve bifurcates into two branches, a medial and a lateral. The authors wondered if the SO when impaired by a trochlear lesion might show compartmental atrophy. Prospective observational study that looked at SO cross section in normal patients and in SO palsy under MRI. 12 normal eyes were studied. 62 patients were recruited that had been determined to have unilateral SO palsy. 18 were considered congenital, 20 traumatic and 24 idiopathic. Mean symptoms lasted around 57 months. All palsied muscles showed significant atrophy by MRI. However, there were 2 different general shapes of the atrophic cross section. It was found that the major and minor axes, cross sectional area, and volume of SO belly were subnormal. The elongate oval shaped SO belly was consistent with palsy of only 1 compartment while the round uniform SO belly was consistent with palsy of both compartments. Further study is needed to see if differences in response of these two patterns to SO palsy surgery.


The authors evaluated the possible effect on the macula of a mechanical force exerted by the inferior oblique muscle. Macular and choroidal thickness measurements obtained by enhanced depth imaging spectral domain optical coherence tomography (EDI SD-OCT) were compared between inferior oblique overaction patients and healthy control subjects. 24 eyes of 24 IOOA subjects were included with a mean age of 7.6 years. There were 25 control patients with a mean age of 9.1 years. There were no morphological abnormalities of the macula in either group. There were no differences in subfoveal macular thickness or choroidal thickness in IOOA patients compared to healthy patients. Statistically significant differences were found in subfoveal choroidal thickness between severe IOOA (thinner) patients and healthy controls. IOOA subgroups were small and there was an age difference between control and IOOA patients. The authors evaluate what role if any, the inferior oblique muscle may have on macular dysfunction.


This study evaluated the accuracy of AS-OCT in measuring the distance from the limbus to rectus muscle insertion compared to intraoperative measurements. 65 muscles of 38 patients were included, including 9 reoperations. 55/56 virgin muscles were successfully imaged and 7/9 reoperations were as well. The two reoperations with measurements that were unobtainable were due to scarring and difficulty differentiating the muscle layer from sclera. The average difference between the AS-OCT measurement and surgical measurement was 0.43mm.
98.4% of measurements were within 2 standard deviations. 90.3% were within 1 mm. This noninvasive imaging procedure could help with preoperative strabismus management.

**Ultrasound Biomicroscopy in Strabismus Surgery: Efficacy in Postoperative Assessment of Horizontal Muscle Insertions**

This double masked prospective study evaluated the efficacy of ultrasound biomicroscopy (UBM) in assessment of extraocular muscle insertion sites after strabismus surgery. It included 16 eyes of 15 patients with deviation <60 prism diopters who underwent primary horizontal strabismus surgery. Preoperative muscle insertion was measured by UBM and compared with intraoperative measurement by caliper. Postoperatively muscle insertion was remeasured by UBM and compared with intraoperative measurement by caliper taken after repositioning the muscle insertion. Clinically limits of agreement of ± 1 mm were taken as acceptable. Results showed that UBM accurately measured preoperative MR muscle insertion in 100% of cases and LR muscle insertion in 87.5% of cases. Post–op UBM at 3 months could visualize new muscle insertion in 100% of operated MR muscles and 50% of operated LR muscles. However, accuracy could be achieved only in 78.6% of cases for MR muscle and for LR in 62.5% of cases (among LR muscles that were visible post-op). Maximum distance posterior to the limbus that the UBM was able to detect MR was 11.2 mm and for LR was 13.5 mm. The authors concluded that UBM does not accurately for predict muscle insertion postoperatively, which is in contradiction of previous reports, and should not be relied upon for surgical decision making in re-operations, the only situation where it is likely to be considered useful by clinicians.

**Strabismus – Superior oblique palsy**


PURPOSE OF REVIEW: This review discusses recent advances in our understanding of the pathology, diagnosis, and treatment of congenital fourth nerve palsies through the use of high-resolution MRI neuroimaging. RECENT FINDINGS: High-definition MRI can now more accurately image the trochlear nerve and has increased our understanding of the pathology of fourth nerve palsies. A more sensitive two-step test is proposed to replace the three-step Parks-Bielschowsky test. High-resolution MRI studies have shown that the majority of congenital superior oblique palsies have an absent trochlear nerve
and atrophic superior oblique muscle resulting in earlier onset and more severe head tilt. Superior oblique tuck combined with inferior oblique recession is a very effective way of eliminating head tilt secondary to congenital fourth nerve palsies with a low incidence of secondary Brown syndrome.

**Strabismus – Childhood XT and ET**

**Intermittent Exotropia and Accommodative Esotropia: Distinct Disorders or Two Ends of a Spectrum? (Editorial)**
Brodsky M. Jung J. *Ophthalmology*. August 2015; 122(8): 1543-1546

Discussion of “phoria adaptation” and its influence in intermittent exotropia (IXT) and accommodative esotropia (AET). Phoria adaptation occurs independently of the immediate vergence system and minimizes the need for vergence control of a deviation. This is responsible for tenacious proximal fusion in IXT which causes the near deviation to be smaller. Conversely, phoria adaptation in AET causes tenacious distance fusion and a larger near deviation. The effects of phoria adaptation become admixed with those of disparity-driven nonaccommodative convergence in IXT and blur-driven accommodative convergence in AET. The authors suggest that IXT and AET exist on a spectrum of disparity-driven convergence accommodation (IXT) to blur-driven accommodation convergence (AET). Phoria adaptation also explains how a distance-near disparity in AET can be managed effectively with medial rectus recessions to target the near esodeviation without overcorrecting a much smaller distance esodeviation.

**A Randomized Trial Comparing Part-time Patching with Observation for Intermittent Exotropia in Children 12 to 35 Months of Age**

Multicenter, randomized clinical trial to determine the effectiveness of part-time patching for treating intermittent exotropia (IXT) in young children. 201 children (ages 12 to 35 months) with IXT. Study criteria were (1) IXT at distance or constant exotropia at distance and either IXT or exophoria at near AND (2) 15-prism diopter (PD) or more exodeviation at distance or near by prism and alternate cover test (PACT) but at least 10 PD exodeviation at distance by PACT. Patients prescribed patching for 3 hours daily for 5 months followed by 1 month of no patching. Control group assigned to observation. 177 patients (88%) completed the 6-month primary outcome examination. Motor deterioration over 6 months was uncommon with or without patching. Motor deterioration (defined as constant XT of \( \geq 10 \) PD at distance and near by SPCT) occurred in 4/87 participants (4.6%) in the observation group and 2/90 (2.2%) in the patching group. The difference was not significant enough to recommend part-time...
patching for treatment of IXT in this age group. These findings may reassure clinicians who believe immediate surgical intervention is necessary to prevent IXT from becoming constant.


This study evaluated the performance of each of a series of specific averaged measures of control of intermittent exotropes. It also defined thresholds for determining change in control over time. A simulated dataset of control scores for 10,000 hypothetical patients based on actual clinical data was created. 152 patients were identified with 2 measures of distance control in a single clinic examination. 84 of these patients had additional exams with 2 measures of control. A Monte Carlo simulation model was created. 95% limits of agreement for a single control score was 2.60, for 3 scores- 1.76 and for an average of 6 scores was 1.28. For less severe initial scores (0,1 or 2) and triple control scores the 95% LOA was 1.33. For more severe initial scores (3, 4 or 5) the 95% LOA was 1.77. Multiple control scores reduce variability, which better allows an assessment of change over time. 6 average scores was not felt to be clinically practical by the authors so they recommend 3 scores. Variability was also lower on the less severe end. Having a true sense of the level of control of intermittent exotropes in one office visit has always been problematic, and the authors attempt to define a minimum standard to improve reliability of the evaluation.

Tenacious Proximal Fusion: The Scobee Phenomenon

This prospective observational study of 10 patients with intermittent exotropia with tenacious proximal fusion (exotropia at near fixation that less than at distance fixation that increases following 1 hours of monocular occlusion) evaluates the effect of the nasal visual field on control of the exotropia at near fixation. The author hypothesizes that the image disparity located on the binasal retina is in part responsible for the control of exotropia at near fixation. The author constructed a device with two 8.5 x 11 inch cardboard panels (one with random letters and the other with small pictures) which were present adjacent to the near target while measuring the exotropia at near. The panels essentially filled the patient’s peripheral vision and presented the same images to the nasal retina of one eye and the temporal retina of the contralateral eye. The purpose was to test the effect of disrupting the usual binasal peripheral retinal stimulation and measure the effect on ocular alignment. Under test conditions using the device, there was a statistically significant increase in the measured angle of exotropia over normal examination conditions; however, the angle of exotropia
was significantly greater following 1 hour of monocular occlusion than when measured using the device without occlusion. The author concludes that normal binasal image disparity contributes but does not fully explain the smaller angle of exotropia at near than at distance in patients with tenacious proximal fusion.

The Long-Term Outcomes in Children Who are Not Compliant with Spectacle Treatment for Accommodative Esotropia. Hussein M, Weakley D, Wirazka T, Paysse E. J AAPOS April 2015; 19(2): 169-171

The authors evaluated the long-term sensory and motor outcomes of children who initially had pure accommodative esotropia and who were noncompliant with spectacle wear. 14 years of medical records were retrospectively reviewed. 82 patients met inclusion criteria. Mean follow-up was 61.4 months. 48/82 had good compliance, with glasses-wear, 25/82 were fair, and 9/82 were poor. Complete lack of stereopsis was seen in 42%, 84% and 89% of the good, fair and poor groups respectively. Poor motor outcomes were seen in 21%, 52% and 78% of the good, fair and poor groups respectively. The fair and poor groups showed a statistically significant greater chance of poor motor and sensory outcomes. This study was retrospective, had no control group, and potential for inaccuracy regarding spectacle compliance. Also the poor wear group was small in subject number, which could skew data. The data reported herein can be used by strabismus specialists to further support the need for good compliance with spectacle wear in accommodative esotropes.

Strabismus – Convergence insufficiency


Retrospective review of 118 adults diagnosed with adult-onset convergence insufficiency (CI) over a 20-year period in Olmsted County, Minnesota. Management data was available on 105 patients. CI constituted 15.7% of all adult-onset strabismus in this population. The prevalence of CI was 1.38% and the incidence increased with increasing age. Median age at diagnosis was 68.5 years (range 21.7-97.1) and 68 (57.6%) were female. Mean initial exodeviation was 14.1 PD at near (range 1-30) and 1.7PD at distance (range 0-10). The Kaplan-Meier rate of exotropia increasing over time by 7PD or more at near was 4.2% at 5 years, 13.5% at 10 years, and 24.4% at 20 years. Most patients were managed conservatively with 92 (88%) patients treated with prisms, 9 (9%) patients with CI exercises, and only 4 (3.84%) patients with surgery. Limitations of this study were lack of a control group and rare documentation of near point of convergence (NPC). Diagnosis was therefore based primarily on distance-near
disparity of deviation. Lack of NPC in most patients is a very important limitation as it likely led to an overestimation of CI in this study.


This study evaluated the efficacy of home-based Computerized Vergence System (CVS) therapy for children with symptomatic convergence insufficiency (CI). This was a retrospective review of patients from 2006 to 2014. Therapy was 15 minutes or less a day, 5 days per week. There were 186 participants with a mean age of 9 years who underwent therapy for an average of 18 weeks. 139 participants had full data. Near point of convergence (NPC) and near convergence amplitudes (NCA) improved significantly. Prior to treatment, 39% reported diplopia and 98% reported asthenopia. At final office assessment, 92% of patients were asymptomatic. Asymptomatic patients did not have better NPC scores compared to symptomatic patients, but they did have significantly higher NCA scores. Near deviations also improved with therapy. The authors felt that post-treatment NCA scores predict clinical success. This was an unmasked study with no control group. Subjective complaints were not quantified.


This is a prospective, randomized observational study of 118 patients aged 9-18 years aimed at evaluating the specificity of the Convergence Insufficiency Symptoms Survey (CISS) as a diagnostic tool. Previous studies have evaluated the CISS in patients previously diagnosed with CI. In this study, 74 subjects had normal binocular vision, 26 had CI and 18 had “partial CI” (meeting fewer than 3 diagnostic CI criteria). The mean CISS scores for the CI group and normal binocular vision group were 12.3 (range 3 to 28) and 14.1 (range 0 to 43), respectively (p=0.32). The authors concluded that the CISS is not an accurate independent tool for diagnosing CI since there was great overlap in the scores of the CI group and normal binocular vision group. The authors reference other papers validate the CISS for use in grading severity of CI once the diagnosis has been made using other clinical means.

**Convergence Insufficiency Symptom Survey Scores for Reading Versus Other Near Visual Activities in SchoolAge Children**


This comparative validity analysis of diagnostic tools to see the difference in
convergence insufficiency symptom survey for reading vs. favorite near visual activities. 100 children were given a survey emphasizing reading vs their favorite near task. They found in this group of 100 children between the ages of 9-18, there was a significant increase in symptoms when the survey asked about reading difficulties vs playing their favorite near task. (Score of 14.1 vs. 6.7) The study concluded that by emphasizing reading, the CI symptom survey may falsely elevate the visual symptoms and overestimate the problem.

**Strabismus – Acquired**


This was a retrospective review to determine the incidence and characteristics of strabismus in NF-1 optic pathway glioma (OPG) patients. This was a 24 year retrospective review from a tertiary referral center. Twenty-two of 76 patients with OPG had strabismus with a mean follow-up of 9.6 years. Of the 22 patients with strabismus, 12 had strabismus at initial presentation and in 3 this was the initial presenting problem. Of the 22 with strabismus, 17 had exotropia (of whom 10 also had vertical deviations). Seven patients also had proptosis (of whom six had a hypotropia in addition to horizontal strabismus). Sensory strabismus was present in 16/22 with vision worse than 20/200 n the OPG-affected eye. Of these, 15/16 had exotropia. Stereovision was present in 5/22 patients. Five patients underwent strabismus surgery but only one had a successful result. This high incidence rate makes thinking of this diagnosis important, especially in the setting of combined vertical-horizontal strabismus

**Heavy Eye Syndrome versus Sagging Eye Syndrome in High Myopia** Tan RJD, and Demer JL. *J AAPOS* December 2015;19:500-506.

The authors sought to differentiate sagging eye syndrome (SES) versus heavy eye syndrome (HES). Medical records and orbital MRIs of highly myopic adults seen for acquired strabismus over a 12-year period were reviewed. Eleven highly myopic subjects were divided into HES and SES groups based on anatomical findings on MRI. HES group consisted of 8 orbits of 5 subjects and the SES groups consisted of 12 orbits of 6 subjects. HES patients had severe superotemporal globe prolapse with displacement of the LR inferiorly and the SR medially. The LR-SR band was thinned (n=6) or ruptured (n=2). SES demonstrated inferior displacement of the LR and degeneration (thinned n=7, ruptures n=5) of the LR-SR band but no globe prolapse. The superior rectus pulley was displaced 2.6mm more medially in HES than in SES. The lateral rectus pulley was 1.0mm higher and 1.2mm more medial in HES than in SES. The mean SR-LR angle in HES was 121’ and in SES it was 104’ which was a
significant difference. Mean axial length was equal between the two groups. All
HES patients had esotropia and hypotropia (average 61 PD esotropia and 26 PD
hypotropia). All 8 had supraduction limitation and 5/8 had abduction limitation.
SES patients had much smaller vertical and horizontal deviations (average 23PD
esotropia and 2PD hypotropia). Limited supraduction as present in 8/12 and all
had full abduction. These distinctions are important because the surgical
treatment of these two conditions is different and the authors recommend
preoperative imaging to help distinguish between these two conditions

Evaluation and Prism Management of Divergence Insufficiency

The author of this review article provides a good discussion of orthoptic
evaluation of divergence insufficiency. Some examination pearls described were:
1) test ocular alignment with patient fixating on an object beyond 20 feet if
esotropia is not seen in the exam lane, 2) place a red filter of one eye to
dissociate to reveal esodeviation not otherwise seen. Prism pearls included
correcting for manifest deviation with base out prism then refining the prism
correction increasing (or decreasing) prism power slightly and asking the patient
“which is best, one or two?” similar to manifest refraction. Give prism in trial
frames to determine patient comfort with resulting prism power. Ideally, then give
4-6 week trial in Fresnel prism and repeat exam before prescribing ground in
prism glasses.

Unmasking Bilateral Inferior Rectus Restriction in Thyroid Eye
Disease: Using Degree of Cyclotropia

The authors reviewed surgical results in 12 patients with stable thyroid eye
disease involving the inferior rectus muscle and manifesting pre-operative
excyclotropia. 4 patients underwent planned bilateral inferior rectus recession
and 8 underwent unilateral IR recession. 4 of the 8 unilateral surgical patients
were successfully corrected and the other 4 patients had reversal of the
hypotropia post-operatively. The successful unilateral surgical cases and
reversal-of-hypotropia surgical cases had 5.5o and 22o of pre-operative
excyclotropia, respectively (p<0.005). The authors conclude that patients with
thyroid eye disease with >15o of pre-operative excyclotropia likely have surgically
significant bilateral IR restriction and should undergo bilateral surgery.
Case Series: Exercise-Induced Esotropia

The authors report a series of 3 cases aged 8-24 in which reproducible comitant esotropia and diplopia were experienced following exercise. Following thorough neurologic evaluation, each patient was diagnosed with exercise induced esotropia which has been reported in 3 other single case reports previously. The authors discuss differential diagnoses such as brain tumors, dolichoectatic vertebral artery, myasthenia gravis, episodic ataxia type 2 and migraine which may be associated with diplopia after exercise. In addition, diseases such as multiple sclerosis, Graves’ disease, acquired intermittent Brown syndrome, and post-concussion convergence insufficiency can be associated with transient diplopia. The authors recommend that patients with newly acquired, exercise-induced diplopia undergo imaging of the brain, orbits, and thorax; serologic studies for myasthenia; and Prostigmin (neostigmine bromide) or Tensilon (edrophonium chloride) test. No treatment plan is suggested for exercise induce esotropia in this case series.

Idiopathic Enlargement of the Extraocular Muscles in Young Patients: A Case Series

This retrospective interventional case series examined 6 young patients with atypical restrictive strabismus with reduced eye movements. All 6 patients had enlarged Extraocular muscles which caused the restrictive movement. There was no identifiable biochemical etiology or significant medical history in any of the patients. MRI imaging is presented showing enlarged muscles. All of the patients were euthyroid and muscle biopsy was inconclusive for any pathology. The authors suggest that EOM enlargement may be on a continuum with congenital fibrosis of the EOM. The authors suggest working these patients up for myosotis, thyroid conditions but also state that parents need to be warned that orthotropia is difficult to achieve in these cases.

Facial Ulcers and Restrictive Strabismus From Delayed Periorbital Granuloma After Poly-L–Lactic Acid Injection
Fuller M, Bradley E. JAMA Ophthalmol September 2015;133(9):1090-1091.

The authors present a case report of restrictive strabismus after poly-L-lactic acid injection, an injectable filler used in cosmetic surgery. Systemic signs and serologic evidence of an automimmune process were present. Biopsy of a periorbital lesion revealed chronic granulomatous reaction and birefringent material consistent with poly-L-lactic acid, a dermal filler which the patient then remembered she had during spa services several years prior to presentation. Importance: Another cause of restrictive strabismus has been identified. Surgeons who perform cosmetic fillers near the orbit should inform their patients
The authors conducted a prospective comparative case study of fixation stability and variability of eye misalignment in a group of 25 alternating exotropes with no amblyopia and a group of 25 normal controls, using video eye trackers. Main outcome measures include documenting spatial and temporal variability in the position of the fixating eye and the nonfixating eye. This variability was quantified by the log area of ellipses containing 95% of eye positions or mean standard deviations of eye position.

The mean amount of exotropia was 14.2 degrees. The mean position variability in the exotropes of the deviating eye was 1.80 log units (95%CI, 1.66-1.93) which is greater the fixating eye, at 1.26 log units (95%CI, 1.17-1.35) (P < .001).

The fixating eye of patients with strabismus was more variable in position than the fixating eye of individuals without strabismus at 0.98 log units (95%CI, 0.88-1.08) (P < .005). This angle of misalignment in exotropes was highly variable, up to a 10 degree (or 20 prism diopter) difference measured in this study.

Importance: Strabismus surgeons seek accurate and reproducible measurements of a patient’s strabismus to guide the surgical dosage. This excellent study calls into question our usual way of measuring strabismus, with alternate prism and cover testing, using absence of refixation as an endpoint for measuring misalignment. The authors, using the latest eye tracking technology, demonstrate that variability in strabismus measurements may partly be due to the biological variability of the condition and not necessarily reflect error on the part of the examiner. Further refinement of this technology may facilitate mass strabismus screenings.

10. STRABISMUS SURGERY

Strabismus surgery for small angles

Small Deviations: Vertical, Horizontal, and Combined

The author discusses 4 methods of single muscle surgery to treat small angle strabismus. The methods are 1) graded marginal tenotomy with intra-operative re-measurement of residual strabismus, 2) in-office mini-tenotomy, 3) mini-plication, 4) recession of only one pole of one muscle. The author reports and example case in which a small medial rectus recession was combined with
recession of only the temporal pole of the inferior rectus to treat small horizontal and vertical deviations in the same patient. The author report the number of one pole recessions that he has performed has increased from less than 5 cases in 2010 to 15+ cases per year from 2012-14.
Comment: Surgical outcomes were not reported but the author has favorable impression of one pole recession surgery for small tropias in patients who are highly motivated to choose over prism glasses.

Adjustable small-incision selective tenotomy and plication for correction of incomitant vertical strabismus and torsion

The authors report a procedure for correction of vertical strabismus that is incomitant in lateral gaze and/or cyclotorsion. The procedure is selective plication or tenotomy of the nasal or temporal fibers of a vertical rectus muscle with an adjustable suture. A flow chart is provided. This was a retrospective review of consecutive patients over a 7-month period. Nine patients with a mean age of 64 years and a mean follow-up of 4.5 months were included. There were 4 plications and 5 tenotomies. Only one patient required postoperative adjustment. Vertical strabismus was corrected within 4 PD in 8/9. 4/8 had torsion reduced to <5'. 8/9 had resolution of diplopia. This technique seems promising in selective patients but the study was small and follow-up was limited. There was no control group

Horizontal muscle surgeries

Comparison of Lateral rectus Muscle Re-recession and Medial Rectus Muscle Resection for Treatment of Postoperative Exotropia

This retrospective non randomized clinical trial assessed the outcomes of unilateral lateral rectus re-recession and medial rectus resection for treatment of persistent exotropia. 40 patients with recurrent exotropia after BLLREC were evaluated. 14 patients were treated with unilateral medial rectus resection and 26 with unilateral lateral rectus re-recession. All patients were followed at least one year. Patients with developmental delays or ocular abnormalities were excluded from the study.

The initial procedure consisted of symmetrical 5-8 mm BLRRec for exotropia. The treatment for recurrent or persistent exotropia was either single medial rectus resection or re-recession of a single lateral rectus. Mean preop deviation was 17.4 diopters in the MR resect group and 18. 1 in the LR re-recess group.
14 patients were treated with MR resection and 26 with re-recess of the lateral rectus with a final position ranging from 15.5 mm to 19 mm from the limbus. At last followup, success (XT less than 10 pd) was achieved in 64% of patients treated with MR resection (9 of the 14 patients). Success was achieved in 73% of patients treated with the LR recession (19 of the 26 patients). Mean followup was 4.5 years in the MR group and 2.9 years in the re-recess group. The final outcome was not statistically significant between the two groups. Both procedures are worth considering in a reop of XT.

**Results of Conservative Management for Consecutive Esotropia after Intermittent Exotropia Surgery**

In this retrospective single center study, the authors investigated results of conservative management for consecutive esotropia following surgery for intermittent exotropia. They followed 149 patients who had surgery for intermittent exotropia. 98% of the patients had received resection/recession procedures, only patients who developed esotropia following surgery for exotropia were included in the study. 149 out of 151 patients were followed with conservative management. 2 patients required repeat operation for persistent esotropia following conservative management. Management included alternate or full time patching if esotropia existed greater than 2-3 weeks following initial surgery. This was continued for 1-2 months following surgery. If esotropia persisted Fresnel patients were utilized. Patients were divided into 2 groups, persistent esotropia which lasted greater than 3 weeks and transient esotropia which lasted 3 weeks or less. Patients were followed on average 31 months and noted that patients with persistent esotropia, recurrence of exotropia occurred in 25%, whereas those with transient esotropia had recurrence rate of 62% after follow up period. The authors state their patients should be advised it could take up to one year after surgery for exotropia for the consecutive esotropia could result and that sensory outcome was not affected by the duration of consecutive esotropia.


Rather than standard motor or sensory success as an evaluation, the authors developed a goal-determined outcomes methodology for exotropia surgery. Potential goals included: binocular potential, restoration of eye contact, resolution of torticollis an resolution of diplopia. 909 surgeries were performed over a 5-year period and 852 surgeries had 2-6 month postop evaluations. Applying goal-specific measures, 62% of patients had excellent outcomes and 16% had good outcomes. Best results were achieved for diplopia and eye contact. Results were worse if standard motor criteria were used. Preoperative strabismus angles >=50
PD at distance, associated DVD, or surgery before 24 months of age were associated with worse results. Excellent outcomes were improved with adjustable sutures and with using SPCT rather than ACT. The concept of goal-determined results is very interesting and changes the paradigm for evaluating success. It clearly is an idea that should continue to be investigated. It allows evaluation of heterogeneous populations. However in regards to this individual paper there are many problems. The specific goal was determined by each surgeon and was not uniform so success is arbitrary. Follow-up was relatively short which is problematic when evaluating exotropia surgery. Finally measuring patients with SPCT versus ACT was not consistent and both measurements were not recorded in most patients. Obviously a group of intermittent exotropes measured by SPCT will have more impressive postoperative results than one measured by ACT.

**Divergence Insufficiency Esotropia: Surgical Treatment**  

The author of this review article describes the this entity sometime called “age-related distance esotropia.” Theories of its etiology are described. The author reviews the literature on surgical results including bilateral lateral rectus resection, unilateral lateral rectus resection and bilateral medial rectus recession as well as a paper showing collapse of distance near incomitance regardless of which type of horizontal muscle corrective surgery is performed. A newer technique under investigation is lateral rectus equatorial myopexy based on the theory that age-related distance esotropia may be due to degeneration of the lateral rectus-superior rectus band leading to inferiorly displaced lateral rectus muscle pulley.

**Comparative study of lateral rectus recession versus recession-resection in unilateral surgery for intermittent exotropia**  

This study compares unilateral lateral rectus recession results to recess-resect for mild-moderate angle exotropia of 20-25 PD. This was a retrospective review of 8 years of surgeries. There were 37 patients in the LR recess group and 33 in the R&R group. The preoperative exotropia measurements at distance and near were 22.2 PD/24/5 PD and 24.5/26.4 PD. Followup was 37.1 months and 44.6 months respectively. At last follow-up no patients in the LR recess group had an overcorrection but 9.1% in the R&R group did. The largest exodrift occurred by 1 month postop in both groups. Median time to exotropia recurrence was 27.0 months in the LR recess group and 41.0 months in the R&R group. Reoperation rates for recurrent exotropia were 18.9% and 30.3% respectively. At day 1 postop the LR recess group had a much higher rate of abduction limitation but this resolved in all cases by month 4. Patients in this study were not randomly assigned to surgery groups. Sensory status was also not evaluated.
In this single surgeon retrospective study, 333 patients who received surgery for the treatment of intermittent exotropia were studied to see if success was related to refractive status. The patients were divided into three groups; hyperopes, emmetropes and myopes. Success was postoperative alignment was recorded at 3, 6 and 12 months post op and last measured follow up appointment. Success was defined as alignment between 5 eso and 15 exotropia. Most of the surgical procedures were recession/resection. They found equal success rates (66%) between the hyperopes and myops and less success rate with emmetropes. The hyperopes demonstrated the most improvement in stereopsis postoperatively. It is noted that up to 60% of the hyperopes were treated with spectacles post operatively. The study is limited by short follow-up period (26 – 35 months) and variability in patient population.

This study sought to identify the types of strabismus surgery which resulted in lateral incomitance, an issue which can cause bothersome diplopia or poor eye contact in side gaze. Study design was a retrospective review of 569 patients who had horizontal strabismus surgery over a 2 year period at one institution with measurements in right and left gaze documented before and after surgery. Main outcome measure was change in comitance, calculated as difference in horizontal alignment between right and left gaze before and after surgery. Symmetrical surgery was defined as operating the same muscle(s) in both eyes and the amount of surgery performed between eyes did not differ by more than 0.5mm. All other procedures were considered asymmetric, including bilateral recession or resection with more than 0.5-mm difference between eyes, unilateral recess-resect procedures, and 3-muscle horizontal surgery. Preoperatively 491 patients had comitant strabismus and 59 developed incomitance after strabismus surgery. Almost 29% (17/59) were symptomatic because of post-operative incomitance. Of those with new post-operative incomitance, 89% (53/59) had asymmetric strabismus surgery. Of those who had preoperative incomitance (n=78), comitance was restored in 36 (46%) of whom 32 had asymmetric surgery (32/36 = 89%).

Importance: Strabismus surgeons need to be aware of the impact on the patient of post-op incomitance, such as diplopia. This study provides evidence that asymmetric surgery is more likely to create incomitance when comitance originally was present.
The Effect of Achieving Immediate Target Angle on Success of Strabismus Surgery in Children

AJO; November 2015; vol 160( 5): pg 914.

This study tried to evaluate the long term success of strabismus surgery if the ideal postoperative target was achieved with surgery. This was an interventional case series. 352 patients with 18 months of follow up were included. All children were below 12 years of age and were evaluated at 1 week postop. The ideal outcome postop was 08 PD ET in Exotropic patients and within 4 PD of Ortho for Esotropic patients. Success was defined as within 10 PD of Ortho. Patients within the target range had a success rate of 75% compared to 57% with those outside of the target range. It was significant for Exotropia but not esotropia. Esotropic surgery results were more likely to be successful than Exotropia.

**Vertical muscle surgeries**

Effect of Combining Oblique Muscle Weakening Procedures with Bimedial Rectus Recessions on the Surgical Correction of Esotropia.

Isaac C, Chalita M. J AAPOS February 2015;19(1):54-56

This was a 10-year retrospective review of the effect of oblique weakening on medial rectus recessions. Inferior oblique weakening surgical procedures were not uniform but superior oblique procedures were. 160 patients met inclusion criteria. The SO surgery group had a higher average age. The authors found inferior oblique surgery did not alter medial rectus recession PD/mm ratio, but superior oblique surgery lowered PD/mm ratio. The effect of inferior oblique surgery may have been hidden because all IO surgeries were combined into one group. Adjusting horizontal rectus surgical dosing when adding vertical surgery is helpful information for strabismus surgeons, but the results of this study must be viewed with caution.

Z-myotomy of the Inferior Oblique for Small Incomitant Hypertropia


This was a retrospective-review of Z-myotomy cases over a 5-year period. 43 Z-myotomies on 38 patients were included. Some patients received surgery on other muscles as well. Mean postoperative follow-up was 31 weeks. On average the Z-myotomy took 5-7 minutes. Overall postoperative ductions improved significantly. 28% of eyes (n=12) had a mild asymptomatic overcorrection. 7% (n=3) had no change in ductions. Postoperative measurements showed an almost complete collapse of the strabismus pattern and effect seemed to correlate with the preoperative deviation. This procedure is irreversible, but it is
faster and avoids the risk of scleral perforation. The authors found the Z-myotomy corrected 100% of the hypertropia in primary position and contralateral gaze and 85% of the hypertropia in ipsilateral head tilt. This study had no control group, was retrospective and not masked. Z-myotomy is a quick, sutureless procedure that can be added to a strabismus surgeons’ armamentarium for inferior oblique procedures.

**Surgical Management of Monocular Elevation Deficiency Combined with Inferior Rectus Restriction**


The authors compared the results of ipsilateral large inferior rectus recession (IR) versus small ipsilateral inferior rectus recession plus contralateral superior rectus recession (IR/SR) in the treatment of double elevator palsy with inferior rectus restriction. This was a retrospective review of surgical/medical records. Ten patients were in the IR group and 13 patients were in the IR/SR group. Mean follow-up was 17.5 months. Both groups showed marked improvement of the vertical alignment in primary position. Primary position success was equal between the two groups but the IR group had 100% consecutive hypertropia in downgaze while this was only seen in 31% of the IR/SR patients. Also upgaze hypotropia was significantly improved in the IR/SR group. Both groups showed improvement in the preoperative chin-up head posture, but ipsilateral head tilt developed in 70% of the IR group and 54% of the IR/SR group. Fundus incyclotorsion developed in the ipsilateral eye in 90% of the iR group and 38% in the IR/SR group, although 85% of the IR/SR group also developed fundus excyclotorsion in the SR recess eye as well. Overall the IR/SR group seems to display better results, probably because it limits the untoward effects of a large IR recess, and matches comitance of the upgaze limitation.

**Surgical management of superior oblique paresis using inferior oblique anterior transposition**


This study reports retrospective data of inferior oblique anterior transposition to treat superior oblique paresis over an eleven-year period. Ninety-six patients underwent 98 IOAT procedures. Mean age at surgery was 37.6 years. Seventy-two cases were congenital, 12 were acquired and 12 were unspecified. Mean follow-up was 5.8 months. Seventy-seven of patients had torticollis preoperatively and post-operatively 52 resolved completely and another 20 improved. Mean vertical correction was 9.5 PD. 20% had some residual inferior oblique overaction and 47% developed underaction (ave -0.6). All cases of underaction were asymptomatic. 27% developed restriction to elevation in abduction (85% of these were <=-1). Four patients had postoperative diplopia in upgaze. Six patients required further surgical intervention. This is an effective surgery in selected cases.
Surgery for Supranuclear Monocular Elevation Deficiency
Struck MC, Larson JC. *Strabismus* December 2015;23(4):176-181

This is a retrospective review of 5 surgically treated patients with supranuclear monocular elevation deficiency (MED), who had intact Bell’s phenomenon, hypotropia, limited elevation above the primary position, and negative forced ductions. Surgery consisted of near maximal superior rectus recession on the contralateral eye, directly suturing the muscle to the sclera 9 to 10.5 mm from the original insertion (average 9.7mm). Average surgical effect was 21 prism diopters of vertical shift. The vertical deviation of the paretic eye in primary position postoperatively was orthotropic for 2, hypotropic for 2, and overcorrected for 1.

The authors conclude that in cases of supranuclear MED, a large contralateral superior rectus recession is a simple and reliable surgical alternative to a Knapp procedure. Nevertheless, the authors fail to address possible complications of this technique, such as limited supraduction of the operated eye and upper eyelid retraction following a large unilateral superior rectus recession.

