What’s New and Important in Pediatric Ophthalmology and Strabismus for 2018
The Complete and Unabridged handout

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1. AMBLYOPIA

Effectiveness of a Binocular Video Game vs Placebo Video Game for Improving Visual Functions in Older Children, Teenagers, and Adults with Amblyopia


This multicenter, double-masked, randomized clinical trial was The Binocular Treatment of Amblyopia Using Videogames from 3/2014 through 6/2016. This study reports 115 participants, from ages 7 to 55 years, with unilateral amblyopia (Snellen vision equivalent of 20/40-20/200) due to anisometropia, strabismus, or both. Results indicate no significant difference detected between the binocular video game treatment group and the placebo video game treatment group in the amblyopic eye visual acuity at 6 weeks. Of the participants, 65 (56.5%) were male and 83 (72.2%) were white and the mean age at randomization was 21.5 years. Compliance with more than 25% of prescribed game play was achieved by 64% of the active group and 83% in the placebo group. At 6 weeks, 36 (64%) participants in the active group achieved fellow eye contrast greater than 0.9 in the binocular video game. Adverse events reported included 3 participants with transient asthenopia, but no reported diplopia. In summary, the authors conclude that this particular dichoptic video game of falling blocks played at home on an iPod Touch for 1 hour a day for 6 weeks did not improve visual outcomes more than the placebo video game despite increases in the fellow eye contrast during the game play. The authors suggest that their results indicate that more engaging video games are needed.

Spectral-Domain Optical Coherence Tomographic Angiography in Children With Amblyopia


This was an observational case-control study of patients at Stein Eye Institute at UCLA from 9/1/2016 through 5/31/2017 to evaluate for retinal and microvascular features using OCTA in children < 18 years old with amblyopia. The authors reported 63 eyes evaluated, 13 (21%) with amblyopia and 50 (79%) without amblyopia (control). Of the 59 patients, the mean age of the amblyopic patient was 8.0 years old as compared to 10.3 years of the control patient. The macular vessel density of the superficial capillary plexus was lower in the amblyopic patients as compared to the controls, in both 3x3mm and 6x6mm scans, with the 6x6mm scans being statistically significant. Macular vessel density of the deep capillary
plexus in the 6x6mm was also lower in the amblyopic patients as compared to the control group. In summary, OCTA reveals a subnormal superficial and deep retinal capillary density in the macula for amblyopic patients as compared to a control group. In summary, this study shows the value of SD-OCT to detect microstructural changes in amblyopic retinas versus non-amblyopic retinas.


Angcang Tang, Taolin Chen, Junran Zhang, Qiyong Gong. J of Ped Ophthal & Strabismus.2017:54(5);303-310

The purpose of this study was to explore the abnormality of spontaneous activity in patients with anisometric amblyopia under resting-state functional magnetic resonance imaging (Rs-fMRI). Twenty-four participants were split into two groups. The anisometric amblyopia group had 10 patients, all of whom had anisometric amblyopia of the right eye, and the control group had 14 healthy subjects. All participants underwent Rs-fMRI scanning. Measurement of amplitude of low frequency fluctuations of the brain, which is a measure of the amplitudes of spontaneous brain activity, was used to investigate brain changes between the anisometric amblyopia and control groups. Compared with an age- and gender-matched control group, the anisometric amblyopia group showed increased amplitude of low frequency fluctuations of spontaneous brain activity in the left superior temporal gyrus, the left inferior parietal lobe, the left pons, and the right inferior semi-lunar lobe. The anisometric amblyopia group also showed decreased amplitude of low frequency fluctuations in the bilateral medial frontal gyrus. The most significant limitation of the study was the sample size. In addition, the different stages of brain development due to age may have influenced the interpretation of the current results when compared with previous studies in children or adults, although age was introduced as a covariate to the amplitude of low-frequency fluctuation calculation. Finally, the current study included only right-sided amblyopia, which may reduce the inference effect on left-sided amblyopia. In possible future studies, aside from grouping the ages by brain development stages, patients with left-sided anisometric amblyopia should be added to compare the differences between these two groups against the control group, which would provide additional data to aid in our understanding of amblyopia and neuroplasticity.

Effect of 4-month intermittent Atropine Penalization in Amblyopic patients for whom Patch Therapy has failed.

Bo Ram Seol, Young Suk Yu, Seong-Joon Kim J of Ped Ophthal & Strabismus.2017;54(6):375-380

The purpose if this retrospective observational study is to evaluate the effect of 4-month intermittent atropine penalization in children with amblyopia for whom
patch therapy had failed and to analyze the factors associated with treatment success. Forty-one children for whom patch therapy had failed were included in the study and received atropine 1% in the sound eye twice a week for 4 months. Treatment success was defined as a best corrected visual acuity (BCVA) improvement of two lines in the amblyopic eye. Age, cause of amblyopia, pretreatment BCVA at the start of atropine penalization in the amblyopic eye, age at the start of eyeglass prescription, age at the start of the patch therapy, type of refraction, type of strabismus, and cause of failure of patch therapy were analyzed and compared between the two groups: failure and success group. The study showed that 48.8% of patients had improvement in their BCVA by two lines. Also, younger age and poor pretreatment BCVA at the start of atropine penalization in the amblyopic eye were the factors associated with treatment success. The study is though limited from its small sample size, retrospective nature. Also, although the study didn’t show any significant side effects from atropine use, it is imperative that clinicians show caution when they use atropine for amblyopia treatment.

Occlusion dose monitoring in amblyopia therapy: status, insights, and future directions

Occlusion therapy remains the mainstay treatment of amblyopia, but its outcome is not assured or universally excellent. Many factors are known to influence treatment outcome, among which compliance is foremost. The occlusion dose monitor (ODM) removes one variable from the treatment equation, because it records the occlusion actually received by-rather than prescribed for-the child. Improvement observed can thus be quantitatively related to the patching received. This review summarizes the insights the ODM has provided to date particularly in elucidating the dose-response relationship. The authors believe that we are entering the era of personalized ophthalmology in which treatments will be tailored to the needs of the individual child and facilitated by the use of wearable monitors. This review article raises some very interesting concepts that may be of use in the future of amblyopia treatment.

Slow reading in children with anisometropic amblyopia is associated with fixation instability and increased saccades.

Previous studies show slow reading in strabismic amblyopia. However, recently the amblyopia, not strabismus, was identified as the key factor in slow reading in children. The authors conducted this cross-sectional study in order to examine reading in anisometropic children and evaluate whether slow reading was associated with ocular motor dysfunction in children with amblyopia. Anisometropic children (7-12 years) with or without amblyopia were compared to age-similar
normal controls. Children silently read a grade-appropriate paragraph during binocular viewing. Reading rate (words/min), number of forward and regressive saccades (per 100 words) and fixation duration were recorded with the ReadAlyzer. Binocular fixation instability was also evaluated (EyeLink 1000). Their results showed that amblyopic anisometropic children read more slowly (n = 25; mean with standard deviation, 149 +/- 42 words/min) than non-amblyopic anisometropic children (n = 15; 196 +/- 80 words/min; P = 0.024) and controls (n = 25; 191 +/- 65 words/min; P = 0.020). Non-amblyopic anisometropic children read at a comparable rate to controls (P = 0.81). Slow reading in amblyopic anisometropic children was correlated with increased forward saccades (r = -0.84, P < 0.001), increased regressive saccades (r = -0.85, P < 0.001), and fellow eye instability during binocular viewing (r = -0.52, P = 0.019). The authors concluded that slow reading in school-age children with anisometric amblyopia is related to increased frequency of saccades and fixation instability of the fellow eye. The relationship of reading rate and the number of saccades is consistent with previous studies of reading in strabismic amblyopia. This is a well-designed study that highlights an oculomotor dysfunction as a possible underlying cause of slow reading in amblyopic patients. It is interesting that the authors did not find a relationship between reading rate and amblyopic eye visual acuity suggesting that the presence, not severity, of amblyopia was sufficient to cause slower reading in anisometropic children.

**Pediatric ophthalmology and childhood reading difficulties: Amblyopia and slow reading.**

This article is part of symposium on childhood reading difficulties. Reading is a major life activity, as recognized by the US Congress in the Americans with Disabilities Act Amendments Act of 2008, and the education code of most US states requires schools to evaluate reading and implement reading programs to addresses students’ reading difficulties. Currently, such legislation is employed to identify accommodations needed for children with bilateral visual impairment and for children with dyslexia and/or related learning disabilities. Yet recent research has shown that children with the most common form of monocular visual impairment-amblyopia-read slowly. Slow reading can be detrimental to academic performance and learning, which in turn may affect self-esteem. The authors suggest that parents and educators work together to implement accommodations (e.g., extra time) to help amblyopic students succeed in their daily school tasks, and improve their performance on the timed, standardized tests. They also propose that children with other visual disorders that cause visual impairment in one eye (e.g., glaucoma, cataract, trauma, etc.) should be considered for academic accommodations. This article overviews some exciting new insights to the mechanisms of slow reading in children with amblyopia.
Balanced Eyes See Stereopsis More Quickly, but Not More Finely

The purpose of this study was to quantify ocular sensory dominance and investigate its relationship to stereopsis. In 69 subjects, ocular dominance was measured by a continuous flashing technique, with the tested eye viewing a Gabor patch increasing in contrast, and the fellow eye viewing a Mondrian noise decreasing in contrast. In each trial, the log ratio of Mondrian to Gabor’s contrasts was recorded as a subject first detected the Gabor. Fifty trials were collected for each eye and an interocular difference was analyzed with a rank-sum test. The z-value was used as the ocular dominance index (ODI) to quantify the degree of ocular dominance. A subject with ODI ≥ 2 was categorized as having a clear ocular dominance, and a subject with ODI < 2 was considered as having balanced eyes (unclear dominance). The stereoacuity was measured with random dot patterns with durations varying from 50 to 1000 ms. The best achievable stereoacuity (Dmin) and the integration time needed to acquire that (Tmin) were calculated. Of 69 subjects, 30 had balanced eyes and 39 had clear ocular dominance. Tmin was significantly longer in subjects with clear ocular dominance than in subjects with balanced eyes (180.18 vs. 121.17 ms, P < 0.01). Tmin was positively correlated with ODI (P < 0.01). However, Dmin (best stereoacuity) in subjects with clear dominance was not different from that in subjects with balanced eyes (40.60 vs. 35.73 arcsec, P = 0.18). This study demonstrates that ocular dominance is not associated with how fine the stereoacuity is, but rather how quickly the best stereoacuity is acquired. This may have implications for athletes undergoing vision training. Also, clinically, the results from this study would support correcting the dominant eye for distance in monovision management, to allow for better binocular summation at middle distances and near stereoacuity since the signals from the eyes are roughly equally blurred.

Optimal Audiovisual Integration in the Ventriloquism Effect But Pervasive Deficits in Unisensory Spatial Localization in Amblyopia

Amblyopia is increasingly recognized to impair audiovisual multisensory processing. This study sought to determine whether audiovisual abnormalities are due to a failure of multisensory integration, or an optimal strategy in the face of unisensory impairment. Fourteen patients with unilateral amblyopia (7 anisotropic, 3 strabismic, 4 mixed mechanism) with mean age of 28.8 years and 16 controls of similar mean age participated. They were asked to localize brief unimodal auditory, unimodal visual, and bimodal audiovisual stimuli during binocular viewing using a location discrimination task. A subset of bimodal trials involved
the ventriloquism effect, an illusion in which auditory and visual stimuli originating from different locations are perceived as originating from a single location. Localization precision and bias were determined by psychometric curve fitting, and observed parameters were compared with predictions from the maximum-likelihood estimation (MLE) model of optimal integration. This study found that spatial localization precision was significantly reduced in the amblyopia group compared to the control group for unimodal visual, unimodal auditory, and bimodal stimuli. Analyses of localization precision and bias for bimodal stimuli showed no significant deviations from the MLE model in the amblyopia or control group, even for the bimodal spatially incongruent subset, demonstrating that audiovisual integration remains intact in unilateral amblyopia, and optimal sensory re-weighting occurs. This study further demonstrates that unilateral amblyopia affects not only binocular vision, regardless of the severity of amblyopia or level of stereopsis, but also auditory localization.


Amblyopia is one of the leading causes of unilateral decreased visual acuity in children. The authors sought to determine the prevalence of amblyopia in a specific region of Iran. They performed a cross-sectional, population-based study on children >1 year old in the second largest city in Iran. The type of amblyopia was classified, as well as the socioeconomic characteristics of the patient population. The prevalence of amblyopia was 4.6% in the 2739 children who met the inclusion and exclusion criteria. The majority (54%) had unilateral amblyopia. Anisometropia was the most common risk factor for amblyopia (45% of patients). The lowest prevalence was in the 5-15 year old group at 2.24% and the highest prevalence was in the 55-65 year old group at 7.14%. There was a disparity by sex, in that more females (5.23%) than males (3.39%) had amblyopia. There was also a disparity by education, in that the prevalence in individuals with no education was 5.71%, a much higher value than those with a university education at 2.59%. The authors conclude that vision screening and amblyopia awareness programs are effective, as the prevalence of amblyopia is lower in younger children than the elderly. Higher education, socioeconomic status, and levels of health knowledge lead to a decrease in the prevalence of visual disorders, including amblyopia.

A Randomized Trial of a Binocular iPad Game Versus Part-Time Patching in Children Aged 13 to 16 Years With Amblyopia

There is emerging evidence that a binocular approach to the treatment of amblyopia can improve amblyopic eye visual acuity in adult patients with strabismic,
anisometropic, and mixed-mechanism amblyopia, and possibly at a greater rate than patching treatment. To achieve a binocular precept, dichoptic displays have been used to present high-contrast images to the amblyopic eye and low-contrast images to the fellow eye in order to overcome binocular suppression commonly found in amblyopia. The purpose of this randomized clinical trial was to compare the improvement in amblyopic eye VA after 16 weeks of home-based treatment with binocular game play on an iPad device prescribed for 1 hour a day vs patching prescribed for 2 hours a day, in teenagers aged 13 to <17 years with amblyopic eye visual acuities of 20/40 to 20/200. One hundred participants aged 13 to <17 years (mean 14.3 years) with amblyopia (20/40 to 20/200, mean 20/63) resulting from strabismus, anisometropia, or both were enrolled into this randomized clinical trial. Participants were randomly assigned to treatment for 16 weeks of either a binocular iPad game prescribed for 1 hour per day (n = 40) or patching of the fellow eye prescribed for 2 hours per day (n = 60). The main outcome measure was change in amblyopic eye VA from baseline to 16 weeks. Mean amblyopic eye VA improved from baseline by 3.5 letters (2-sided 95% confidence interval [CI]: 1.3–5.7 letters) in the binocular group and by 6.5 letters (2-sided 95% CI: 4.4–8.5 letters) in the patching group. After adjusting for baseline VA, the difference between the binocular and patching groups was -2.7 letters (95% CI:-5.7 to 0.3 letters, P=0.82) or 0.5 lines, favoring patching. In the binocular group, treatment adherence data from the iPad device indicated that only 13% of participants completed >75% of prescribed treatment. The authors concurrently conducted a parallel study of binocular treatment in younger children aged 5–12 years, which showed greater VA improvement than the current study. Although this younger group also had poor adherence to treatment, they had a higher median proportion of treatment hours than the teenager group. The authors conclude that, in teenagers aged 13 to <17 years, improvement in amblyopic eye VA with the binocular iPad game used in this study was not found to be better than patching, and was possibly worse. Nevertheless, it remains unclear whether the minimal treatment response to binocular treatment was owing to poor treatment adherence or lack of treatment effect.

Elbow splinting as a method to increase patching compliance in amblyopia therapy.


Patching of the contralateral is an effective therapy to treat unilateral amblyopia. Unfortunately, compliance rates are relatively poor. The aim of this study was to assess the efficacy, safety, and parental acceptance of using elbow restraints as a tool to improve occlusion therapy compliance in children with amblyopia. Children 6 years old or younger diagnosed with amblyopia who had attempted patching therapy for a minimum of 3 months, fitted for elbow splints due to low treatment adherence. Non-compliance was defined as patching less than 50% of the specified amount of time, or consistently removing the patch during daily activi-
ties. Parents/guardians were instructed to continue to attempt patching the non-amblyopic eye for the predetermined amount of time, and to employ the elbow splints if the child removed the patch, until the child was fully compliant with daily patching. Forty-one patients were included, 16 females, 25 males, with a median age of 37 months (12–68) months. Mean follow-up duration was 4.9 ± 1.6 months. Sixty percent of the patients had esotropic amblyopia. The mean amount of daily patching prescribed prior to the use of elbow splints was 4.95 ± 1.5 h and the mean amount of actual patching achieved was only 1.5 ± 1.7 h. Following the use of elbow splints, the mean amount of patching increased to 3.4 ± 1.3 h. Visual acuity improved in 95% of the children. The median amount of time the splints were used to improve patching compliance was 7 days. Eighty-three percent of parents/guardians said that they would recommend using the elbow splints as a method to increase patching compliance. Elbow splints are a safe method of increasing compliance with patching. Elbow splints are easily removed by the parents yet difficult to remove by the children on their own. Parents found the temporary unhappiness was an acceptable side effect in order to aid in the restoration of vision in the amblyopic eye.