Transposition surgeries


This was a retrospective analysis of the results of three different full tendon vertical rectus transposition (VRT) techniques for complete abducens palsy performed by one surgeon. Surgeries were performed over 23 years. Group 1- simple VRT (n=9); Group 2- VRT with vertical rectus resection 4mm prior to transposition (n=7); Group 3- full VRT with myopexy sutures (n=10). Surgeical choice was not randomized. 26 patients met inclusion criteria (1 bilateral). Mean age was 43.1 years and mean postoperative follow-up was 8.1 months. Group 2 had the largest mean reduction of esotropia, the greatest improvement in mean abduction and had the only patient with primary position overcorrection. Mean alignment change for the three procedures showed no significant difference. No procedure led to limitation of adduction worse than -1 and there was no difference between the groups. No intraoperative complications occurred and there were no cases of anterior segment ischemia. Three patients developed postoperative vertical deviations. FTT was found to be the least effective procedure. The results of this study must be viewed in light of the small numbers of patients in each group and possible selection bias for which procedure was performed based on deviation size or etiology of the abducens palsy.
Comparison of Augmented Superior Rectus Transposition with Medial Rectus Recession for Surgical Management of Esotropic Duane Retraction Syndrome


This study compares the results of augmented SRT with or without MR recess (SRT group) with unilateral or bilateral MR recess (MRc group) alone for the treatment of esotropic Duane syndrome. Patients underwent surgery over a six-year period and results were reviewed retrospectively. The SRT group consisted of 8 patients (2 SRT alone and 6 with MR recess; ave age 12 years) and the MRc group consisted of 13 patients (6 patients unilateral MR recess and 7 bilateral MR recess; ave age 13 years). Strabismus and motility were comparable preoperatively between the two groups.

SRT surgery reduced the esotropia from 20 PD to 3 PD, and decreased the AHP from 14’ to 2’. Abduction deficit improved from -3.6 to -2.4 and defined success was 87%. There were no new vertical deviations.

MRc surgery reduced the esotropia from 24 PD to 4 PD and decreased the AHP from 18’ to 3’. Abduction deficit improved from -3.6 to -3.3 and defined success was 77%. Postoperative adduction deficit was found in 3/8 SRT patients and 3/13 MRc patients.

Overall, results between the two groups were similar except the SRT procedure improved abduction more but produced more adduction limitation. Multiple surgeons performed MRc and a single surgeon performed SRT which could affect results.

Plication Augmentation of the Modified Hummelsheim Procedure for Treatment of Large-angle Esotropia Due to Abducens Nerve Palsy and Type 1 Duane Syndrome


The authors added plication of the lateral rectus to a Hummelsheim augmented with ‘Foster’ modification in the treatment of complete abducens nerve palsy and type 1 Duane syndrome. Medical records were reviewed retrospectively. There were 9 patients with abducens palsies with a mean age of 39 years and average follow-up of 28 weeks. 6/7 patients with tight intraoperative medial rectus muscles additionally received botulinum toxin injection or recession of the medial rectus. All 9 patients had a large reduction in their esotropia and limitation of abduction improved from a range of -5 to -8 preop to -2 to -4 postop. One patient had an induced vertical strabismus and there were no other complications. There were four patients with Duane syndrome with an average age of 11.5 years and an average follow-up of 31 weeks. These patients also had improved esotropic deviations and improved adduction (-4/-5 to -1/-3). No complications were noted.

The problem with this paper is there is no way to determine if the plication of the lateral rectus had any effect on results. There was no control group, and it is
unclear whether plicating a lateral rectus in the setting of a complete sixth nerve palsy, has any effect. Therefore this paper merely becomes a report of surgical results in treating type 1 Duane syndrome and 6th nerve palsy.

**Adjustable sutures**


This retrospective cross-sectional study looked at the association of strabismus surgery reoperation rate with adjustable vs. conventional sutures. 526 patients out of 6178 had reoperation (8.5%). Reoperations were in 8.1% of adjustable suture surgeries and after 8.6% with conventional sutures. When horizontal muscles were operated upon, the reoperation rate was lower for adjustable sutures (5.8%) compared to conventional (7.8%) after controlling for known confounding variables. When vertical muscles were operated upon, reoperation were 15.2% after adjustable surgery and 10.4% after conventional surgery. This data was taken from insurance company information and not medical health records, which allows for some limitations to the study.

When evaluating the success of adjustable surgery, it is important to separate the horizontal surgical results from the vertical surgical results. The younger the patient, the lower the reoperation rate as well.


This study evaluated postoperative shifts in non-thyroid patients following suture adjustment between postoperative day 1 and 2 months. This was a retrospective review of consecutive adults patients. The inferior rectus recessions were performed with two different types of sutures whereas the superior rectus recessions were only performed with one type. The cases were a mix of paralytic strabismus, childhood strabismus, orbital disease, or post-eye surgery. 60 patients met inclusion criteria. Suture type did not affect results. Mean shift was 1.1 PD undercorrection for superior rectus and 1.0 PD for inferior rectus recession. However, mean results may not have been the best way to report the data since there were under- and overcorrections, which tend to neutralize each other. Preoperative deviation was not a factor and there was no difference in results between the superior and inferior rectus recessions. This study has many problems. It was retrospective, patients were not age-matched and subjects had many different causes for strabismus. It is difficult to cull any useful data for clinical practice when multiple causes of strabismus, multiple suture types,
multiple muscles operated on, and mean data combining under and overcorrections are combined.


The authors attempt to characterize the friction created by various knots used in adjustable sutures. A tying board was created to model sliding of adjustable knots along the pole sutures. The authors compared a cinch knot, sliding noose knot, and a simple square knot. Average force needed to overcome static friction on first movement for the sliding noose knot was 240 gf, the cinch knot 150 gf, and the square knot 110 gf. The difference for the first movement was found to be statistically significant, but this difference did not persist for the fifth movement for all knots. The difference in force required for the first movement compared to the second and in comparison to the fifth movement was also statistically significant. Overall the sliding noose knot maintained the most friction. The square knot held the least force and the authors would not recommend using it for adjustable sutures. This study is limited by all knot tying being performed by one surgeon (potential user bias), and the in vivo nature of this research (therefore viscoelastic effect or the effect of other surgical field fluids were not considered, nor was scleral friction). Holding forces and ease of movement must be evaluated when determining the best options for adjustable suture surgery.

**Strabismus surgery - Misc**


This prospective interventional study assesses the efficacy of botulinum toxin (Novotox) injection under general anesthesia in patients with cerebral palsy (CP) and esotropia. Forty-four patients (21 males) with the mean age of 47.56 ± 35.86 months were included. The mean esotropia was 52.27 ± 18.40 PD (25–123 PD). The range of follow-up was 12–24 months. Thirty patients (68.18%) were treated successfully (orthotropia ± 10 PD) one year after surgery. Twelve patients required reinjection. The rates of success, consecutive exotropia, and residual esotropia were 61.4%, 13.63%, and 25% in the last follow-up, respectively. Complications included ptosis in 97% at the first month (severe in 38.6%) and subconjunctival hemorrhage. In this study, lower age, more ptosis, larger pre-injection deviation, and less deviation one month after injection were significantly associated with better results. The authors conclude that botulinum toxin injection is a reasonable, less invasive therapeutic alternative for the patient with esotropia and CP. The main limitation of the study is the lack of long-term follow-up.
Instructions to Patients and Families Following Strabismus Surgery


PURPOSE: To analyze postoperative instructions provided to patients and families after strabismus surgery. METHODS: In April 2012, a 12-question electronic survey was sent to all members of the American Association for Pediatric Ophthalmology and Strabismus (AAPOS) regarding their instructions to patients undergoing strabismus surgery. The questions specifically addressed patients’ daily activities, such as their resumption of school and work, sports, swimming, normal showering and bathing, and contact lens use. RESULTS: One hundred two responses were completed; 96% were from pediatric ophthalmologists regularly performing strabismus surgery. Participation was greater by North American members (86%) and respondents with more than 10 years of experience (75%). Fifty percent of the respondents advised patients to resume normal showering and bathing 24 hours after surgery but 27% recommended waiting until the 2nd or 3rd day while 20% recommended waiting 1 week. Conversely, respondents recommended that children wait 3 to 4 days before resuming schoolwork (52%) and at least 2 weeks before playing in a sandbox (47%). Furthermore, respondents indicated that patients should refrain from participating in sports-related activities for at least 1 week (43%) and should not go swimming for at least 2 weeks (56%). Finally, 47% advised their patients not to wear contact lenses for 2 weeks after surgery. CONCLUSIONS: Most AAPOS members agree in postoperative infections except with respect to resumption of normal bathing. The study was somewhat limited by it’s survey format and low response rate.

Quantitative Intraoperative Torsional Forced Duction Test


The authors developed a method for quantifying intraoperative torsional forced duction testing. Assessment was made on 33 eyes with various types of oblique dysfunction and 31 controls. The new torsional forced duction test enables quantitative assessment of SO and IO tightness and laxity with good reproducibility. Under general anesthesia the 12 and 6 o’clock positions of the limbus were marked and the globe was maximally excyclorotated without retroplacement until the first resistance was felt. The angle of rotation, in degrees, was read on a Mendez ring.

Minimally Invasive Strabismus Surgery (MISS) Compared with the Fornix Approach in Pediatric Horizontal Strabismus Surgery

Sanz P, Sanchez P, Dominguez I. Strabismus December 2015;23(4):159-163
Minimally invasive strabismus surgery (MISS) obviates large muscle dissections and large conjunctival incisions and enables minimal anatomical disruption of muscles and surrounding tissue. This study compares MISS with the fornix approach in horizontal strabismus operations in 16 children ≤12 years old. MISS was performed in one eye, and fornix opening in the contralateral eye. Operations were done on 9 medial rectus and 7 lateral rectus muscles. Recession was performed in 14 muscles (mean, 5 mm) and plication in 2 (5.5 mm and 7 mm, respectively). Differences between MISS and the fornix approach were not statistically significant for VA, conjunctival hyperemia, or swelling at days 1 and 7 after surgery. Nevertheless, moderate and severe conjunctival hyperemia was more frequent in the fornix approach than in MISS at days 1 and 7. Operating time was not significantly different between the groups, although surgery took longer in MISS (14.43 minutes) vs control (12.37 minutes). Unfortunately, the study is limited by the small number of cases and the fact that postoperative ocular examinations were performed by the surgeons who performed the surgeries.


This retrospective cross-sectional study looked at predictors of reoperation and abnormal binocularity outcomes following strabismus surgery. Of 11,115 total children who underwent strabismus surgery, 7.7% had reoperation and 12.1% had abnormal Binocularity, and 18% had one of these outcomes during the first year. Younger age was associated with reoperation and abnormal binocularity. Adjustable sutures were associated with a higher reoperation rate. In addition, hyperopia, Botox injections and superior oblique surgery resulted in higher reoperation rates.


The authors report a 2-year experience in creating a sustainable pediatric ophthalmology outreach program in Guatemala City, Guatemala. The medical team consisted of 3 pediatric ophthalmologists, 1 orthoptist (2 in year 2), pediatric recovery room nurses, pediatric surgical operating room technicians, an anesthesiology team and a pharmacist. In year one, 37 children underwent surgical intervention and this increased to 58 in year two. There were no major postoperative surgical complications or anesthesia complications. The number of prescreened children also increased in year two, after the addition of a local pediatric ophthalmologist. The authors faced numerous challenges with this
project and they discuss strategies to continue to provide outreach programs in rural and poor settings in the future.

11. **ANTERIOR SEGMENT**

*Anterior segment disorders - surgical procedures*

**Robotically Assisted Amniotic Membrane Transplant Surgery**
Bourcier T, Becmeur PH, Mutter D
*JAMA Ophthalmol.* Feb 2015;133(2):213-4

The uses of amniotic membrane transplantation in pediatric ophthalmology and strabismus include prevention of cicatricial changes in Stevens Johnson syndrome and similar conditions, for treatment of conjunctival scarring after strabismus surgery and for treatment of persistent epithelial defects. The authors describe the first human cases of robotically assisted ocular surgery using the daVinci SiSurgical System and its feasibility and safety in performing amniotic membrane transplantation. The 3 patients did well but the operative time was prolonged compared to non-robotic surgery. The authors are confident, however, that with further refinement of robotic systems, the advantages will become apparent, including better precision and maneuverability, scalability of motion, tremor filtration, better ergonomics, the ability to simultaneously manipulate 3 surgical instruments and cameras, improved patient access to surgeons, and enhanced surgical training.

**Corneal collagen crosslinking in children with keratoconus.**
McAnena L, O'Keefe M
*J AAPOS.* June 2015;19:228-32

Corneal crosslinking (CXL) outcomes were evaluated in consecutive patients <=18 years of age over a four-year period. 25 eyes of 14 patients with a mean age of 16.2 years were included. Mean uncorrected acuity was not significantly different between preoperative and 1-year follow-up. However, mean best-corrected acuity improved significantly. Mean spherical equivalent was -4.42 D preoperatively and -5.5 D at final follow-up. Mean cylinder was 3.65 D pre- and 4.5 D at one-year follow-up. These values were not significantly changed. Tomographic data showed no change at 1-year in astigmatism, Kmax, Kmin, or Kmean. At 1-year, Kmax showed regression in 5 eyes, stabilization in 13 eyes, and progression in 7 eyes. There was a significant reduction in corneal thickness at the thinnest measured area at 3 and 6 months follow-up. Data for 2 and 3 years postop is provided but many patients were lost to follow-up. This is an exciting new treatment option for keratoconus patients.
Combined Cataract Surgery and Aniridia Ring Implantation in Oculocutaneous Albinism
Farahi A, Hashemi H, Mehravaran S

The authors present results of cataract surgery combined with aniridia ring implantation in six patients (twelve eyes) with oculocutaneous albinism (OCA) in terms of vision, refraction, eye movements, and subjective photophobia and glare. These were adult patients, and five of the six had visually significant cataracts. The patients underwent phacoemulsification and posterior chamber intraocular lens (PC IOL) implantation. They also had 2 Morcher aniridia rings inserted intracapsularly anterior to the IOL. Two rings were implanted because each ring has opaque leaflets comprising about 50% of the ring diameter. In addition to improved uncorrected and corrected distance visual acuity and significant reduction of refractive error, all patients had a marked reduction of glare and photophobia after surgery, as assessed by a questionnaire. In light of these study results, the authors suggest a follow up study be performed to assess the outcomes of refractive lens exchange with implantation of a PC IOL and prosthetic iris device in OCA patients seeking refractive correction. However, there are other options for managing photophobia in oculocutaneous albinism, including colored contact lenses and tinted glasses, as this is a small study with insufficient follow up to determine long-term safety.

Outcomes of a Modified Capsular Tension Ring with a Single Black Occluder Paddle for Eyes with Congenital and Acquired Iris Defects: Report 2
Date R, Olson M, Masket S, Miller K, et al.
Journal of Cataract & Refractive Surgery. September 2015; 41(9):1934–4

This study evaluated the safety and efficacy of Morcher 96F iris diaphragm implantation to manage small defects of the human iris. This devise is a modified capsular tension ring (CTR) with a 90-degree segmental occluder paddle made from black PMMA.
The study was a prospective nonrandomized interventional case series from UCLA that included 16 patients who underwent CTR implantation. 14 of the 16 iris defects were acquired due to trauma or prior surgery and two were congenital iris colobomas. There were no intraoperative complications. Three adverse events were reported: 1 ocular hypertension, 1 postoperative retinal detachment, and 1 25-degree rotation of the CTR. There were 4 secondary surgical interventions. There was a statistically significant improvement in the median CDVA of 2.5 Snellen lines (P < .01), with 4 patients having minor decreases in CDVA for reasons unrelated to the device. There was a statistically significant improvement in the median CDVA with glare of 8 Snellen lines (P < .01), but 2 patients had a decrease in CDVA with glare for reasons unrelated to the device.
The authors conclude that iris diaphragm CTR implantation was relatively safe and effective at reducing light and glare sensitivity in eyes with small iris defects.

**Results of Deep Anterior Lamellar Keratoplasty for Advanced Keratoconus in Children Less Than 18 Years**

R. Aurora, P. Jain, A. Maned hand, J. Goyal.

This retrospective non comparative interventional case series looked at the outcomes of deep anterior lamellar Keratoplasty in children with advanced Keratoconus. DALK is a newer alternative for stromal corneal pathology and is gaining popularity over PKP. DALK has an advantage over PKP because the host maintains their own endothelium with lower chance of rejection and shorter duration of postop steroids. 20 eyes of 16 patients underwent deep lamellar Keratoplasty. The mean age of the patients was 14 years. The mean preop vision was 20/320. The mean postoperative vision was 20/80 uncorrected. BCVA was 20/160 preop and 20/40 postop. At the final follow up, 18 patients had clear grafts in the visual axis. Complications included 1 patient with graft rejection, 2 shield ulcer, 2 graft infection, and 4 interface vascularization. Only 1 patient went on to PKP.

**Anterior segment disorders – nonsurgical management**

**Blepharokeratoconjunctivitis in children.**

Hammersmith KM.

PURPOSE: Review the current literature on pediatric blepharokeratoconjunctivitis (BKC) to enhance the understanding on the incidence, clinical course, and treatment options. RECENT FINDINGS: Pediatric BKC is a disorder with a wide spectrum of clinical manifestations, is commonly misdiagnosed as HSV keratitis and is frequently associated with recurrent chalazia. Therapies target both the infectious and inflammatory components of this disorder. There is no consensus on the appropriate dose of oral erythromycin to treat pediatric BKC. Lower potency topical steroids such as loteprednol and fluorometholone are often effective in treating the inflammatory component of BKC. SUMMARY: Pediatric BKC is a disorder with a wide spectrum of clinical manifestations and severity, which is often overlooked or misdiagnosed.

**Besifloxacin in the management of bacterial infections of the ocular surface**

Deschênes J, Blondeau J
Besifloxacin ophthalmic suspension 0.6% is a chlorofluoroquinolone developed solely for ophthalmic use with demonstrated safety and efficacy in the treatment of acute bacterial conjunctivitis. Most cases of acute bacterial conjunctivitis are self-limiting; however, topical antibacterial treatment offers several benefits. These include shorter disease duration; prevention of spread of infection; reduction in adverse events (AEs), including those threatening vision; and reduced disease recurrence. In the following section, they discuss antibiotic resistance and the development of newer fluoroquinolones to combat drug-resistant strains. A study examining the in vitro activity of various antibiotics, including besifloxacin, against 2690 bacterial isolates showed that besifloxacin had higher potency against gram-positive pathogens and anaerobes, and was equivalent to comparator fluoroquinolones against most gram-negative pathogens, is likely to be associated with a lower rate of resistance development compared with other topical antibiotics and is, therefore, an excellent choice for the treatment of acute bacterial conjunctivitis.

**Anterior segment biometry and refraction**

**Comparison Of Refractive Error And Central Corneal Thickness In Neonates Of Diabetic And Healthy Mothers**

Göncü T, Çakmak A, Akal A, Çakmak S


This is a study that compared a small group of newborns (16) born to diabetic mothers to normal newborns (17). Retinoscopy and pachymetry were done within 1 week of birth.

Results: The mean spherical equivalent for both eyes in the diabetic group was +2.9 ± 2.6 and significantly greater than that of the nondiabetic group (+1.3 ± 2.1 D) (p = 0.008). The mean sphere value was +2.6 ± 2.4 D in the diabetic group and +1.0 ± 2.0 D in the nondiabetic group, significantly higher in the diabetic group (p = 0.008). There was no statistically significant difference between groups (p = 0.95) in astigmatic error. The mean central corneal thickness in the nondiabetic group was 542.9 ± 21.9 μm whereas it was 592.0 ± 40.2 μm in the diabetic group, which was significantly thicker (p = 0.05).

Conclusion: The small study showed that neonates of diabetic mothers seem to be more hypermetropic and have thicker corneas compared to full-term healthy neonates.
The effects of methylphenidate on refraction and anterior segment parameters in children with attention deficit hyperactivity disorder.
Larranaga-Fragoso P, Noval S, Rivero JC and Boto-de-los-Bueis A.
J AAPOS. August 2015;19:322-6

Methylphenidate is frequently used to treat ADHD and the authors evaluated its' ocular side effects. Children were invited to participate in a prospective pilot study over a 4-month period. Fourteen patients were recruited with a mean age of 11 years. Mean IOP was not statistically significant when compared at baseline, and 3 and 9 months after starting treatment. Cup/disk ratio also did not change. Refraction did not change. Anterior chamber volume and anterior chamber angle were similarly unaffected by this medication, but post-cycloplegic anterior chamber depth (ACD) decreased significantly 9-months after treatment was started. However the ACD decrease was less than the amount that another published paper determined was a risk factor for angle closure. The study methods state that ACD, ACA, and ACV were measured pre-cycloplegia however the data table shows pre- and postcycloplegia measurements. Obviously cycloplegia on an individual visit increased ACV and ACD. However the table data does not seem to justify the contention that ACD decreased significantly post-cycloplegia when comparing baseline and 9-month data. Also even if this decrease did occur, it would only be a concern in a dilated state such as during an eye exam. This study has a conflict between the table of data and the written information and should not have been published without rectifying this.

Structural Changes of the Anterior Chamber Following Cataract Surgery During Infancy
Nguyen M, Shainberg M, Beck A, Lambert S

This study from Emory University used anterior segment OCT to study the anterior chamber anatomy of eyes that had undergone unilateral pediatric cataract surgery. Seven children were assessed with AS-OCT. They had unilateral cataract surgery at a mean age of 2.2 months (range 0.9 to 4.2 months). Of the 7 treated eyes, 5 were aphakic and 2 were pseudophakic. Patients were examined at a mean age of 9.2 years (range 6.6 to 12.5 years). The study found that angle opening distance was larger in pseudophakic eyes than in aphakic eyes, and that treated eyes had larger mean angle opening distances and anterior chamber angles than fellow untreated eyes. The authors do not address what these anatomical differences in anterior chamber anatomy mean. However, this is the first study to demonstrate the feasibility of using AS-OCT to assess structural changes in the anterior chamber in pediatric eyes after infantile cataract surgery. It is worth speculating whether AS-OCT could be
utilized to provide anatomical clues regarding the elusive pathophysiology of pediatric aphakic glaucoma in future studies.

**Effects of Birth Weight on Anterior Segment Measurements in FullTerm Children Without Low Birth Weight by Dual-Scheimpflug Analyzer**


This retrospective cohort study analyzed 78 healthy right eyes of children between 3 and 6 years of age. The eyes were scanned with the Galilei Dual-Scheimpflug Analyzer which is a device that can accurately assess the corneal thicknesses, posterior corneal curvature, total corneal power and anterior chamber volume. The analyzer also has a placido disc based topography so it can give topographic data as well. A scan was performed on all as well. Mean age was 55.86 months, 3426.3 grams at birth, and 39.4 weeks of gestation. There was a moderate correlation between lens thickness, vitreous length, axial length, and anterior chamber volume and birth weight. No correlation was found between anterior chamber depth and birth weight. Corneal thickness only weakly correlated with birth weight. In this study, they concluded that preschoolers who were heavier at birth had thicker corneal and lens, longer axial lengths, and flatter corneal curve.

12. **CATARACT**

13. **CATARACT SURGERY**

*Pediatric cataract surgery outcomes*

**Outcomes after Secondary Intraocular Lens Implantation in Children**

Shenoy B, Mittal V, Gupta A, Sachdeva V, Kekunnaya R.  

This retrospective study looked at 174 eyes in 104 children who had secondary lens implantation. The mean age was 6.08 years and mean follow up was 25.7 months. Mean follow up duration was 25.7 months with 31 eyes having follow up of 3-6 months, 30 eyes having 6-12 months, and 49 eyes with 13-24 months, 41 eyes having 24-48 months, and the rest having 48 to 120 months. Bilateral
surgery was performed in 70 of 104 eyes. Most children underwent secondary IOL placement between 2-8 years of age.

Nystagmus was present in 44 eyes prior to surgery; strabismus seen in 42 eyes prior to surgery. An additional 17 developed strabismus after surgery. The lens was placed in the ciliary sulcus in the majority of eyes with only 2 lens being placed in the bag. The Soemmering ring was not debulked at time of surgery in cases where the capsular bag failed to be opened. PMMA lenses were implanted in 81% of eyes and the rest received an acrylic hydrophobic or hydrophilic lens. No cases of iris chafing, erosion of the haptics, chronic uveitis, retinal detachment were seen. The most common complication was secondary membrane (17 eyes), optic capture (15 eyes), IOL decentration (9 eyes), and glaucoma (11 eyes). 11 eyes (5%) developed glaucoma after surgery. 51 eyes (35%) achieved best vision of 20/40 or better in the bilateral surgical group. This study suggests that ciliary sulcus placement of the lens without debulking Soemmering ring provides successful outcome.

Pediatric Bag-In-The-Lens Intraocular Lens Implantation: Long-Term Follow-up
Van Looveren J, Dhubhghail S, Godts D, Bakker E, et al.

This Belgian prospective case series evaluated long-term results of pediatric cataract surgery using the bag-in-the-lens (BIL) intraocular lens (IOL) implantation technique. Forty-six eyes of 31 children had a complete follow-up of 5 years or more after BIL IOL implantation. Sixteen cases were unilateral and 15 were bilateral. Patient age at time of surgery ranged from 2 months to 14 years. The mean refraction at the end of follow-up was -2.0 D ± 3.7 (SD). In bilateral cases, a corrected distance visual acuity (CDVA) of better than 0.5 was attained in 86.7% and a CDVA of 1.0 was achieved in 56.7%. In unilateral cases, 31.2% achieved a CDVA of better than 0.5 but none obtained a CDVA of 1.0. A clear visual axis was maintained in 91.3% of cases during follow-up. Visual axis reopacification was detected in 4 eyes of 3 cases, all due to inadequate BIL IOL positioning. Other than 1 case of glaucoma, no severe complications were detected. Long-term follow-up results show that BIL IOL implantation is a safe, well-tolerated approach for treating pediatric cataract with a low rate of visual axis reopacification and secondary interventions. The visual axis reopacification rates are lower than those typically reported for cataract surgeries with in the bag or sulcus IOL placement. Furthermore, this technique does not require an anterior vitrectomy. Note that the senior author, Dr. Tassignon, has intellectual property rights to the bag-in-the-lens intraocular lens, with both United States and European Union patents.
Long-Term Postoperative Outcomes After Bilateral Congenital Cataract Surgery in Eyes with Microphthalmos

This study from India assessed children with microphthalmos who had bilateral congenital cataract surgery. Eyes with other structural anomalies such as colobomas were excluded. Microphthalmos was defined as an eye that has an axial length (AL) 2 standard deviations smaller than what is normally expected at that age. All eyes were left aphakic. One of the 2 eyes was randomly selected for analysis. The study included 72 eyes of 36 children. The mean age of the patients was 4.8 months ± 6.2 (SD) (range 0.5 to 15 months). Postoperative complications included secondary glaucoma (11/36, 30.6%), visual axis obscuration (4/36, 11.1%), and posterior synechiae (10/36, 27.8%). This study provides some baseline data on complication rates after congenital cataract surgery in microphthalmic eyes. In the current study, the prevalence of postoperative glaucoma was higher when cataract surgery was performed before 3 months of age, and the authors suggest delaying cataract surgery in microphthalmic eye with bilateral congenital cataracts until after three months. Note that this is later than what is typical practice for bilateral congenital cataracts in average-sized eyes.

Long Term Outcomes of Iris sutured posterior chamber Intraocular lenses in Children.
AJO. Jan 2016;161:44-9

This was a retrospective interventional case study that evaluated long term complications in 12 pediatric patients (17 eyes) who had a foldable iris sutured PCIOL lens implanted between 2004 2007. In an aphakic child, there is only 4 methods of lens implantation: sulcus fixated, anterior chamber lenses, scleral sutured and iris sutured. This study is an extension study looking at long term follow up of the same previously published cohort. Five patients had Marfans, 6 patients had idiopathic ectopic lentis, 4 had traumatic cataracts. There were no intraoperative complications however, 7 of the 17 eyes had dislocation of their IOLs. The dislocation occurred at a mean of 12 months after the primary procedure. IOL type and suture type did not affect dislocation. This procedure should be considered with caution in the pediatric patient.
Pediatric cataract surgery complications

Spectral-domain optical coherence tomography measurements of central foveal thickness before and after cataract surgery in children.

In this retrospective cohort study of 11 eyes, the authors compare macular thickness before and after cataract surgery and intraocular lens (IOL) implantation in pediatric eyes. Eleven eyes of patients with mean age of 5.8 years (range 3 to 14 years) were included in the study. Eight of the eleven eyes also underwent posterior capsulorrhexis with anterior vitrectomy. There was an increase in mean macular thickness of 12% at 1 and 9% at 3 months, which then reached baseline values after 3 months and was stable over the 12 month follow up period. The result was statistically significant but not clinically significant. None of the eyes developed cystoid macular edema. This study corroborates finding in prior studies that cystoid macular edema is rare after pediatric cataract surgery.

Posterior Capsule Opacification in Pediatric Eyes With and Without Traumatic Cataract.
Trivedi RH1, Wilson ME.

The authors performed a retrospective case control study comparing the rate of visually significant posterior capsule opacification (PCO) in pediatric eyes with and without traumatic cataract. 29 eyes operated for pediatric traumatic cataract, which received in the bag IOL fixation, were compared to 29 eyes operated on for nontraumatic cataract. The eyes were matched by age, follow up, and IOL type. Mean age at surgery was 7 years for both group. The rate of PCO was statistically significantly different between the 2 groups (12/29 eyes versus 2/29 eyes) (P = .002). This difference was more marked for those with intact posterior capsules (9/12 eyes [75%] and 1/12 eyes [8%] (P = .001) compared with eyes with primary posterior capsulectomy and vitrectomy (3/17 [18%] and 1/17 [6%] (P = .6). For eyes with intact posterior capsules, the duration between cataract surgery and intervention for PCO was 4 to 15 months in the traumatic cataract group; 1 eye in the nontraumatic cataract group required intervention 20 months after surgery. This research supports the common perception that eyes with traumatic cataract were more likely to develop PCO than eyes without traumatic cataract. The authors suggest that primary posterior capsulectomy and vitrectomy should be considered for children having traumatic cataract surgery, irrespective of age at the time of surgery. However, most of the patients with traumatic cataract and intact posterior capsules went on to have successful YAG
laser posterior capsulectomies, so an alternative argument is that undergoing this relatively minor procedure in the older child may be better than a longer and perhaps less predictable surgery for posterior capsulectomy / anterior vitrectomy at the original surgery. If follow up is in question, however, primary posterior capsulectomy and anterior vitrectomy for most pediatric traumatic cataracts appears prudent.

**Pediatric cataract surgery in regions with limited medical resources**

**Cataract Surgery Outcomes in Bangladeshi Children**


The study included a total of 407 participants who had previously undergone bilateral cataract surgery as children and had a mean follow-up of 8.8 years. Children were examined and parental questionnaires were completed. Mean age at examination was 16 years (range 5-28 yrs). 22% had presenting binocular VA > 20/60 and 53% had VA < 20/200. After refraction, 33% had VA > 20/60 and 33% had VA < 20/200. Factors that predicted poor VA were nystagmus (50%), longer delay in presentation, and magnitude of absolute spherical equivalent refractive error. School attendance (69%) was associated with better vision, however, gender was not. This is the first study reporting pediatric cataract surgical outcomes in Bangladesh. Outcomes were poor compared to the United States where 68% children achieve 20/40 or better. Results were also poor compared with other developing countries. Results from Nepal, India, and Tanzania show final VA of 20/60 or better in 40.5%-62% children. This is attributed to inadequate eye care services in Bangladesh and not to increased post-operative complications.

**Pediatric cataract surgery – other topics**

**Cost of Intraocular Lens versus Contact Lens Treatment after Unilateral Congenital Cataract Surgery in the Infant Aphakia Treatment Study at Age 5 Years**


This is a retrospective cost analysis of a prospective, randomized clinical trial. The Infant Aphakia Treatment Study is a muticenter (n = 12), randomized clinical trial comparing the optical treatment of aphakia with either primary IOL
implantation (n = 57) or contact lens correction (n = 57) in 114 infants with unilateral congenital cataract. 

Main Outcome Measures: The mean cost of cataract surgery and all additional surgeries, examinations and supplies used up to 5 years of age. 

Results: The 5-year treatment cost of an infant with a unilateral congenital cataract corrected optically with intraocular lens was $27,090 versus $25,331 for a patient treated with a contact lens after initial cataract surgery. The total cost of supplies was $3,204 in the IOL group and $7,728 in the contact lens group. 

Conclusions: Unilateral cataract surgery in infancy coupled with primary IOL implantation is approximately 7% more expensive than aphakia and contact lens correction. PATIENT COSTS ARE MORE THAN DOUBLE WITH CONTACT LENS VERSUS IOL TREATMENT.

**Femtosecond Laser-Assisted Pediatric Cataract Surgery: Bochum Formula.**

Dick HB1, Schelenz D2, Schultz T. 

This is a. The purpose of the study was to assess anterior capsulotomy enlargement after femtosecond laser treatment. The authors found that the pediatric capsule enlarged approximately 1/3 larger than the programmed capsule diameter. The authors developed a formula to help predict capsular enlargement, prospective case series from a German university hospital of 22 eyes of 18 children who underwent femtosecond laser-assisted pediatric cataract surgery noting that younger children had more enlargement than older children. This research is important when implanting pediatric IOLs that require a particular capsule size, such as the bag-in-the-lens IOL (Morcher GmbH) used in some European pediatric cataract surgeries.

The paper also provides helpful technical descriptions regarding how to perform femtosecond laser-assisted pediatric cataract surgery. The authors were successful in using the laser to perform both anterior and posterior capsulotomies.

**Corneal Changes in Children after Unilateral Cataract Surgery in the Infant Aphakia Treatment Study**


Data from the Infant Aphakia Treatment Study (ATS) which is a multicenter randomized, controlled trial of the treatment of unilateral congenital cataract with aphakic contact lens (CL) versus primary intraocular lens (IOL) implant. All patients underwent cataract surgery between 1 and 6 months of age. There were 114 patients enrolled in ATS. This paper reports the endothelial cell (EC)
characteristics and central corneal thickness (CCT) at the 5-year examination. The EC density, coefficient of variation (CV), and percent hexagonal cells were measured by noncontact specular microscopy. The CCT was measured using contact pachymetry. Fellow eyes served as controls. A total of 105 subjects (52 with CL, 53 with IOL) had data recorded. Mean EC densities were higher in aphakic eyes compared with fellow eyes (3921 vs. 3495 cells/mm²). However, mean CV was higher (27 vs. 24) and mean percent hexagonal cells was lower (72% vs. 76%) in aphakic eyes compared with fellow eyes and this thought to be due to corneal polymegathism caused by extended CL wear. Mean CCT of aphakic eyes was higher than in controls (637 vs. 563 μm). There was no difference in EC density in eyes treated with IOLs compared with fellow eyes (3445 and 3487 cells/mm²). Means for CV (25 vs. 24) and percent hexagonal cells (74 vs. 76%) were also not significantly different. Mean CCT was higher in eyes with IOLs (605 vs. 571 μm) compared with fellow eyes. Compared with treated eyes without glaucoma or glaucoma suspect, treated eyes with glaucoma had lower EC density (3289 vs. 3783 cells/mm²) and treated eyes with glaucoma suspect had greater mean corneal thickness (660 vs. 612 μm). Cataract extraction during infancy with IOL implantation was not associated with a reduced EC count in treated compared with fellow eyes, although CCT was increased. Both groups had increased CCT when compared to fellow eyes and this may be due to abnormalities in anterior segment anatomy in eyes with congenital cataract. Extended-wear aphakic CLs may cause corneal polymegathism with increased EC density and CCT. Glaucoma diagnosis was associated with reduced EC counts and increased CCT.