Binocular Therapy for Childhood Amblyopia Improves Vision Without Breaking Interocular Suppression

Binocular treatments for amblyopia can produce rapid gains in visual function, thought to be a result of reduced interocular suppression. The authors of this study aimed to develop an effective home-based binocular treatment system for amblyopia that would engage high levels of compliance but that would also allow the assessment of the role of suppression in children’s response to binocular treatment. Twenty-two children (3-11 years) with anisometropic (n=7, group 1) and strabismic or combined mechanism amblyopia (group 2; n=6 and 9, respectively) were treated for a maximum of 8 (group 1) or 24 weeks (group 2). Treatment consisted of balanced binocular viewing (BBV) therapy, involving daily viewing of dichoptic movies with shutter glasses (blurring the image to the fellow eye so that monocular acuity was matched across eyes), interrupted by gameplay to monitor compliance and suppression. The treatment elicited high levels of compliance (89.4% ± 24.2% of daily dose in 68.23% of days on treatment) and led to a mean visual acuity improvement of 0.27 logMAR (SD 0.22) for the amblyopic eye. However, acuity gains were not correlated with a reduction in suppression. A statistically significant reduction in interocular suppression was observed in only 6 of 22 children, of whom 4 had combined mechanism and 2 purely strabismic amblyopia; further 5 children showed a significant increase in suppression. This study, though small, is important in that it reports a new binocular treatment of amblyopia with comparable success rates to previous binocular treatments, and is the only unsupervised binocular vision treatment that also supports remote monitoring of compliance and suppression.
The purpose of this study is to evaluate the role of monocular video game play as an adjuvant to occlusion therapy in the treatment of anisometropic amblyopia. In a prospective randomized study design, 68 children with ages ranging from 6 to 14 years who had anisometropic amblyopia with a best corrected visual acuity (BCVA) in the amblyopic eye of better than 6/36 and worse than 6/12 and no manifest strabismus were recruited. They were randomly allocated into two groups: 34 children received 1 hour per day of video game play for the first month plus 6 hours per day of occlusion therapy (video game and occlusion group) and 34 children received 6 hours per day of occlusion therapy alone (occlusion only group). Patients were then evaluated at baseline and 1 and 3 months after treatment for BCVA, stereoacuity, and contrast sensitivity. The study showed that in the video game and occlusion group, BCVA improved from $0.61 \pm 0.12$ logarithm of the minimum angle of resolution (logMAR) at baseline to $0.51 \pm 0.14$ logMAR ($P = .001$) at 1 month and $0.40 \pm 0.15$ logMAR ($P = .001$) at 3 months. In the occlusion only group, BCVA improved from $0.65 \pm 0.09$ logMAR at baseline to $0.60 \pm 0.10$ logMAR ($P = .001$) at 1 month and $0.48 \pm 0.10$ logMAR ($P = .001$) at 3 months. There was significantly more improvement in the video game and occlusion group compared to the occlusion only group ($P = .003$ at 1 month and $P = .027$ at 3 months). The authors conclude that video game play along with part-time occlusion therapy has an advantage in visual recovery in previously untreated anisometropic amblyopia in children. This effect is greater after 1 month, and more precisely after 3 months, in children younger than 10 years.

Comparison of quantitative measurement of foveal avascular zone and macular vessel density in eyes of children with amblyopia and healthy controls: an optical coherence tomography angiography study.


Optical coherence tomography angiography (OCTA) is a relatively new and non-invasive imaging technique that uses motion control contrast imaging to obtain high resolution volumetric blood flow information and generate angiographic images. The purpose of this cross-sectional study was to quantify vessel density of superficial capillary plexus (SCP), deep capillary plexus (DCP), and the foveal avascular zone (FAZ) of children's amblyopic eyes and to compare the measurements with those of companion eyes and age-matched controls. Fifteen pa-
Patients with strabismic amblyopia (Mean age 8.2 ± 2.3 years), and 15 age-matched controls (Mean age 8.6 ± 2.2 years) were included. The mean SCP at 1 mm, 2 mm, and 3 mm zones were (in the order amblyopic eye, companion eye, control) 1.399 +/- 0.088, 5.854 +/- 0.195, 12.866 +/- 0.346; 1.467 +/- 0.084, 5.979 +/- 0.182, 12.965 +/- 0.321; and 1.559 +/- 0.052, 6.343 +/- 0.190, 13.819 +/- 0.423. SCP was significantly lower in amblyopic eyes than in companion eyes and controls (P < 0.05). The mean DCP at 1 mm, 2 mm, and 3 mm zones were 1.425 +/- 0.069, 6.038 +/- 0.186, 13.522 +/- 0.336; 1.525 +/- 0.072, 6.427 +/- 0.190, 14.286 +/- 0.322; and 1.685 +/- 0.074, 6.895 +/- 0.198, 15.355 +/- 0.356. DCP was significantly lower in amblyopic eyes than companion eyes and controls (P < 0.05). There was no significant difference in FAZ among groups (P > 0.05). The authors conclude that in their cohort of patients vessel density of SCP and DCP of eyes with amblyopia is lower than that of the companion eye and age-matched controls. This study introduces this novel technology and highlights some possibly anatomical differences between amblyopic eyes and controls.

This study is limited by its small sample size and its cross-sectional nature. Normative data is still absent and hence the clinical relevance of these findings still needs to be explored.

**Use of Video Games for the Treatment of Amblyopia**

The author reviews the use of video games, videos and dichoptic stimulation for amblyopia therapy. The most prominent defects in amblyopia are the crowding effect and suppression. Suppression seems to respond to video game therapy. There are 3 approaches to using video games: 1) monocular approach with patching the non-amblyopic eye and using the game which improves aspects related to crowding. Some small studies have shown improvement in both adults and children. 2) dichoptic viewing- the same background is presented in both eyes but enriched for the amblyopic eye. This addresses suppression. A number of studies in different age groups showed improvement but suffered from significant limitations due to design. If the theory is addressing antisuppression a fundamental issue in assessing improvement is the lack of standardization in quantifying suppression. One of the important outcomes of the majority of the studies is that dichoptic viewing conditions may be the important feature rather than the type of game or video viewed. 3) using video games to develop stereopsis. 2015 meta-analysis of behavioral training showed improvement of 0.17logMAR based on all of the case series reported and applied across modalities whether dichoptic, monocular video gaming or perceptual learning. Age was not a factor in determining response. In summary, there are multiple approaches and theories to using video games/videos for amblyopia therapy. The fundamental question is whether or not this is superior to conventional treatment. The most definitive trial to date is a PEDIG trial using dichoptic stimulation vs. patching which found that it was ‘noninferior’ to patching but the trend favored patching. Most studies that included adults showed improvement in these patients which is an
exciting possibility for further research but there is a lack of well controlled RCT’s and most studies should be considered exploratory

**Is the 15Δ Base in Prism Test Reliable for Detection of Amblyopia in Anisometropic Patients?**


A 10 to 20PD base down prism induced tropia test can be used to detect amblyopia by monitoring for changes in fixation. Alternatively, the authors postulate that a 15PD base in prism test can be used to optically induce horizontal strabismus and thus predict the presence of amblyopia. A retrospective case review was conducted on 152 heterophoric children with a median age of 5.4 years. The overall sensitivity of the 15PD base in prism test was 34.3%, specificity 88.0%, positive predictive value 85.4%, and negative predictive value 39.6%. Therefore there was low sensitivity and high false negatives with the 15 PD base in testing. The authors acknowledge that there are several limitations of the study including the unknown effect of the fixation object, comparison of the horizontal prism with prior studies using a vertical prism, and the difficulty of assessing movements in young children. They recommend future prospective studies in order to further evaluate the accuracy of this test.

2.**VISION SCREENING**

**Inability of Open-Field Autorefractration to eliminate Accommodation in Preschoolers.**


The purpose of this study is to evaluate the effectiveness of the Shin-Nippon NVision-K 5001 autorefractometer based on the open-field refractometry principle in refractive measurements of preschool children and to determine its ability to eliminate accommodation adequately. The refractive results of 114 preschool children who presented to the ophthalmology outpatient department for screening were evaluated. The measurements were obtained before and after cycloplegia with the Shin-Nippon NVision-K 5001 autorefractometer and after cycloplegia with retinoscopy, which is the gold standard. The results underwent vectorial transformation to produce the spherical equivalent (M) and two Jackson cross-cylinder (J0 and J45) values. All results were then subjected to statistical analysis. The difference between the measurements was evaluated with repeated measures analysis of variance. Although statistically significantly more myopic results were obtained with non-cycloplegic measurements using the Shin-Nippon NVision-K 5001 autorefractometer (P < .001), no difference was observed in cylindrical values (P > .05). Cycloplegic J0 measurements were significantly lower (P < .001), but no difference was found between J45 values before and after cy-
cloplegia ($P > .05$). The authors conclude that the Shin-Nippon NVision-K 5001/Grand Seiko WR-5100K open-field autorefractometer seems to be inadequate in eliminating accommodation in childhood. Measurements under cycloplegia continue to be the best method to ensure accurate results.