Evaluation of Artisan aphakic intraocular lens in cases of pediatric aphakia with insufficient capsular support.
Gawdat GI, Taher SG, Salama MM, Ali AA.
J AAPOS. June 2015;19:242-6

The Artisan IOL is of a different design than previous iris-fixated IOLs. The authors looked at the postoperative outcomes of its use in aphakic pediatric eyes lacking adequate capsular support. 25 eyes of 18 patients were included. 18 cases were primary implantation with lensectomy and 7 underwent secondary implantation. The mean age was 7.86 years. There were statistically significant improvements in acuity for both traumatic aphakia cases and for subluxed lens cases. IOP measurements did not change significantly during the postoperative period. The mean CECD decreased significantly with a mean loss of 19%. No spontaneous decentrations occurred but two cases had further trauma with de-enclavation of one claw. 2 of 25 cases had iritis with incipient papillary membrane and fine keratic precipitates treated with topical cycloplegia and steroids. One patient had pupillary block relieved with a peripheral iridectomy. Artisan aphakic intraocular lenses can be considered when adequate capsular support is lacking.
Cataract surgery in children with congenital keratolenticular adhesion (Peters anomaly type 2).
Medsinge A, Nischal KK.
_J AAPOS_. February 2015;19:24-8

Visual and surgical outcomes in patients operated on using a lensectomy technique developed to prevent further corneal opacification after surgical removal of the cataract were reported. This was a retrospective review of consecutive children operated on over an 11-year period. The technique is described. 4 eyes of 3 patients with KLA (mean age 37 months, mean follow-up 3.3 years) had surgery and none had a complicated postoperative course. Corneal opacities did not progress. 1 eye received an IOL implant. This technique minimized corneal endothelial cell decompensation postoperatively. This study provides detail on a surgical technique that can be helpful when patients have this complicated ocular condition.

Image-Guided Femtosecond Laser–Assisted Cataract Surgery in Peters Anomaly Type 2
Hou J, Crispim J, Cortina M, de la Cruz J.

The authors describe a technique for image-guided femtosecond laser–assisted cataract surgery in a case of type 2 Peters anomaly, characterized by corneal leukoma with cataract and corneolenticular adhesions. A six year old boy with a central corneal opacity but clear peripheral cornea had visual acuity in his better eye slip from 20/100 to finger counting due to cataract progression. Because his other eye had done poorly after corneal transplantation, the authors attempted cataract removal alone. Femtosecond laser technology enabled reliable construction of a complete capsulotomy despite central corneal opacification and a tented anterior capsule, and the patient then underwent cataract extraction alone, leaving his cornea as is. This surgical technique could be applied in specific situations of type 2 Peters anomaly, sparing the child the penetrating keratoplasty that comes with extremely high long term risks.

Lens regeneration using endogenous stem cells with gain of visual function.
_Nature_. March 2016;531(7594):323-8

The repair and regeneration of tissues using endogenous stem cells represents an ultimate goal in regenerative medicine. This is the first study demonstrating the regeneration of a human lens. The authors isolate lens epithelial stem/progenitor cells (LECs) in mammals and show that Pax6 and Bmi1 are required for LEC renewal. They design a surgical method of cataract removal
that preserves endogenous LECs and achieves functional lens regeneration in rabbits and macaques. They then perform this technique in 12 infants (24 eyes) ages <24 months with bilateral congenital cataracts. The control group was 25 infants (50 eyes) who underwent standard cataract surgery with either intraocular lens implantation or aphakia. In the new technique, the authors perform a 1.0-1.5 mm peripheral anterior capsuorrhexis and remove the cataractous lens through this small opening, leaving most of the anterior capsule and posterior capsule intact, and leaving most of the LECs. Then, over the next three to six months, they observe the LECs recreate a lens with refractive power and some accommodating ability. The small peripheral anterior capsular opening heals, leaving a peripheral scar in the lens. They use Teller acuity cards to measure postoperative visual acuity, showing approximately 20/200 average acuity six months later. They show slit lamp photographs and clear fundus photographs through the regenerated lenses, proving relatively normal lens shape and clarity.

The authors harness what we previously deemed a complication of infantile cataract surgery: Soemmering’s ring formation and visual axis opacification, and use the ability of LECs to proliferate to an advantage. This approach demonstrates a novel treatment strategy for infantile cataracts, and it’s exciting to envision whether this approach could even be utilized in adult eyes. This study is a breakthrough for medicine in general, showing functional tissue regeneration using endogenous stem cells. Finally, the study is an exceptional example of translational research, truly taking what is learned from the laboratory bench to the bedside!

Critiques of this study include: The control group did not undergo standard of care as practiced in the United States (undergoing YAG laser to the posterior capsule three months postoperatively rather than a primary posterior capsulectomy / anterior vitrectomy). The control group eyes were not directly compared to the study group eyes in terms of visual acuity outcomes. The main statistical comparison was preoperative versus postoperative visual acuity in the experimental group, rather than postoperative visual acuity in the experimental group vs postoperative visual acuity in the control group, and that set the bar low for showing a successful treatment effect. Those measuring visual acuity with Teller cards could not truly be masked to experimental vs. control treatment group owing to the need for aphakic correction in the control group. Refractive correction is not discussed in this paper. Amblyopia is also not discussed; what impact will that 3-6 month delay in waiting for a lens to grow back play on final visual outcome? Many of these questions pertinent to the pediatric ophthalmologist will hopefully be addressed in a subsequent paper giving more details.
**Pediatric glaucoma - surgical management**

**Valved Glaucoma Drainage Devices in Pediatric Glaucoma Retrospective Long-term Outcomes**  
Chen A, Yu F, Law SK, Giaconi JA, et.al.  
*JAMA Ophthalmol.* September 2015;133(9):1030-5

This is a retrospective study looking at long term outcomes of initial and repeat glaucoma drainage devices (GDD) in a cohort of children with glaucoma. The authors also wanted to identify risk factors associated with GDD failure. One hundred nineteen eyes of 89 patients less than 18 years of age with glaucoma were studied. The glaucoma drainage device implanted was a silicone or polypropylene Ahmed valve. Success was defined as a final intraocular pressure of 5 to 21mmHg, as well as a 20% reduction from baseline intraocular pressure, with or without medications. The group was subdivided into primary glaucoma (congenital and juvenile glaucoma), uveitic glaucoma (mainly juvenile idiopathic arthritis) and secondary glaucoma (anterior segment dysgenesis, phakomatoses, retinopathy of prematurity, previous cataract surgery, steroid induced, and trauma). At 5 years post-op first GDD, the average success rate was 55% with an average intraocular pressure reduction of 13 mmHg and there was no difference in mean number of glaucoma meds pre-op versus post-op. At 5 years post-op a subsequent GDD, the success rate was 52.8%. Older age at GDD implantation, a diagnosis of uveitic glaucoma, and polypropylene GDDs were associated with higher survival rates for GDD.

**Gonioscopy assisted transluminal trabeculotomy: an ab interno circumferential trabeculotomy for the treatment of primary congenital glaucoma and juvenile open angle glaucoma.**  
*Br J Ophthalmol.* August 2015;99:1092-6

This is an introduction to a novel ab interno 360° trabeculotomy surgery for treating primary congenital glaucoma (PCG) and juvenile open angle glaucoma (JOAG). Gonioscopy assisted transluminal trabeculotomy (GATT) is approached from a paracentesis created temporally. A goniotomy is then performed nasally and a microcather is advanced in Schlemm’s canal circumferentially 360° within the anterior chamber. The progress of the microcatheter is noted by observing the illuminated tip. Traction is first placed on the distal and then on the proximal tips to create the 360° trabeculotomy. The advantage of this procedure is that there is no manipulation of conjunctival tissue that will affect the success of trabeculectomy, if necessary, later in life. The authors presented preliminary
results of interventions performed on 14 eyes of 10 patients, with an age range from 17 months to 30 years (mean = 18.4 yrs), during a mean follow-up time of 20.4 months (range 12-33 months). In all eyes, the mean decrease in IOP was 12.5 mmHg and the mean decrease in IOP lowering medications was 1.8. The investigators reported that there were no major complications after this procedure. The rate of hyphema was comparable to that of trabeculotomy ab externo. The surgery is technically more challenging than goniotomy or trabeculotomy ab externo. Visibility of anterior chamber is important since surgery is performed using a gonioscopic view.

Comparison of 360-degree versus traditional trabeculotomy in pediatric glaucoma.
*J AAPOS.* April 2015;19:143-9

This study compared IOP control and surgical success of traditional (<360 degree)(Group 1) with 360-degree trabeculotomy (Group 2). 12 years of records were retrospectively reviewed. Group 1 had 77 eyes of 56 patients and group 2 had 14 eyes of 10 patients. Age at surgery was 1.52 years and 0.61 years respectively. 1 year after surgery both group showed significant decreased IOP. At 1-month IOP dropped from 28.75mm Hg to 19.63mm Hg in group 1 and from 30.36mm Hg to 12.17mm Hg in group 2. At 1-year IOP was 17.05mm Hg and 11.00mm Hg respectively. Group 2 IOP was statistically significantly lower than group 2 at 1, 3 and 12 months postoperatively but not at 6-month follow-up. 42% (32/77) patients required reoperation within the first year in group 1 versus 2/14 (14%) in group 2. Success at 1-year was 58.44% for group 1 and 85.71% for group 2. Group 1 showed a 3.9% complication rate (hyphema n=2, and iris prolapse n=1), versus a 21.43% complication rate in group 2 (hyphema n=3). The subset of primary glaucoma patients also showed robust IOP lowering in both groups but overall success rates were better in group 2 patients. Also group 2 patients required fewer postoperative IOP lowering medications. This study is limited by the small number of patients in group 2. Group 2 experienced a more pronounced effect but greater complications.

The use of irradiated corneal patch grafts in pediatric Ahmed drainage implant surgery
Nolan KW, Lucas J, Abbasian J.
*J AAPOS.* October 2015;19:445-9

An alternative material for a patch graft is irradiated cornea. It provides good cosmesis and allows visualization of the underlying tube. Medical records of 6 different glaucoma surgeons over a 14-year period were reviewed. Twenty-five procedures on 20 patients met inclusion criteria. Tube erosion through the patch graft and overlying conjunctiva occurred on two separate procedures in 1 eye. This same patient had the only persistent inflammation reported in the series.
Two cases of wound dehiscence secondary to broken conjunctival limbal sutures occurred. There were no cases of endophthalmitis over an average of 24.8 months of follow-up. The surgical technique is described. This technique utilizes donated corneal tissue that is not felt suitable for corneal transplants, provides, excellent cosmesis, and clarity to facilitate suture lysis, and makes infectious agent transmission unlikely. Complication occurrence was rare.

**Evaluation the adjunctive use of combined bevacizumab and mitomycin to trabeculectomy in management of recurrent pediatric glaucoma**

In this prospective trial, the authors investigate if the use of bevacizumab at the time of trabeculectomy improves long term pressure control for children with congenital glaucoma undergoing repeat glaucoma surgery. 12 children between the ages of 7 months to 4 years were included in the study. They all had the diagnosis of pediatric glaucoma and all had had previous surgery but had poor IOP control prior to entering this study. Each child in the study underwent surgery in both eyes. In one eye the received trabeculectomy with mitomycin, in the fellow eye they received trabeculectomy with mitomycin with the addition of subconjunctival bevacizumab 2.5 mg over the scleral flap at the completion of the surgical case. At the one-year post op follow, the eye receiving the bevacizumab had lower IOP compared to the fellow eye (12.8 vs. 15.6 mmHg). There was no difference in complication rates between the two groups. This adjuvant therapy may be useful not only for pediatric glaucoma but for adults as well.

**Potential Effect of Tumor Necrosis Factor Inhibitors on Trabeculectomy With Mitomycin C for Patients With Juvenile Idiopathic Arthritis–Related Uveitic Glaucoma: A Retrospective Analysis**

This is a retrospective observational study which seeks to determine if systemic treatment with a tumor necrosis factor (TNF) inhibitor changes the success rate of trabeculectomy with mitomycin C (MMC trab) in uveitic glaucoma patients with juvenile idiopathic arthritis. Young age and chronic inflammation decrease the success rate of filtering surgery. Most patients with uveitic glaucoma will require surgery to control their intraocular pressure. Twenty-nine consecutive patients underwent an MMC trab and 15/29 (52%) patients were on systemic anti-TNF treatment at the time of surgery. Main outcome measure was Kaplan Meier survival curves of MMC trabs. Failure occurred if IOP >21mmHg with need for
post op glaucoma medicines or need for further glaucoma surgery. The success rate of trabeculectomy for patients who were treated with TNF inhibitors was 73% at 1, 5, and 10 years after surgery, whereas the success rates of trabeculectomy for patients who were not treated with TNF inhibitors were 57%, 16%, and 0% at 1, 5, and 10 years after surgery, respectively (P = .01).

Importance: Treatment with TNF inhibitors was associated with a high trabeculectomy success rate for patients who did not have prior ocular surgery. The trabeculectomies performed on patients who received TNF inhibitors at the time of surgery were successful for a longer length of time (median, 3.2 years) than those performed on patients who did not receive TNF inhibitors (median, 1.2 years).

**Pediatric glaucoma - medical management**

**Periocular skin hyperpigmentation in children treated with prostaglandin analogues.**

_J AAPOS. February 2015;19:49-53_

Objective and subjective measures were used to classify periocular skin hyperpigmentation in children with glaucoma who were taking PGA for more than 6 months. Objective measurements were taken with a chromameter. 55 eyes were evaluated. Mean age was 9.0 years and mean duration of treatment was 14.8 months. The treated side upper lid had a pigmentation score of 8.7, which was significantly greater than the ipsilateral cheek. The lower lid score of 5.1 was also significantly greater than the ipsilateral cheek. The upper lid was score was significantly greater than the lower lid score. These differences compared to the cheek were not found on the nontreated eye side of patients with unilateral glaucoma but there was still a 1.9 difference between the upper and lower lid scores. Duration of treatment did not alter results, nor did the complexion of the child. Only 20% of parents questioned noted the change. Results may have been augmented because the authors used the eye with the higher score in bilateral glaucoma cases. Also this study enrolled Saudi children so pigment changes may be different in children of other races. Although the findings of this study may not be generalizable, it adds to the literature by evaluating periocular skin pigment changes in children after PGA use.
Intraocular pressure control with echothiophate iodide in children’s eyes with glaucoma after cataract extraction.
Kraus CL, Trivedi RH and Wilson ME.
J AAPOS. April 2015;19:116-8

The authors evaluated echothiophate iodide (EI) for its potential side effects and IOP-lowering ability in aphakic and pseudophakic children with glaucoma. This was a retrospective review of 21 years of patients. 32 eyes (27 aphakic and 5 pseudophakic) of 21 children met inclusion criteria. 29/32 eyes received EI as an adjuvant therapy. Mean IOP dropped 9.5mm Hg with the addition of EI and overall was reduced in 31 of 32 eyes. Three eyes had acceptable IOP on EI alone. Average duration of use was 3.5 years. The only reported side effect was transient redness in 3/32 eyes. No retinal detachments or iris cysts were observed or reported. EI can be added as a medical treatment option for aphakic and pseudophakic children with glaucoma.

Pediatric glaucoma – corneal biometry, OCT and visual field

Ely A, El-Dairi M, Freedman S.
Am J Ophthal. Nov 2015; 158(5);905-15

This retrospective study tried to identify optic nerve head cupping reversal and looked at OCT and HVF changes as well. Sequential surgical cases of juvenile glaucoma or primary congenital glaucoma were examined. Group 1 had preoperative and postoperative photos and OCT while group 2 had preop clinical optic nerve assesments and post op imaging. 9 eyes were in group 1; 24 eyes were in group 2. 56% of group 1 showed cupping reversal. HVF showed no real change. In group 2, 14 eyes demonstrated cupping reversal. However, some eyes still showed continued nerve fiber layer thinning posteropatively. This suggests that cupping reversal in pediatric glaucoma may not be a predictor of improved optic nerve health.

Visual field loss in primary congenital glaucoma.
J AAPOS. April 2015;19:124-9

Perimetry was evaluated in a cohort of patients with primary congenital glaucoma (PCG) having a controlled IOP of <=14mm Hg to determine typical defects and correlate their severity with clinical risk factors. This was a cross-sectional study of consecutive patients over a 1-year period. Humphrey field analyzer (HFA) was performed on 56 PCG eyes of 47 children and Goldmann perimetry on 44 PCG
eyes of 30 children. Mean age of patients who underwent HFA was 12.2 years. 79% of fields were reliable. False-positive were the most common cause of unreliability. Of the 44 reliable and reproducible fields, 32 (73%) had a visual field defect (11- mild, 12-moderate, and 9-severe). Goldmann perimetry patients mean age was 11.6 years. Control patients had significantly higher mean global visual field extents for all three targets than PCG patients. Overall, a definite scotoma was present in 41% of eyes (n=36). These divided into single arcuate (n=12), biarcuate (n=7), paracentral (n=8), nasal step (n=5), and only a central island of vision (n=4). Results were similar to those reported for adult patients. Baseline IOP, especially >30mm Hg was significantly associated with visual field loss. HFA was recommended over Goldmann to document and demonstrate progression of visual field defects. Data on visual field defects in children with PCG are limited because of testing difficulty and this study attempts to provide some information about associated visual field defects.

**Optic nerve morphology in normal children**
*J AAPOS.* December 2015;19:526-30

The authors provide a normative database of pediatric eyes analyzed with the Optovue OCT. These were compared to adult data in the Optovue database. Eighty-three healthy 5-year old children were recruited and six were excluded from analysis. The average RNFL (retinal nerve fiber layer) thickness was 103.92 μm, the mean GCC (ganglion cell complex) thickness was 98.36 μm. No statistical difference was identified between the children and adults aged 18-25 years and 40-45 years with respect to either measurement. However adults 55-60 years showed thinner RNFL and GCC. Children’s ONHs (optic nerve heads) were statistically less cupped but the difference in disk area compared to adults was marginal. Most of the patients in this study were Caucasian and they were all 5 years old so caution must be used when applying the data to other groups. However, normative data can be helpful since it is currently lacking in this age group.

**Pediatric glaucoma – other topics**

**Primary Congenital Glaucoma Outcomes: Lessons From 23 Years of Follow-up**

This retrospective study was analyzing the effects of age at presentation on congenital glaucoma and whether there were critical ages for glaucoma progression and surgical management. They looked at 192 surgical procedures on 117 eyes over a 23 year time period. They found that children diagnosed
under 3 months of age had a visual outcome of 20/200 or worse despite successful glaucoma control. The age of presentation did not affect surgical success. There appeared to be glaucoma progression around 2 and 5 years of age requiring further surgery. In addition, the surgeons in this study found that 78.9% of cases undergoing primary trabeculotomy were controlled with one surgery which opened 4 clock hours. Therefore, only 21% of cases required more than 120 degrees of angle opened.

**Movement of Retinal Vessels to Optic Nerve Head with Intraocular Pressure Elevation in a Child – case report**
*Ophthalmology*. July 2015; 122(7):1532-4

Retinal vasculature around the optic nerve head is not a static structure in patients with glaucoma. Nasal displacement of retinal vessels occurs and is especially common in younger patients, and may be associated with more rapid field loss. This is a case report of a 4 year old girl with juvenile idiopathic arthritis who developed glaucoma. Disc photos at initial presentation and many months later show movement of the retinal vessels onto the disc.

**In vitro characteristics of Tenon’s fibroblast lines derived from pediatric and adult eyes do not fully explain pediatric glaucoma surgery failure: a preliminary report**
Baig NB, Shields B, Darr DJ, Buckley EG, et al.
*J AAPOS*. October 2015;19:455-61

The authors hypothesized that age-related differences in outcomes of glaucoma-filtration surgery may be influenced by intrinsic properties of Tenon’s capsule fibroblasts. They compared in vitro characteristics of Tenon’s capsule fibroblast lines from children and older adults. Fibroblast cell lines were derived from 6 eyes of 5 children (median age 2.45 years) and 7 eyes of 7 adults (median age 71 years). From day 0 to day 14, fibroblasts increased in number for both groups, albeit at a statistically different (slower) rate in older adults. Mean doubling times were shorter for the young line at high-plating densities but not at low-plating densities. There was no significant difference in wound closure or collagen synthesis when comparing young versus old lines. The authors felt the in vitro differences between the two groups were modest, and therefore other factors must mediate the higher failure rates of pediatric glaucoma filtration surgery.

**Peripheral Retinal Degenerations and Rhegmatogenous Detachment in Primary Congenital Glaucoma**
*Retina*. January 2016; 36:188-91
The authors of this study sought to determine the prevalence of peripheral retinal degeneration (PRD) and rhegmatogenous retinal detachment (RRD) in patients with primary congenital glaucoma. The records of 310 eyes (180 patients) with primary congenital glaucoma operated from the year 2000 onwards were evaluated and the prevalence of RRD was noted. Those children who were old enough to cooperate and had sufficient media clarity were screened with indirect ophthalmoscopy and the prevalence of PRD was estimated in this subset. RRD was detected in 13/310 eyes (4%); mean axial length of these eyes was 26.3 mm. Among the eyes screened for PRD (n=60), prevalence of pathologic PRD (lattice with or without atrophic holes and isolated holes/tears) was 15%. Mean axial length was significantly greater in eyes with pathologic PRD than in those without (28.1 mm vs. 25.8 mm). For axial length >26 mm, the odds of having a pathologic PRD were 14.4 times more than those with axial length <26 mm. The authors conclude that the prevalence of PRD among eyes with primary congenital glaucoma is high, and peripheral retinal screening should be performed, especially in eyes with axial length >26 mm. This study was limited in that only a subset of subjects could be examined for PRD due to cooperation and media challenges. Nevertheless, it is known that the risk of RD is exponentially increased in high myopes with lattice degeneration. A longitudinal study to detect the percentage of patients with primary congenital glaucoma with pathologic PRDs that ultimately develop RRD would be useful.

15.REFRACTIVE SURGERY

Visual Acuity Improvement in Adult Amblyopic Eyes With an Iris-Fixated Phakic Intraocular Lens: Long-Term Results.
Venter JA, Pelouskova M, Schallhorn SC, Collins BM

This retrospective case series evaluated the effect of implanting Artisan iris-fixated phakic intraocular lenses in adult amblyopic eyes. Patients underwent phakic Artisan lens implantation if they had high refractive error not amenable to corneal refractive surgery. The study analyzed 5 year follow up data. Group 1 comprised 82 eyes with myopia (mean -13.4 D) or myopic astigmatism, and Group 2 contained 21 eyes with hyperopia (mean +6.8 D) or hyperopic astigmatism. The mean CDVA improved from 0.51 ± 0.15 logMAR to 0.34 ± 0.16 logMAR (P<.001) in Group 1 and from 0.54 ± 0.17 log MAR to 0.46 ± 0.14 logMAR in Group 2 (P<.005). The mean gain in CDVA was statistically significantly greater in Group 1 than in Group 2.

The study suggests that phakic intraocular lenses are an alternative to spectacle and contact lenses for correcting high ametropia in amblyopic adults. This study also raises the question of whether the improved visual acuity in the
adult (primarily myopic) amblyopic eyes occurred due to cortical plasticity. However, alternative explanations exist: (1) the Artisan lens was closer to the eye’s nodal point than a contact lens or spectacle lens, and thus increased image magnification, and (2) the postoperative refraction could be better optimized once a large amount of ametropia was corrected by the Artisan lens.

**Evaluation of Artisan aphakic intraocular lens in cases of pediatric aphakia with insufficient capsular support.**
Gawdat GI, Taher SG, Salama MM, Ali AA.
*J AAPOS.* June 2015;19:242-6

The Artisan IOL is of a different design than previous iris-fixated IOLs. The authors looked at the postoperative outcomes of its use in aphakic pediatric eyes lacking adequate capsular support. 25 eyes of 18 patients were included. 18 cases were primary implantation with lensectomy and 7 underwent secondary implantation. The mean age was 7.86 years. There were statistically significant improvements in acuity for both traumatic aphakia cases and for subluxed lens cases. IOP measurements did not change significantly during the postoperative period. The mean CECD decreased significantly with a mean loss of 19%. No spontaneous decentrations occurred but two cases had further trauma with de-enclavation of one claw. 2 of 25 cases had iritis with incipient papillary membrane and fine keratic precipitates treated with topical cycloplegia and steroids. One patient had pupillary block relieved with a peripheral iridectomy. Artisan aphakic intraocular lenses can be considered when adequate capsular support is lacking.

**Photorefractive Keratectomy in 22 Adult Eyes With Infantile Nystagmus Syndrome**

This study analyzed the visual and refractive outcomes of photorefractive keratectomy (PRK) in eleven adult patients with infantile nystagmus syndrome. PRK was performed under topical anesthesia using an eye-tracking excimer laser. As is expected among nystagmus patients, the preoperative refractive error included significant astigmatism (mean -3.40 ± 1.31 D [SD]). PRK was successful in reducing the astigmatism to -0.70 D ± 0.81 [SD], P < .0001. The mean binocular postoperative UDVA was better than the mean preoperative CDVA (0.15 ± 0.14 logMAR versus 0.23 ± 0.23 logMAR) (P = .05). This study provides evidence that PRK is an alternative to spectacles or contact lenses for the correction of refractive error, including moderate astigmatism, among adult infantile nystagmus patients.
Implantation of Spherical and Toric Copolymer Phakic Intraocular Lens to Manage Amblyopia Due to Anisometropic Hyperopia and Myopia in Pediatric Patients
Emara K, Al Abdulsalam O, Al Habash A.

The authors implanted the Visian Implantable Collamer Lens phakic intraocular lens (pIOL) in children with refractory amblyopia due to high anisometropic myopia or hyperopia. These children were not compliant with spectacle/contact lens correction. 11 eyes (9 myopic, 2 hyperopic) of 11 patients aged 5 to 15 years were identified. Of the 9 myopic eyes, 6 eyes received spherical pIOLs and 3 received toric pIOLs. Both hyperopic eyes received spherical pIOLs. Preoperatively, the mean cycloplegic refractive spherical equivalent (CRSE) was -11 D (range -7.8 to -21.9 D) in myopic eyes, and +8.8 D (range +8.6 to +8.9 D) in the two hyperopic eyes. The mean corrected distance visual acuity (CDVA) was 20/171 (range 20/40 to 20/400) in myopic eyes, and 20/130 (range 20/60 to 20/200) in hyperopic eyes. At a mean follow-up of 16.8 months in myopic eyes, the mean CRSE was -1.4 D (range 0 to -2.3 D), and mean CDVA was 20/51 (range 20/20 to 20/100). In the two hyperopic eyes, at a mean follow-up of 15 months, the CRSE was +1.8 D and +1.9 D, and the CDVA had improved to 20/25 in both eyes. The two hyperopic eyes had minor complications: an IOP spike on postoperative day one and pigment deposition on the pIOL.

The authors conclude that pIOL implantation may be considered a treatment option for refractory amblyopia due to anisometropic hyperopia or myopia in children who are noncompliant with conventional therapy. Corneal refractive surgery is typically limited to refractive errors of +5 D to -10 D, and pIOL can be considered for refractive errors outside of that range.

Visual Outcomes in Adult Amblyopic Eyes with Moderate Myopia After Corneal Laser Surgery Versus Copolymer Phakic Intraocular Lens Implant

The authors assessed visual acuity and refractive correction in moderately myopic adult eyes with suboptimal preoperative corrected distance visual acuity (CDVA) after laser in situ keratomileusis (LASIK) or insertion of a posterior chamber Implantable Collamer Lens phakic intraocular lens (pIOL). This retrospective study sample included 1310 eyes that had LASIK and 94 that had insertion of a pIOL from July 2002 to September 2013. Suboptimal preoperative CDVA was defined as equal to 0.7 or below (< 20/28) and moderate myopia as a spherical equivalent of -5 to -10 D. Please note that the study title calls these adult amblyopic eyes, but amblyopia was not confirmed. The inclusion criterion
was poor preoperative corrected distance visual acuity and the absence of organic eye disease; the authors did not attempt to prove amblyopia as the reason for poor CDVA. The preoperative mean CDVA was very similar between the LASIK and pIOL groups: 20/33. Postoperative uncorrected distance visual acuity (UDVA) was 20/27 (0.13 \pm 0.12 \text{logMAR}) in the LASIK group and 20/26 (0.12 \pm 0.09 \text{logMAR}) in the pIOL group. Postoperative CDVA was 20/26 (0.11 \pm 0.10 \text{logMAR}) in the LASIK group and 20/24 (0.08 \pm 0.07 \text{logMAR}) in the pIOL group. Compared with preoperative values, amblyopic eyes with moderate myopia post LASIK or post pIOL demonstrated a statistically significant improvement in UDVA and CDVA (P < .001). The pIOL group performed significantly better than the LASIK group, though the small difference may not be clinically meaningful.

16. GENETICS


The authors retrospectively analyzed the association between mutations affecting the Wnt-signaling receptor protein (FZD4) and inherited vitreoretinopathies and retinopathy of prematurity (ROP). There were 421 participants with vitreoretinopathies and 98 full-term healthy infant controls included. Analysis of the FZD4 gene was performed with Sanger sequencing. Participants with a diagnosis of familial exudative vitreoretinopathy (FEVR), Norrie disease, Coats’ disease, bilateral persistent fetal vasculature, and ROP were reviewed for the presence of a FZD4 variant. The sequence variation p.[P33S;P168S], the most prevalent FZD4 variant, was statistically significant for ROP and FEVR compared with full-term newborns. In addition, infants expressing the sequence variation tended to have significantly lower birth weights for respective gestational age. This suggests that the FZD4 p.[P33S;P168S] variant may be a risk factor for retinopathy and restricted intrauterine growth. Therefore, testing for FZD4 gene mutations may be useful in patients with suspected FEVR and ROP. Furthermore, the relatively high prevalence of the p.[P33S;P168S] variant in ROP and intrauterine growth restriction suggests that it also may be a marker for increased risk of developing ROP and preterm birth.
Novel FRMD7 Mutations and Genomic Rearrangement Expand the Molecular Pathogenesis of X-Linked Idiopathic Nystagmus


Idiopathic infantile nystagmus (IIN; OMIM 31700) with X-linked inheritance is one of the most common forms of infantile nystagmus. To date three X-linked loci have been identified including: Xp11.4-p11.3 (calcium/calmodulin-dependent serine protein kinase [CASK]), Xp22 (GPR143), and Xq26-q27 (FRMD7). The authors investigated the role of mutations and copy number variations (CNV) of FRMD7 and GPR143 in the molecular pathogenesis of IIN in 49 unrelated Belgian probands. Molecular testing was performed using Sanger sequencing, targeted next generation sequencing (NGS) and CNV analysis with multiplex ligation–dependent probe amplification (MLPA). In 11/49 probands, nine unique FRMD7 changes and four known mutations were found. No GPR143 mutations or CNVs were found in the remainder of the probands (38/49). Overall, genetic defects of FRMD7 were found in 22.4% of probands, including the first reported genomic rearrangement of FRMD7 in IIN, expanding its mutational spectrum. Finally, the authors generated a discovery cohort of IIN patients potentially harboring either hidden a variation of FRMD7 or mutations in genes at known or novel loci sustaining the genetic heterogeneity of IIN.

Submicroscopic Deletions at 13q32.1 Cause Congenital Microcoria


Congenital microcoria (MCOR), which is characterized by inability of the iris to dilate owing to absence of dilator pupillae muscle, is a rare autosomal-dominant disorder with only twelve MCOR-affected families reported to date. In some families there has been confirmed linkage to a unique 8 Mb locus on chromosome 13q31–q32. However, other families were inconsistent with the 13q31–q32 region, supporting genetic heterogeneity of the disease. The authors used whole-genome oligonucleotide array comparative genomic hybridization (CGH) to identified deletions at 13q32.1 segregating with MCOR in six families originating from France, Japan, and Mexico. Heterozygote 13q32.1 deletions were found in all six MCOR-affected families. The deletions varied from 35 kbp to 80 kbp in size, but invariably encompassed or interrupted only two genes: TGDS, encoding the TDP-glucose 4,6-dehydratase, and GPR180, encoding the G protein-coupled receptor 180. Unlike TGDS, which has no known function in muscle cells, GPR180 is involved in the regulation of smooth muscle cell growth. The identification of a null GPR180 mutation segregating over two generations with iridocorneal angle dysgenesis, which can be regarded as a MCOR endophenotype, is consistent with the view that deletions of this gene, with or without the loss of elements regulating the expression of neighboring genes, are the cause of MCOR. Further studies will hopefully allow the identification of the
molecular mechanisms underlying this rare disease.


Microphthalmia with linear skin defects (MLS) syndrome is an X-linked male-lethal disorder also known as MIDAS (microphthalmia, dermal aplasia, and sclerocornea). Additional clinical features include neurological and cardiac abnormalities. Heterozygous mutations in HCCS or COX7B have been identified in MLS-affected females. Both genes encode proteins involved in the structure and function of complexes III and IV, which form the terminal segment of the mitochondrial respiratory chain (MRC). However, not all individuals with MLS syndrome carry a mutation in either HCCS or COX7B. The majority of MLS-affected females have severe skewing of X chromosome inactivation, suggesting that mutations in HCCS, COX7B, and other as-yet unidentified X-linked gene(s) cause selective loss of cells in which the mutated X chromosome is active. By applying whole-exome sequencing and filtering for X-chromosomal variants, the authors identified a de novo nonsense mutation in NDUFB11 (Xp11.23) in one female individual and a heterozygous 1-bp deletion in a second individual, her asymptomatic mother, and an affected aborted fetus of the subject’s mother. NDUFB11 encodes one of 30 poorly characterized supernumerary subunits of NADH:ubiquinone oxidoreductase, known as complex I (cI), the first and largest enzyme of the MRC. By shRNA-mediated NDUFB11 knockdown in HeLa cells, the authors demonstrated that NDUFB11 is essential for cI assembly and activity as well as cell growth and survival. These results demonstrate that X-linked genetic defects leading to the complete inactivation of complex I, III, or IV underlie MLS syndrome. The data reveal an unexpected role of cI dysfunction in a developmental phenotype, further underscoring the existence of a group of mitochondrial diseases associated with neurocutaneous manifestations.


Multiple pterygium syndrome (MPS) is a phenotypically and genetically heterogeneous group of rare Mendelian conditions characterized by multiple pterygia, scoliosis, and congenital contractures of the limbs. MPS typically segregates as an autosomal-recessive disorder, but rare instances of autosomal-dominant transmission have been reported. Whereas several mutations causing recessive MPS have been identified, the genetic basis of dominant MPS remains unknown. The authors identified four families affected by dominantly transmitted MPS characterized by pterygia, camptodactyly of the hands, vertebral fusions,
and scoliosis. Exome sequencing identified predicted protein-altering mutations in embryonic myosin heavy chain (MYH3) in three families. MYH3 mutations underlie distal arthrogryposis (DA) types 1, 2A, and 2B, but all mutations reported to date occur in the head and neck domains. In contrast, two of the mutations found to cause MPS in this study occurred in the tail domain. The phenotypic overlap among persons with MPS, coupled with physical findings distinct from other conditions caused by mutations in MYH3, suggests that the developmental mechanism underlying MPS differs from that of other conditions and/or that certain functions of embryonic myosin might be perturbed by disruption of specific residues and/or domains. Moreover, the vertebral fusions in persons with MPS, coupled with evidence of MYH3 expression in bone, suggest that embryonic myosin plays a role in skeletal development.

**Unique Variants in OPN1LW Cause Both Syndromic and Nonsyndromic X-Linked High Myopia Mapped to MYP1.**

Though MYP1 is a locus for X-linked syndromic and nonsyndromic high myopia, the genetic defects in MYP1 responsible for these phenotypes have not been clear. Recently, unique haplotypes in OPN1LW were found to be responsible for X-linked syndromic high myopia mapped to MYP1. The current study tested if such variants in OPN1LW were also responsible for X-linked nonsyndromic high myopia mapped to MYP1. The proband of a family previously mapped to MYP1 was initially analyzed using whole-exome sequencing and whole-genome sequencing. Additional probands with early-onset high myopia were analyzed using whole-exome sequencing. Variants in OPN1LW were selected and confirmed by Sanger sequencing. Long-range and second PCR were used to determine the haplotype and the first gene of the red-green gene array. Candidate variants were further validated in family members and controls. The unique LVAVA haplotype in OPN1LW was detected in the family with X-linked nonsyndromic high myopia mapped to MYP1. In addition, this haplotype and a novel frameshift mutation (c.617_620dup, p.Phe208Argfs*51) in OPN1LW were detected in two other families with X-linked high myopia. The unique haplotype cosegregated with high myopia in the two families. OPN1LW was not present in 247 male controls. Reevaluation of the clinical data in both families with the unique haplotype suggested nonsyndromic high myopia. This study confirms that unique variants in OPN1LW are responsible for both syndromic and nonsyndromic X-linked high myopia mapped to MYP1.
Lack of Interphotoreceptor Retinoid Binding Protein Caused by Homozygous Mutation of RBP3 Is Associated With High Myopia and Retinal Dystrophy


The RBP3 gene encodes the interphotoreceptor retinoid binding protein (IRBP), a glycoprotein exclusively expressed by photoreceptors and the pineal gland. This study includes four patients from two consanguineous families with a similar childhood-onset retinal dystrophy resulting from novel homozygous nonsense mutations in RBP3. Whole exome sequencing and subsequent direct Sanger sequencing were utilized. Detailed phenotyping was performed, including full clinical evaluation, electroretinography, fundus photography, fundus autofluorescence (FAF) imaging, and spectral-domain optical coherence tomography (OCT). Two novel homozygous nonsense mutations (c.1530T>A;p.Y510* and c.3454G>T;p.E1152*) in RBP3 were identified in four patients from two families. All four patients had a similar, unusual retinal dystrophy characterized by childhood onset high myopia, generalized rod and cone dysfunction, and an unremarkable fundus appearance. The FAF imaging showed multiple paracentral foci of low autofluorescence in one patient and patchy increased FAF in the region of the vascular arcades in another. The OCT showed loss of outer retinal bands over peripheral macular areas in all 4 cases. To our knowledge, this report is the first to describe the retinal dystrophy in children caused by homozygous nonsense RBP3 mutations, highlighting the requirement for IRBP in normal eye development and visual function. Longitudinal study will reveal if the four children reported here will progress to a more typical retinitis pigmentosa phenotype described previously in adults with RBP3 mutations. The RBP3-related disease should be considered in children with high myopia and retinal dystrophy, particularly when there are no significant fundus changes.

Homozygosity for Frameshift Mutations in XYLT2 Result in a Spondylo-Ocular Syndrome with Bone Fragility, Cataracts, and Hearing Defects


Heparan and chondroitin/dermatan sulfated proteoglycans have a wide range of roles in cellular and tissue homeostasis including growth factor function, morphogen gradient formation, and co-receptor activity. Proteoglycan assembly initiates with a xylose monosaccharide covalently attached by either xylosyltransferase (XylT) I or II. The authors identified three individuals from two families were found that exhibited similar phenotypes. The index case subjects were two brothers, individuals 1 and 2, who presented with osteoporosis, cataracts, sensorineural hearing loss, and mild learning defects. Whole exome sequence analyses showed that both individuals had a homozygous c.692dup
mutation (GenBank: NM_022167.3) in the xylosyltransferase II locus (XYLT2) (MIM: 608125), causing reduced XYL2 mRNA and low circulating XylT activity. In an unrelated boy (individual 3) from the second family, we noted low serum XylT activity. Sanger sequencing of XYL2 in this individual revealed a c.520del mutation in exon 2 that resulted in a frameshift and premature stop codon (p.Ala174Profs*35). Fibroblasts from individuals 1 and 2 showed a range of defects including reduced XylT activity, GAG incorporation of $^{35}$SO$_4$, and heparan sulfate proteoglycan assembly. These studies demonstrate that human XylT2 deficiency results in vertebral compression fractures, sensorineural hearing loss, eye defects, and heart defects, a phenotype that is similar to the autosomal-recessive disorder spondylo-ocular syndrome of unknown cause. This phenotype is different from what has been reported in individuals with other linker enzyme deficiencies. These studies illustrate that the cells of the lens, retina, heart muscle, inner ear, and bone are dependent on XylT2 for proteoglycan assembly in humans.

**Ophthalmic and molecular genetic findings in Kniest dysplasia**
P I Sergouniotis, G S Fincham, A M McNinch, C Spickett, A V Poulson, A J Richards and M P Snead
Eye 29: 475-482; January 2015

In this case study and series review, the ophthalmic features of 7 patients with the diagnosis of Kniest dysplasia are described. Kniest dysplasia is one of the collagenopathies causing short stature involves abnormal type II collagen. Ophthalmic features include high myopia in normal vitreous gel architecture with an increased risk of retinal detachment.

**Occurrence of CYP1B1 Mutations in Juvenile Open-Angle Glaucoma With Advanced Visual Field Loss**

The genetic basis of juvenile open angle glaucoma (JOAG), which can be considered a neurodegenerative disorder of onset after age 4 and before age 30-40, is poorly understood. The authors assess the prevalence of pathogenic CYP1B1 sequence variants in an Australian cohort of patients, 118 of whom had advanced JOAG, 42 of whom had nonadvanced JOAG and 8 of whom did not have glaucoma and served as controls. Advanced JOAG was defined as visual field loss in 2 of the 4 central fixation squares on visual field testing. Family history is quite predictive of development of primary open angle glaucoma, which includes JOAG, with a 9 times greater risk in first degree relatives. Defects in the MYOC gene are responsible for 4% of advanced POAG cases and 17% of advanced JOAG cases. Mutations in CYP1B1 were identified in patients with congenital glaucoma, a much more rare condition. The authors conclude that enrichment of CYP1B1 pathogenic variants had the more severe phenotype of JOAG.
Occurrence of CYP1B1 Mutations in Juvenile Open-Angle Glaucoma With Advanced Visual Field Loss


Juvenile open-angle glaucoma (JOAG), which is an early onset form of primary open-angle glaucoma (POAG), displays a strong heritability but is genetically heterogeneous. Pathogenic variants of CYP1B1 have been associated with JOAG among different populations with variable frequencies. However, most studies involving cases of JOAG included small cohorts, and none assessed severe cases as defined by their visual field (VF) loss. In this study, the prevalence of pathogenic CYP1B1 sequence variants is investigated in a large cohort of Australian patients with JOAG and severe VF loss. The study included 160 patients with JOAG classified as advanced (n = 118) and nonadvanced (n = 42) through the Australian and New Zealand Registry of Advanced Glaucoma from January 1, 2007, through April 1, 2014. Eighty individuals with no evidence of glaucoma served as a control group. JOAG was defined as a diagnosis before age 40 years and advanced JOAG as VF loss in 2 of the 4 central fixation squares on a reliable VF test result. Direct sequencing of the entire coding region of CYP1B1 was performed. Seven different pathogenic variants were identified among 8 of 118 patients with advanced JOAG (6.8%) but none among the patients with nonadvanced JOAG. Three patients were homozygous or compound heterozygous for CYP1B1 pathogenic variants and five patients were heterozygous. The allele frequency among the patients with advanced JOAG (4.7%) was higher than among the controls (0.6%) or among the control population from the Exome Aggregation Consortium database (2.4%). Individuals with CYP1B1 pathogenic variants had worse mean (SD) deviation on visual fields than patients without CYP1B1 pathogenic variants. This study revealed that patients with advanced JOAG based had an enrichment of CYP1B1 pathogenic variants (6.8%) compared with unaffected controls and patients with non-advanced JOAG. This finding is consistent with previous smaller studies among white individuals. It was also confirmed that CYP1B1 mutations tend to result in more severe glaucoma than in patients without CYP1B1 mutations. Since these individuals are at high risk for preventable blindness, early identification through genetic testing for adequate glaucoma intervention is important.

A de novo mutation in TEAD1 causes non–X-linked Aicardi syndrome


Aicardi syndrome (AIC) is a congenital neurodevelopmental disorder characterized by infantile spasms, agenesis of the corpus callosum, and chorioretinal lacunae. Variation in phenotype and disease severity is well documented, but chorioretinal lacunae represent the most constant pathological feature. Aicardi syndrome is believed to be an X-linked–dominant disorder
occurring almost exclusively in females (with early embryonic lethality in males), although 46, XY males with AIC have been described. The authors performed exome/genome sequencing of 10 girls diagnosed with AIC and their parents. They identified a de novo mutation in autosomal gene TEAD1, expressed in the retina and brain, in a patient with AIC. Mutations in TEAD1 have previously been associated with Sveinsson’s chorioretinal atrophy, characterized by chorioretinal degeneration. This demonstrates that TEAD1 mutations can lead to different chorioretinal complications. In addition, they found that altered expression of genes associated with synaptic plasticity, neuronal development, retinal development, and cell cycle control/apoptosis is an important underlying potential pathogenic mechanism shared among cases. Last, they found a case with skewed X inactivation, supporting the idea that nonrandom X inactivation might be important in AIC. The data from this study suggest that AIC is a genetically heterogeneous disease and is not restricted to the X chromosome. Thus, males with similar features should be considered for diagnosis of AIC.

**Correlation of Retinal Structure and Function in Choroideremia.**

Choroideremia, which is an X-linked inherited retinal degeneration caused by defects in the *CHM* gene, affects the retina, retinal pigment epithelium (RPE), and choroid. It is characterized by childhood nyctalopia and peripheral field loss that gradually encroaches centripetally, typically resulting in significant vision loss in men by middle age. It is unclear whether photoreceptor loss occurs primarily or if it is secondary to degeneration of the underlying RPE. The authors explored this relationship by examining female carriers, whose fundi typically demonstrate patchy X chromosomal inactivation (XCI) with areas of degenerative change interspersed with normal tissue. Fundus autofluorescence (AF) and microperimetry (MP) data were used to analyze 24 eyes of 12 choroideremia carriers. No study to date has assessed retinal function using MP over normal and abnormal areas of AF. Four characteristic AF patterns were defined: fine, coarse, geographic and male pattern. All female choroideremia carriers in this cohort had a reduction in MTS that was symmetrical in both eyes but variable between individuals. There was a similar AF mosaic in relatives suggesting consistency in the underlying mechanism(s) of phenotypic variability. Frequently observed was abnormal retinal function in areas of dysfunctional RPE. But, there was little evidence of significantly abnormal retinal function in regions of relatively higher AF. Because it would be predicted to be CHM-affected photoreceptors overlying some of these regions of relatively greater AF, the observations suggest that photoreceptor function is not impaired enough to be detected using this method. The data suggests that RPE degeneration and reduced retinal function in choroideremia are related nonlinearly. Furthermore, based on this study, a multimodal, deep phenotyping approach to all choroideremia carriers, including the use of microperimetry and AF, is recommended. This study also
provides evidence that some female carriers may benefit from gene replacement therapy.

**Association of Retinal Artery and Other Inner Retinal Structures With Distribution of Tapetal-like Reflex in Oguchi’s Disease.**


Oguchi’s disease is an unusual form of congenital stationary night blindness that is characterized by a golden or grayish-white tapetal-like reflex (Mizuo-Nakamura phenomenon) of the fundus, which disappears after a long period of dark-adaptation. Mutations in the arrestin gene, *SAG*, or the rhodopsin kinase gene, *GRK1*, have been identified as the causative genes. Most Japanese patients have mutations in the *SAG* gene. This study reports novel ophthalmoscopic features of patients with Oguchi’s disease, and describes how they may be related to the unusual tapetal-like fundus appearance. Twenty-one eyes of 11 patients with Oguchi’s disease were investigated. Genetic screening of seven cases showed homozygous mutations in the *SAG* gene (c.926delA). The retinal appearance was retrospectively assessed through fundus photographs and optical coherence tomographic (OCT)/fundus autofluorescence (AF) images. In 11 eyes of 7 patients, clearly demarcated dark regions without tapetal-like reflex were observed in the midperipheral retinal regions. In the dark regions, OCT showed lower reflectances in the photoreceptor layer but the AF images had normal reflectances. In nine eyes of six patients, the dark regions were partially demarcated by retinal arteries but not by veins. In nine eyes of five patients, the extent of the dark regions either increased or decreased during the course of the disease process, and these changes were not due to the state of adaptation or a posterior vitreous detachment. In all eyes, the peripheral retinal arteries but not veins had either high or low reflective regions along one side. Although the alterations of the outer retinal layers are believed to be most responsible for the abnormal tapetal-like reflex in patients with Oguchi’s disease, these ophthalmoscopic features cannot be explained solely by the abnormality of the outer retina. The findings suggest that the appearance of tapetal-like reflex is strongly affected by alterations of structures in the inner retinal layers.

**Association Between Missense Mutations in the BBS2 Gene and Nonsyndromic Retinitis Pigmentosa**


The authors discover several missense mutations in the BBS2 gene responsible for nonsyndromic retinitis pigmentosa. Bardet-Biedl syndrome (BBS) is an autosomal recessive disease that is heterogeneous both clinically and genetically and is characterized by such features like retinal degeneration, polydactyly, renal and gonadal malformations, obesity, and learning disabilities or secondary
features including speech disorders, developmental delay, ataxia, diabetes mellitus, dysmorphic features, and cognitive impairment. The clinical diagnosis of BBS is based on the presence of at least 4 primary features or a combination of 3 primary and 2 (or more) secondary features. Retinitis pigmentosa is an inherited retinal degeneration that affects photoreceptors and pigment epithelial function and is one of the most heterogeneous genetic diseases in humans. A total of 36 genes have been identified as the cause of nonsyndromic autosomal recessive RP. Although the patients in this study did not show the major clinical features of BBS, the retinal involvement seems to be as severe as that in patients with BBS due to BBS2 mutations and points to the overlap of these 2 diseases.


Next-generation sequencing (NGS) has been demonstrated to be an effective strategy for the detection of mutations in retinal dystrophies, a group of inherited diseases that are highly heterogeneous. The authors applied NGS to a Spanish cohort of autosomal dominant retinitis pigmentosa (RP) patients in order to determine causative mutations. Index cases of 59 Spanish families with initial diagnosis of autosomal dominant RP and unsuccessfully studied for mutations in the most common RP causal genes, were selected for application of a NGS-based approach with a custom panel for 73 genes related to retinal dystrophies. Candidate variants were select based on frequency, pathogenicity, inherited model, and phenotype. Subsequently, confirmation by Sanger sequencing, cosegregation analysis, and population studies, was applied for determining the implication of those variants in the pathology. Overall 31 candidate variants were selected. From them, 17 variants were considered as mutations causative of the disease, 64% (11/17) of them were novel and 36% (6/17) were known RP-related mutations. Therefore, 16 families were characterized rendering a mutation detection rate of 27% (16/59). Of them, 5% (3/59) of cases displayed mutations in recessive or X-linked genes (ABCA4, RPGR, and RP2) allowing a genetic and clinical reclassification of those families. Furthermore, seven novel variants with uncertain significance and seven novel variants probably not causative of disease were also found. NGS is a fast, effective, and reliable tool to detect known and novel mutations in autosomal dominant RP patients allowing genetic reclassification in some cases and increasing the knowledge of pathogenesis in retinal dystrophies.

There have been several human clinical trials demonstrating the efficacy of gene therapy in LCA type 2 (caused by RPE65 variants). One of the principal criteria for successful gene therapy in inherited retinal disorders is the degree of cellular preservation of the diseased retina. This study looked at OCT findings in LCA type 4 (due to variants in the gene Aryl-hydrocarbon-interacting protein-like 1 or AIPL1). Recent electrophysiologic findings suggest there may be some preservation of retinal function in young children with AIPL1 mutations. 42 patients with AIPL1 mutations and LCA4 phenotype from 18 countries were assessed (age range from 6 months to 43 years). OCT images were obtained in 19 patients of which 13 had good quality scans. 3 of these 13 patients showed relative preservation of the inner segment ellipsoid layer and outer nuclear layer at the fovea – and these were the youngest patients in the cohort (< 1 year of age). It is possible that the majority of LCA AIPL1 patients retain preserved foveal outer retinal structure when very young and this may provide a therapeutic window for future gene therapy trials in this condition.

**Communicating the Promise for Ocular Gene Therapies:**
**Challenges and Recommendations**
Benjaminy S, Kowal S, Macdonald I, Bubela T. AJO September 2015; 160(3); pg. 408.

This paper was a literature review to identify challenges and pose solutions about ocular gene therapy between patient and clinician. It was suggested that even though ocular gene therapy trials are available, we are many years off from treating hereditary retinopathies. Be careful not to promote overly positive message.


This is a report of three patients with Leber’s congenital amaurosis due to the RPE65 mutation, who underwent gene therapy, and were followed for nearly six years. Gene therapy consisted of a single subretinal extrafoveal injection of a vector with the RPE 65 gene. Of fifteen patients who received such an injection, only three met inclusion criteria: follow up for 4.5 years or longer, ability to undergo elaborate testing, maintaining foveal fixation, no ocular complications, and no cataract. These patients were subject to vision sensitivity testing and OCT measurements of outer nuclear layer thickness. Vision sensitivity increased in the first six months and up to three years, but then declined thereafter to near pre-treatment levels. OCT testing showed a progressive loss of photoreceptors in both the gene therapy treated and untreated portions of the retina. The RPE65 gene mutation study was a landmark in the field of gene therapy for any human disease; these results showing decline in effect over time are discouraging.

This was a phase 1-2 study of twelve RPE65 gene-therapy treated patients with long term follow up. A difference between this study and the Jacobson et al. study is that this protocol intentionally delivered the vector subfoveally. Four participants were administered a lower dose of the vector, and 8 were administered a higher dose. Five of the eight patients given a higher vector dose had improved visual sensitivities, as compared with one of four who received the lower dose. Improvements in retinal sensitivity were evident in six human participants for up to 3 years, peaking at 6 to 12 months after treatment and then declining. Like in the Jacobsen et al study, these are discouraging results suggesting that initial benefits of RPE65 gene-therapy are short lasting. The authors do not recommend delivering the vector subfoveally in the future, as there is no benefit to the foveal photoreceptors, yet an adverse effect from the temporary foveal detachment.


Leber’s congenital amaurosis (LCA) is a group of heterogeneous disorders characterized by an early-onset rod-cone dystrophy and severe visual loss. Type 4 LCA is caused by variants in the gene Aryl-hydrocarbon-interacting protein-like 1 (AIPL1), which plays a role in molecular chaperoning within photoreceptors. One of the principal criteria for successful gene therapy of inherited retinal disorders is a degree of cellular preservation of the diseased retina, to allow for the potential of functional restoration. Given the very poor prognosis of severe and rapidly progressive visual loss of AIPL1 LCA, the authors utilized optical coherence tomography (OCT) determine if there was an early window of opportunity during which patients might be suitable for a human treatment trial. Data was compiled on 42 patients with molecularly confirmed AIPL1 mutations and a LCA4 phenotype from 18 countries. The age of these patients ranged from 0.5 to 43 years old (median, 8); 24 patients (57%) were <10 years old and 10 (24%) were <5 years old. OCT images were obtained for 19 patients (45%). Of these 19 patients, 6 (32%) had poor quality scans or scans that were not foveal. Of the remaining 13 patients in whom good OCT images had been obtained, nine (69%) had no evidence of photoreceptor structure at the macula. However, three of the 13 patients (23%) demonstrated significant outer retinal structure. These three patients were the youngest in the cohort, each being ≤1 year of age. This study shows that there is promising evidence from high resolution OCT imaging that, in the very youngest AIPL1 LCA patients imaged, there is relative preservation of foveal outer retinal structure. Additionally, the three youngest
children in this cohort represent the youngest AIPL1 LCA patients in the literature to date that demonstrate foveal outer retinal structure and possible candidates for gene therapy. A human gene therapy based approach may be worthy of consideration in a small group of selected patients with preserved outer retinal structure in AIPL1 LCA. The results of this study also suggest that intervention may need to be initiated in the first few years of life.

**Next-Generation Sequencing and Novel Variant Determination in a Cohort of 92 Familial Exudative Vitreoretinopathy Patients.**

Familial exudative vitreoretinopathy (FEVR) is a genetic disorder affecting retinal blood vessel development in young children. Four genes involved in the Wnt signaling pathway have been previously linked to FEVR: NDP, FDZ4, LRP5, and TSPAN12. The contribution of mutations in each known FEVR disease gene to the disease has not been well documented. To gain a clearer picture of the mutation spectrum in FEVR patients, sequencing libraries from 92 FEVR patients were generated using a custom capture panel to enrich for 163 known retinal disease-causing genes in humans. Samples were processed using next generation sequencing (NGS) techniques followed by data analysis to identify and classify single nucleotide variants and small insertions and deletions. Sanger validation and segregation testing were used to verify suspected variants. Of the cohort of 92, 45 patients were potentially solved (48.9%). Solved cases resulted from the determination of 49 unique mutations, 41 of which are novel. Of the novel variants discovered, 13 were highly likely to cause FEVR due to the nature of these variants (frameshifting indels, splicing mutations, and nonsense variants types). Specifically, mutations in LRP5, FZD4, TSPAN12, NDP, and ZNF408 accounted for 19.6%, 15.2%, 8.7%, 6.5%, and 1.1% of patients, respectively. This is the largest study of a FEVR cohort using NGS to date. In conclusion, the authors were able to determine probable disease-causing variants in a large number of FEVR patients (approximately 50%), the majority of which were novel. Knowledge of these variants will help to further characterize and diagnose FEVR. Molecular diagnosis, together with clinical phenotype, potentially provides useful information for disease diagnosis, prognosis, and genetic counseling. This is particularly valuable given the phenotypic variation found even within the same family.

**Characterization of Abnormal Optic Nerve Head Morphology in Albinism Using Optical Coherence Tomography**

Albinism is a group of congenital disorders in melanin biosynthesis affecting
approximately 1 in 4000 people. Although chiasmal abnormalities are well
documented, little is known about the morphology of the optic nerve head (ONH)
in albinism. The authors sought to characterize abnormalities in three-
dimensional ONH morphology in people with albinism (PWA) using spectral-
domain optical coherence tomography (SD-OCT) and to determine whether ONH
abnormalities relate to other retinal and clinical abnormalities. Spectral-domain
OCT was used to obtain three-dimensional images from 56 PWA and 60 age-
and sex-matched control subjects. B-scans were corrected for nystagmus-
associated motion artifacts. Disc, cup, and rim ONH dimensions and peripapillary
retinal nerve fiber layer (ppRNFL) thickness were calculated using Copernicus
and ImageJ software. Median disc areas were similar in PWA (median = 1.65
mm²) and controls (1.71 mm², P < 0.128), although discs were significantly
elongated horizontally in PWA (P < 0.001). In contrast, median optic cup area in
PWA (0.088 mm²) was 23.7% of that in controls (0.373 mm², P < 0.001), with
39.4% of eyes in PWA not demonstrating a measurable optic cup. This led to
significantly smaller cup to disc ratios in PWA (P < 0.001). Median rim volume in
PWA (0.273 mm³) was 136.6% of that in controls (0.200 mm³). The ppRNFL was
significantly thinner in PWA compared with controls (P < 0.001), especially in the
temporal quadrant. In PWA, ppRNFL thickness was correlated to ganglion cell
thickness at the central fovea (P < 0.007). Several ONH abnormalities, such as
cup to disc ratio, were related to higher refractive errors in PWA. This study
revealed that ocular maldevelopment is not just limited to the retina but also
involves the ONH in PWA. Reduced ppRNFL thickness is consistent with
previous reports of reduced ganglion cell numbers in PWA. The thicker rim
volumes may be a result of incomplete maturation of the ONH.

Objective Analysis of Hyperreflective Outer Retinal Bands
Imaged by Optical Coherence Tomography in Patients With
Stargardt Disease


The purpose of this study was to develop an objective, semiautomated algorithm
for analyzing the layers of the outer retina imaged by spectral-domain OCT (SD-
OCT) in patients with Stargardt disease (STGD1). The authors focused on the
three outermost retinal bands, the retinal pigment epithelium (RPE) complex,
interdigitation zone (IZ), and ellipsoid zone (EZ), with a particular emphasis on
the IZ, as little has been reported regarding this band in STGD1. Horizontal
macular B-scans were acquired from 20 visually normal controls and 20
genetically confirmed stage 1 STGD1 patients. The number of outer retinal bands
was quantified using a semiautomated algorithm that detected bands using the
second derivative of longitudinal reflectivity profiles. The RPE complex and EZ
bands were detected throughout the B-scan in all controls. The RPE complex
was detected throughout the B-scan in all patients, but was atrophic appearing in
some locations. The EZ band was detected only outside the central lesion.
Interdigitation zone band detection varied as a function of eccentricity for both
groups, with detection for controls being highest in the para- and perifovea and
lowest in the fovea and near periphery. In STGD1 patients, the IZ band was
generally not present in the fovea or para- or perifovea due to the central lesion.
Outside of the lesion, the IZ band was detected in 26% of patients (mean
detection across the near periphery), which was approximately half of the
detection in controls. An objective approach for quantifying the number of outer
retinal OCT bands found reduced IZ detection in STGD1 patients. This occurred
even outside the central lesion, demonstrating an inability to image the IZ,
possibly due to enhanced RPE reflectivity or abnormal outer retinal structure.
This finding sheds more light onto the pathogenesis of STGD1.

The current status of molecular diagnosis of inherited retinal
dystrophies Chiang JP¹, Trzupek K. Curr Opin Ophthalmol. 2015

We are witnessing lightning-fast advances in the molecular diagnosis of inherited
retinal dystrophies, mainly due to the widespread use of next-generation
sequencing technologies. The purpose of this review was to highlight the breadth
of findings from this in-depth testing approach, and to propose changes to our
traditional testing and diagnostic paradigms. Lessons learned from modern
molecular testing suggest that the previous concept of inherited retinal
dystrophies as a group of 'single gene diseases' may require a significant
update. Now all of the known retinal dystrophies genes can now be sequenced.
In many cases, this nonhypothesis driven testing strategy is uncovering
mutations in unsuspected genes, generating data that challenges established
concepts of genetic mechanisms and provides insights regarding genes
previously thought to be exclusively related to syndromic disease. Recent
advances in testing have improved not only the breadth, but also the depth of
genetic data. For example, deep intronic sequencing has uncovered many novel
intrinsic mutations/variations in the ABCA4 gene. Currently, in approximately 50-
60% of patients with nonsyndromic retinal dystrophy, the disease mechanism
can be identified. The presence of pathogenic alleles in more than one gene is
not uncommon. Retinal dystrophy, with relatively defined clinical presentations
and a large but limited number of genes involved, is becoming a model for the
next-generation study of molecular disease mechanisms.

The John Pratt-Johnson Annual Lecture - Congenital and
Genetic Ocular Motility Disorders: Update and Considerations

The lecturer presents a review of known loci and genes associated with
congenital cranial dysinnervation syndromes including CFEOM1 (12q12 KIF21A),
CFEOM2 (11q13.2 PHOX2A), CFEOM3A (16q24, TUBB3), CFEOM3B (12q12 KIF21A), CFEOM3C (13q), Duane radial ray syndrome (2q13 SALL4), DRS1 (8q13 del, cytogenetic), DRS2 (2q31 CHN1), Moebius syndrome (sporadic) and horizontal gaze palsy with progressive scoliosis (11q23-25 ROBO3), Athabaskan brainstem dysgenesis syndrome (7p15.3 HOXA1), Bosley-Salih-Aloainy syndrome (7p15.3 HOXA1). The lecturer advocates the following to narrow a differential before attempting genetic diagnosis: 1) note congenital onset of motility disorder and family history, 2) allow for some variability among individuals with the same condition, even within the same family, 3) remember 1 or 2 cardinal features of each condition, 4) remember that some CCDDs only ocular motility and others involve neurological problems or other systems.

Comment: This is a practical review article focusing on the many developments over the past 10 years in our understanding of CCDDs.


The purpose of this longitudinal study was to investigate retinal development in infants and young children with achromatopsia (ACHM). The authors studied in vivo foveal development using coherence tomography (OCT) in a cohort of ten children with a confirmed genetic diagnosis of ACHM. The mean age at the time of examination was 40.6 months. The cohort was compared to a control group. In all the participants with ACHM, foveal hypoplasia was evident on OCT at each visit. A delay in photoreceptor migration into the central fovea was also noted in the youngest ACHM participants. There was evidence of photoreceptor disruption (consisting of ellipsoid disruption and/or a hyporeflective zone) in the ACHM group. Overall retinal thickness measurements and rate of increase in retinal thickness with age were reduced significantly at the fovea, parafovea and perifovea in ACHM participants. The foveal inner retinal layers (IRLs) were five times thicker in ACHM than mean control values (P < 0.0001), as a result of significantly increased thicknesses of the ganglion cell (GCL), inner plexiform, inner nuclear (INL), and outer plexiform (OPL) layers. There was an age-related decrease in foveal IRL thickness in ACHM, owing to regression of the GCL, INL, and OPL. In contrast, the foveal outer retinal layers (ORLs) in ACHM were significantly thinner, being 0.6 times thinner than mean control values (P < 0.0001), which was attributable to reductions in the photoreceptor inner segment (IS), outer segment (OS), and outer nuclear layer. The perifoveal IRLs were significantly thinner in ACHM (P < 0.01), which was attributable to changes specifically in the plexiform layers. The parafoveal ORLs were uniformly thinner in ACHM at all ages (P < 0.0001), owing to reductions in IS, OS, and retinal pigment epithelium (RPE) measurements. Perifoveal ORL thickness in ACHM did not differ from controls at birth. However, after 12 months of age a significant
intergroup difference emerged, with thinner perifoveal ORLs in ACHM. In summary, the authors revealed that retinal development is not arrested in children with ACHM, but is ongoing albeit at a reduced rate and magnitude in comparison with controls, with consequences for all retinal layers. This suggests that ACHM is a continuously altering and progressive process in the developing retina. Given this information, it is important to consider gene therapy at an early age, while the photoreceptors are still developing, and thereby potentially facilitating normal retinal maturation.


This paper described the clinical characteristics associated with a newly identified autosomal recessive bestrophinopathy (ARB) mutation in two family members (66-year-old brother and 52-year-old sister). Whole-cell patch clamping of ARB alleles was conducted to confirm that this mutation leads to altered \( \text{BEST1} \) function in a recessive manner. The related patients presented with reduced visual acuity and bilateral symmetrical subretinal deposits of hyperautofluorescent materials in the posterior pole. Spectral-domain OCT showed macular thinning with submacular fluid. The female patient had concomitant macular edema associated with branched retinal vein occlusion in the left eye, which responded favorably to intravitreal bevacizumab injections. Genetic analysis for bestrophin-1 (\( \text{BEST1} \)) mutations was conducted through direct Sanger sequencing. This demonstrated that both patients were compound heterozygous for one novel (Leu40Pro) and one previously identified (Ala195Val) \( \text{BEST1} \) variant. The effect of ARB-associated mutations of \( \text{BEST1} \) on the cellular localization was determined by in vitro experiments. Whole-cell patch clamping was conducted to measure the chloride conductance of wild-type \( \text{BEST1} \) and the identified \( \text{BEST1} \) mutants in transfected HEK293T cells. HEK293T cells transfected with the identified \( \text{BEST1} \) mutant showed significantly small currents compared to those transfected with the wild-type gene, whereas cells cotransfected with mutant and wild-type \( \text{BEST1} \) showed good chloride conductance. Cellular localization of \( \text{BEST1} \) was well conserved to the plasma membrane in the mutants. In conclusion, the authors identified and described the phenotype and in vitro functional aspects of a new \( \text{BEST1} \) mutation causing ARB. Furthermore, the autosomal recessive nature and clinical features that mimic other more common macular diseases indicate that clinically suspected cases of ARB warrant genetic confirmation to confirm the diagnosis.

**Fundus Autofluorescence and SD-OCT Document Rapid Progression in Autosomal Dominant Vitreoretinochoroidopathy (ADVIRC) Associated with a c.256G > A Mutation in \( \text{BEST1} \).**
Pathogenic mutations in the bestrophin-1 (BEST1) gene are associated with a heterogeneous spectrum of retinal dystrophies including autosomal dominant Best disease (MIM 153700), autosomal dominant vitreoretinochoroidopathy (ADVIRC) (MIM 193220), and autosomal recessive bestrophinopathy (ARB) (MIM 611809). ADVIRC is a rare autosomal dominant retinal dystrophy first described in 1982 with characteristic signs of retinal and vitreous degeneration predominantly in the retinal periphery. To date, four heterozygous ADVIRC mutations have been identified in the BEST1 gene. In contrast to missense mutations causing classical Best disease, these mutations are thought to affect splicing regulators resulting in partially functional bestrophin-1 protein. The focus of this paper is to report the variability of clinical findings, rapid concentric progression, and successful treatment of macular edema in autosomal dominant vitreoretinochoroidopathy (ADVIRC) associated with a heterozygous c.256G4A missense mutation in the bestrophin-1 (BEST1) gene. Three affected members of a four-generation ADVIRC family were examined with fundus autofluorescence (FAF), near-infrared autofluorescence (NIA) and spectral domain optical coherence tomography (SD-OCT). Direct sequence analysis of coding and flanking intronic regions of the BEST1 gene was performed. The authors found that disease manifestations presented with high variability with visual problems manifesting between 10 and 40 years of age. Two probands showed marked signs of peripheral degeneration, while this retinal area was not noticeably affected in the third. Cystoid macular edema was present in one proband, which responded to long-term treatment with topical dorzolamide with improved visual acuity. FAF and NIA revealed midperipheral retinal degeneration in areas that appeared normal on ophthalmoscopy. The full-field ERG was markedly reduced in two probands. Within a 5-year period a marked increase in concentric progression of degeneration including the posterior pole was documented with FAF, NIA and SD-OCT in one proband after the age of 63 years. Direct sequence analysis of the BEST1 gene revealed a heterozygous c.256G4A missense mutation in the three affected probands. The findings in this family emphasize the previously noted variability of clinical manifestations in BEST1-associated ADVIRC and the relevance of FAF and NIA imaging. In addition, the study reveals that the cystoid macular edema and vascular leakage can be successfully treated using dorzolamide.