**Outcome of universal newborn eye screening with wide-field digital retinal image acquisition system: a pilot study.**


Universal newborn eye screening is an emerging concept for early intervention of many eye diseases that present at birth. The purpose was to analyze the outcome of this universal newborn eye screening with wide-field digital retinal imaging (WFDRI), assess the cost-benefit margin and compare it with few similar studies reported so far in the literature. Pupillary dilation with a mixture of 2.5% phenylephrine hydrochloride and 0.5% cyclopentolate eye drops. Assessment of red reflex with the help of the illumination from the Ret Cam 130-degree lens; imaging of the external structures of both eyes including eye lids and anterior segments of each eye and entire fundus imaging with five fundus photographs included the posterior pole, including disc and fovea, superior retina-optic disc at the inferior pole of the field of view, inferior retina-optic disc at the superior pole of the field of view, temporal-optic disc at the nasal most part of field of view and nasal retina-optic disc at the temporal most part of the field of view. In addition, the superotemporal, inferotemporal, inferonasal, superonasal quadrant retina were also imaged when required. A total of 1152 babies were examined. Average time to examination was 3.68 days (median: 3.08 days; range 0–21 days). The mean GA and BW were 39.07 weeks (SD: 1.19) and 2.88 kg (SD: 0.46) respectively. Most babies were delivered by lower segment caesarean section (78.4%) Ocular abnormality of any kind was seen in 14.9%, Retinal hemorrhages were the major finding (13.28%); it was of varying severity- superficial, subhyaloid and vitreous hemorrhages. Most were bilateral (77%). Hemorrhages were distributed in all quadrants with varying severity with a tendency to be more around the optic nerve and along the retinal vessels Retinal hemorrhages were seen in 47.6% of babies born by normal vaginal delivery and 5.2% born by LSCS. The majority of the findings were retinal hemorrhages which usually do not require treatment and the ones that required treatment could have been detected by a routine red reflex test too.

**Use of the Spot Vision Screener for patients with developmental disability.**

The aim of this cross-sectional study was to determine whether the Spot Vision Screener effectively detects amblyopia risk factors in patients with developmental disability. Children with developmental disability presenting for complete pediatric ophthalmologic examination were prospectively enrolled between June 2012 and March 2016. The following data were analyzed: presence of amblyopia risk factors according to the AAPOS guidelines, refraction, eye alignment, and other ocular pathology. A total of 100 children (average age, 5.7 years; range, 2.2-9.2 years) were included. The Spot was able to evaluate successfully 91% of the patients enrolled in the study. The prevalence of amblyopia risk factors in this cohort was 38%. The sensitivity of the Spot Vision Screener in detecting amblyopia risk factors was 84%; the specificity, 62%. The positive predictive value (PPV) was 58%; the negative predictive value (NPV), 86%. The authors conclude in their cohort of patients the Spot Vision Screener provided good sensitivity and adequate specificity for a screening examination. Automated screeners may be useful in screening children with developmental disability. Adjustments in referral criteria on the screener may be appropriate for certain patients or subgroups with developmental disability. Further investigation of criteria modifications appropriate for children with disabilities are warranted and may improve the PPV.

Pediatric ophthalmology and childhood reading difficulties:
Overview of reading development and assessments for the pediatric ophthalmologist.

This article is part of symposium on childhood reading difficulties. Reading difficulties are common in the pediatric population, and large socioeconomic disparities exist. In the United States 46% of white children achieved expected reading proficiency by the end of fourth grade, while only 21% of Hispanic and 18% of African American children were reading at the expected level. Reading is an involved cognitive process with many subskills; likewise, development of reading proficiency is a complex and continuous process. Failure to achieve reading proficiency or even early difficulty with reading can affect a child's academic performance for years to come. Some studies suggest reading proficiency may be related to later success in life. Although many problems with reading are not related to vision, a vision assessment is recommended for children with reading difficulties and a suspected vision problem. The process of reading development as well as the varied educational assessments of reading are presented here for pediatric ophthalmologists, who are often called upon to provide baseline evaluation and management recommendations.

Do the near computerised and non-computerised crowded Kay picture tests produce the same measure of visual acuity?
Dawkins, Bjerre Br Ir Orthopt J 2016; 13: 22-28
Tablet computer apps have been developed to assess visual acuity (VA). It has been advocated that the apps could assist in vision screening. The iSight app presents 4 different Kay pictures in a line surrounded by a crowding bar. The validity of the distance iSight pictures as a screening tool has been proven. The goal of this study is to determine the validity of the crowded Kay pictures on the iSight app compared to printed crowded Kay picture testing in amblyopic and non-amblyopic children. The authors found that there was no statistically significant difference between the inter-ocular VA difference for each of the two tests in either the amblyopic or the non-amblyopic participants. The two tests are comparable in their ability to detect amblyopia. The study had a small sample size with a power of only 38%; it also did not assess test-retest variability which can affect validity. The authors conclude that near crowded Kay pictures using the iSight tablet app agreed well with printed near crowded Kay pictures.

**The redevelopement of the Kay picture test for visual acuity**
Milling, Newsham, Tidbury, O'Connor, Kay *Br Ir Orthopt J* 2016; 13: 14-21

In the UK the Kay pictures is the leading assessment for visual acuity (VA) in pre-literate practice. Previous literature has shown that crowded Kay picture testing is repeatable and comparable. The purpose of the study is to validate the design of updated optotypes in the Kay picture acuity tests to improve resolution acuity, recognition of the pictures, repeatability, and comparisons with gold standard logMAR acuity assessments. The study had four phases: compare the adult resolution acuity of 25 picture optotypes, to assess the recognition of these pictures in children, to assess the resolution acuity of the reduced number of picture optotypes, and to compare the final picture selection to current tests and assess the test-retest reliability of the updates Kay pictures acuity test. The study narrowed the 25 optotypes to 6 that had equal resolution acuity and recognition. The authors conclude that the revised Kay picture optotypes were shown to be a repeatable method of pediatric VA assessment, highly comparable with the gold standard ETDRS VA assessment.

**Community vision screening in preschoolers: initial experience using the Plusoptix S12C automated photoscreening camera**

Pediatric vision screening is a practical way of identifying children with potential vision that require more through evaluation. This paper describes the use of the Plusoptix S12C vision screener in the iSee vision screening program in Ontario. The iSee (Ivey Special Eye Examination) vision screening research program provided vision screening for preschool children. Over 9 months, vision screening was provided at 119 child care centers and programs. 1321 children were included in the final analysis, with a mean age of 34.1 months. 80 children (6.1%) were identified with amblyogenic risk factors and referred to an optometrist. Anisome-
tropia was the most common reason for referral (62.5%). 3.0% of screens were inconclusive. Optometrists’ reports were received from 26 of the referred children, of which screening findings were confirmed in 72.0% (although 40 of the referred children were examined by an optometrist by 3 months). The positive predictive value for any risk factor was 81.8%. It was noted that 40 children who were referred did not have any available record of follow-up. The authors conclude that the program was successful in identifying amblyogenic risk factors that otherwise may have gone unnoticed. However the results were likely influenced by the limited number of optometrists’ reports received and limited follow-up.

Final Visual Outcomes and Treatment Received for Children Referred from a UK Primary School Visual Screening Program: A Comparison of An Orthoptic-led Program with Orthoptic-delivered Services.

Long-term studies identifying the visual outcomes of children found to have reduced vision on screening tests have not been performed. The purpose of this study was to examine the treatment received after being identified as having reduced vision at school screening, to identify the level of improvement in vision as a result of treatment and to quantify the amount of time taken to achieve maximum visual acuity. Overall 7807 children were screened during a 11 month period. Eleven percent failed the screen and were referred for further evaluation (319 to General Optometry and 547 to Community Children’s Eye Service). 79.4% of the 547 referred to CCES attended the appointment and 86.4% (375) of these were found to have reduced vision. The majority of these children (82.7%, 310 children) were prescribed glasses. Thirty-one (8.3%) of the 375 were found to have strabismus, with the majority having esotropia. Of the 375 positive referrals, 47 (12.5%) did not present for follow up. At the conclusion of the study, 299 (79.7%) of the 375 with an abnormal vision had normal vision at the completion of treatment. The authors conclude that children who complete the recommended course of treatment have a 93% chance of normal visual acuity in each eye.