Bestrophinopathies result from mutations within the BEST1 gene. To date, there have been >100 BEST1 mutations described. The vast majority of these are
formed of heterozygous missense mutations; however there have been
descriptions of biallelic mutations causing the recessive forms of the disease.
The recessive form is often the form which gives rise to the rarer complication of
choroidal neovascularization. Treatment options studied in patients with macular
changes associated with BEST1 mutations include photodynamic therapy, argon
laser therapy, and intravitreal combinations of anti-VEGF therapy and
triamcinolone. There have also been a few cases reported of treatments in
children with intravitreal bevacizumab with subsequent good visual recovery. The
authors describe a 9-year-old female child with treated choroidal
neovascularization secondary to Best disease with a newly identified genetic
mutation, c.563T>C(p.Phe188Ser). In this case report, the child experienced
deteriorating vision to 3/18 over several months due to the development of a
choroidal neovascular membrane. She was treated with three injections of
bevacizumab with recovery to 6/12 vision and no subsequent recurrence over the
follow-up period of 2 years. There were no secondary complications from the
drug. Genetic analysis revealed a novel heterozygous mutation in the BEST1
gene, with no evidence of disease in the family. In conclusion, the authors
described a novel mutation within the BEST1 gene of the heterozygous form,
giving rise to vitelliform lesions and secondary neovascularization successfully
treated in a child with a course of bevacizumab. Intravitreal anti-VEGF appears to
be a promising and safe treatment of CNVM secondary to maculopathies
associated with BEST1 mutations in the pediatric population with good visual
recovery. Prompt recognition and treatment of choroidal neovascularization can
effectively restore vision.

**Immunosuppressive Treatment for Retinal Degeneration in

Juvenile Neuronal Ceroid Lipofuscinosis (JNCL) presents with progressive vision
loss at 4–7 years of age. Blindness typically results within 2 years, followed by
neurologic decline and death. Data for the natural history of the ERG response in
JNCL is sparse, but published reports suggest progression from a recordable,
electronegative standard combined response (SCR), to non-recordable over 1–2
years with useful vision undergoing simultaneous loss. Currently there is no
treatment for JNCL. It is postulated that neuroinflammation plays a role in the
neurodegeneration. The JNCL mouse model has demonstrated decreased
neuroinflammation and improved motor skills with immunosuppression. Based on
this work, a short-term human clinical trial of mycophenolate mofetil has begun,
however long-term effects, and whether immunosuppression modulates vision
loss, have not been studied. The objective of this retrospective case report was
to determine whether treatment with immunosuppression affects visual outcome
in JNCL. Over two years the authors treated a JNCL patient with
immunosuppressive therapy and comprehensively characterized visual function.
The patient was 7.5 years old at the time of presentation. She was noted to have an intense anterior vitreous inflammatory response. Because an immune component was suspected, commercial anti-retinal antibody (ARA) testing was obtained, followed shortly thereafter by molecular genetic testing for JNCL. Commercial ARA testing reported seven different ARA. Genetic testing of the CLN3 gene was positive for two disease-causing mutations. A combination of topical prednisolone acetate, topical nepafenac, posterior subtenon of triamcinolone, and systemic mycophenolate mofetil were used at varying times. Nine months after starting immunosuppression there was a small increase in ERG b-wave amplitudes, but it was not maintained. At the conclusion of the report, the patient continued to have ambulatory vision and essentially full V4e isopters on GVF. Binocular visual acuity was 20/400 at distance and 20/80 at near. Autoimmune retinopathy is a well-described entity, and has been shown to be ameliorated with immunosuppressive therapy but has not been documented as part of a genetic retino-neurodegeneration. The significance of ARA in this patient is unknown. Based on parent reported data and examinations, children with JNCL demonstrate complete vision loss by a median age of 10 years. At this patient’s last visit she was 9 and 10/12 years old at and still has ambulatory vision and reading large print. This case suggests that there is an inflammatory component to the rapid retinal degeneration in JNCL. Furthermore, the authors propose that local and/or systemic immunosuppression may affect the course of JNCL retinal degeneration if started early in the course of vision loss. However, additional research in a large group of subjects regarding long-term outcome, safety of administration as well as other clinical impacts is needed.


Bietti crystalline dystrophy is a rare (1:67,000) autosomal recessive retinal degenerative disease that was first reported in 1937. The disease is characterized by the presence of shiny yellow deposits on the cornea and posterior pole of the retina, and progressive atrophy of the retina, choriocapillaris, and choroid. The symptoms of Bietti crystalline dystrophy are similar to those of retinitis pigmentosa (RP): night blindness, gradual constriction of the visual field, abnormal retinal electrophysiology, and decreased visual acuity. CYP4V2, the only reported gene associated with the disease, is expressed in the retina and retinal pigment epithelium (RPE). It is unclear whether the pathogenesis of Bietti crystalline dystrophy is a disorder of RPE and/or the photoreceptors. Several reports have suggested that RPE dysfunction is the primary change in Bietti crystalline dystrophy with CYP4V2 mutations. Adaptive optics scanning laser ophthalmoscopy (AO-SLO) allows high-quality noninvasive imaging of photoreceptors. Prior to this study, there have not been any reported characterizations of photoreceptors in Bietti crystalline dystrophy patients. The
authors evaluated photoreceptors in individuals with CYP4V2 mutations using AO-SLO. Seven eyes of seven Bietti crystalline dystrophy patients with CYP4V2 mutations and twelve normal eyes of twelve age- and axial length-matched healthy controls were studied. All participants underwent ophthalmologic examinations and AO-SLO assessments. All patients underwent spectral-domain optical coherence tomography, fundus autofluorescence, Humphrey field analysis, and electroretinography. AO-SLO images were analyzed 0.5 mm and 1.0 mm from the center of the fovea in the superior, inferior, nasal, and temporal quadrants. Compared to controls, Bietti crystalline dystrophy patients showed a significant reduction in cone density at 0.5 mm from the center of the fovea, but not at 1.0 mm. In addition, there was no correlation between cone density and mean deviation measured using a Humphrey field analysis or visual acuity in patients. Cone density 1.0 mm from the center of the fovea did not decrease, regardless of the remarkable RPE atrophy observed in fundus autofluorescence images. This is consistent with previous reports suggesting that RPE dysfunction is the primary change in Bietti crystalline dystrophy, whereas the photoreceptors are secondarily affected. This implies that restoration of RPE function via emerging therapies such as transplantation or gene therapy may revive cone function and some central vision in patients with Bietti crystalline dystrophy.


Choroideremia is a progressive X-linked inherited retinal degeneration affecting the retinal pigment epithelium (RPE), choroid, and outer retina. Early symptoms include nyctalopia, reduction in peripheral vision, and loss of visual acuity (VA), resulting in legal blindness around the third to fourth decade. The disease is caused by mutation of the CHM gene, which codes for Rab escort protein-1 (REP1). Choroideremia patients can maintain excellent foveal VA until very late in the disease process; however, this does not exclude the presence of a color vision defect. Since the choroideremia gene is also expressed in cones and these cells are dependent on surrounding retinal cells that also express REP1 as part of the cone visual cycle, it would not be unexpected to find subtle defects in color vision in these patients before the onset of degeneration. The authors prospectively characterized defects in color vision in thirty patients (41 eyes) with choroideremia. The patients were compared to 10 age-matched male controls (19 eyes) with visual acuity of ≥ 6/36 attending outpatient clinics in Oxford Eye Hospital. Color vision testing was performed with the Farnsworth-Munsell 100 hue test. To exclude changes caused by degeneration of the fovea, a subgroup of 14 patients with a visual acuity ≥ 6/6 was analyzed. Calculated color vision total error scores were compared between the groups and related to a range of factors using a random-effects model. Mean color vision total error scores were 120 in the < 6/6 choroideremia group, 206 in the < 6/6 visual acuity choroideremia group, and 47 in the control group. Covariate analysis showed a
significant difference in color vision total error score between the groups (P < .001 between each group). In conclusion, patients with choroideremia have a functional defect in color vision compared with age-matched controls. The color vision defect deteriorates as the degeneration encroaches on the fovea. The presence of an early functional defect in color vision provides a useful biomarker against which to assess successful gene transfer in gene therapy trials. Assessing color vision before and after gene therapy may provide further information about effects on cones from this primarily RPE-rod disorder. The observations from the current study, however, suggest that visual function in cones is also impaired in REP1 deficiency, albeit in a subtler manner when compared to rods.


The first of the classic macular dystrophies to have its gene mapped to a chromosome, North Carolina macular dystrophy (NCMD), is the last to have its specific disease-causing mutations identified. In the decades since the MCDR1 locus was mapped, many additional families with NCMD have been described, including 2 families that link to a separate locus on chromosome 5 (MCDR3). The critical region on chromosome 6 has been considerably narrowed, and all of the coding regions of genes within this interval have been exhaustively studied by us and other investigators. The failure of these experiments to identify plausible disease-causing mutations in any of these kindreds suggested that the mutations were likely to exist in nonexomic DNA and to affect the expression of a nearby gene or genes rather than the structure of its gene product. The purpose of this study was to take advantage of whole-genome sequencing to comprehensively screen the nonexomic sequences within the MCDR1 and MCDR3 loci to identify disease-causing mutations in families affected with these diseases. Using whole-genome sequencing coupled with reverse transcription polymerase chain reaction (RT-PCR) analysis of gene expression in human retinal cells, the authors identified specific mutations causing NCMD. A total of 141 members of 12 families with NCMD and 261 unrelated control individuals were included. Genome sequencing was performed on 8 affected individuals from 3 families affected with chromosome 6-linked NCMD (MCDR1) and 2 individuals affected with chromosome 5-linked NCMD (MCDR3). Variants observed in the MCDR1 locus with frequencies <1% in published databases were confirmed using Sanger sequencing. Confirmed variants absent from all published databases were sought in 8 additional MCDR1 families and 261 controls. The RT-PCR analysis of selected genes was performed in stem cell-derived human retinal cells. The results revealed five sequenced individuals with MCDR1-linked NCMD shared a haplotype of 14 rare variants spanning 1 Mb of the disease-causing allele. One of these variants (V1) was absent from all published databases and all 261 controls, but was found in 5 additional NCMD kindreds. This variant lies in a DNase 1
hypersensitivity site (DHS) upstream of both the PRDM13 and CCNC genes. Sanger sequencing of 1 kb centered on V1 was performed in the remaining 4 NCMD probands, and 2 additional novel single nucleotide variants (V2 in 3 families and V3 in 1 family) were identified in the DHS within 134 bp of the location of V1. A complete duplication of the PRDM13 gene was also discovered in a single family (V4). The RT-PCR analysis of PRDM13 expression in developing retinal cells revealed marked developmental regulation. Next-generation sequencing of 2 individuals with MCDR3-linked NCMD revealed a 900-kb duplication that included the entire IRX1 gene (V5). The 5 mutations V1 to V5 segregated perfectly in the 102 affected and 39 unaffected members of the 12 NCMD families. In conclusion, the authors identified 5 rare mutations, each capable of arresting human macular development. Four of these strongly implicate the involvement of PRDM13 in macular development, whereas the pathophysiologic mechanism of the fifth remains unknown but may involve the developmental dysregulation of IRX1.


Usher syndrome (USH) is characterized by vision and hearing loss, and is the most common cause of deafblindness. It is an autosomal recessively inherited group of disorders, divided into three major clinical subtypes that are differentiated by the severity of hearing loss and the presence of vestibular dysfunction. Vision loss due to retinitis pigmentosa (RP) is a hallmark of all three USH subtypes. In addition to clinical heterogeneity, Usher syndrome displays genetic heterogeneity, with 12 causative genes identified to date. Six genes have been associated with USH type 1, namely CDH23, CIB2, MYO7A, PCDH15, USH1C, and USH1G. The gene MYO7A was the first USH gene identified and has since been recognized as the most frequent cause of USH type 1, which is the most severe form of USH. Research over the past 25 years at the University of Cape Town has led to the identification of causative mutations in 17% of the 1416 families in the Retinal Degenerative Diseases (RDD) biorepository in South Africa. A low rate of mutation detection has been observed in patients of indigenous African origin, hinting at novel genes and mutations in this population. Recently, however, data from the authors’ translational research program showed two unrelated indigenous African families with Usher syndrome (USH), with the same homozygous MYO7A mutation. Therefore, the extent to which this mutation contributes toward the disease burden in South Africa was investigated. Cohorts of unrelated indigenous South African probands with different RDD diagnoses were tested for the MYO7A c.6377delC mutation. Familial cosegregation analysis was performed for homozygous probands, clinical data were evaluated, and SNP haplotypes were analyzed. This homozygous MYO7A mutation underlies a remarkable 43% of indigenous African USH cases.
investigated in this study, the majority of which (60%) were diagnosed clinically with Type 2 USH. All homozygotes shared a common haplotype. This mutation does not appear to cause nonsyndromic vision loss. Of interest is the origin of this common mutation relevant to the Bantu population migration into southern Africa. Finally, further investigation of the phenotype may elucidate the disease biology, and perhaps reveal a larger cohort with the same mutation, with which to assess the impact of environmental and genetic modifiers and evaluate therapeutic trials.


Retinitis pigmentosa (RP) is a set of hereditary retinal dystrophies affecting more than 1 million people worldwide. It is a progressive disease that typically presents with degeneration of the rod photoreceptors, followed by loss of cone photoreceptor function. The clinical presentation of RP is highly variable and is matched by an impressive genetic heterogeneity: currently, mutations in 55 genes have been implicated in the pathogenesis of autosomal recessive RP (arRP). In 2010, two back-to-back studies revealed null-mutations in FAM161A as a cause of arRP in the Israeli and German population, respectively. In this study, the authors aimed to explore the contribution of FAM161A mutations to the genetic spectrum of arRP in the Dutch and Belgian populations. They also investigated whether common FAM161A-associated phenotypic features could be identified. Homozygosity mapping in 230 Dutch individuals with suspected arRP yielded five individuals with a homozygous region harboring FAM161A. Sanger sequencing revealed a homozygous nonsense mutation (p.[Arg437*]) in one individual. Subsequent ARMS analysis and Sanger sequencing in Dutch and Belgian arRP patients resulted in the identification of seven additional individuals carrying the mutation, either homozygously or compound heterozygously with another mutation. Haplotype analysis identified a shared haplotype block of 409 kb surrounding the p.(Arg437*) mutation in all patients, suggesting a founder effect. Although the age of onset was variable among patients, all eight developed pronounced outer retinal loss with severe visual field defects and a bull's eye-like maculopathy, followed by loss of central vision within 2 decades after the initial diagnosis in five subjects. Overall, the authors discovered that a founder mutation in FAM161A p.(Arg437*) underlies approximately 2% of arRP cases in the Dutch and Belgian populations. The age of onset of the retinal dystrophy appears variable, but progression can be steep, with almost complete loss of central vision later in life.

Retinitis pigmentosa (RP) refers to a large group of genetically heterogeneous disorders characterized by early rod photoreceptor dysfunction followed by progressive rod and cone photoreceptor dysfunction and death. The prevalence of RP is approximately 1 in 3000-4500 persons. X-linked RP (XLRP) accounts for approximately 10-15% of RP cases and, in general, causes some of the severest clinical forms of RP. Mutations in the retinitis pigmentosa GTPase regulator (RPGR) gene are found in approximately 30–70% of XLRP families. The authors sought to phenotypically and genotypically characterize a large Puerto Rican kindred with X-linked retinitis pigmentosa associated with a novel RP GTPase regulator (RPGR) genotype. A total of 100 family members of a single kindred with X-linked RP were evaluated with ophthalmic examinations and blood DNA analysis. Visual fields, OCT, and full-field ERG were obtained on all affected males and carriers. Of the 100 family members examined, 13 were affected males and 18 were carriers. A deletion of 2 base pair of the RPGR gene in the ORF15 region at position c.2267-2268 (Lys756del2aaAG hemi) was identified with the affected and carriers. Best eye visual acuity was correlated with age with hand motion acuity by age 35 and light perception to no light perception by age 50–60. Visual fields were minimally plottable by age 40, and ERG responses reached non-detectable levels by late teens. Carriers had no or mild visual symptoms. All carriers had visual acuity of at least 20/50 or better in one eye, and the amount of retinal degeneration was variable with ERG responses ranging from severely impaired to normal. In conclusion, profound visual loss occurred by the second decade of life with progression to near no light perception by age 60 in this kindred of X-linked RP associated with the RPGR genotype. Female carriers maintained visual acuity with age and were identifiable by clinical and ERG examination. This large kindred of XLRP provides us with a comprehensive phenotyping of affected males and female carriers of a novel RPGR gene mutation. The information from this study is important to determine the optimal age for intervention, as new RP treatments are being developed and tested.


Juvenile X-linked retinoschisis (XLRS) is a congenital macular degeneration affecting 1/5000 to 1/25,000 worldwide. The gene associated with XLRS, Retinoschisin (RS1), translates to a retinoschisin protein (RS1). Shape discrimination hyperacuity (SDH) and contour integration perimetry (CIP)
patients with intermediate AMD show significant deficits, with macular edema exacerbating the loss of the ability to detect distortions in circular shapes. These tests assess the global integration of visual stimuli over a large retinal area. Due to the foveal edema in XLRS the authors hypothesized that the global integration measured by SDH/CIP may be affected, although some patients retain a relatively good BCVA. Spectral-domain optical coherence tomography (SDOCT) studies in XLRS have been reported, but rarely correlated with fundus-guided perimetry or shape discrimination. The authors compared structural properties from SDOCT and psychophysical measures from a subset of patients enrolled in a larger multicenter natural history study of XLRS. A subset of males (n = 24) participating in a larger natural history study of XLRS underwent high-resolution SDOCT. Total retina (TR) thickness and outer segment (OS) thickness were measured manually. SDH and CIP were performed on an iPad with the myVisionTrack application. Sensitivity was measured with fundus-guided perimetry (4-2 threshold testing strategy; 10-2 grid, spot size 3, 68 points). Mean macular OS thickness was less in XLRS patients than in controls but mean TR thickness was comparable. For patients, total sensitivity was lower than for controls and had a strong correlation with photoreceptor OS and a weak correlation with TR thickness. The XLRS subjects had a logMAR best corrected visual acuity (BCVA) of 0.5 ± 0.3 that was associated with OS but not TR thickness. Shape DH and CIP inner ring correlated with OS but not TR thickness. When considered from a single visit, OS thickness within the macula is more closely associated with macular function than TR thickness within the macula in patients with XLRS. In conclusion, the data presented here are consistent with previous measures of schisis cavities and decreased photoreceptor sensitivity in patients with XLRS. New findings include measures of OS length and the relationship between OS length and macular function based on microperimetry, SDH, CIP, and BCVA. Psychophysical outcome measures in these patients will be imperative when deciphering the effectiveness of therapies in future clinical trials for XLRS.


Oculocutaneous albinism (OCA) is an autosomal recessive condition that affects melanin production in the skin, hair, and eyes. All individuals with OCA have some degree of foveal hypoplasia, contributing to the frequent but variable reduction in visual acuity. Posterior staphyloma is typically associated with myopic degeneration and has not been recognized as a cause of reduced visual acuity in albinism. The authors report 3 cases of posterior staphyloma, each with oculocutaneous albinism (OCA) defined by phenotype and genotype. Two cases are biological sisters with OCA type 2; one was myopic and the other was hyperopic. The third case involves a man with OCA associated with Hermansky-Pudlak syndrome (HPS-5). This is first known report of posterior staphyloma in...
albinism. In summary, staphyloma may be another cause of reduced visual acuity in albinism, particularly with increasing age. It may occur in association with myopia or hyperopia.


Monogenic forms of nonsyndromic high myopia have been described in the genetics literature and are likely underrecognized as Mendelian disease by ophthalmologists. Genes associated with autosomal dominant nonsyndromic high myopia include zinc finger protein 644 (ZNF644), SCO2 cytochrome c oxidase assembly protein (SCO2), solute carrier family 39 zinc carrier member 5 (SLC39A5), procollagen proline 2-oxoglutarate-4-dioxygenase alpha subunit isoform 2 (P4HA2), and coiled coil containing domain 111 (CCDC111). In regard to autosomal recessive nonsyndromic high myopia, the only associated gene to date is low-density lipoprotein receptor-associated protein 1 (LRPAP1). Clinical characterization of the LRPAP1-related ophthalmic phenotype is needed to facilitate phenotype recognition, directed genetic testing, genetic counseling, and research for gene-directed treatments. In this report, the authors define the clinical and biometric features of children with high myopia related to recessive LRPAP1 mutations on the basis of our experience with the phenotype.

Seven consecutive families (12 children) with recessive LRPAP1 mutations were identified, and all affected individuals had homozygous mutations. The 12 affected children from these 7 families ranged in age from 2 to 16 years (median, 6 years). Cycloplegic refraction, axial length, anterior chamber depth, and keratometry ranges were as follows: -17 to -32 D (mean = median = -24); 29.64 to 37.65 mm (mean = median = 33.6); 3.04 to 3.17 mm (mean = median = 3.11); 40.34 to 45.14 D (mean = 41.8 = median = 41.6), respectively. Clinical appearance of the retina was typical for very high myopia (diffuse severe chorioretinal atrophy and optic nerve head peripapillary conus in all affected children), but neither lacquer crack nor neovascularization was seen. Vitreopathy was not appreciated clinically. The affected children were not dysmorphic. Best corrected visual acuity ranged from 20/60 to 20/200 and was considered stable. All children were or had been hyperactive before 6 years of age but not after that age. In summary, the clinical and biometric features described in this report characterize LRPAP1-related high myopia and have important implications for potential gene-related therapy.

**Exome Sequencing on 298 Probands With Early-Onset High Myopia: Approximately One-Fourth Show Potential Pathogenic**

High myopia, defined as a refractive error of at least -6.0 diopters (D) or an axial length of at least 26 mm, is a leading cause of blindness. Genetic factors are well known to play an important role in the development of high myopia, as confirmed by a number of studies. Early-onset high myopia (eoHM), occurring before school age, is an ideal model for monogenic studies of high myopia because of the minimum influence of environment (e.g., such as near work). Six genes have been identified in patients with high myopia, including **SCO2**, **ZNF644**, **LRPAP1**, **SLC39A5**, **LEPREL1**, and **CTSH**. High myopia has also been identified as a symptom of various forms of retinal dystrophies as well as systemic syndromes caused by a series of known genes. In this study, the authors used data obtained from whole exome sequencing in 298 patients with eoHM to attempt to verify mutations in all the genes responsible for retinal diseases and genes responsible for systemic diseases accompanied by high myopia. Variants from 234 genes were selected and analyzed by multistep bioinformatics analyses. Systematic analysis of variants in the 234 genes identified potential pathogenic mutations in 34 of 234 genes in 71 of 298 (23.8%) probands. Of the 71 probands, 44 (62.0%) had mutations in 11 genes responsible for ocular diseases accompanied by high myopia, including **COL2A1**, **COL11A1**, **PRPH2**, **FBN1**, **GNAT1**, **OPA1**, **PAX2**, **GUCY2D**, **TSPAN12**, **CACNA1F**, and **RPGR**. Initial clinical records of the 71 patients with mutations did not show recognizable signs of original diseases other than high myopia. Mutations in genes known to be responsible for retinal diseases were found in approximately one-fourth of the probands with early-onset high myopia. The high mutation frequency of RetNet genes in these patients can provide clues for genetic screening and further specific clinical examinations of high myopia to promote long-term follow-up assessment and prompt treatment of some diseases. Furthermore, this study expands the list of candidate genes associated with eoHM.


Heterozygous **OPA1** mutations cause autosomal dominant optic atrophy (DOA), which is the most common form of inherited mitochondrial blindness with a minimum prevalence of 1 in 25 000 in the general population. Infantile-onset encephalopathy and hypertrophic cardiomyopathy caused by mitochondrial oxidative phosphorylation defects are genetically heterogeneous with defects involving both the mitochondrial and nuclear genomes. The authors identified the causative genetic defect in two siblings from a consanguineous family presenting with lethal infantile encephalopathy, hypertrophic cardiomyopathy and optic atrophy. Molecular genetic analysis was done by a combined approach involving
genome-wide autozygosity mapping and next-generation exome sequencing. Both affected sisters presented with a similar cluster of neurodevelopmental deficits marked by failure to thrive, generalized neuromuscular weakness and optic atrophy. The disease progression was ultimately fatal with severe encephalopathy and hypertrophic cardiomyopathy. Mitochondrial respiratory chain complex activities were globally decreased in skeletal muscle biopsies. They were found to be homozygous for a novel c.1601T>G (p.Leu534Arg) mutation in the \textit{OPA1} gene, which resulted in a marked loss of steady-state levels of the native \textit{OPA1} protein. Severe mtDNA depletion was observed in DNA extracted from the patients’ muscle biopsies. Mitochondrial morphology was consistent with abnormal mitochondrial membrane fusion. The authors established, for the first time, a causal link between a pathogenic homozygous \textit{OPA1} mutation and human disease. The fatal multisystemic manifestations observed further extend the complex phenotype associated with pathogenic \textit{OPA1} mutations, in particular the previously unreported association with hypertrophic cardiomyopathy. The findings further emphasise the vital role played by \textit{OPA1} in mitochondrial biogenesis and mtDNA maintenance. Homozygous OPA1 mutations have not been reported previously and the unexpected association with cardiac involvement further broadens the genotypic and phenotypic spectrum associated with syndromic DOA.


Sensorineural hearing loss (SNHL) is the most common sensory deficit in developed societies. Usher syndrome is the most common cause of deafblindness, with an estimated prevalence of 4.4-6.2 per 100,000 in the population. The retinitis pigmentosa (RP) associated with Usher syndrome is typical, with nyctalopia (night blindness), progressive visual field constriction, and later loss of visual acuity. The guidelines of the National Deaf Children’s Society recommend that children with SNHL be routinely screened for ophthalmological problems and suggest electroretinography (ERG) to exclude Usher syndrome. An ERG is recommended to rule a retinal dystrophy in the absence of signs or symptoms. The present study reports the nature and prevalence of abnormal ERG findings in a cohort of children with SNHL undergoing ERG with the aim of identifying risk factors for the diagnosis of Usher syndrome. The medical records of children (<18 years of age) with SNHL referred for ERG at Moorfields Eye Hospital, London, between January 2009 and December 2011 were retrospectively reviewed. Patients were included if they had been referred with SNHL by an audiological medicine consultant and the primary indication for electrodiagnostic testing was possible Usher syndrome. A total of 84 cases met inclusion criteria of which 13 (15%) had ERG findings showing rod-cone dysfunction clinically consistent with a diagnosis of Usher syndrome. Two patients with retinal pigmentary changes had normal ERGs and were diagnosed
with rubella retinopathy based on the clinical findings. Risk factor analysis showed that age of ≥ 8 years at the time of ERG, sex, and bilateral hearing loss were not predictive of a diagnosis of Usher syndrome. However, the presence of or referral for cochlear implants, having relevant symptoms and/or clinical signs consistent with a retinal dystrophy, and profound hearing loss were all highly predictive. In conclusion, ERG is a useful diagnostic tool in children with SNHL and should be performed in children with SNHL who have cochlear implants and/or have signs or symptoms of retinal dystrophy. This study reveals that a focused approach could have potential cost-saving benefit.


In the UK, congenital and childhood cataract (CCC) has a reported incidence of 3.5 per 10,000 by age 15 years, with an estimate of around 200,000 children globally are sightless due to cataract. Determination of the precise cause is necessary to ensure prompt management of multisystemic complications. Among the numerous causes of childhood cataract, a large proportion of cases are genetic, accounting for as many as 50% of cases, including many syndromic conditions (e.g., Stickler, Cockayne, Nance-Horan, and Warburg-MICRO syndromes). A small and poorly defined subset result from biochemical defects (e.g., galactosaemia, galactokinase deficiency, and disorders of cholesterol or peroxisome biogenesis). Owing to a lack of wide-scale genetic analyses of large cohorts of patients, awareness of these disorders is low, despite the fact that early diagnosis can be crucial because a number are amenable to therapeutic intervention. The authors screened 50 patients diagnosed with bilateral CCC by cataract-targeted next-generation sequencing (NGS) for 115 genes associated with all forms of CCC, or by whole exome sequencing in combination with autozygosity mapping. Putative pathogenic variants were identified in 75% of cases (n = 38). The study demonstrated that 15.7% of suspected cataract-causing variants identified occurred in genes associated with inborn errors of metabolism (n = 6). Putative pathogenic variants in 6 different genes associated with 6 different inborn errors of metabolism were identified, including peroxisome biogenesis disorder 14B, lathosterolosis, galactokinase deficiency, and cerebrotendinous xanthomatosis. Importantly, 5 of 6 of the metabolic disorders identified herein are amenable to treatment, either by dietary management or preventative therapies. These outcomes highlight the importance of early identification of the precise molecular cause to prevent the onset of other disease manifestations by timely therapeutic intervention to improve outcomes in this patient group. The findings presented confirm that inborn errors of metabolism complicated by pediatric cataract are also efficiently and accurately diagnosed by NGS. Traditional routes to the diagnosis of pediatric cataract are heavily reliant on accurate, multidisciplinary clinical phenotyping and numerous diagnostic tests are required to establish an underlying cause. The authors revealed that on
average 13 diagnostic tests were ordered in the children presented. The use of NGS as a frontline means of diagnosis in pediatric cataract cases could remove the reliance on disease recognition, facilitate early diagnosis, and enable personalized therapeutic intervention.


Tuberous sclerosis complex (TSC) is an autosomal dominant multisystem disease, caused by mutation in the TSC1 or TSC2 genes, associated with many features, including intellectual disability (ID). ID is defined as an IQ <2 SDs of the mean (IQ/ developmental quotient (DQ)<70), and associated functional impairment in daily life. To date, only three studies of genotype-phenotype associations in TSC used validated and standardized measures of intellectual ability/developmental level. These studies, however, had methodological weaknesses, particularly in the psychometric approach to IQ/DQ data. The authors examined psychometric profiles of patients with TSC1 or TSC2 mutations and tested whether different mutation types were associated with different degrees of intellectual ability. One hundred subjects with known TSC1/TSC2 mutations were assessed using a range of IQ or DQ measures. Effects of mutations on TSC1/TSC2 proteins were inferred from sequence data and published biochemical studies. Most individuals with TSC1 mutations fell on a normal distribution identical to the general population, with ~10% showing profound ID. Of individuals with TSC2 mutations, 34% showed profound ID, and the remainder a pattern of IQ/DQ more variable and shifted to the left than in TSC1 or the general population. Truncating TSC1 mutations were all predicted to be subject to nonsense-mediated mRNA decay. Mutations predicted to result in unstable protein were associated with less severe effects on IQ/DQ. There was a statistically significant negative correlation between length of predicted aberrant C-terminal tails arising from frameshift mutations in TSC1 and IQ/DQ; for TSC2 a positive but not statistically significant correlation was observed. The authors propose a model where (i) IQ/DQ correlates inversely with predicted levels and/or deleterious biochemical effects of mutant TSC1 or TSC2 protein, and (ii) longer aberrant C-terminal tails arising from frameshift mutations are more detrimental for TSC1 and less for TSC2. These predictions of the model require replication and biochemical testing. In conclusion, larger-scale exploration of the relationship between the molecular consequences of TSC mutations, including direct measurements of levels and function of mutant proteins in vivo, and intellectual phenotype is required to confirm our findings and may lead to discoveries of direct relevance in the clinical setting.
Clinical and molecular predictors of mortality in neurofibromatosis 2: a UK national analysis of 1192 patients.

Neurofibromatosis 2 (NF2) is an autosomal-dominant tumor predisposition syndrome characterized by bilateral vestibular schwannomas, considerable morbidity and reduced life expectancy. Although genotype–phenotype correlations are well established in NF2, little is known about effects of mutation type or location within the gene on mortality. Improvements in NF2 diagnosis and management have occurred, but their effect on patient survival is unknown. The authors evaluated clinical and molecular predictors of mortality in 1192 patients (771 with known causal mutations) identified through the UK National NF2 Registry. The study included 241 deaths during 10 995 patient-years of follow-up since diagnosis. Early age at diagnosis and the presence of intracranial meningiomas were associated with increased mortality, and having a mosaic, rather than non-mosaic, NF2 mutation was associated with reduced mortality. Patients with splice-site or missense mutations had lower mortality than patients with truncating mutations. Patients with splice-site mutations in exons 6-15 had lower mortality than patients with splice-site mutations in exons 1-5. The mortality of patients with NF2 diagnosed in more recent decades was lower than that of patients diagnosed earlier. This study confirms the adverse effects on mortality of younger age at diagnosis of NF2, the presence of intracranial meningiomas and the presence of a non-mosaic, rather than mosaic, NF2 mutation. The authors found that the mortality rate among patients with NF2 has improved since 1980. The development of NF2 specialist centers has greatly increased the availability of high-quality diagnostic, medical and surgical services for patients with NF2 throughout the UK. These centers also provide patients with NF2 the opportunity to participate in clinical trials of novel therapeutics.


Neurofibromatosis type 1 (NF1) is an autosomal dominant disorder with an approximate worldwide incidence of 1 in 3,500. The most common NF1-associated tumor in children is optic pathway glioma (OPG), seen in 15%-20% of patients. OPG represents 2%-5% of all childhood brain tumors; as many as 70% of these cases are associated with NF1. Strabismus has only been occasionally mentioned in the literature as a presenting symptom of NF1-associated OPG. The purpose of this retrospective study was to define the incidence and characteristics of strabismus and examine the outcomes of strabismus surgery in a set of pediatric patients with NF1-associated OPG. The medical records of consecutive patients diagnosed with NF1 and OPG at a neurofibromatosis clinic
since 1985 were reviewed. A total of 76 patients were included. Of these, 22 (28.9%) had strabismus: 5 (22.7%) had esotropia and 17 (77.2%) had exotropia; of those with exotropia, 10 (45%) also had hypotropia. In 12 patients (54.5%), strabismus was present at the first ophthalmologic examination. The development of strabismus preceded the diagnosis of both NF1 and OPG in 4 (5.3%) patients and the diagnosis of OPG in another 2 (2.6%) patients with known NF1. In 16 (76%) patients, the strabismus was sensory. Five patients (22.7%) underwent surgery, which resulted in a deviation angle of <10D in 1 patient, <20D in 2 patients, and >20D in 2 patients. In conclusion, strabismus was the presenting symptom and led to the diagnosis of OPG in a subset of patients, including those who did not have a previous diagnosis of NF1. These findings underscore the importance of determining visual acuity, optic nerve appearance, and the possibility of Lisch nodules during the initial evaluation of strabismus. Exotropia, especially associated with a hypotropia, was the most common strabismic deviation seen in these patients. Sensory strabismus was the most common type seen in this population. Deviations of <10D may be difficult to achieve with strabismus surgery.


Children with retinal dystrophies often have nonspecific strabismus, but vertical incomitant deviations are uncommon, even with profound visual loss. The authors report 4 children from 3 consanguineous families with bilateral elevation deficiency in the context of retinal dystrophy. All were found to harbor recessive mutations in retinal dehydrogenase 12 (RDH12). This suggests that elevation deficiency may be a recurrent finding for a subset of children with this form of retinal dystrophy. The main differential diagnosis for elevation deficiency with retinal dystrophy has classically been neurological disease, which is typically acquired and of later onset. Such neurological disease includes Kearns-Sayre syndrome and related mitochondrial disorders, spinocerebellar ataxia, and potentially neurodegeneration with brain iron accumulation. Further studies are needed to better understand how frequently elevation deficiency occurs in RDH12-related retinopathy and potentially in other genetic forms of retinal dystrophy.