Semistructured Observation of Population-based Eye Screening in The Netherlands.

The current screening program in the Netherlands consists of 7 eye exams as part of a population-based, comprehensive, no-cost voluntary screening. These exams are performed at 1, 2, 3, 6-9, 14-24, 36 and 45 months. The authors note that vision screening is only effective at detecting amblyopia due to refractive error in children in whom the vision can be checked. They sought to determine why detection of amblyopia in younger children is low with the current testing methods by performing an observational study evaluating the performance of eye
screening tests. They found that the Hirschberg test, fundus red reflex, and VA were adequately tested in most cases. However the cover-uncover test, alternating cover test, and ocular motility were often performed inadequately. They suggested that the performance of these tests could be improved with extra teaching. Alternatively, they suggest that terminating this part of the screening due to the low effectiveness when performed by untrained general practitioners/pediatricians with limited experience with eye examinations may be indicated.


The purpose of this study is to evaluate the usefulness of the Plus Lens Test and the Spot Vision Screener in detecting high hyperopia in a pediatric population. In this prospective study, 109 children were included and were screened with the Spot and Plus lens test prior to a scheduled pediatric ophthalmology visit. The following data were analyzed: cycloplegic refraction, Plus Lens test result, Spot Vision Screener result, demographic data. The sensitivity/specificity and positive/negative predictive values were calculated for both tests in detecting hyperopia as determined by the “gold-standard” cycloplegic refraction. The study showed that compared to cycloplegic refraction, the Spot Vision Screener sensitivity for +3.50 D hyperopia was 31.25% and the specificity was 100%. For the Plus Lens test sensitivity for +3.50 D of hyperopia was 43.75% and the specificity was 89.25%. Spot vision Screener sensitivity increased with higher degrees of hyperopia. The authors conclude that the Spot Vision Screener as well as the Plus Lens Test demonstrated moderate sensitivity with good specificity in detecting high hyperopia. This is a good study that showed that the above test are only marginally useful in detecting high hyperopia. Further research needs to be done in order to maximize detection of high hyperopia with vision screening.

Comparison of cycloplegic refraction between Grand Seiko autorefractor and Retinomax autorefractor in the Vision in Preschoolers-Hyperopia in Preschoolers (VIP-HIP) Study.

The purpose of this cross-sectional study was to evaluate the agreement of cycloplegic refractive error measurements between the Grand Seiko and Retinomax autorefractors in 4- and 5-year-old children. Cycloplegic refractive error of children was measured using both instruments during a comprehensive eye examination. Accommodative error was measured using the Grand Seiko. The differences in sphere, cylinder, spherical equivalent (SE) and inter-eye vector dioptric distance (VDD) between autorefractors were assessed using the Bland-
Altman plot and 95% limits of agreement (95% LoA). A total of 702 examinations were included; 27% were Hispanic, and 69% were African American. Mean age±SD was 58±5.6 months (range, 45 to 72 months). Compared to the Retinomax, the Grand Seiko provided statistically significantly larger values of sphere (mean difference, 0.34 D; 95% LoA, -0.46 to 1.14 D), SE (mean, 0.25 D; 95% LoA, -0.55 to 1.05 D), VDD (mean, 0.19 D; 95% LoA, -0.67 to 1.05 D), and more cylinder (mean, -0.18 D; 95% LoA, -0.91 to 0.55 D). The Grand Seiko measured ≥0.5 D than Retinomax in 43.1% of eyes for sphere and 29.8% of eyes for SE. In multivariate analysis, hyperopic eyes with SE of >4 D (based on the average of two autorefractors) had larger differences in sphere (mean, 0.66 D vs 0.35 D; P < 0.0001) and SE (0.57 D vs 0.26 D; P < 0.0001) than eyes with SE of ≤4 D. The authors conclude that under cycloplegia, the Grand Seiko provided higher measures of sphere, more cylinder, and higher SE than the Retinomax. Higher refractive errors were associated with larger differences in sphere and SE between the Grand Seiko and Retinomax.

This study provides the largest sample size to date for assessing the agreement between the Grand Seiko and Retinomax autorefractors and the only study for comparing measures of cycloplegic refractive error in young children. Several limitations were raised in the discussion, including: (1) Measurements were always performed with the Grand Seiko first and consequently with the Retinomax, and thus a systemic bias could have been introduced; (2) The study did not include refractive error measurements from cycloplegic retinoscopy, the gold standard for measuring refractive error, and thus it could not make definite inferences on which device provides more accurate measurements of refractive error; (3) Finally, the children examined were limited to those believed to be candidates for the VIP-HIP study based on screening results consistent with emmetropia or moderate hyperopia (3–6 D); therefore, children with severe myopia or astigmatism were under-represented.

Performance of the Spot Vision Screener in Children Younger than 3 Years of Age.

American Academy of Pediatrics advocates for instrument based vision screening beginning at the age of 12 months old, but United States Preventative Services Task Forces states that there is insufficient evidence to recommend vision screening in children less than 3 years old. While there is certainly a large advantage to identify younger children who are at risk for amblyopia, there is also risk of over examining children. The authors sought to determine the use of the Spot vision screener for the detection of amblyopia risk factors in children aged 6 months to 3 years as recommended by the American Academy of Pediatrics to determine the sensitivity and specificity of this screening tool in this age group. This was a reliability analysis of 184 children tested with the Spot vision screener and then had a comprehensive eye exam within 6 months of screening that included a cycloplegic refraction and sensorimotor exam by a pediatric ophthalm-
mologist who was masked to the Spot vision screening results. 89.7% of children had readings obtained by the vision screener and of those the sensitivity was 89.8% and the specificity was 70.4% of detecting amblyopia risk factors. The positive predictive value in the general population was estimated at 43.1% and the negative predictive value was estimated to be 96.5%. This data supports the use of instrument based vision screening in this young age group.

Validation of an instrument to assess visual ability in children with visual impairment in China.


In children with visual impairment, routine assessments such as visual acuity, contrast sensitivity, and visual field may not reveal the true impact on daily activities that the children experience. Other tools such as questionnaires have been developed to better assess impact and outcomes measures after rehabilitation. The Cardiff Visual Ability Questionnaire for Children (CVAQC) is one such tool that focuses on school activities. For this report, the authors translated the original English CVAQC to Mandarin and administered it to children 8-18 with visual impairment (0.3 LogMAR or less). 114 children completed the form. The most common form of visual impairment was infantile nystagmus (43%). 3 questions were removed from the 25-item list due to cultural adaption reasons or missing data. The tool was found to be reliable and easy to administer. Rasch analysis confirmed reliability. There were moderate correlations of the questionnaire with contrast sensitivity and visual acuity. Although the children tested were only from one low vision clinic, the authors conclude that it covers important school aged activities in their population and has the efficacy to monitor visual ability before and after rehabilitation in children.

Normative pediatric data for three tests of functional vision


There are a number of methods to monitor functional vision, although consensus of which to use in a preschool vision screening program is not clear. Normative data ranges for tests may also vary by different tests for a single aspect of functional vision, creating issues with referral criteria. The authors of this study performed a prospective analysis of three different tests for preschool vision screening. Monocular visual acuity was measuring using the PVVAT (Precision Vision Visual Acuity Testing) system, stereoacuity was measured using the Pass Test 3 Stereotest, and refractive error (non-cycloplegic) determined using the PlusoptiX S09 Vision Screener. Mean visual acuity improved from age 3 to 5, with lower limits improving from 0.54 logMAR to 0.32 logMAR. Mean stereoacuity improved from 104 to 81 arsec from 3 to 5 years of age. Mean spherical (0.29D at 3 years, 0.24D at 5 years) and mean cylindrical refractive error (0.39D at 3 years, 0.31D
at 5 years) remain fairly stable. Note that visual acuity scores were worse than those from other studies. Stereoacuity norms were similar to previous studies. Refractive errors, while stable, were lower than those obtained in a previous study using the Welch-Allyn SureSight Autorefractor. However, the lower limits for cylindrical and upper limits for spherical refractive error obtained were in agreement with the manufacturer-suggested criteria. Altogether, the study provides normative data for these 3 tests, which can be used to help establish referral criteria.