Malignant hyperthermia susceptibility is a rare pharmacogenic disorder of skeletal muscle calcium regulation caused by mutations in the skeletal muscle ryanodine receptor 1 gene (RYR1). It is important to identify children who are
candidates for ophthalmic surgery who might harbor \textit{RYR1} mutations because intraoperative malignant hyperthermia is potentially lethal. Ophthalmoplegia has been reported infrequently as part of \textit{RYR1}-related myopathy, but isolated ptosis has not been described. The authors report 2 siblings with congenital ptosis and scoliosis who were considered for ptosis surgery but were found to harbor underlying recessive \textit{RYR1} mutations. No other dysmorphic features were noted. In this case series the authors report for the first time congenital ptosis as the only ophthalmic findings in 2 siblings with scoliosis and underlying recessive \textit{RYR1} mutations and highlight the importance of suspicion for malignant hyperthermia susceptibility with this phenotype.


Wiedemann-Rautenstrauch syndrome (WRS) is a rare neonatal congenital disorder characterized by a progeroid appearance at birth. Other diagnostic features include failure to thrive, abnormal facial appearance, pseudohydrocephalus, craniofacial disproportion, prominent scalp veins, absence of subcutaneous fat, sparse scalp hair, hypotrichosis of the eyebrows and eyelashes, and neonatal teeth. In contrast to other progeroid syndromes, the phenotypic features of WRS are present from birth. There have been approximately 30 documented cases in the literature since it was first reported in the late 1970s. To date, there have been no reports summarizing the ocular manifestations of the condition. The authors report the ocular manifestations of WRS in a 6-year-old boy and compare the findings to previously reported cases. In the prior cases, the most commonly reported ophthalmic features in WRS were deep set eyes, hypotrichosis of eyebrows and eyelashes, proptosis, upward slanting palpebral fissures, and lower lid entropion. The ophthalmic findings in this case are consistent with these commonly described features. In addition, this is the first time the findings of thin central corneas and lagophthalmos in WRS have been reported. In conclusion, Patients with WRS may be at greater risk of corneal perforation due to decreased corneal and possibly limbal thicknesses. Clinicians should consider this potential risk in management of WRS patients.

\textbf{A novel OPA1 mutation causing variable age of onset autosomal dominant optic atrophy plus in an Australian family.} Ahmad KE, Davis RL, Sue CM. J Neurol October 2015; 262(10):2323-8.

Pathogenic mutations in the \textit{OPA1} gene can be associated with Autosomal Dominant Optic Atrophy (ADOA). In approximately 20 % of patients with \textit{OPA1} mutations, a more complex neurodegenerative disorder with extraocular manifestations, known as ADOA Plus, can arise. 12 members of a multigenerational family were assessed clinically and screened for a genetic
mutation in OPA1. Eight family members displayed manifestations consistent with ADOA Plus and four did not. Affected members of the oldest available generation displayed the most severe phenotype, which included severe optic atrophy, deafness, ptosis, ophthalmoplegia, proximal myopathy, neuropathy and ataxia. The next generation was less severely affected but several members displayed manifestations only after the fifth decade. Genetic analysis revealed a heterozygous variant in the OPA1 gene (c.1053T>A, p.Asp351Glu) that segregated with disease. The affected family members described here exhibited visual loss later than is typical for OPA1-related disease, as well as later onset of other neurological abnormalities in the fifth or sixth decades of life that progressed to severe neurological disability by the seventh decade. These findings expand the clinical spectrum of OPA1-related disease associated with a novel OPA1 mutation.

17. TRAUMA

NON-ACCIDENTAL HEAD TRAUMA


This article seeks to answer three questions regarding the experience of pediatric ophthalmologists with abusive head trauma. 875 pediatric ophthalmologists and active members of the American Association for Pediatric Ophthalmology and Strabismus (AAPOS) were sent a survey. The response rate was 15% (132 surveys). The use of retinal photography, presence of a child abuse team and geographic location had no impact on how often pediatric ophthalmologists were subpoenaed or testified in court. The median number of missed clinic days was 1.0 with an estimated cost of $3,000 in lost revenue when members testified in court. This article may be limited by the low response rate but serves to document that pediatric ophthalmologists have little power to prevent being subpoenaed or having to testify in court when involved in abusive head trauma cases. Court testimony results in significant loss of revenue.


This study evaluated the use of BAmyloid precursor and Ubiquitin and glial fibrillation acid protein as a diagnostic tool to help differentiate between head
trauma due to abuse and nonabusive head trauma. This was a retrospective crosssectional study. 74 eyes of 37 infants was studied. In the abusive head trauma group, positive BAPP and Ubiquitin stain of the retina was more likely than in the control. This study looked at how Immunohistochemistry studies post mortem could help differentiate out abuse. The expression of BAPP and Ubiquitin reveals axonal injury in the brain. They found there is a distinctive pattern in the eyes as well. This may be useful in cases where the eye exam is not definitive in post mortem scenerios.


This was a case-control study of retinal hemorrhages (RH) in the setting of abusive head trauma (AHT). The authors determined potential risk factors. This was a retrospective review over 47 months. The case group had at least one RH (n=65) and the control group (n=103) had no RH. Mean age was 9.3 months. Of 103 children with RH, 22 had subretinal hemorrhage, 9 had retinoschisis and 1 had a vitreous hemorrhage. The case group had statistically significantly greater age, symptoms of lethargy, altered mental status, seizure, vomiting, subdural hemorrhage, other radiologic findings, skull fracture without intracranial hemorrhage, and nonskull fracture without intracranial hemorrhage. Lethargy or altered mental status, were the only presenting signs that strongly correlated with the presence of RH. Patients with fractures but no intracranial hemorrhage were not found to have RH. Mortality was 4x higher in the case group compared to the control group. Persistent traumatic brain injury was found in 18% of the case group patients and 0% of the control group patients. Feeding tube placement was also more likely in the case group. This study can help define clinical features to distinguish AHT from other causes of pediatric head injury.


Recently, the relevance of retinal hemorrhages in helping make a diagnosis of non-accidental trauma in children has been challenged. Lawyers and non-ophthalmology medical professionals assert that retinal hemorrhages could be due to conditions other than trauma, such as after a vaccination. This was a retrospective cohort study to determine the prevalence of retinal hemorrhages in 5177 children age 1 to 23 months who underwent a fundus exam at one institution for any reason. Children were excluded if there was a history of prior ocular surgery or active retinal neovascularization. The main outcome measures were the prevalence and causes of retinal hemorrhage, as well as the temporal association between vaccination injection within 7, 14, or 21 days preceding the
eye exam and retinal hemorrhage. Out of 7675 fundus exams of 5177 children, 9 children had retinal hemorrhages for a prevalence of 0.17%. All 9 had non-ocular signs consistent with abusive head trauma. Among a subset of 2210 children who had vaccination history documented and underwent 3425 fundus exams, none had retinal hemorrhage who had been vaccinated within 7 days, one had retinal hemorrhage within 14 days, and none had retinal hemorrhage within 21 days of the fundus exam.

Importance: This article rebuts the dangerous trend of discounting retinal hemorrhages caused by abusive head trauma. Dr. William Good, in his invited commentary on this important article, says it best. “Our responsibility to come to the infant’s aid has been bolstered. Confronting the reality of abuse is difficult. One more vestige of doubt about the cause of retinal hemorrhages can be laid to rest.”

**MISCELLANEOUS**

**Emergency Eye Rinse for Chemical Injuries New Considerations**

Copious irrigation with a pH neutral solution, either water, normal saline or balanced salt solution, has been the classical teaching regarding the management of a chemical exposure to the eye. The authors seek to raise awareness that a more effective treatment is available, but it is not yet approved by the US Food and Drug administration. The authors highlight a major gap in our care of chemical burn patients since lavage of the eye does not always prevent injury to the cornea or prevent glaucoma and optic neuropathy in severe cases. The reason for post lavage eye injury is that intraocular pH is not always normalized. Another agent for rinsing the eye is potentially more effective in neutralizing intraocular pH, that is, buffered liquids like borate and Diphoterine, an amphoteric buffer. There is a borate-buffered solution that is sterile, preservative free, single use, and available in the United States (Cederroth). Both substances have been shown to be superior to saline in the ex vivo model and has been used successfully in Europe. Barriers to adopting this rinse include that the FDA does not have a monograph for over-the-counter ophthalmic drug products for emergency first-aid use. It is this monograph which drug manufacturers use as a guide for the formulation and production of a drug.


This study examines trends and risk factors for paintball and airsoft pediatric ocular injuries using a nationally representative sample. Data was obtained from consumer product injury emergency department visits. In 2012, approximately
3161 children 2-18 years of age were treated in US emergency departments for eye injuries secondary to nonpowder gun use. This was a leading cause of pediatric eye injury requiring hospital admission. From 2006 to 2010 the rate decreased by 722% but then it rebounded sharply by 511% from 2010 to 2012. Air guns are the major cause of pediatric nonpowder gun-related eye injuries. Air guns are 4x more likely to result in a foreign body injury and 3x more likely to cause an ocular puncture injury, compared to paintball injuries. These data also reflect the trend of declining paintball gun sales and rising airsoft gun sales. This reinforces the need for eye-care providers to ask their patients about recreational activities and counsel eye protection usage.

18. RETINA

OCT IMAGING IN DISEASE

Familial Exudative Vitreoretinopathy: Spectral-Domain Optical Coherence Tomography of the Vitreoretinal Interface, Retina, and Choroid

Y Yonekawa, BJ Thomas, KA Drenser, MT Trese, et al
Ophthalmology November 2015; 122:2270-2277

This is a retrospective observational case series. 346 patients with familial exudative vitreoretinopathy (FEVR) were identified and treated between from 2009 to 2014. Of these, 74 eyes from 41 patients underwent 225 imaging sessions with spectral domain OCT (SD-OCT). Interpretable images were acquired in 67 eyes and 50 eyes had microstructural findings. All eyes with FEVR severity ≥ stage 2 had abnormalities. A broad spectrum of features were found: various forms of posterior hyaloidal organization, vitreomacular traction (VMT), vitreopapillary traction, vitreo-fold traction, vitreo-laser scar adhesion, diminished foveal contour, persistent fetal foveal architecture, cystoid macular edema (CME), intraretinal exudates and subretinal lipid aggregation, dry or edematous radial folds, and disruption of the ellipsoid zone. Mean foveal, central macular, and choroidal thicknesses were 305±145 μm, 337±160 μm, and 216±64 μm, respectively. In stages 1 to 2, greater foveal and central macular thicknesses correlated with poorer BCVA, but not choroidal thickness. Posterior hyaloidal organization, VMT, CME, exudation, and disruption of the ellipsoid zone were associated with poorer BCVA. Spectral-domain OCT detected all cases of angiographic edema and areas of outer retinal dysfunction that were hypoautofluorescent on fluorescein angiography. Microstructural-genetic associations were not identified. Spectral-domain OCT imaging identified microstructural anomalies in the majority of patients with FEVR and this could serve to improve the diagnosis, treatment, and pathophysiologic understanding of this disease.

Spectral domain OCT was used to document changes in the pediatric retina after unprotected solar viewing. This was a prospective, observational case series. Two children (4 eyes) viewed a partial eclipse and 1 child (1 eye) viewed the transit of Venus. Initial visual loss was mild to moderate (20/20 to 20/40). At presentation, there was significant foveal pathology, even with normal acuity. Disruption of the ellipsoid zone and interdigitation zone was present in all eyes. In the eyes with decreased visual acuity, there was apparent disruption of the outer nuclear layer and/or external limiting membrane. These later changes resolved over time, but the changes in the ellipsoid zone and interdigitation zone persisted. This article uses OCT to help define specific retinal layer pathology as a result of solar retinopathy.

**Retinal Structure And Function In Perinatally HIV-Infected And Cart-Treated Children: A Matched Case–Control Study.**

Subtle structural and functional neuroretinal changes have been described in human immunodeficiency virus (HIV)–infected adults without retinitis treated with combination antiretroviral therapy (cART), thought to be part of an “HIV-associated neuroretinal disorder”. However, studies on this subject in HIV-infected children are scarce. The authors studied 33 perinatally HIV-infected children on cART (median age 13.7 years [interquartile range (IQR), 12.2–15.8], median CD4+ T-cell count 760 cells/mm3, 82% with an undetectable HIV viral load) and 36 age-, sex-, ethnicity-, and socioeconomically matched healthy controls (median age 12.1 years [IQR, 11.5–15.8]). Contrast sensitivity was significantly lower in the HIV-infected group (1.74 vs. 1.76 logCS; P = 0.006). The patients had a significantly thinner foveal thickness (-11.2 µm, P = 0.012), which was associated with a higher peak HIV VL (-10.3 µm per log copy/mL, P = 0.016). There was no significant difference in peripapillary retinal nerve fiber layer (RNFL) thickness or visual outcome. The results of this study are contrary to a previous study that showed thicker fovea and thinner peripapillary RNFL thickness in children with HIV. However, this study is likely more accurate, as it used spectral-domain OCT rather than time-domain OCT, and adjusted for known confounders. Though visual outcome did not appear affected in the HIV-infected children, it is possible that vision loss might become more prevalent and symptomatic with time. Longitudinal studies are warranted to investigate the effect of chronic HIV infection and long-term cART on the retinal structure and visual function of both HIV-infected adults and children.

The authors highlight the utility of SD-OCT to correlate form (retinal lesions) and function (visual acuity) in patients with Stargardt's disease. Stargardt's disease is a progressive retinal degeneration of the macula from a defect in the ABCA4 gene and is inherited in an autosomal recessive fashion. Twenty six eyes of 13 patients with Stargardt's were evaluated with SD-OCT and the authors make a new discovery that the retinal flecks seen as hyperreflective foci on OCT were found even in superficial retinal layers and the choroid, not only in deeper retina layers and the RPE. These hyperreflective lesions correlated with visual acuity, such that the more hyperreflective lesions noted on OCT, the worse the visual acuity.


Ocular changes in some types of the mucopolysaccharidoses (MPS) include corneal clouding, glaucoma, pigmentary retinopathy, optic disc edema, and optic atrophy. Pigmentary retinopathy has been reported in MPS I (Hurler disease), MPS I-S (Scheie syndrome), MPS I-H/S (Hurler/Scheie), MPS II (Hunter disease), MPS III (Sanfilippo syndrome), and MPS IV A (Morquio A syndrome). Clinical signs of retinopathy include atrophy of the retinal pigment epithelium (RPE), arteriolar narrowing, and later bone spicules. Histopathologic examinations have demonstrated widespread loss of RPE and photoreceptors. However, there have been no histopathologic descriptions of the retinas in mild forms of MPS. Using optical coherence tomography (OCT), the authors attempted to provide a detailed morphologic description of the retina and choroid in cases with MPS. A total of 42 eyes of 21 consecutive patients with MPS were enrolled in this study, including 3 patients with MPS I, 5 patients with MPS II, 8 patients with MPS IV A, and 5 patients with MPS VI. Patients underwent infrared fundus imaging and spectral-domain (SD) OCT with enhanced depth imaging. Imaging demonstrated the presence of parafoveal retinal folds, a fuzzy and thickened ELM, and thinning of the choroid at depigmented retinopathy areas. These chorioretinal changes were noted in the MPS type I, II, and VI, but not in MPS IV A. Pigmentary retinopathy has previously been reported in MPS I, MPS I-S, MPS I-H/S, MPS II, MPS III, and MPS IV A, but has never in MPS VI. This study is the first to report chorioretinal changes in MPS VI. There is controversy as to whether enzyme replacement therapy is effective for ocular complications of MPS. One major argument is that enzymes cannot pass the blood-retinal barrier to exert an influence. This study revealed choroidal thinning at areas of retinal hypopigmentation. This finding may have important implications, as the choroid is located outside the blood-retinal barrier. Therefore, enzyme
replacement therapy performed in the early stages of the disease might prevent chorioidal thinning caused by glycosaminoglycan (GAG) accumulation in the sclera, and slow down the progression of retinal changes caused by MPS. Furthermore, SD OCT with enhanced depth imaging might help to investigate the pathophysiology and follow the disease course of the chorioretinopathy caused by MPS.


This cohort study evaluated the RNFL thickness in very preterm (less than 32 weeks) vs. term newborn infants. SD OCT was performed prospectively. 57 term babies and 134 preterm babies were enrolled. RNFL was thinner for very preterm babies vs. term babies at the paillomacular bundle (61 vs 72 microns). There was a weak correlation between RNFL thickness and birth weight and gestational age. In addition, in babies undergoing MRI, thinner paillomacular bundle RNFL correlated with higher global brain MRI lesion burden and lower cognitive and motor skills.


The authors attempt to relate posterior segment microanatomy evaluated by perinatal spectral domain OCT to visual acuity, brain abnormalities, and neurodevelopment. Thirteen infants (11 preterm and 2 term births) were imaged in the nursery with portable SD-OCT and then had visual acuity and sensorimotor testing at age 9 – 15 months or 4 – 5 years. Their medical records were reviewed for brain MRI reports and Bayley scales testing at age 18 – 24 months. Eight children with age-appropriate macular microanatomy without edema on perinatal SD-OCT had >=20/40 or within normal limits grating visual acuity, as well as appropriate neurodevelopmental outcomes and no clinical indication for brain MRI while in the nursery. The five children with perinatal macular edema had suboptimal visual acuity and sensorimotor deficits, MRI abnormalities, or poor neurodevelopment. Macular edema persisted in 1 infant through 9-months corrected age, and this child had subnormal acuity and strabismus. The authors conclude that retinal microanatomy observed in infancy might relate to subsequent vision and other CNS events. One important point, however, is that other eye findings as well as brain and neurodevelopmental abnormalities may also impact visual acuity, and therefore CME on bedside OCT may reflect the presence of other abnormalities rather than indicate a direct retinal cause of subnormal acuity. Only 13 infants who were imaged in infancy had follow-up visual acuity assessed at a later date, and this limited population may not
represent the balance of health and disease in the larger population. Finally, visual acuity assessed at 9 – 15 months with grating acuity is not directly comparable to optotype acuity at 4 – 5 years so comparisons between these time points are limited.

**OCT IMAGING – DATA ON NORMAL EYES**


This study attempted to collect descriptive information to develop normative data. Healthy infants between 37-42 weeks postmenstrual age were imaged and a hand held spectral domain OCT was utilized. Average RNFL thickness for 4 temporal 45-degree sectors and the temporal quadrant were calculated and compared between all infants. The results were collected on 50 infants. The RNFL thickness was most regular at 1.5 mm radial distance from the optic nerve. There was no significant difference between race, sex, gestational age, or birth weight. Normative data was presented for future references.


Changes in different retinal layer thicknesses are associated with a variety of retinal diseases that can begin in childhood. These investigators sought to improve understanding of the average thickness distribution across the posterior pole in a healthy pediatric population. High-resolution macular spectral domain OCT scans from 196 children with normal ocular health and minimal refractive error were analyzed to determine total retinal thickness and thickness of 6 different retinal layers across the central 5mm of the posterior pole. The mean total retinal thickness in the central 1-mm foveal zone was 255 +/- 16 microns. This increased significantly with age (mean increase of 1.8 microns per year) in childhood. Changes with the highest statistical significance were found in the outer retinal layers in the central foveal region. Therefore, the authors state that a clinical observation of thinning in the outer retinal layers in childhood should raise suspicion for a retinal abnormality. The cross-sectional nature of this study is a weakness, and longitudinal studies would provide greater insight into the nature and time-course of retinal thickness changes with age in childhood.
**Choroidal Thickness and Volume in a Healthy Pediatric Population and its Relationship with Age, Axial Length, Ametropia, and Sex**


It has been reported that choroidal thickness (CT) in healthy adults decreases with age, level of myopia, and axial length (AL). Studies of CT in a healthy pediatric population are limited. This study evaluated CT and volume in healthy children using enhanced depth imaging spectral domain optic coherence tomography (EDI SD-OCT) and its association with age, sex, AL, and refractive error. Ninety-three eyes from 93 healthy pediatric individuals were examined and an ETDRS grid was applied to analyze CT and volume in each of its 9 sectors. The mean subfoveal CT and volume were 314.22 microns and 0.25 mm³, respectively. The nasal CT and volume of the inner and outer rings were lower than the temporal area of the same ring and lower than the subfoveal CT. A negative correlation between the subfoveal CT and AL was found; estimation of the variation in the subfoveal CT in relationship to the AL was -13.55 microns per mm. A positive correlation between the subfoveal CT and refractive error was found; variation in subfoveal CT with refractive error was 7.52 microns per diopter. In this population, CT and volume showed an increase with age after adjusting for AL, suggesting a possible bimodal growth of CT during an individual’s lifetime with evolution in childhood followed by a progressive reduction in adulthood.

One study limitation is that CT was determined manually. In addition, height and weight were not measured, though previous authors have found correlation with choroidal volume. All of the subjects in this study were white which may limit application to differing populations.

**INCONTINENTIA PIGMENTI**

**Extended Follow-up of Treated and Untreated Retinopathy in Incontinentia Pigmenti Analysis of Peripheral Vascular Changes and Incidence of Retinal Detachment**


The authors seek to determine which patients with incontinentia pigmenti (IP) are at risk for developing retinal detachment. Incontinentia pigmenti, also known as Bloch-Sulzberger syndrome, is a rare X-linked dominant disease affecting the eyes, central nervous system, skin, and teeth. Affected infants are typically female because the responsible mutations in nuclear factor-κB essential modulator (NEMO) gene are lethal to males in utero. This was an observational cohort study of 50 eyes in 25 females with IP and followed prospectively over at least 6 months. In fact the median follow up was 9.3 years. The odds of retinal detachment were increased if there was retinal neovascularization (odds ratio,
11.61; 95%CI, 1.34-100.56; P = .03) or ischemic optic neuropathy (odds ratio, 5.27; 95%CI, 1.61-17.23; P = .006) on initial examination. A bimodal distribution of retinal detachments was observed, with most tractional detachments (7 eyes) occurring by age 2.5 years (median, 1.5 years; range, 14 days-7.0 years) and most rhegmatogenous detachments (4 eyes) occurring in adults (median age, 31.5 years; range, 14.0-47.0 years).


The authors describe foveal abnormalities using SD-OCT in several patients, some with vision loss and all with biopsy proven incontinentia pigmenti, also known as Bloch-Sulzberger syndrome, an X-linked disorder which is lethal in males. Characteristic skin findings are a hallmark of this syndrome and 18-30% will experience neurologic or retinal problems. Foveal abnormalities found on fluorescein angiography and SD-OCT include foveal hypoplasia, which was determined by calculating the foveal parafoveal ratio, inner foveal disorganization and thinning. These findings did not necessarily correlate with peripheral changes such as avascular retina or neovascularization. The authors stress the importance of a coordinated approach with dermatology and neurology, as well as judicious use of exams under anesthesia to perform fluorescein angiography to identify and treat with laser areas of extraretinal neovascularization and areas of non-perfusion. SD-OCT should be used to detect macular abnormalities. Identification and treatment of amblyopia and strabismus are also requisite for achieving best visual outcomes in these children.

**COAT’S DISEASE**

**Intraoperative Fluorescein Angiography-Guided Treatment in Children with Early Coat’s Disease** Suzani M, Moore AT *Ophthalmology* June 2015; 122(6) pp.1195-1202

Historically, children with Coat’s disease have been treated with laser photocoagulation and/or cryotherapy based on direct visualization of telangiectatic vessels during examination under anesthesia. With the recent advent of the RetCam, intraoperative wide-field fluorescein angiography (FA) has been used in treating many pediatric retinal diseases. This is a retrospective review of 20 children (ages 2-15 years) diagnosed with early Coat’s disease (6 with Stage 2 and 14 with Stage 2a) and treated using intraoperative FA at the Moorfields Eye Hospital. Patients had at least 3 months follow-up (median
duration 21 months) after treatment. The purpose of the study was to determine if treatment based on intraoperative FA would result in fewer treatment sessions and improved outcome due to better visualization of the full extent of retinovascular abnormalities (such as microaneurysms and capillary nonperfusion). Use of intraoperative FA led to good anatomic and visual outcomes. 15 eyes were stabilized with 1 treatment and 5 eyes needed a second treatment. None of the patients demonstrated progression of disease to a more severe stage. 12 eyes had a final VA of 0.4 logMAR or better, 6 patients had VA between 0.4 and 1.0 logMAR, and 2 patients had VA worse than 1.0 logMAR.

Childhood Retinal Angiomatous Proliferation with Chorioretinal Anastomosis in Coats Disease: A Reappraisal of Macular Fibrosis Using Multimodal Imaging


In Coats’ original articles, he noticed a temporal macular neovascular lesion in >50% of the originally described cases. This nodular entity was recognized as a common feature of Coats disease, and was described by others as “subretinal mounds” and later “macular fibrosis”. The authors of this report observed a temporal macular choroidal neovascular lesion in multiple children undergoing examination under anesthesia for presumed Coats disease. Using color fundus photography, wide-field FA, and spectral domain OCT, they describe the unique morphologic features of retinal angiomatous proliferation (RAP) and chorioretinal anastomoses. The study was a prospective observational case series of 21 consecutive patients with Coats disease examined over a 1-year period. RAP and chorioretinal anastomoses were present in 5 of the patients (24%). Although the series was relatively small and lacked ICG angiography, the authors conclude that Type III choroidal neovascularization commonly occurs in childhood Coats disease and frequently involves a large-caliber chorioretinal anastomosis, thus redefining the previously described subretinal mounds and macular fibrosis.

Transcleral Drainage of Subretinal Fluid, Anti-Vascular Endothelial Growth Factor, and Wide-Field Imaging-Guided Laser in Coats Exudative Retinal Detachment


The management of advanced (Stage 3 and 4) stages of Coats disease varies greatly and has included sclerotomy and drainage of subretinal fluid (SRF), buckling or encirclement, and vitrectomy with gas or long-term oil tamponade. The authors of this study present a new therapeutic approach for exudative RD in Stage 3 Coats disease by combining transscleral drainage of SRF, intravitreal anti-VEGF injection, and wide-field image-guided laser photocoagulation. Eight
eyes in 8 children with advanced Coats disease manifested as total or subtotal RD underwent surgical drainage of exudative SRF followed by intravitreal injection of bevacizumab and laser photocoagulation. In all eyes, SRF was eliminated after SRF drainage and administration of 1 – 2 intravitreal injections. Patients required up to 4 sessions of laser. All patients had total retinal reattachment and resolution of subretinal exudates. At the last follow-up (up to 60 months), no patient showed recurrent SRF and no ocular complications were noted, though 3 of the 8 patients developed cataracts within the follow-up period. This study is limited by a small number of patients, but the authors present a novel therapeutic approach that allows for successful treatment of advanced cases of exudative RD in Coats disease without the need for vitrectomy. In eyes with a poor visual prognosis, treatment may prevent the development of iris rubeosis, phthisis bulbi, or a blind painful eye.

**MISCELLANEOUS**

**Visual Outcome in Early Vitrectomy for Posterior Persistent Fetal Vasculature Associated with Traction Retinal Detachment**

This study investigated the anatomic and visual outcomes of vitrectomy for the treatment of unilateral posterior persistent fetal vasculature with traction retinal detachment in 11 patients. 6/10 eyes that had surgery at age 13 months or younger had 20/800 or better vision at last follow-up; 2 had 20/60 visual acuity. All 10 of these patients had their retinas reattached postoperatively with significant reversal of retinal dragging. One patient underwent surgical intervention at 33 months of age and had persistent traction retinal detachment and postoperative visual acuity of hand motion. Postoperative glaucoma was diagnosed in 4 patients (36%). Follow-up in the study was variable but was 10 months or longer in all patients. The study was limited by the small sample size and lack of control group. Compliance with amblyopia therapy was also not recorded. Despite these limitations, this study suggests that surgical intervention at a younger age may offer improved visual potential.

**Peripheral Retinal Vasculopathy in Childhood Glaucoma**

In this retrospective study, 12 patients with childhood glaucoma underwent wide-field fluorescein angiography after surgical or medical treatment of glaucoma. Twelve eyes of 6 patients had primary congenital glaucoma, 5 eyes of 3 patients glaucoma associated with congenital cataract surgery, 4 eyes of 2 patients glaucoma associated with a systemic condition, and 1 eye of 1 patient had
phacomatosis pigmentovascularis Type II. RetCam fundus photography and digital fluorescein angiography were performed under general anesthesia. In this series, peripheral retinal nonperfusion affected 20 eyes (91%). Other features included circumferential branching of the retinal vessels parallel to the ora serrata in 77%, venous shunts in 50%, and abnormal capillary branching patterns such as capillary dilatation (41%) and tortuous capillary tangles (18%). Leakage at the junction of vascular and avascular retina was uncommon (13.6%), and none of the eyes demonstrated retinal neovascularization or fibrovascular proliferation. A significant limitation of this study is one of selection bias, as FA was only performed in patients that were suspected to have incomplete vascularization based on clinical exam and photography. Also, all FAs were performed after treatment of glaucoma or cataract, and some findings may have been secondary to postoperative inflammation. Longer follow-up would be useful to assess for long-term retinal vascular changes and any delayed sequelae.

Sirolimus for Retinal Astrocytic Hamartoma Associated with Tuberous Sclerosis Complex


Tuberous sclerosis complex (TSC) is a genetic disease characterized by the presence of benign tumors (hamartomas) in multiple organs, including the eyes. The efficacy of the mammalian target of rapamycin (mTOR) inhibitors (sirolimus and everolimus) has been demonstrated in several TSC-related lesions, including subependymal giant cell astrocytomas, renal angiomyolipomas, and pulmonary lymphangioleiomyomatosis. Retinal astrocytic hamartomas (RAHs) are present in approximately 44% of patients with TSC. There is currently no medical treatment available for controlling the size of these tumors. The authors sought to determine whether sirolimus is effective for RAHs. Eligible patients met the following inclusion criteria: (1) male or female patients aged 10-60; (2) RAHs associated with a definitive diagnosis of TSC; (3) treatment with sirolimus for subependymal giant cell astrocytomas, renal angiomyolipomas, or pulmonary lymphangioleiomyomatosis; (4) ≥1 RAH located in the posterior pole of the retina detected by spectral-domain optical coherence tomography (SD OCT); and (5) follow-up examination of the eyes available ≥6 months with sirolimus therapy. Oral sirolimus was administered at an initial daily dose of 1-2 mg and was then titrated, targeting a trough serum concentration of 5-10 ng/ml. Seven consecutive patients (4 men and 3 women) with a mean age of 22 years (range, 13-33) were enrolled. The patients were followed every 3-6 months, and the last evaluation of eyes was scheduled after 6 months of treatment. Each eye underwent a complete ophthalmic examination at baseline and ≥6 months after treatment, including best-corrected visual acuity testing, slit-lamp examination, color fundus photography, and SD OCT analysis. There were 24 RAHs in the 14 eyes of the 7 patients, including 1 partially calcified and 23 uncalcified lesions. Twenty RAHs located in the posterior pole were measured. Sirolimus was associated with a mean reduction in RAH thickness of 13.9%. All lesions demonstrated
improvement, and there was no increase in size for any of the lesions observed in this study. Because the RAHs in this study did not affect the macula regions, volume reduction did not have an impact on visual acuity. Adverse effects reported in this study included oral ulcers (n = 4), hyperlipidemia (n = 2), and irregular menses (n = 1). There were no complications in the eyes. No patient discontinued the use of sirolimus because of adverse effects. Overall, the study found that treatment with sirolimus for an average period of 7.9 months resulted in a significant decrease in the size of RAHs. Thus, mTOR inhibitors may provide effective treatment for RAHs in TSC. This report should stimulate further studies regarding medical treatment of RAHs in TSC.


The authors present long-term follow-up data on the largest series of children treated with intravitreal bevacizumab (IVB) for pediatric retinal and choroidal conditions other than ROP. Data was accumulated from patients receiving an intravitreal injection over an 8-year period. One hundred and three eyes of 98 patients were treated (8 eyes with LP vision or worse were excluded). Average age was 8.7 years and a total of 352 injections occurred with average follow-up of 679 days. The most common clinical diagnoses were neovascular membrane, Coats disease, FEVR and cystoid macular edema. The top indications for IVB were intra- or subretinal fluid/exudation, or neovascularization or hemorrhage. Average vision improved from 20/224 at baseline to 20/120 at 6 months and 20/156 at final followup. Mean central macular thickness improved and no patients required enucleation or evisceration. There was no significant change in mean IOP but three eyes did develop ocular hypertension that was felt to be attributable to IVB. Eight eyes required cataract surgery but IVB was not felt to be the cause of this in any case. Mean systolic blood pressure did not change significantly over time, but mean diastolic blood pressure statistically significantly changed at 12 months compared to baseline. It is not clear if this is a valid finding, or directly related to IVB. In addition the ideal dosing and best anti-VEGF agent are not known so more research is needed to investigate the optimal treatment regimen and side effects.


It is known that female carriers of X-linked retinitis pigmentosa (XLRP) are sometimes symptomatic. This study aimed to expand knowledge of the frequency and severity of visual function loss in XLRP carriers. Two hundred
seventy-six XLRP carriers with cross-sectional data (n = 242) and longitudinal
data (n = 34; median follow-up, 16 years; follow-up range, 3-37 years)
participated. Half of the carriers were from RPGR- or RP2-genotyped families.
The main outcome measures were visual acuities, visual field areas, final dark
adaptation thresholds, and full-field electroretinography (ERG) responses to 0.5-
Hz and 30-Hz flashes. In genotyped families, 40% of carriers showed a baseline
abnormality on at least 1 of 3 psychophysical tests. There was a wide range of
function among carriers. For example, 3 of 121 (2%) genotyped carriers were
legally blind because of poor visual acuity, some as young as 35 years. Visual
fields were less affected than visual acuity. In all carriers, the average ERG
amplitude to 30-Hz flashes was approximately 50% of normal, and the average
exponential rate of amplitude loss over time was half that of XLRP males
(3.7%/year vs. 7.4%/year, respectively). Among obligate carriers with affected
fathers, sons, or both, 53 of 55 (96%) had abnormal baseline ERG results. Some
carriers who initially had completely normal fundi in both eyes went on to
experience moderately decreased vision, although not legal blindness. Among
carriers with RAGR mutations, those with mutations in ORF15, compared with
those in exons 1-14, had worse final dark adaptation thresholds and lower 0.5-Hz
and 30-Hz ERG amplitudes. Most carriers of XLRP had mildly or moderately
reduced visual function but rarely became legally blind. In most cases, obligate
carriers could be identified by ERG testing. In conclusion, carriers of RPGR
ORF15 mutations tended to have worse visual function than carriers of RPGR
exon 1 through 14 mutations. Most carriers of XLRP had mildly or moderately
reduced visual function but rarely became legally blind. In most cases, obligate
carriers could be identified by ERG testing. In conclusion, carriers of RPGR
ORF15 mutations tended to have worse visual function than carriers of RPGR
exon 1 through 14 mutations. Because XLRP carrier ERG amplitudes and decay
rates over time were on average half of those of affected men, these
observations were consistent with the Lyon hypothesis of random X-inactivation.
From a family planning perspective, it is important to counsel carriers that
affected males have a worse visual prognosis than female carriers, and that,
although rare, even female carriers can have significant impairment of retinal
function.

Clinical And Echographic Features Of Retinochoroidal And

Currently, management of retinochoroidal and optic nerve colobomas involves
early recognition and treatment of any associated complications. The rate of
retinal detachment in eyes with retinochoroidal colobomas is significantly higher
than the general population risk, and this is attributed to impaired differentiation
and stability of the retina, which predisposes to retinal breaks often at the
junction of the undifferentiated (intercalary membrane) and differentiated retina.
The study is a nonrandomized consecutive case series of 140 colobomatous
eyes in 98 patients (age range, 0–83 years). The authors found that increased
relative coloboma excavation was significantly associated with an increased risk
of retinal detachment. A relative coloboma excavation (ratio of coloboma depth to
axial length) greater than 0.15 was associated with an increased risk of retinal
detachment (52%), compared to those with a relative coloboma excavation less than 0.15 (23%, \( P = 0.014 \)). The presence of any structural abnormality and the presence of a retrobulbar cyst were associated with increased risk of retinal detachment and severe visual impairment (worse than 20/200). Increased coloboma depth, width, volume, and relative coloboma excavation were not associated with increased risk of severe visual impairment. This is the first study to use echography to evaluate this cohort of patients. Measuring relative coloboma excavation upon presentation, in combination with clinical information, may alter follow-up and assist in the diagnosis of retinal detachment. The authors provide a promising method of early detection of those at risk for retinal detachment, thus potentially improving visual outcome in these patients.


This study evaluated a cohort of children with sensorineural hearing loss (SNHL). ERG’s were performed to look for abnormal ERG findings and to identify risk factors for the diagnosis of Usher syndrome. This was a 3-year retrospective review. Eight-four subjects met inclusion criteria with a median age of 87 months. Sixteen patients had symptoms suggestive of a possible retinal dystrophy (most commonly nyctalopia). Twelve patients had retinal pigmentary changes. ERG showed rod-cone dysfunction consistent with RP (Usher syndrome) in 13 patients (15%). Highly significant risk factors included the presence of or referral for cochlear implants, signs/symptoms of a retinal dystrophy and profound hearing loss. ERG was also helpful in diagnosing rubella retinopathy (pigmentary changes with a normal ERG). ERG can show changes prior to the patient developing signs/symptoms and is recommended in patients with a high index of suspicion for a retinal disorder of this type.


The authors of this review article describe pathophysiology, assessment and treatment of macular diplopia, which is described as “fighting” between central and peripheral fusion. The symptoms are cause by macular pathology such as epiretinal membrane, scar, AMD and subretinal neovascular membrane. Interesting points in this paper includes how peripheral fusion is dominant under photopic conditions and central fusion is dominant under scotopic conditions. Steps are described on how to perform the almost pathognomonic light on/off test. In brief, while fixating on a 20/70 distant optotype, the patient experiences diplopia while viewing with the room lights on but with the room lights turned off, the patient is able to fuse and eliminate diplopia since there is no stimulation of peripheral sensory fusion. Prism glasses are typically not helpful. Other options
include total occlusion of one eye, graded blur of one eye with Bangerter filter, sectoral occlusion of one portion of one eye and monovision. The authors suggest that these options are frequently not acceptable and they advocate for educating patients to ignore the distorted second image by “concentrating on the clear image

In addition, they recommend diminishing peripheral illumination when using devices such as smart phones, e-readers and computers to promote central fusion.

Comment: This is a nice review of the topic with some useful pearls (mentioned above).


This review article summarizes completed and ongoing human trials for treatment of retinal diseases with stem cell therapy. Retinal diseases discussed include: age-related macular degeneration, Stargardt's macular dystrophy, retinitis pigmentosa, and ischemic retinopathies. There remains much work to be done before we can offer our patients stem cell therapy but current studies are promising. Challenges to bring stem cell therapy from the bench to the bedside include: optimization of stem cell delivery methods, cell survival and cell differentiation. Published trials have not reported severe complications after stem cell therapy such as tumorigenicity. This article is a good summary of the origin of stem cell therapy, it's challenges and current registered clinical trials.


Autosomal dominant Stargardt-like macular dystrophy is a rare juvenile macular dystrophy typically caused by mutations in *ELOVL4* and *PROM1* genes. Only a few pedigrees are described in the literature, and this report attempts to further characterize the early stages of maculopathy using advanced imaging techniques. A retrospective medical record review was performed for 5 patients from 2 families with *ELOVL4* mutation and one patient with *PROM1* mutation. All patients had reduced central visual acuity with varying degrees of foveal atrophy. In the *ELOVL4* group, BCVA ranged from 20/25 to 20/200. Early pathologic changes included thickening of the external limiting membrane and outer nuclear atrophy followed by RPE loss in later stages. Adaptive optics imaging revealed photoreceptor loss even in early stages with good visual acuity. The *PROM1* patient also had similar central vision loss with significant outer nuclear atrophy. In contrast to *ELOVL4* mutation, there was more diffuse and patchy RPE loss throughout the macula.
The natural history of \textit{ELVOL4}- and \textit{PROM1}-associated maculopathy seems to be similar to Stargardt disease. Understanding the level of photoreceptor pathology early in the disease course while acuity is still good will become increasingly important as gene therapy becomes more widespread. Imaging modalities such as adaptive optics have been critical in revealing these changes. Early intervention will be important it has been shown that significant photoreceptor loss occurs before the development of visual symptoms.

\textbf{Cobalamin C Deficiency Shows A Rapidly Progressing Maculopathy With Severe Photoreceptor And Ganglion Cell Loss}


Cobalamin C (cblC) disease is the most common inborn error of vitamin B12 metabolism (1:100,000 live births), and patients with this autosomal recessive disorder show homocysteinemia, homocystinuria, and methylmalonic aciduria and acidemia. Ocular changes range from limited maculopathies to a progressive retina-wide degeneration and severe central vision loss and prior to this study were described in case reports, a few case series, and a single histopathological report. This study aimed to describe in detail the retinal structure and function in a group of 11 patients with cblC disease. The patients underwent complete ophthalmic examinations, fundus photography, near-infrared reflectance imaging, and spectral-domain optical coherence tomography. Electroretinograms were performed in selected patients. Late-onset patients (onset after 1 year of age) had normal exams. All early-onset (onset before one year of age) patients had a maculopathy, with older patients (>7 years of age) developing retina-wide degeneration. Three patients had pseudocolobomas. Maculopathy in early-onset patients was unusually fast-progressing (over first 2 years of life), with severe central outer nuclear layer and ganglion cell layer loss, and an abnormally thickened inner retina likely due to remodeling response. This study increases our understanding of the visual dysfunction and retinal structural abnormalities resulting from cblC disease and \textit{MMACHC} mutations.

\textbf{Development of Retinal Layers in Prenatal Human Retina}


This qualitative and quantitative descriptive study looked at the developmental sequence of retinal layers so that an understanding of pathological events that may affect retinal development could occur. Aborted fetuses were used for the collection of subjects between 622 weeks. Eyes from fetal week 2440 were obtained with support of the NICU and Lions eye Bank. Abnormally appearing eyes were eliminated from this evaluation. Axial length and eye diameter doubled between week 7 and 11. It doubled again by week 14 and week 27. At fetal week
11, the fovea can be reliably identified since it is the only retinal area with 5 layers. The nasal retina between the fovea and optic nerve is never more than 4 mm long and stabilizes at 3 mm shortly before birth. It became apparent from this study that different stages of development occur in the central, mid peripheral and far peripheral retina. The IPL develops first at week 8, the OPL is much slower upto week 20. Outer segments on rods and cones do not occur until close to birth. IPL reaches far periphery by 20 weeks, OPL reaches far periphery by 30 week.

19. RETINOBLASTOMA / INTRAOCULAR TUMORS

RETINOBLASTOMA

Association of Cone-Rod Homeobox Transcription Factor Messenger RNA With Pediatric Metastatic Retinoblastoma

Disseminated retinoblastoma (RB) is rare but usually fatal. RB may disseminate to the central nervous system via direct extension through the optic nerve or hematogenously. The main site of metastasis is the bone marrow, followed by bones and liver. The authors query whether identification of small amounts of tumor cells in extraocular sites might be a tool for designing appropriate and timely treatments. The authors propose a surrogate for the detection of small amounts of tumor cells, that is, cone-rod homeobox (CRX) transcription factor as a lineage-specific molecular marker for metastatic retinoblastoma. They measured CRX from bone marrow, peripheral blood, and cerebrospinal fluid at diagnosis, after induction chemotherapy, and during follow-up. The authors conclude that CRX mRNA is a novel marker for retinoblastoma at extraocular sites and even with bone marrow remission, detection of CRX mRNA suggests persistent disease, perhaps in a sanctuary site such as the cerebrospinal fluid.

Retinoblastoma Information: Can Graphics Be The Solution?
Chiu HH, Dimaras H, Downie R, Gallie B, CAN J OPHTHALMOL JUNE 2015. 50 (3)

A cross-sectional observational study was conducted. Parents of children with the diagnosis of retinoblastoma were recruited from January through August 2009 at an urban quaternary care pediatric hospital in Canada. A 19-item questionnaire with a predetermined template of correct answers validated by retinoblastoma experts was constructed to evaluate parents' comprehension of the treatment of bilateral retinoblastoma
Participants who were parents of children with unilateral versus bilateral retinoblastoma were roughly equal (n 1/4 23 [51%] and n 1/4 22 [49%], respectively), parents who spoke English as a first language scored approximately 20% higher than parents who spoke another language. This study evaluated parents’ comprehension of treatment choices for 2 eyes instead of 1 eye and also distinguished between unilateral and bilateral disease.ower education level was not associated with a lower comprehension score of bilateral retinoblastoma treatment. This finding has significant implications on informed consent for investigators. It supports the use of a visual tool for communicating medical information as complex as treatment choices for 2 eyes in bilateral retinoblastoma.


CDC25, a family of protein phosphatases, have a crucial role in the growth and inhibition of the cell cycle. They are also the key components of the checkpoint pathways that become activated in the event of DNA damage. In humans, three isoforms, CDC25A, CDC25B, and CDC25C, which act at different checkpoints of the cell cycle, have been identified. CDC25A regulates entry into the S phase, S phase progression and mitosis and CDC25B and CDC25C are mainly required for entry into mitosis (G2/M checkpoint). This is a study conducted from All India Institute of Medical Sciences in New Delhi. The authors studied 109 eyes that underwent primary enucleation. Of these, 84 were unilateral and 25 were bilateral retinoblastomas. The authors found that both CDC25A and CDC25B were expressed in the retinoblastoma samples. CDC25B was more frequently expressed in poorly differentiated retinoblastoma samples as compared with CDC25A. Both isoforms of CDC25 phosphatases significantly correlated with massive choroidal invasion and optic nerve invasion. CDC25 phosphatases are direct transcriptional targets of the E2F-RB1 complex and their expression may contribute to the development of retinoblastoma.

Local chemotherapy has recently emerged as a way to salvage globes with advanced intraocular RB that would have previously been enucleated. However, since local chemotherapy has minimal systemic effect, it does not protect against systemic disease in high-risk eyes. The authors argue that clinical RB staging must be able to predict the likelihood of high risk features before local chemotherapy instead of systemic chemotherapy is implemented for eyes with advanced intraocular RB. This retrospective study evaluated 50 primarily enucleated eyes from 49 RB patients. Main outcome measures included demographics, TNM stage, International Classification of Retinoblastoma (ICRB) group, Reese-Ellsworth stage, choroid, optic nerve, and anterior chamber invasion. They found that higher tumor clinical TNM stage and more advanced ICRB group at presentation are associated with higher frequency of high risk pathologic features ad may predict which patients should receive adjuvant chemotherapy. This was not the case for the Reese-Ellsworth staging system, which was developed to predict the probability of maintaining sight and local disease control but not to predict the likelihood of metastases or patient survival.


There is some controversy regarding the exact definition of a high-risk histopathologic feature and whether or not anterior chamber seeds and iris infiltration are considered high-risk features of retinoblastoma. Through a case-control study the authors sought to identify the clinical features predictive of high-risk retinoblastoma on histopathology. High-risk features on histopathology were defined as the presence of anterior chamber seeds, iris infiltration, ciliary body infiltration, massive (≥3 mm) choroidal invasion, postlaminar optic nerve invasion, invasion of optic nerve transection, combined nonmassive choroidal and prelaminar/laminar optic nerve invasion, or scleral/extrascleral infiltration. The study included 403 patients who underwent primary enucleation for the treatment of retinoblastoma. On histopathology 145 (36%) participants had high-risk features on histopathology (cases) and 258 (64%) participants had no high-risk features (controls). The histopathologic high-risk features in the 145 patients included anterior chamber seeds (17%), iris infiltration (8%), ciliary body infiltration (12%), massive (≥3 mm) choroidal invasion (48%), postlaminar optic nerve invasion (49%), invasion of optic nerve transection (2%), combined choroidal and optic nerve invasion (12%), scleral infiltration (14%), and extrascleral involvement (6%). The mean number of high-risk features was two. The significant clinical features in cases versus controls included prolonged duration of symptoms of >6 months (21% vs. 7%; P < 0.001), poor visual acuity at presentation (74% vs. 64%; P . 0.05), buphthalmos (16% vs. 7%; P . 0.005), secondary glaucoma (47% vs. 15%; P < 0.001), iris neovascularization (46% vs.
22%; P < 0.001), ectropion uveae (39% vs. 14%; P < 0.001), and orbital cellulitis (3% vs. <1%; P < 0.05). Importantly, the clinical features at presentation predictive of high-risk features on histopathology included prolonged duration of symptoms of >6 months and secondary glaucoma. Consequently, globe-preserving methods of treatment should be used with caution in patients with these features.

The Classification of Vitreous Seeds in Retinoblastoma and Response to Intravitreal Melphalan


Vitreous seeds have been recognized as the defining feature for treatment failure by the Reese and Ellsworth classification group (Vb) and the International Classification of Retinoblastoma group (D). With the increased adoption of intravitreal melphalan, salvage rates for eyes with vitreous seeds are surpassing all historical data. As a result, the authors chose to evaluate the clinical characteristics of the three classifications of vitreous seeds in retinoblastoma, dust (class 1), spheres (class 2), and clouds (class 3), and their responses to intravitreal melphalan. A total of 87 patient eyes received 475 intravitreal injections of melphalan (median dose, 30 mg) given weekly, a median of 5 times (range, 1-12 times). At presentation, the vitreous seeds were classified into 3 groups: dust, spheres, and clouds. Indirect ophthalmoscopy, fundus photography, ultrasonography, and ultrasonic biomicroscopy were used to evaluate clinical response to weekly intravitreal melphalan injections and time to regression of vitreous seeds. Kaplan-Meier estimates of time to regression and ocular survival, patient survival, and event-free survival (EFS) were calculated and then compared using the Mantel-Cox test of curve. The difference in time to regression was significantly different for the 3 seed classes (P < 0.0001): the median time to regression was 0.6, 1.7, and 7.7 months for dust, spheres, and clouds, respectively. Eyes with dust received significantly fewer injections and a lower median and cumulative dose of melphalan, whereas eyes with clouds received significantly more injections and a higher median and cumulative dose of melphalan. Overall, the 2-year Kaplan-Meier estimates for ocular survival, patient survival, and EFS (related to target seeds) were 90.4% (95% confidence interval [CI], 79.7-95.6), 100%, and 98.5% (95% CI, 90-99.7), respectively. In conclusion, distinguishing vitreous seeds into 3 classes based on morphologic features can provide valuable clinical information. This classification seems to be predictive of the time it will take seeds to regress and the number of injections and amount of melphalan that are used.

Enucleation vs Ophthalmic Artery Chemosurgery for Advanced Intraocular Retinoblastoma A Retrospective Analysis

Orbital recurrence of retinoblastoma after intraarterial chemotherapy is studied in this retrospective review of patients from a single ophthalmic oncologic academic practice. One hundred forty eyes in 139 patients with Reese Ellsworth Group 5 or International Classification of retinoblastoma group D or E were included of whom 63 eyes were enucleated and 77 eyes received intraarterial chemotherapy, designated ophthalmic artery chemosurgery (OAC) by the authors. Patients were accumulated from February 2006 to March 2014 and were analyzed to determine incidence of and time to orbital recurrence, metastasis and death in the period August 2014-March 2015.

The incidence of orbital recurrence in the enucleation group was 7.9% (n=5) and in the OAC group was 1.3% (n=1) during median follow-up times of 42.6 months and 38.7 months, respectively. The incidence of metastatic disease in the enucleation group was 7.9% (n=5) and in the OAC group 4.2% (n=3). The mortality rate during the time period studied was 3.2% (n=2) in the enucleation group and no deaths occurred in the OAC group. Analysis of a number of features of the 2 groups revealed more eyes with iris neovascularization in the enucleation group (25.4%) than in the OAC group (5.2%) and more eyes with group E retinoblastoma in the enucleation group (87.3%) than in the OAC group (29.9%). The authors state none of these differences between the 2 groups could explain the different outcomes between the 2 groups and that ophthalmic artery chemosurgery is superior to enucleation in risk for orbital recurrence, metastasis and death.


This study attempted to characterize treatment patterns, survival, and second tumor occurrence in patients with retinoblastoma. The study utilized data from Surveillance Epidemiology and End Results dataset (SEER). Data was reviewed from 1975 to 2010. The SEER data only captures 28% of all newly diagnosed cancer cases in the US. Total of 1452 cases of retinoblastoma were identified. Mean age was 1 year and 74% white. 28% had bilateral disease. At initial presentation, 76% were localized disease. Of the patients with localized disease, 55% underwent surgical intervention alone. 26% had surgery plus chemotherapy. Over time, there was a dramatic decrease in the use of radiation from 15% to 4.9%. There was an increase in use of chemotherapy from 16% to 50%. The 5 year survival increased from 1980 to 2010 from 93.7% to 97%. Risk of developing second malignant neoplasms was highest in patients who underwent radiotherapy with sarcoma being the most common.

This study looked at the incidence of trilateral retinoblastoma. This was a systemic review and metaanalysis where they searched scientific literature between 1966 to 2015. 23 retinoblastoma cohorts were included from 26 studies. The chance of developing trilateral retinoblastoma amongst bilateral cases was 5.3%. A Pineal RB incidence was 4.2% and non pineal was 0.8%. These results show that trilateral retinoblastoma has much lower incidence then was previously suggested in literature. More than 50% of trilateral retinoblastomas were present at time of diagnosis of ocular lesions. Therefore, baseline screening may be useful


Diffuse anterior retinoblastoma is an extremely rare variant of retinoblastoma with involvement of the anterior segment and no apparent retinal involvement. Previously published studies have been managed with enucleation. The authors present 3 cases (mean age at presentation 5.7 years) which they treated with plaque radiotherapy and chemotherapy thereby preserving the globe and vision.


The authors represent many of the specialized treatment centers in the United States who care for children with retinoblastoma. This article highlights the rapid advances and changes in treatment paradigms over the last 10 years. These advances include intravitreal chemotherapy, such as with melphalan, and intraophthalmic artery chemotherapy, 2 modalities which have virtually replaced external beam radiotherapy and have reduced the enucleation rate by 90%, with little adverse effect on survival.

Importance: The pace at which new medical knowledge is added to our literature is accelerating. The authors provide a valuable update on the latest treatment paradigms for retinoblastoma treatment.

In this brief report, the authors describe anterior segment seeding in eyes with retinoblastoma which failed to respond to intraophthalmic artery chemotherapy (IAC). This was a retrospective case series of 12 eyes, which were enucleated because of persistent viable vitreous seeds. The histopathologic findings included: 4 eyes (33%) with no viable retinal tumor; the remainder had poorly differentiated tumor (6 eyes [50%]) or moderately differentiated tumor (2 eyes [17%]). Anterior segment involvement occurred in 8/12 eyes including the ciliary body and/or ciliary muscle, iris, and cornea.

Importance: Although salvaging an eye with extensive retinoblastoma despite systemic chemoreduction is a laudable goal, IAC may not be successful in retaining the eye, especially if vitreous seeding is present. This article also demonstrated tumor involvement of the anterior segment on histopathology in 67% of the examined eyes, which may not always be apparent on clinical exam.

NON-RETINOBLASTOMA


This longitudinal cohort study evaluated changes in the Circumpapillary RNFL thickness when measured with OCT in children with Glioma. Either a handheld OCT or table top OCT was used for this study. The RNFL was compared between the eye that lost VA to the more stable eyes. 55 eyes were included in this study. 10 eyes from 7 patients noted vision changes. 45 of 39 patients showed stability. The percent decline in RNFL thickness was highest in the superior and inferior quadrants. Therefore, OCT measurements of RNFL thickness could be a good predictor of visual loss from a Glioma and could help make treatment decisions.


A 17-year-old Asian male reported seeing a black spot in the left eye with no other associated symptoms. He was previously treated for cerebellar medulloblastoma with brain and spine metastases with subtotal tumour resection. An elevated yellow-red circular mass that was a disc diameter in size with indistinct borders in the middle third of the superotemporal arcade associated with a boat-shaped subhyaloid and vitreous hemorrhage along the inferotemporal arcade was seen in the left eye, showed early blocked
fluorescence with central mottling and late leakage. By month 23, repeat OCT of
the lesion showed increase in vertical and horizontal dimensions, with posterior
shadowing and thickening of the neurosensory retina more evident nasal to the
mass. Retinal vasoproliferative tumours (VPT) are rare and are seen between
the third and fifth decade of life, but they may present in childhood, results from a
reactive process with glial and vascular proliferation, and presents as a solitary,
unilateral, elevated, globular, yellow-pink vascular mass commonly in the inferior
peripheral retina.

**Juvenile Xanthogranuloma Involving the Eye and Ocular
Adnexa: Tumor Control, Visual Outcomes, and Globe Salvage in
30 Patients**  
WA Samara, CTL Khoo, EAT Say, JSaktanaste, et al
Ophthalmology October 2015; 122:2130-2138

This is a retrospective case series of the clinical features and treatment
outcomes of ocular juvenile xanthogranuloma (JXG). The medical records of 30
patients (31 eyes and 32 tumors) with JXG were reviewed. The mean patient
age at presentation was 51 months (median, 15 months; range, 1–443 months).
Eye redness (12/30, 40%) and hyphema (4/30, 13%) were the most common
presenting symptoms. Cutaneous JXG was concurrently present in 3 patients
(3/30, 10%), and spinal JXG was present in 1 patient (1/30, 3%). The ocular
tissue affected by JXG included the iris (21/31, 68%), conjunctiva (6/31, 19%),
eyelid (2/31, 6%), choroid (2/31, 6%), and orbit (1/31, 3%). Those with iris JXG
presented at a median age of 13 months compared with 30 months for those with
conjunctival JXG. In the iris JXG group, mean IOP was 19 mmHg (median, 18
mmHg; range, 11–30 mmHg) and hyphema was noted in 8 eyes (8/21, 38%).
The iris tumor was nodular (16/21, 76%) or diffuse (5/21, 24%). Fine-needle
aspiration biopsy was used in 10 cases and confirmed JXG cytologically in all
cases. The iris lesion was treated with topical (18/21, 86%) and/or periocular
(4/21, 19%) corticosteroids. The eyelid, conjunctiva, and orbital JXG were
treated with excisional biopsy in 5 patients (5/9, 56%), topical corticosteroids in 2
patients (2/9, 22%), and observation in 2 patients (2/9, 22%). Of 28 patients with
a mean follow-up of 15 months (median, 6 months; range, 1–68 months), tumor
regression was achieved in all cases, without recurrence. Two patients were lost
to follow-up. Upon follow-up of the iris JXG group, visual acuity was stable or
improved (18/19 patients, 95%) and IOP was controlled long-term without
medication (14/21 patients, 74%). No eyes were managed with enucleation.
Ocular JXG preferentially affects the iris and is often isolated without cutaneous
involvement. Iris JXG responds to topical or periocular corticosteroids, often with
stabilization or improvement of vision and IOP.
Intraocular Medulloepitheliomas and Embryonal Tumors With Multilayered Rosettes of the Brain: Comparative Roles of LIN28A and C19MC

This retrospective study compared immunohistochemical and genetic overlaps and differences between intraocular medulloepitheliomas and embryonal tumors with rosettes of the brain. 19 of the 20 intraocular medulloepitheliomas were either diffusely or focally LIN28A positive. The more intensely positive, the more likely aggressive behavior. By evaluating for LIN28A, you may be able to predict more aggressive tumors.

20. ORBIT

Pediatric orbital cellulitis in the Haemophilus influenzae era.

Medical records for a largely vaccinated population spanning 11 years were retrospectively reviewed. 101 patients had orbital cellulitis of whom 71 were treated with IV antibiotics without surgical intervention. 65/71 had been treated with Hib vaccine. 68/71 had blood cultures performed. 3 patients had positive cultures (Streptococcus pyogenes n=1, and coagulase-negative Staphylococcus n=2). 30/101 required surgical drainage- these patients had larger abscesses, underwent a longer course of IV antibiotics and inpatient hospital duration. 24/30 had blood cultures with 1 positive result (S. pyogenes). 18 patients had positive cultures from their surgical drainage. Of these 4 showed H. flu growth (1-predominant bacterium and 3-mixed). These 4 patients were older and had larger abscesses and lower white blood counts. It cannot be confirmed that the positive H. flu cultures were due to serotype b because this was not evaluated with serotyping and biotyping. This article discusses the changes in orbital cellulitis since introduction of the Hib vaccine.

Subperiosteal Abscess of the Orbit- evolving pathogens and the therapeutic protocol
J Liao, G Harris Ophthalmology March 2015;122(3) pp.639-647

This is a comparative case series. 94 patients ≤18 years with sinusitis-related subperiosteal abscess (SPA) treated from 2002 to 2012 were compared to cohorts treated from earlier time frames (1977-1992, 1988-1999, and 1999-2008). Culture results, surgical outcomes, overall and age-related outcomes were looked at. The authors followed a consistent management protocol throughout all series as follows: all patients ≥9 years undergo prompt surgical
Patients <9 years receive medical therapy unless they have compromised vision, large or nonmedial SPAs, frontal sinus or intracranial involvement, or risk factors for anaerobic infection. In the current cohort, 53 patients (56%) recovered with medical therapy alone and 41 (44%) underwent surgical drainage, which was similar to previous cohorts. Culture results showed an increase in Strep anginosus, Staph aureus, and group A beta-strep. MRSA accounted for 4 out of 7 staph aureus isolates. In the earlier cohorts, patients ≥9 years old had a higher proportion of positive cultures with more varied pathogens than younger patients. In the current series both groups had similar culture yields and aerobic pathogens. Anaerobes were isolated only from patients ≥9 years old in both series. In cases positive for MRSA and other aggressive aerobes, initial findings prompted early drainage and outcomes were not compromised by adherence to the treatment protocol. The proportion of children <9 years requiring surgery for sinusitis-related SPA has remained a minority (15%–32.5%), without a clear upward trend over 25 years. Anaerobes are not a factor in the younger subgroup, but more aggressive aerobic pathogens, including MRSA, have emerged.

Bilateral Orbital Abscesses after Strabismus Surgery
Case report of a healthy 3 year old who developed bilateral orbital abscesses after uncomplicated strabismus surgery on the medial recti and inferior oblique muscles. The report reviews infectious orbital complications after strabismus surgery which has an incidence of 1 case per 1,100 surgeries. In the authors review of literature there was rare reports of orbital abscesses after strabismus surgery. They maintain that clinicians should have a high index of suspicion as these patients require prompt treatment with IV antibiotics and surgical evacuation of the abscesses. They also advise preoperative evaluations of upper respiratory infections which can complicate strabismus surgery.

Cases of cavernous sinus thrombosis in children were reviewed over a 13-year period. Nine patients were identified with a mean age of 11.4 years. All 9 patients had an infectious sinusitis involving the sphenoid or ethmoid sinus. 7/9 also had a maxillary sinusitis. 4 cases had orbital involvement, all of whom had permanent decreased visual acuity compared to 1/5 without orbital involvement. 5/9 had intracranial involvement that includes meningitis and epidural abscess. 4/5 developed an abscess of the planum sphenoidale. There were three cases of cerebral infarcts but no cases that resulted in mortality. 8 patients had ophthalmoplegia and one had a frozen globe. 5 patients had permanent motility
defects. This is the largest review of cavernous sinus thrombosis in the post-antibiotic era.

**Management of Orbital and Periocular Vascular Anomalies**


This article was a major review of the authors’ experience along with a literature review of treatment modalities available for treating orbital and periocular vascular anomalies. Treatment can be particularly challenging due to the risk of retrobulbar hemorrhage and the propensity of these lesions to recur, as well as their proximity or invasion of important orbital structures. The article reviews the different types of malformations including arteriovenous malformations, arteriovenous fistulas, venous malformations and lymphatic malformations. Orbital vascular tumors including hemangiomas, hemangiopericytomas and hemangioblastomas are also reviewed. A combination of endovascular, percutaneous and open surgical techniques is discussed as management options.

**Hydroxyapatite Orbital Implant in Children Following Enucleation: Analysis of 531 Sockets**


Following enucleation in children several available orbital implants are available. This study retrospectively reviewed 531 enucleated sockets which received hydroxyapatite (HA) orbital implants. The technique for HA implantation involved suturing the extraocular muscles to the orbital implant. Implant motility was found to be excellent or fair in 97% of cases. 99% of the patients reported excellent overall satisfaction with the cosmetic outcome. Implant exposure rate was 3%, much lower than other studies. This was a large series showing HA orbital implants to have low complication rates and good motility with high patient cosmetic satisfaction on long term follow up.

**Dermis-Fat Graft in Children as Primary and Secondary Orbital Implant**


The purpose of this study was to provide indications for the use of autogenous dermis-fat graft. The study evaluated the outcomes of the procedure as a primary orbital implant at time of evisceration and in children with congenital anophthalmia and as a secondary implant following exposure of other implants and in contracted sockets.
All patients had satisfactory orbital volume although one required surgical debulking for excessive growth of the implant. Motility of the prosthesis was satisfactory in all patients except in patients with congenital anophthalmia. The authors concluded the dermis-fat graft was useful as both a primary and secondary implant in children.

**Vertical Diplopia and Ptosis from Removal of the Orbital Roof in Pterional Craniotomy** S Desai, M Lawton, M McDermott, J Horton
*Ophthalmology* March 2015;122(3) pp.631-638

The authors describe a newly recognized syndrome and present 8 cases with neuro-ophthalmic symptoms after orbito-zygomatic-pterional craniotomy for meningioma removal or aneurysm clipping. Cardinal features were ptosis, limited elevation, and hypotropia. Three patients also had limitation of downgaze and 2 patients had limitation of abduction. Imaging showed loss of the fat layers that normally envelop the superior rectus and levator. The muscles appeared tethered to the surgical defect in the orbital roof. Physical injury during surgery also may cause paresis of the superior rectus. Patients with limited downgaze may have scarring of the superior rectus. Limitation of abduction may have been due to adhesion of the lateral rectus. In all 8 cases, ptosis and dection deficits improved spontaneously in the months after surgery. Prism glasses were prescribed to alleviate diplopia in the short term. Surgical correction of ptosis (levator advancement) or diplopia (inferior rectus recession on an adjustable suture) was necessary in half the patients. Follow-up at 6.5 years showed slight limitation of elevation and depression in all patients, but orthotropic alignment in primary gaze.

**21. OCULOPLASTICS**

**Proximal drainage plus massage of lacrimal sac improves the symptoms of congenital dacryocystocele**s Lin Chen, Jing Fang

This retrospective study was to compare traditional management of congenital dacryocystoceles (lacrimal sac massage) with the modified massage treatment of lacrimal sac massage and proximal drainage in 77 patients. Of those that failed massage or modified massage, underwent probing.

**Results** There was a decompression success rate of 100% in the modified group and 31% in the traditional group. After two weeks, only 30% had resolution after conservative treatment the traditional group, compared to 80% in the modified group. In both groups, the addition of probing, 100% of the modified...
group were successful compared the 78% of the traditional group.

Conclusions
Proximal drainage plus massage has the advantage of high efficiency and safety for the treatment of congenital dacryocystoceles.


Bacteremia following surgical procedures is a well-documented entity. The authors aimed to study the incidence of bacteremia post nasolacrimal duct probing. A prospective interventional study was performed on thirty-one eyes of 25 patients who underwent probing. One patient presented with an acute dacryocystitis at the time of the probe. Blood was drawn before and after probing and blood cultures were performed using the BacT/ALERT microbial detection system. All pre and post cultures were negative except the one with acute dacryocystitis. The authors conclude that nasolacrimal duct probing does not induce bacteremia in routine cases and preoperative antibiotic prophylaxis is not needed for systemically healthy patients.


Congenital nasolacrimal duct obstruction (CNLDO) has been described as simple or complex based on intraoperative findings. Complex variations include ducts that fail to open through the nasal mucosa (buried probe). This report reviews twenty eyes endoscopically diagnosed as buried probe variant of complex CNLDO. Epiphora and discharge were the most common presenting symptoms (77%). 41% had associated lacrimal and nasal anomalies including punctal agenesis, incomplete punctal canalization, atonic lacrimal sac and impacted inferior turbinate. All but two patients had the buried probe exteriorized by tilting the probe under endoscopic guidance to create an opening. The other two patients required a vertical mucosal incision to be made. At 3 month follow up anatomical success was noted in 81.8% and functional success in 72.7%. The authors conclude that buried probe is an uncommon variant noted more commonly in older children. Endoscopic guidance is crucial for diagnosis. Satisfactory outcomes can be achieved.
**Initial management of congenital canalicular atresia.** Soliman M and Lueder GT. *J AAPOS* 2015;19:220-222

The authors report their experience treating canalicular atresia. This was a retrospective review of medical records over a twenty-year period. 15 patients (19 eyes) were included. 10 patients had epiphora and crusting and 5 had epiphora only. Mean age at surgery was 16.5 months. 11/19 had upper canalicular atresia. Probing through the patent canaliculus was performed successfully in all patients. 18/19 had a membranous obstruction and 1 had a bony obstruction. Good outcomes occurred in 9/11 upper and 4/8 lower atretic cases.


Congenital lacrimal fistula result abnormal embryonal developments at the optic end of the naso-optic fissure. This study focuses solely on the histopathology of the excised fistulae along with their immunophenotyping. Twelve fistulae were studies. In 83%, the deeper parts were lined with hypertrophied stratified squamous epithelium, similar to canalicular tissue. 17% originated from the lacrimal sac and were lined with columnar epithelium. Immunophenotyping revealed a mix of T and B lymphocyte infiltration revealing chronic inflammation, more so in older children.

**Canalicular laceration repair using a viscoelastic injection to locate and dilate the proximal torn edge.** Orge FH and Dar SA. *J AAPOS* June 2015;19:217-219

Viscoelastic deployed superficially near the injured canaliculus and then injecting it into the proximal torn end when it is visible helps tamponade any slow bleeding and retract surrounding tissue. It also dilates the torn canaliculus allowing easier intubation and avoiding risk of iatrogenic injury of the intact canaliculus during repair. This study was a retrospective review over a seven-year period. 17 cases were included with a mean age of 6.27 years. 11 cases involved the lower lid, 4 cases involved the upper lid and 2 cases involved both. All patients had good anatomic repair with no iatrogenic injury. The authors point out the high viscosity makes the viscoelastic linger at the cusp of the cut ends of the lumen and makes relocating the proximal edge easier. This is a useful oculoplastics technique that lid surgeons should know to help facilitate canalicular laceration repair.
Improvement in Levator Function after Anterior Levator Resection for the Treatment of Congenital Ptosis


The traditional approach for surgical correction in congenital ptosis includes frontalis sling for severe ptosis with poor levator function and levator resection for ptosis with fair to good levator function. Preferred approach when levator function is fair to poor remains a matter of debate. The authors looked at 42 eyelids of patients with severe or moderate ptosis who underwent levator resection and evaluated the lid height as well as any change in levator function. The overall success rate was 78.6% with a mean improvement in levator function after surgery of 2.9mm. On the basis of the data, the authors conclude that the improvement in levator function after resection surgery may influence surgical outcome.