3. REFRACTIVE ERROR

Prevalence and Risk Factors

Risk factors for myopia progression in second-grade primary school children in Taipei: a population-based cohort study

The prevalence of high myopia in Taiwan in 18 year-old students increased from 10.9% in 1983 to 21% in 2000. The prevalence high myopia in freshman at National Taiwan University reached 38.4% in 2005. This study explored the progression and risk factors in second graders in Taipei. Data from the Taipei myopic investigation study (MIT) was used. 1-year follow-up data was evaluated in children noted to have myopia on first examination. A total of 3256 children (mean age 7.49 years) were included in the analysis. They found baseline spherical equivalent (SE) of -1.43D. The average change in SE over 1 year was -0.42D. 24.54% of the patients showed fast myopia progression (more than -1.0D change). Fast myopic progression was associated with a greater myopic SE at baseline and a shorter eye-object distance when doing near work (based on questionnaire data). More outdoor activity time was not associated with slow myopia progression. The data suggest that increased distance when doing near work and including short rest between periods of near work could be helpful in decreasing the speed of myopia progression in young children.

Environmental factors explain socioeconomic prevalence differences in myopia in 6-year-old children
Risk factors for myopia include education, ethnicity, and other socioeconomic factors. Higher education has been shown to increase risk, and prevalence rates are high in East Asia. Other lifestyle factors have also been implicated, especially time spent outdoors and certain indoor activities. This study examined whether the differences in myopia prevalence could be explained by lifestyle factors. 5711 six-year old children were included. These children were part of a cohort study called Generation R undertaken in The Netherlands. Visual acuity and refraction were measured, and questionnaires were analyzed for socioeconomic and behavior factors. Myopia was present in 2.4% of children. These children spent more time indoors, had lower vitamin D, higher BMI, and participated less in sports. Other risk factors included non-European descent, low maternal education, and low family income. The authors conclude that environmental factors are strong risk factors for myopia, even at age 6 years. The difference in prevalence among socioeconomic groups were largely explained by environmental risk factors, which can be modified (more outdoor activity) to decrease risk.

**Spectacle Wear Among Children in a School-Based Program for Ready-Made vs Custom-Made Spectacles in India: A Randomized Clinical Trial**


In a school-based eye health program in India, 460 children were randomized to custom-made versus ready-made spectacles. The 23,345 children, ages 11 to 15 years, had a visual acuity screening in an urban school setting and 460 were eligible: 232 for ready-made and 228 for custom-made. At 3-4-month follow-up, the rates of wearing both spectacles types were not statistically significant. In summary, most children were eligible for ready-made spectacles and the proportion wearing them was not inferior to custom-made. In the future, the significant financial burden of custom-made spectacles could be reduced or avoided by using ready-made spectacles for school in India.

**Ocular Biometry and Determinants of Refractive error in a Founder Population of European Ancestry.**


Worldwide, the prevalence of myopia is increasing. According to the National Health and Nutrition Examination Survey, 41% of US adults are now myopic compared to 25% of US adults in the 1970s. By 2050, it has been estimated that nearly half of the world’s population will have myopia, and 10% will have high myopia. Understanding factors that contribute to myopia has become increasingly important to address a growing public health concern. Previous studies have found a positive association between myopia, education, and near activities, while others have noted a negative association with outdoor exposure. This study
reports refractive error and biometry in a founder population of European ancestry, the Hutterites, and discusses risk factors contributing to myopia. As a genetically isolated population with a communal lifestyle, the Hutterites present a unique opportunity to study risk factors for myopia. This is the first epidemiological report of refractive error among the Hutterites. This cross-sectional study included complete eye exams with retinoscopy and biometry. A total of 939 study participants, ages 6 to 89, were examined. Females were significantly more myopic than males (SE $-0.87 \pm 2.07$ and $-0.40 \pm 1.49$ in females and males, respectively, $p < 0.0001$). Males had significantly longer axial lengths, while females had steeper corneas. Hutterite females are more myopic than males, a finding which has only been reported in a few other populations. Hutterite children complete compulsory education through the 8th grade, after which women and men assume gender-specific occupational tasks. Men often work outside on the farm, while women engage in more domestic activities inside. These occupational differences likely contribute to the increased myopia comparing females to males, and their uniform lifestyle reduces the impact of potential confounding factors, such as education and income. In conclusion, the Hutterites are more myopic than most other North American and European populations. Greater time spent doing near work and less time spent outdoors likely explain the increased myopia comparing females to males.

**Reducing the Progression of Myopia**

**Atropine for the Prevention of Myopia Progression in Children: A Report by the American Academy of Ophthalmology**  

This is a literature review of the efficacy of topical atropine for the prevention of myopic progression in children. Literature searches were last conducted in December 2016 in the PubMed database with no date restrictions, but were limited to studies published in English, and in the Cochrane Library database without any restrictions. This resulted in 98 citations, 23 of which were reviewed in full text. Of these, 17 articles were deemed appropriate for inclusion in this assessment and subsequently were assigned a level of evidence rating by the panel methodologist. Seventeen level I, II, and III studies were identified. Most of the studies reported less myopic progression in children treated with atropine compared with various control groups. All 8 of the level I and II studies that evaluated primarily myopic progression revealed less myopic progression with atropine (myopic progression ranging from 0.04±0.63 to 0.47±0.91 diopters (D)/year) compared with control participants (myopic progression ranging from 0.38±0.39 to 1.19±2.48 D/year). In studies that evaluated myopic progression after cessation of treatment, a rebound effect was noted. Several studies evaluated the optimal dosage of atropine with regard to myopic progression, rebound af-
ter treatment cessation, and minimization of side effects. Lower dosages of atro-
pine (0.5%, 0.1%, and 0.01%) were found to be slightly less effective dur-
ing treatment periods of 1 to 2 years, but they were associated with less rebound
myopic progression (for atropine 0.01%, mean myopic progression af-
fter treatment cessation of 0.28±0.33 D/year, compared with atropine 0.5%,
0.87±0.52 D/year), fewer side effects, and similar long-term results for myopic
progression after the study period and rebound effect were considered. All doses
of atropine studied did show reduction in accommodative ability after 2 years of
treatment and 1 year of wash-out period. Studies looked at other parameters
such as effect on ocular biometry, accommodation, and pupil size. Axial length
elongation is reduced in atropine than control groups. In the ATOM 2 trial, there
was an average accommodation reduction of -2.56 D less than that measured at
baseline for all of the atropine groups (0.5%, 0.1% and 0.01%) that showed dose
response. The most robust and well-designed studies were carried out in Asian
populations. Studies involving patients of other ethnic backgrounds failed to pro-
vide sufficient evidence of an effect of atropine on myopic progression. Level I
evidence supports the use of atropine to prevent myopic progression. Although
there are reports of myopic rebound after treatment is discontinued, this seems
to be minimized by using low doses (especially atropine 0.01%).

Update on Orthokeratology in Managing Progressive Myopia in
Children: Efficacy, Mechanisms and concerns.
Xintong Li, Ilana B. Friedman, Norman B.Medow, Cheng Zhang Journal of Pedi-
atric Ophthalmology & Strabismus May/June 2017; 54(3): 142-148

Myopia is an important public health issue, and high myopia may lead to severe
complications if left untreated. Orthokeratology lenses, worn overnight to reshape
the cornea, are one of many recent modalities used to slow down the progres-
sion of myopia in children. This treatment has been proven successful, as evi-
denced by decreased spherical refractive error and axial length relative to con-
trol at interval follow-up ranging from 6 months to 5 years. In this systematic re-
view, the authors collected publishes controlled studies that analyzed the efficacy
of orthokeratology lens wear and calculated longitudinal relative changes in axial
length, revealing a weighted average of -45.1% change in axial length at the 2
year follow-up. The exact mechanism by which orthokeratology lenses reduce
myopia progression is unknown, but research shows that the corneal reshaping
decreases peripheral defocus and therefore increases peripheral myopic defocus
to likely reduce stimuli for axial elongation and subsequent development of myo-
pia. Use of orthokeratology lenses is felt to be generally safe, but cases of asso-
ciated infectious keratitis may have a higher incidence of virulent organisms such
as Pseudomonas, Acanthamoeba, and antibacterial-resistant strains of Staphy-
lococcus, partially due to the required overnight use of these lenses. Or-
thokeratology is regarded as one of the most effective non-pharmacologic
measures to slow down progression of myopia in children and, with regular fol-
low-up to ensure safety, continues to be one of the most effective treatments for
myopia management around the world.
Efficacy and Adverse Effects of Atropine in Childhood Myopia: A Meta-analysis

This was a meta-analysis of 19 studies which included 3137 children in which atropine treatment was effective at slowing the progression of myopia. The authors included randomized clinical trials and cohort studies. The meta-analysis found that all doses of atropine were equally effective at slowing the progression of myopia and high doses of atropine were associated with more adverse effects, such as photophobia. Also, there was not a difference in adverse effects between Asian and white patients. In summary, the results suggest that the efficacy of atropine is dose independent and adverse side effects is dose dependent. This meta-analysis is helpful as the PEDIG (pediatric eye disease investigator group) will launch a study of dilute atropine treatment to slow the progression of myopia in children.

Current Approaches to Myopia Control

The author reviews the various proposed treatments for retarding the progression of myopia. He begins with a discussion of the reason for concern in that high-grade myopia is a leading cause of blindness due to retinal detachment, macular degeneration, premature cataract and glaucoma. There is increasingly early onset and high progression rates. The approach includes to slow the onset and reduce or prevent progression. Outdoor time has been correlated with a decrease in the onset of myopia with ideal exposure 2-3 hours per day. However, this does not decrease progression of myopia. Atropine 0.1% in a large RCT appears to have a good risk-benefit ratio with no clinically significant visual side effects, with a reasonable and clinically significant 50% reduction in myopia progression. Atropine 1% had a greater effect but significant increase in myopia on washout and required photochromic progressive lenses due to dilation of the pupil and poor accommodation. Orthokeratology also appears to slow axial length elongation by about 40% but does have risks of corneal problems. An area for future study is to determine the length of the treatment and when it can be stopped with minimal risk of regression and to make sure that there are no long-term adverse effects.

Miscellaneous

Progression of high anisometropia in children
The purpose of this retrospective study was to investigate the onset and rate of progression of high anisometropia in myopic children younger than 13 years. The study included children with myopia of more than 4.00 diopters (D) in the more ametropic eye and a difference in spherical equivalent refraction of 4.00 D between both eyes. All children had a complete ophthalmologic examination, including measurement of visual acuity and cycloplegic refraction every 3 to 6 months for at least 5 years. Change in the spherical equivalent and the cylindrical error for both eyes and changes in the difference in spherical equivalent refraction between both eyes were calculated for each patient at each visit. Linear, polynomial, logarithmic, and exponential fitting models were tested for both eyes and for the anisometropic difference between both eyes. The regression line with the greatest $R^2$ value was considered best fit. The study showed that sixty-three patients fulfilled the inclusion criteria. The more ametropic eye grew in a regular fashion during the first 2 years of life, followed by a rapid decrease in the rate of growth to become almost stable after 4 years of age. The increase in myopia best fit a third-degree polynomial (cubic) model ($R^2 = 0.98$). The less ametropic eye showed only a small increase in myopia during the follow-up period. The anisometropic difference between both eyes increased gradually during the first 2 years, then remained stable. The authors conclude that high anisometropic amblyopia progresses rapidly before becoming stable.

**Significant Axial Elongation with Minimal Change in Refraction in 3- to 6-Year-Old Chinese Preschoolers: The Shenzhen Kindergarten Eye Study.**

Scarce data are available on ocular biometry on children of preschool age. Early onset emmetropia is a major risk factor for the subsequent development of myopia. This study focuses on biometry of eyes in children 3 to 6 years of age when these measures are poorly understood. The purpose of the study is to understand the biometry changes in this age group and how it correlates to the refractive error change in this cohort. This population-based cross-sectional study included 1255 of Chinese preschoolers 3 to 6 years of age from 8 representative kindergartens in Shenzhen Kindergarten Eye Study. Successful biometric measurements were obtained in 1133 children, and complete cycloplegic refraction was obtained in 1127 children. Biometric measurements including axial length (AL), anterior chamber depth (ACD), and corneal radius of curvature (CR) were obtained from partial-coherence laser interferometry (IOL Master) before cycloplegia. Lens power was derived from the Bennett-Rabbetts method. Lens power (LP) and AL-to-CR ratio were calculated. Cycloplegic refraction (3 drops of 1% cyclopentolate) was measured using an autorefractor (KR8800; Topcon Corp., Tokyo, Japan), and spherical equivalent refraction (SER) was calculated. Biometric and refractive parameters were assessed as a function of age and gender. Multiple regression analysis was performed to explore the associations...
between refraction and ocular biometry. Among the 1127 children (99.5%) with successful cycloplegic refraction, mean SER was 1.37±0.63 diopters (D). Prevalence of myopia increased from 0% at 3 years of age to 3.7% (95% confidence interval, 1.0%-6.5%) at 6 years of age. Biometric parameters followed Gaussian distributions with means of 22.39±0.68 mm for AL, 7.79±0.25 mm for CR, and 24.61±1.42 D for calculated LP; and non-Gaussian distributions with means of 3.34±0.24 mm for ACD and 2.88±0.06 for AL-to-CR ratio. Axial length, ACD, and AL-to-CR ratio increased from 3 to 6 years of age, CR remained stable, whereas LP declined. Overall, SER declined slightly. For the SER variance, AL explained 18.6% and AL-to-CR ratio explained 39.8%, whereas AL, CR, and LP accounted for 80.0% after adjusting for age and gender. In conclusion, young Chinese children are predominantly mildly hyperopic, with a low prevalence of myopia by the age of 6 years. An increase of 1 mm in AL was associated with only 0.45 D of myopic change. Decreases in LP reduce the myopic shifts that normally would be associated with increases in AL, and thus play a key role in refractive development in this age group. However, it’s important to keep in mind that LP is a calculated value based modified Bennett-Rabbetts method.

**Choroidal thickness and ametropia in children: a longitudinal study**

The authors studied the relationship between subfoveal choroidal thickness, refraction, and axial length in 229 eyes of 115 children aged 2 to 16 years. Cycloplegic refraction under cycloplegia, axial length, and subfoveal ChT were measured at baseline and over a 15-month follow-up period. They found that subfoveal choroid was thinner in myopic children, and that subfoveal choroidal thickness was related to axial length. After 15 months of follow-up, subfoveal choroidal thickness had decreased in myopic eyes and increased in nonmyopic eyes. The authors concluded that a thinner choroid may predict the onset, or progression, of myopia, but that additional studies, with longer follow-up, are necessary to confirm this hypothesis. Previous studies have shown the choroid to play an important role in the process of emmetropization. This study contributes to our knowledge of the pathogenesis of myopia, which could aid in the development of future treatments to prevent its occurrence and/or progression.

**Development of Refractive Errors—What Can We Learn From Inherited Retinal Dystrophies?**

This is a case control study of patients with known inherited retinal dystrophies (IRD) in two eye centers in the Netherlands. The reference population was the Rotterdam III population based study patients. The purpose of this study was to
evaluate the refractive errors in patients with IRD. The authors explain that if the retina-to-sclera signalizing cascade causes myopia, and IRDs are caused by dysfunction of a single retinal type, then looking at the affected cell type, causal gene, and refractive errors may provide insight to the causes of myopia. Distributions and mean spherical equivalents were calculated and risks of myopia and hyperopia were calculated. The retinal dystrophies were grouped into those which affect the RPE (Stargardt, Best, pattern dystrophies), cone dominated dystrophies (achromatopsia, cone-rod dystrophies), rod dominated dystrophies (retinitis pigmentosa), and bipolar cell dysfunctions (congenital stationary night blindness). The authors found that bipolar cell related dystrophies (CSNB) were associated with the highest risk of high myopia (-6D or more) (OR = 239.7) followed by cone related dystrophies (OR = 19.5). Bipolar cell related dystrophies were also associated with high hyperopia (+6D or more). Cone dystrophies and retinitis pigmentosa mostly led to mild myopia (-1.5 to -3 D). The authors concluded the bipolar cells may be important in the development of myopia. They looked further into the genes causing bipolar cell dysfunction as well as those which cause high refractive error and found significant overlap. The authors speculate that mutations in the IRD genes can cause retinal dystrophies and genetic variants may cause myopia. The authors point out that this study doesn’t prove causation, and that this is the first systemic evaluation of refractive errors in IRD. Note that this study was not done using pediatric patients, but is relevant to the pediatric ophthalmologist.

A comparison of the conventional and modified push-up methods of measuring the near point of accommodation

Measuring accommodation is used to assess accommodation deficits. It is most commonly performed using a Royal Air Force (RAF) rule subjectively. The near point of accommodation is the point nearest the subject that can be seen clearly and is measured with the RAF rule. This can be done with conventional push-up method of moving a clear target toward a subject until it blurs or the modified push-up method of moving a blurred target away from a subject until it becomes clear. The article compares the validity of the two methods in young visually normal patients. The near point of accommodation was measured monocularly and binocularly for both methods. The conventional push-up method resulted in near points of accommodation slightly closer to patients than the modified push-up method. The difference was found to be statistically significant but not clinically significant. The authors conclude that both methods are accurate, and consistency amongst testing methods is essential for accuracy and standardization.