Modified Hotz Procedure Combined with Modified Z-Epicanthoplasty Versus Modified Hotz Procedure Alone for Epiblepharon Repair

Ni J, et al. *Ophthal Plast Reconstr Surg*

This was a study of 130 eyes of 71 Chinese patients who underwent congenital lower eyelid epiblepharon correction surgery. 59 eyes were operated on with the modified Hotz procedure while 71 eyes had the modified Hotz procedure combined with modified Z-epicanthoplasty. In both groups all of the inverted cilia were corrected successfully. In group 1 the outcome was excellent (no cilium-ocular touching) in 78%, while in group 2, 98.6% had excellent outcomes. 22% of group 1 had fair or poor outcome while only one eye (1.6%) in group 2 had a fair result. The authors state that the modified Hotz procedure combined with the modified Z-epicanthoplasty is a more effective way to correct lower eyelid epiblepharon. Their results also showed that the combined procedure did not produce obvious lower eyelid or medial canthus scars.

The incidence, embryology, and oculofacial abnormalities associated with eyelid colobomas


This single author study reports 55 patients with eyelid coloboma is seen over a 20 year period. 93% involve the upper lid and were unilateral in 76%. Only 29% of the lid colobomas were isolated finding where the other 62% being associated with cranial facial or ocular anomalies. Size of the coloboma strongly correlate with other association with other cranial facial defects.
Current trends in the management of thyroid eye disease.

Corticosteroids continue to be the primary medical therapy for thyroid eye disease (TED) although steroid sparing agents such as rituximab are under investigation. Recent research suggest that IV corticosteroids may be more effective than oral corticosteroids in the treatment of active TED. However, a survey of ASORPS members found most continue to prefer the use of oral corticosteroids. Oral corticosteroids are likely more popular due the complex logistics associated with IV corticosteroid administration. There is renewed interest in the role of radiation therapy to reduce active TED and reduce the risk of compressive optic neuropathy. Dietary supplementation with selenium and vitamin D may aid in the treatment of TED. Multiple orbital decompression techniques have been described. Orbital decompression procedures include: endonasal endoscopic orbital floor decompression, stereotactic navigation via a electromagnetic image-guided endoscopic system and balanced orbital decompression. Balanced orbital decompression is a technique where the medial and lateral orbital walls are decompressed simultaneously. In theory, balanced orbital decompressions reduce horizontal globe shifts and may reduce postoperative diplopia. Violation of the periorbita during decompression may result in increased postoperative diplopia. Immediate orbital decompression surgery has no advantage over IV corticosteroids for short term visual acuity outcomes. Orbital decompression is typically performed after the resolution of active TED. This article is a good review regarding the management of TED.

22. INFECTIONS


This was a randomized, placebo-controlled trial of oral valganciclovir therapy in neonates with symptomatic congenital CMV disease, comparing 6 months of therapy with 6 weeks of therapy. Previous studies have shown the efficacy of six weeks of intravenous ganciclovir therapy in symptomatic congenital CMV disease. The primary end point was the change in hearing in the better ear ("best-ear" hearing) from baseline to 6 months. Secondary end points included the change in hearing from baseline to follow-up at 12 and 24 months and neurodevelopmental outcomes.

A total of 96 neonates underwent randomization, of whom 86 had follow-up data at 6 months that could be evaluated. Best-ear hearing at 6 months was similar in
the 6-month group and the 6-week. Total-ear hearing (hearing in one or both ears that could be evaluated) was more likely to be improved or to remain normal at 12 months in the 6-month group than in the 6-week group (73% vs. 57%, P=0.01). The benefit in total-ear hearing was maintained at 24 months (77% vs. 64%, P=0.04). At 24 months, the 6-month group, as compared with the 6-week group, had better neurodevelopmental scores on a language-composite component (P=0.004) and on a receptive-communication scale (P=0.003).

In conclusion, treating symptomatic congenital CMV disease with valganciclovir for 6 months, as compared with 6 weeks, modestly improved hearing and developmental outcomes in the longer term. There are two take home points for the ophthalmologist consulting on a neonate with symptomatic congenital CMV: 1) based on the results of this trial, anticipate that the baby will be treated with oral valganciclovir for six months; 2) the rate of chorioretinitis is low (in this study, chorioretinitis affected just 3 of 96 = 3% of babies.)

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**Prevalence of gonococcal conjunctivitis in adults and neonates**

L McAnena, S J Knowles, A Curry and L Cassidy *Eye* 29: 875-880 April 2015

In this epidemiologic study conducted in Dublin, the authors investigate the prevalence of gonococcal conjunctivitis in adults and children over a two year period (2011 – 2013). In 2756 live births, there were _no cases of neonatal gonococcal conjunctivitis_. In the adult population, the prevalence of gonococcal conjunctivitis was 0.19 cases per 1000 eye emergency attendees. Of those cases with gonococcal conjunctivitis, all were __ and ceftriaxone sensitive. They state that PCR is the gold standard for diagnosing gonococcal infection. The authors recommend that pending PCR results with patients high suspicion for gonococcal conjunctivitis be treated with 1 gram of ceftriaxone with frequent saline lavage and topical ofloxacin as well as empiric treatment for chlamydia treated with azithromycin 1 gram orally as a single dose or doxycycline 100mg orally twice daily for 7 days.

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PURPOSE OF REVIEW: To summarize recent advances on ocular Demodex infestation. RECENT FINDINGS: Demodex infestation is a potential cause of ocular surface inflammation. The pathogenesis of Demodex in eliciting ocular surface inflammation has been further clarified. Cliradex is currently the treatment of choice, it comprises the most active ingredient of tea tree oil, that is terpinen-4-ol, which helps eradicate Demodex mites and reduce ocular surface inflammation. SUMMARY: Demodex causes chronic anterior and posterior blepharitis, meibomian gland dysfunction, recurrent chalazia, and refractory
keratoconjunctivitis. The lash sampling and microscopic counting method and in-vivo confocal microscopy are key diagnostic methods. Cliradex shows promising potential to reduce Demodex counts with additional antibacterial, antifungal, and anti-inflammatory actions. Ocular demodicosis is a common eye disease but is often overlooked.

Phthiriasis Palpebrarum in a Child Micali G, Lacarrubba F

A 6-year-old boy presented with persistent erythema and pruritus of the eyelids, which had been previously diagnosed as atopic dermatitis and unsuccessfully treated with topical glucocorticoids and systemic antihistamines for 2 weeks. Dermatoscopy showed several crab lice (Phthirus pubis) on the eyelashes along with their ovoid nits. A diagnosis of phthiriasis palpebrarum was made; the patient was treated with topical 5% yellow mercuric oxide ointment four times daily for 2 weeks, and the symptoms resolved completely. This case report reminds pediatric ophthalmologists to consider lice in the differential diagnosis of atopic eyelid dermatitis and to look at the eyelashes closely with slit lamp examination.

23. PEDIATRICS/ INFANTILE DISEASE/ SYNDROMES

Prenatal Factors in Singletons with Cerebral Palsy Born at or Near Term Nelson K, Blair E N Engl J Med. September 2015; 373:946-953

This is a review article discussing the causes of cerebral palsy among term babies. Cerebral palsy is a disorder of movement affecting activities of daily living that is due to nonprogressive cerebral defects. Although cerebral palsy is common among ultra premies, ultra premies account for a small proportion of surviving children, and thus most children with cerebral palsy are actually those who are born near term. There is a widespread notion that birth asphyxia is the main cause of cerebral palsy in term babies. However, the authors explain that birth asphyxia plays a relatively minor role, accounting for less than 10% of cases. The main associations with cerebral palsy are congenital malformations (primarily of the brain followed by the heart) and intrauterine growth restriction, and thus cerebral palsy results from abnormal prenatal development rather than from events taking place at the time of birth. According to the authors, it is thus not surprising that increased electronic fetal monitoring and surgical deliveries have not decreased the rate of cerebral palsy. As pediatric ophthalmologists, we frequently examine patients with cerebral palsy and should be aware that most were term babies without birth asphyxia.
Human Milk Feeding as a Protective Factor for Retinopathy of Prematurity: A Meta-analysis  Zhou J, Shukla V, John D, Chen C  *Pediatrics* Dec 2015; 136: (6) e1576-e1586

The aim of this meta-analysis was to pool currently available data on incidence of ROP in infants fed human milk versus formula published through February 2015.  

**RESULTS:** Five studies with 2208 preterm infants were included. Searches including various proportions of human milk versus formula, any-stage ROP, and severe ROP were defined to pool data for analyses. For any-stage ROP, the ORs (95% confidence intervals [CIs]) were as follows: exclusive human milk versus any formula, 0.29 (0.12 to 0.72); mainly human milk versus mainly formula, 0.51 (0.26 to 1.03); any human milk versus exclusive formula, 0.54 (0.15 to 1.96); and exclusive human milk versus exclusive formula, 0.25 (0.13 to 0.49).  

For severe ROP, they were 0.11 (0.04 to 0.30), 0.16 (0.06 to 0.43), 0.42 (0.08 to 2.18), and 0.10 (0.04 to 0.29), respectively.  

**CONCLUSIONS:** In very preterm newborns, human milk feeding potentially plays a protective role in preventing any-stage ROP and severe ROP.

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Choroidal involvement was considered to be a rare finding in neurofibromatosis type 1 (NF1), mainly related to the fact that they are asymptomatic and undetectable via conventional ophthalmoscopy or fluorescein angiography. NF1-related choroidal abnormalities were originally described as hypofluorescent patches in the early choroidal angiographic phases when performing indocyanin-green angiography. More recently, confocal near-infrared (NIR) reflectance imaging, a non-invasive tool, has shown superior visability of these choroidal features, and choroidal abnormalities now appear to be frequent in adult NF1 patients. Thus, this study aimed to evaluate the feasibility of NIR choroidal imaging acquisition in pediatric patients with NF1, evaluate it as a diagnostic criterion, and to compare it with the established criteria of the original NIH Consensus Development Conference. This was an institutional, observational, masked, cross-sectional study with prospective enrollment of 140 pediatric patients (0-16 years old) affected by NF1, 59 suspected, and 42 healthy subjects. Two masked operators assessed NF1-related choroidal abnormalities via NIR confocal ophthalmoscopy. NF1-related choroidal abnormalities were detected in 72 affected (61%) and 1 suspected (2%) child. No healthy subject had choroidal abnormalities. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were: 0.60, 0.97, 0.98, and 0.46 respectively. Compared with standard NIH criteria, the presence of NF1-related
choroidal abnormalities was the third parameter for PPV, and fourth for sensitivity, specificity, and NPV. Compared to Lisch nodules, NF1 related choroidal abnormalities had a higher specificity and PPV. This study found 82% feasibility for performing confocal NIR imaging in the population they examined (detection of Lisch nodules feasibility was 87%), but had a higher interobserver agreement compared to Lisch nodules. The use of this sign moved one patient (a 2-year-old boy) from the suspected to the affected group. Choroidal abnormalities represent a new diagnostic sign in NF1 children. NF1-related choroidal abnormalities could anticipate NF1 diagnosis, though the main obstacle is cooperation required by very young children.


GD2 is the ideal therapeutic target for neuroblastoma therapies because it is uniformly expressed on the surface of almost all neuroblastoma cells yet restricted expression on normal cells. However, anti-GD2 antibodies cause significant neuropathic pain. Anti-GD2 antibodies also cause mydriasis and decreased accommodation. 39 patients with refractory or recurrent neuroblastoma were enrolled (1 withdrew consent) and received hu14.18K322A treatment and the authors retrospectively reviewed charts for documentation of ocular side effects. This method could underestimate side effects based on rigor of reporting. 13/38 (34%) had papillary involvement and 9/38 (24%) had accommodation impairment. A dose effect was observed. Median time to onset of mydriasis was 5.5 days from initial dose and median time to onset of impaired accommodation was 12.5 days. 2/5 patients with mydriasis only had resolution at a median of 95 days after discontinuation of treatment. The other 3 patients had disease progression and returned to their referring institution. 8/9 impaired accommodation patients resolved at a median of 186 days. This study used higher antibody doses than prior studies of this treatment. Patients and their families can be counseled on potential ocular side effects of this treatment.

24. UVEITIS/ SYSTEMIC


The objective of this study was to explore the association of known HLA-DRB1 alleles in a cohort of children with oligoarticular and polyarticular juvenile
idiopathic arthritis (JIA) who develop uveitis. High-resolution HLA-DRB1 genotyping was performed in 107 children with oligoarticular and polyarticular rheumatoid factor (RF) negative JIA and 373 non-Hispanic white controls. There were 47 children with JIA-associated uveitis and 60 with JIA alone. Compared to controls, only children with JIA-associated uveitis had increased odds of carriage of HLA-DRB1*11, HLA-DRB1*08, and *13. Also, compared to controls and children with JIA alone, those with JIA-associated uveitis had increased odds of carriage of HLA-DRB1*11 and *13. This new finding that carriage of HLA-DRB1*11 and *13 appears to increase the risk of uveitis in children with JIA, may eventually lead to improvements in the screening algorithm for patients with JIA.

Uveitis Reactivation in Children Treated With Tumor Necrosis Factor Alpha Inhibitors


This retrospective study evaluated reactivation of uveitis in children treated with anti-TNFα. It is common practice among rheumatologists to maintain quiescence for 1-2 years before discontinuing systemic medication. In addition, it is believed that recurrence is lower in children treated with prolonged therapy. 50 children were observed. 39 met study criteria for the primary outcome of time to reactivation of uveitis while under treatment. 19 subjects discontinued therapy following quiescence and met inclusion for the secondary outcome of time to reactivation of uveitis. In the first group, 27.8% reactivated within 12 months of quiescence. The reactivation of uveitis with 12 months of discontinuing the treatment was much higher (63.8%) The likelihood of reactivation was higher with medications of adalimumab vs. infliximab and with older age. This study suggests that 75% of children remaining on anti-TNFα achieve quiescence at 1 year. Reactivation occurs at higher percentage after stoppage of treatment.

The Association of Race with Childhood Uveitis


This was a retrospective cohort study which attempted to identify risk factors for severe uveitis. 85 children had their records reviewed and were included in the study. Severe uveitis definition: VA less than 20/200 or history of ocular complications. Race only evaluated non-Hispanic African Americans and non-Hispanic white children. 27 children had VA less than 20/200. There was an increase in the number of African American children with this level of vision (72% vs 4%) in the white children. There was also more bilateral disease, intermediate uveitis in the African American group of children. Being an African American child was a significant predictor of blindness.
Outcome of Treating Pediatric Uveitis with Dexamethasone Implants
AJO Jan 2016: vol. 161; pg. 110.

This retrospective interventional study describes the outcome of the eyes in children with uveitis following repeated treatment with Dexamethasone. 22 eyes of 16 children with uveitis were evaluated. These patients were treated with 35 Dexamethasone implants. Intravitreal implants have shown up to 6 months of control of symptoms. The effects of these implants have been reported for a single use, no one has looked at repeated implantation and the outcomes. The children they followed had either panuveitis or intermediate uveitis. Average age at time of first implantation was 13 years. Some children prior to implantation were being treated with steroids and steroid sparing agents. BCVA improved significantly from .55 logmars to .37 logmars. OCT testing showed that central retinal thickness (CRT) decreased significantly as well by an average of 219 microns. Vitreous haze improved significantly as well. Relapse occurred about 9 months after implantation with an overall relapse rate of 61%. Systemic medication was able to be stopped and the patients did not require restarting systemic meds for average of 16 months. Posterior subcapsular cataract developed in 2 patients. None were visually significant. Only 5 eyes had increased IOP of greater than 21 mmHg. 3 patients required topical treatment for IOP and 1 patient required revision of filtration procedure.

The Risk of Intraocular Pressure Elevation in Pediatric Noninfectious Uveitis
S. Kothari, C.S. Foster, M. Pistilli, T.L. Liesegang, et al

This is a multicenter retrospective cohort study. Data is from the Systemic Immunosuppressive Therapy for Eye Diseases Research Group. Medical records were reviewed of 916 children (1593 eyes) <18 years old at presentation with noninfectious uveitis followed up between January 1978 and December 2007 (median follow-up 1.25 years) at 5 academic centers. Prevalence and incidence of IOP of ≥ 21 mmHg and ≥ 30 mmHg and incidence of a rise in IOP by ≥10 mmHg were the main outcome measures. To avoid underascertainment, outcomes were counted as present when IOP-lowering therapies were in use. Initially, 251 (15.8%) and 46 eyes (2.9%) had IOP ≥21 mmHg and ≥30 mmHg, respectively. Factors significantly associated with presenting IOP elevation included age of 6 to 12 years (versus other pediatric ages), prior cataract surgery, pars plana vitrectomy, duration of uveitis ≥6 months, contralateral IOP elevation, presenting visual acuity worse than 20/40, and topical corticosteroid use (in a dose-response relationship). At follow-up, the estimated incidence of any observed IOP elevation to ≥21 mmHg, to ≥30 mmHg, and increase in IOP by ≥10 mmHg was 33.4%, 14.8%, and 24.4%, respectively.
within 2 years. Factors associated with IOP elevation during follow-up included pars plana vitrectomy, contralateral IOP elevation, and the use of ocular (topical, peri-ocular, or intraocular) corticosteroids in a dose and route dependant relationship. Immunosuppressive therapy did not increase IOP. Pediatric eyes with noninfectious uveitis should be followed closely for IOP elevation, especially in the presence of risk factors such as the use of local corticosteroids and contralateral IOP elevation.

**Antibody Production against B19 Virus in Ocular Fluid of JIA-Associated Uveitis Patients (Case Report)**


Analysis of intraocular fluids of patients with chronic bilateral anterior uveitis (AU) and concurrent juvenile idiopathic arthritis (JIA) for indication of parvovirus B19 (B19V) infection. Intraocular fluid was analyzed by Goldmann-Witmer coefficient (GWC) assay. Patients were seropositive for B19V IgG but not IgM. 7 of 13 (54%) of patients with JIA and 3 of 45 (7%) of patients with idiopathic AU had positive intraocular B19V antibodies. Additionally, 9 patients with herpetic AU and 14 noninflammatory controls were all negative for intraocular B19V antibodies. B19V has been implicated in JIA and some cases of uveitis. This is the first report of B19V in JIA-associated uveitis specifically. The presence of B19V antibodies in the JIA patients with uveitis suggests that the uveitis is a B19V driven process either due to low-grade infection or a virus triggered autoimmune response.


Panuveitis with orbital inflammatory syndrome (OIS) is rare with few reported cases in the world literature. A 49-year-old previously healthy female presented with a 3-day history of rapidly progressive vision loss OU, high fever with new-onset tender cervical lymphadenopathy, and rapidly progressive hip and shoulder pain. She received an influenza vaccination 4 days before the onset. Later that day, the patient had decreased ocular motility but no frank proptosis, suggestive of a rapidly progressive OIS in conjunction with panuveitis, and the patient underwent urgent magnetic resonance imaging, she was started on high-dose IV methylprednisolone (1 g) tid for 3 days. She had an immediate improvement in her systemic polyarthritis and her eye pain decreased rapidly. At 1-year follow-up, her vision was 20/20 OD, but she remained no light perception OS. A 57-year-old male presented with decreased vision OD over a 6-week period. His community ophthalmologist initially recorded OD vision at 20/40 and intraocular
pressure (IOP) of 9. During follow-up, his vision decreased to 20/60 and IOP increased to 34. He had received a flu shot 3 days before the onset of symptoms.

A 57-year-old male presented with decreased vision OD over a 6-week period. His community ophthalmologist initially recorded OD vision at 20/40 and intraocular pressure (IOP) of 9. During follow-up, his vision decreased to 20/60 and IOP increased to 34. He had received a flu shot 3 days before the onset of symptoms. Forty-eight hours later, there was worsening proptosis, restriction of extraocular movements, and lid retraction with protrusion of orbital contents, during his admission, he developed lower motor neuron weakness and was diagnosed with Guillain-Barré syndrome by the neurology service. He was treated with pooled IV immunoglobulin for 48 hours with improvement in his symptoms. Their 2 cases exhibit the rare presentation of noninfectious panuveitis with OIS and are difficult to immediately distinguish from an infectious endophthalmitis, panophthalmitis, or orbital cellulitis. However, it is imperative that the clinician be aware of panuveitis with OIS and that this inflammatory, potentially blinding disorder be considered as a potential diagnosis, particularly after a vaccination.

**Ocular Involvement Following Postnatally Acquired Toxoplasma gondii Infection in Southern Brazil: A 28-year Experience**


This retrospective longitudinal study evaluated the incidence and risk factor for ocular involvement among patients with postnatally acquired toxoplasmosis. There is a high prevalence of toxo in the southern Brazil region. 302 patients with + IgM for toxoplasmosis were evaluated. 5 eyes were found with inactive retinochoroidal scars and were excluded from the analysis. Isolated intraocular inflammation was present in 30 patients at baseline (9.9%); it was unilateral in 27 patients. In all patients except 2, inflammation was observed within 3 months of the first positive IgM test. Men were more likely to have ocular disease or clinically apparent systemic disease. Patients greater than 40 years of age at first IgM testing had the greater risk of necrotizing retinochoroiditis. Important to remember that first presentation of toxo could be isolated intraocular inflammation and could develop as long as 12 years after infection. Presentation in southern Brazil is different than in the USA where only 14% of the general population is infected with T gondii by age 40 years.

**Ophthalmic manifestations in recently diagnosed childhood leukemia**

Between January 2005 and December 2014, 185 patients with leukemia, and a median age of 6.0 years (range 0.5-18.0 years), were retrospectively given a complete ophthalmic examination at the time of diagnosis. The median follow-up time of 36.0 months (range 0.5-108.0 months). Ocular signs were present in 24.3% of the patients at the time of diagnosis and 37.8% of them were symptomatic. The prevalence of ocular involvement was higher in patients with acute myelocytic leukemia (36.4%) compared to patients with acute lymphocytic leukemia (20.4%). Fatality rate was significantly higher in subjects with AML compared with ALL, but was not significantly different between patients with and without ocular involvement. Platelet counts were significantly lower in patients with ocular signs, but not hemoglobin levels or white blood cell counts. Routine ophthalmic examination should be performed in recently diagnosed children with leukemia, as ocular signs may be present at the time of diagnosis even without symptoms.

**Risk Factors for Developing Thyroid-Associated Ophthalmopathy Among Individuals With Graves Disease**


The study seeks to identify risk factors for patients with Graves disease (GD) to develop thyroid associated ophthalmopathy. This was a longitudinal cohort study of all patients 18 years and older with newly diagnosed GD identified in a large US healthcare system in which patients with Graves disease who obtained at least one eye exams during the study period 2001-2009 were evaluated. Main outcome measure were hazard ratio with 95% confidence intervals of developing TAO via multivariate Cox regression with adjustment for possible confounders such as sociodemographic factors, systemic medical conditions, thyrotropin levels, and medical and surgical interventions for management of hyperthyroidism Of 8404 patients with who met inclusion criteria, 8.8% developed GD.

Surgical thyroidectomy, alone or in combination with medical therapy, was associated with a 74% decreased hazard for TAO (adjusted HR, 0.26 [95%CI, 0.12-0.51]) compared with radioactive iodine therapy alone. Statin use (for 60 days in the past year vs <60 days or nonuse) was associated with a 40% decreased hazard (adjusted HR, 0.60 [CI,0.37-0.93]). No significant association was found for the use of nonstatin cholesterol lowering medications or cyclooxygenase 2 inhibitors and the development of TAO.

**Ocular Complications in Children with Diabetes Mellitus**

Current guidelines by the American Academy of Ophthalmology encourage annual screening examinations for all patients with type 1 diabetes mellitus (DM) to begin 5 years after diagnosis of DM. However, the age at diagnosis and prevalence of diabetic retinopathy (DR) among children are not well established, with varied reports in the literature and there is very little information about other diabetic ocular complications in children. Some data are available with regard to modifiable risk factors to prevent the development of ophthalmic complications of DM, but not particularly in the very young. The effectiveness of annual eye examinations in diabetic children is unclear. The authors sought to determine the prevalence and onset of ocular pathology, identify risk factors for ocular disease, and recommend a screening regimen for asymptomatic children with DM. This a retrospective, consecutive cohort study of 370 children (mean 11.2 yrs, range 1-17.5 yrs) with DM (type 1 or 2) with mean duration of 5.2 yrs (range 0.1-16.2 yrs). Patients underwent 693 examinations over a 4-year period. Mean hemoglobin A1C (Hb A1C) was 8.6 (range 5-14). No children were found to have DR. 12 children had cataract and 5 underwent surgery, however they were identified by decreased vision, not diabetic screening. 19 children had strabismus, but only 1 was microvascular paralytic strabismus. 41 children had high refractive error. There were no associations between these conditions and duration or control of DM. A review of the literature showed the youngest reported age at diagnosis of vision threatening DR was 15 years, and the shortest duration of disease was 5 years. It appears that DR is rare in children regardless of duration and control of DM. On the basis or their study and literature review the authors propose that screening examinations for type 1 DM could begin at age 15 years or 5 years after diagnosis, whichever occurs later, unless the child is considered high risk by the endocrinologist.


Thirty-eight children diagnosed with allergic asthma (mean age 9.8 ± 2.8 years, age range 6-13 years) and 40 age-similar controls were enrolled in this study. All children with asthma were taking inhaled fluticasone propionate at a dosage of 250 μg or more per day for at least 1 year. The RNFL thickness measurements were performed using Cirrus HD spectral-domain OCT 400. Central subfield thickness, cube average thickness, and cube volume were also measured. Asthmatic children had similar peripapillary RNFL measurements compared to controls on spectral-domain OCT. Raised eosinophil counts in asthmatic children were found to be significantly associated with cube average thickness.
Pediatric Ophthalmology Practice Efficiency: Utilization of Orthoptists as Partners in the Pediatric Eye Care Team

The author analyzed 6-month expenses and income related directly and indirectly to the addition of an orthoptist to a pediatric ophthalmology private practice in Texas. The orthoptist operated independently in an orthoptic clinic with indirect supervision by a physician via chart review. Expenses included salary, payroll tax, medical insurance, 401k, educational expenses, society membership expenses, examination room overhead (one room), increased, support staff costs for orthoptist's clinic. Direct revenue included collections stemming from the orthoptist's charges for sensory motor examinations (92060) and E&M level 1 (99211). Indirect revenue resulted from the transfer of some established patients to the orthoptic clinic and increased number of new patients on the surgeon's schedule and increased surgical volume. Total annualized expenses and income attributed to the new orthoptist were $101,000 and $172,320, respectively, for a net revenue of $71,320.


This study evaluated the psychological effect of cycloplegic eyedrops in Asian children and to identify factors that contribute to success. Consecutive patients 2-12 years of age were recruited. 298 children with a mean age of 5.9 years were recruited. 80% were of Chinese ethnicity and slightly more than half had previously received eyedrops. 13% of children were uncooperative. Uncooperative behavior was linked to younger age, male sex, ‘demanding, aggressive’ type, and prior eyedrop experience. Each cycle of drops lowered the uncooperative rate. Children who were uncooperative with the drops reported significantly higher pain scores, and became more uncooperative with the doctors for the post-cycloplegia portion of the examination. In general, anxiety declined after drop administration had been completed. The more cooperative nature of female patients is in contradistinction to other papers based in other countries and may be country-specific. Anticipatory factors seem to increase anxiety. Clearly eye-care providers need a specific plan in regards to drop administration to limit the number of uncooperative children. This, will in turn, shorten the length of time to administer drops, make the rest of the eye exam easier, and improve patient satisfaction with the exam which will make subsequent examinations easier and less anxiety-provoking.
Analysis of online patient education materials in pediatric ophthalmology

The average American comprehends at an 8th grade level. This study looked at the readability of online information for 10 pediatric ophthalmology conditions (PEMs) by looking at the first 10 articles on Google for each condition. Reading ease was given a score 0-100. Mean grade level of the articles was 11.75. Only 12% of the articles were written below a high school level and only 2% met recommended criteria. Cataracts, glaucoma, nystagmus and retinoblastoma were written at statistically higher levels than stye. Wikepedia was written at the highest grade level, and WebMD was written at the lowest grade level. The authors recommend ‘dumbing down’ patient information articles as the main way to correct this which is a sad commentary on our society.

Impact of Free Glasses and a Teacher Incentive on Children’s Use of Eyeglasses: A ClusterRandomized Controlled Trial

This cluster randomized controlled trial looked at 728 children who met enrollment criteria of vision worse than 6/12 in either eye were randomly allocated to to intervention or control. 693 children completed the study. Spectacle wear was higher in the intervention group at 6 months (68% vs. 23%). Intervention described as free glasses and education of parents and teachers. Also teachers were told that if greater than 80% of children given glasses were wearing them on 2 unannounced class visits, the teacher would receive a tablet computer. The control group was given a glasses prescription with a letter to the parents about their child’s status. However, free glasses were not promoted and the teachers received no incentive.

Safety of Spectacles for Children’s Vision: A Cluster - Randomized Controlled Trial

This study evaluated safety of children’s glasses in rural China where there is a belief that glasses will harm the child’s vision. This study was an exploratory of a cluster randomized, investigator masked, controlled trial. The children were randomly assigned to 1 of 3 interventions: free glasses provided in class, vouchers for free glasses, or glasses prescription only. 5852 myopic children
were enrolled and randomized. The final visual acuity in the free glasses and voucher group were more successful than the group who just got prescriptions.

**Strabismus Surgical Subspecialization: A Population-Based Analysis**


The authors observe that performance of strabismus surgery is increasingly shifting from general ophthalmologists to strabismus surgeons and they determine in this study surgeon level strabismus surgery rates in a population based study in Ontario Canada. The percentage of ophthalmologists who provided strabismus surgery decreased from 37.7% to 12.5%, a 66.8% decline from the baseline level. Of ophthalmologists who provided strabismus surgery during the same period, the mean number of strabismus procedures per surgeon grew from 16.2 to 55.3 per year, a 241.4%. These trends occurred at all career stages. The authors conclude that this trend has implications on the delivery of eye care, as well as on the training of ophthalmology residents to meet the future eye care needs of their patients.


PURPOSE: To evaluate and compare trends in different categories of pediatric and adult ophthalmology publications. METHODS: Publications in ophthalmology between January 1, 1998, and December 31, 2012, were retrieved from PubMed. An age filter separated pediatric from adult articles. RESULTS: There was a significant linear increase in the number of publications in both pediatric and adult publications. There was an increase over time in pediatric and adult clinical trials, letters to the editor, meta-analyses, and systematic reviews. There was a significant increase in adult randomized controlled trials only. No meaningful statistical analyses could be conducted for practice guidelines. CONCLUSIONS: Pediatric and adult ophthalmology have demonstrated a significant increase in annual published articles. Practicing ophthalmologists have an increasing number of articles to read and might become more and more dependent on search engines and reviews to remain informed, emphasizing the need for official practice guidelines to help ophthalmologists deliver safe, efficient and effective care.

This article discusses a committee formed at the University of Iowa Department of Ophthalmology to address the lack of resident curriculum for extraocular muscle surgery. This included web-based learning, reading list and wet laboratory session. Seven residents scores were evaluated. Comfort passing scleral sutures, isolating and suturing muscles and identifying instruments all improved. Testing also improved (65% pre- and 91% post-). This paper can provide a blueprint for other residency programs around the country and the world to improve resident knowledge and facility with strabismus surgery.

**Direct ophthalmoscopy should be taught to undergraduate medical students—yes** I H Yusuf, J F Salmon and C K Patel

_Eye_ 29: 987-989; June 5, 2015

**Direct ophthalmoscopy should be taught to undergraduate medical students—No** RMJ Purbrick and NV Chong _Eye_ 29: 990-991; June 2015

In an interesting editorial in the journal _EYE_ the two authors debate the value the teaching direct ophthalmoscopy to medical students. Both authors acknowledge that proficiency and the use of the direct ophthalmoscope is low in medical students trained in the United Kingdom with less than 20% failure to detect papilloedema or arterial occlusion and less than 50% feel comfortable to using the direct ophthalmoscope. The authors who do not recommend teaching direct ophthalmoscopy recommend the routine use of fundus photography and spending time training primary care physicians to recognize any changes of systemic disease in a photograph rather than looking at the eye. The authors who support training medical students to use the direct ophthalmoscope argues that non-mydriatic fundus cameras are not widely available are expensive and will never likely be used in the developing world. He argues that relegating fundus screening to non-specialists will lead to devaluing role of ophthalmologists as integral members of the healthcare system.

**Sentinel Events, Serious Reportable Events, and Root Cause Analysis**


In an effort to reduce adverse events which harm patients, the authors define sentinel events and distinguish them from serious reportable events. They go on to describe root cause analysis as a method of prevention of such events. Sentinel event was defined by the Joint Commission to describe unexpected occurrences that resulted in death or serious physical or psychological injury to a patient. An ophthalmic example is insertion of the wrong intraocular lens. The National Quality Forum coined the term serious reportable events (SREs) to refer
to “preventable, serious, and unambiguous adverse events that should never occur.” Serious reportable events in ophthalmology include surgery on the wrong patient, surgery on the wrong eye, wrong procedure performed, patient death or serious injury with a medication error, and unintended retention of a foreign object after surgery. To minimize these events, root cause analysis is employed which uses a systematic approach to determine underlying causes for errors resulting in poor patient care. This includes inquiry into (1) the flow process (2) human factors (3) human resource issues, (4) communication issues, (5) equipment issues, (6) environmental issues, and (7) policies and procedures.


This study is a retrospective analysis of the 140 claims closed in the field of pediatric ophthalmology & strabismus (POS) over a 25-year period. One hundred and seventeen cases (unique plaintiffs) resulted in 140 closed claims against one or more physicians and/or entities. Defendants (n=119) had a mean age of 45 years and the majority were not subspecialists. The most common plaintiff age was less than 1 year, and the most cases occurred in Texas. The top four case originations in order were the office, surgical setting, hospital inpatient, and the emergency room. The top three allegations were related to treatment, followed by surgery, followed by diagnosis. Of the 44 claims closed with indemnity payment, the average payment was $470,695 ($556,106 inflation-adjusted). Individual claims resulted in an indemnity payment in 35% of cases and entity claims resulted in a payment in 9.5%. There were no cases where the payment exceeded the insured’s limit of liability. Strabismus was the top cause of individual cases but ROP was the highest percentage of closed cases with an indemnity payment, and the highest mean payment. In lawsuits against individual physicians, the most frequent risk management factors were informed consent, follow-up and the litigation process. For entities the most frequent risk was the litigation itself (most of these were dismissed). POS cases are relatively infrequent but have higher mean indemnity payments compared to all claims at OMIC.