Dynamic cues to binocular depth
Tidbury, O’Connor, Wuerger Br Ir Orthopt J 2016; 13: 29-34
Patients with stereoacuity deficits when tested clinically often experience 3D volumetric depth when viewing stereoscopic stimuli such as 3D videos. The difference between the clinically measurable stereopsis and patient’s perceived depth perception may be due to limitations of clinical tests. Current clinical testing only measures static binocular disparity. Dynamic disparity is an important tool in detection of motion of depth and determination of shape. Motion in depth contains two binocular clues: changes in disparity over time (CDOT) and interocular velocity differences (IOVD). The experiment compared static versus dynamic conditions on stereopsis measurements while eliminating monocular cues to depth. The study found that dynamic disparity information benefits individual’s depth perception, explaining why a patient without clinically measurable stereopsis can perceive 3D cinema.

Involvement of Multiple Molecular Pathways in the Genetics of Ocular Refraction and Myopia


As the prevalence of myopia has increased worldwide in the last three decades, recent studies have shown that refractive development is influenced by environmental, behavioral, and inherited factors. This review paper analyzes recent progress in the genetics of refractive error and myopia. Genome-wide association and sequencing studies have increased our understanding of the genetics involved in refractive error. Candidate genes have been identified. All genetic loci discovered to date indicate that refractive development is a heterogeneous process mediated by a number of overlapping biological processes. However, the exact mechanisms by which these biological networks regulate eye growth are poorly understood. Several individual genes and/or molecular pathways have been investigated in animal models, but a systematic network-based approach in modeling human refractive development is necessary to understand the complex interplay between genes and environment in refractive error. The authors predict that new biomedical technologies and better-designed studies will continue to refine our understanding of the genetics and molecular pathways of refractive error, and may lead to preventive or therapeutic measures to combat the myopia epidemic.

Development of Refractive Errors—What Can We Learn From Inherited Retinal Dystrophies?


It is known that refractive errors are common in patients with inherited retinal dystrophies (IRD), such as retinitis pigmentosa (RP, in particular in X-linked forms), congenital stationary night blindness, Stargardt disease, and Best macular dystrophy. It is unknown which retinal cells are involved in the retina-to-sclera signal-
ing cascade causing myopia. As IRDs are characterized by dysfunction of a single retinal cell type and have a high risk of refractive errors, a study investigating the affected cell type, causal gene, and refractive error in IRDs may provide insight herein. A total of 302 patients with IRD from 2 ophthalmic-genetic centers in the Netherlands were included in this study. Distributions and mean spherical equivalent (SE) were calculated for main affected cell type and causal gene; and risks of myopia and hyperopia were evaluated using logistic regression. Bipolar cell-related dystrophies were associated with the highest risk of SE high myopia 239.7; odds ratio (OR) mild hyperopia 263.2, both P < .0001; SE -6.86 diopters (D) (standard deviation [SD] 6.38), followed by cone-dominated dystrophies (OR high myopia 19.5, P < .0001; OR high hyperopia 10.7, P = .033; SE -3.10 D [SD 4.49]); rod-dominated dystrophies (OR high myopia 10.1, P < .0001; OR high hyperopia 9.7, P = .001; SE -2.27 D [SD 4.65]), and retinal pigment epithelium (RPE)-related dystrophies (OR low myopia 2.7; P = .001; OR high hyperopia 5.8; P = .025; SE -0.10 D [SD 3.09]). Mutations in RPGR (SE -7.63 D [SD 3.31]) and CACNA1F (SE -5.33 D [SD 3.10]) coincided with the highest degree of myopia and in CABP4 (SE 4.81 D [SD 0.35]) with the highest degree of hyperopia. In conclusion, the authors showed that many genes involved in IRD coincide with myopia. Most genes cause a relatively mild myopia, but several genes causing bipolar cell dysfunctions and RP particularly predispose to high myopia. The authors determined critical sites for refractive error development: transport between inner and outer segment of the photoreceptor, calcium-dependent glutamate release by photoreceptors, and bipolar neurotransmission and routing. These retinal sites are candidates for more in-depth investigation by future functional studies of myopia.

Lower urinary cotinine level is associated with a trend toward more myopic refractive errors in Korean adolescents.


The incidence of myopia has increased worldwide suggesting environmental influences other than genetic factors. For example, the incidence of high myopia of more than 6 D myopia in Korean patients between 13-18 years-old is 8.9%. Previous studies reported on the general roles of acetylcholine signaling through muscarinic and/or nicotinic acetylcholine receptors (nAChRs) and the retinal dopamine signaling pathway regulating ocular emetropization. nAChRs play a role from the earliest stages of development of the vertebrate retina to later stages of neuronal growth and synaptogenesis. Pharmacologic blockade of nAChRs affects the development of form-deprivation myopia. Epidemiological studies have shown an inverse relationship between parental smoking and childhood myopia in Caucasian, Egyptian and Singaporean populations. nAChR signaling would have a potential role to modulate the eye growth and subsequent refractive development. Cotinine, a major metabolite of nicotine is the most appropriate parameter to assess tobacco exposure. Urinary cotinine is an ideal biochemical marker for measuring the level of exposure to tobacco smoke. The purpose of the
study was to assess the association between urinary cotinine refractive errors among Korean adolescents. Korea National Health and Nutrition Examination Survey (KNHANES) is a nationwide, population-based, cross-sectional health examination survey conducted since July 1998 to monitor the general health and nutritional status of the South Korean population. The KNHANES comprises a health interview survey, nutrition survey, and health examination survey. Data from KNHANES between 2008-2011 were used to estimate the association between urinary cotinine levels and refractive errors in Korean adolescents. Mean study population age 15.5 ± 0.1 years. A total of 1139 adolescents aged 12–18 years were included in this study. Spherical equivalents (SE) were calculated as the spherical value plus half of the cylindrical value. Mean refractive errors were −3.1 D, −2.8 D, and −2.2 D in the low (T1), middle (T2), and high (T3) urinary cotinine level groups, respectively (P = 0.002). The prevalence of myopia in subjects with low cotinine levels was 35% mild myopia (−0.5 to −3.0 D), 30% moderate myopia (−3.0 to −6.0 D), and 15% high myopia (more than 6.0 D). A trend toward decreased myopia was observed in subjects with higher urinary cotinine level (P for trend = 0.003). The mean refractive error value was significantly less myopic in subjects with higher urinary cotinine level regardless of adjustment for confounding variables.

The results of this research suggest an inverse association between urinary cotinine level and myopic refractive errors in Korean adolescents. Urinary cotinine level was an independent factor associated with refractive error after adjustment for potential confounding factors, such as age, sex, area of residence, parental income, receipt of national basic livelihood security, physical activity, and serum vitamin D level. Previous studies have suggested a relation between higher hyperopia and parental smoking. The findings support that nAChRs might play a role in human refractive development. Nicotine stimulates retinal angiogenesis, accelerates diabetic retinal changes, alters retinal pigment epithelial cell morphology and function, and modifies electroretinogram responses.

The Response AC/A Ratio Before and After the Onset of Myopia

The purpose of this study was to investigate the ratio of accommodative convergence per diopter of accommodation (AC/A ratio) before, during, and after myopia onset. There were 698 children aged 6-14 years who became myopic and 430 emmetropic children participating in the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error included in the study. The response AC/A ratio of children who became myopic were compared with age-, sex-, and ethnicity-matched model estimates for emmetropic children from 5 years before through 5 years after the onset of myopia, and was found to not be significantly different between the two groups 5 years before onset, then increased monotonically in children who became myopic until reaching a plateau at myopia onset of about
7Δ/D at myopia onset (without further increase) compared to about 4Δ/D for children who remained emmetropic. An increasing AC/A ratio was found to be an early sign of becoming myopic, was related to greater accommodative lag, but did not affect the rate of myopia progression regardless of level of near work. The association with accommodative lag suggests that the AC/A ratio increase was from greater neural effort needed per diopter of accommodation rather than change in the accommodative convergence cross-link gain relationship. Still, nothing predicts future myopia onset better than a child’s current low hyperopic to emmetropic refractive error. However given the data of this study in light of previous studies, accommodative, peripheral refractive, and crystalline lens optical findings in myopia might have a common source: an increasing ciliary muscle dysfunction prior to onset that reaches a maximum at onset. The studies strengths include large size and ethnic diversity of the sample and extensive follow-up. A major limitation was that measurements were done with or without correction based on whether the child brought glasses to the appointment or not.

**Fusional Amplitudes: Developing Testing Standards**

Assessing vergence is an important part of the clinical exam in patients with diplopia, however there is no standardized method of testing. Prior studies by this author found that convergence was affected by encouragement, and divergence was reduced if tested after convergence. Therefore, the author sought to create guidelines for assessing fusional amplitudes. One hundred adult patients with an average age of 38 years (range 20-70 years) with normal vision and binocular function underwent testing of convergence and divergence fusional amplitudes in a modified crossover design study, both with and without encouragement. The author found that divergence should be assessed prior to convergence in the asymptomatic patient and that near amplitudes were significantly higher for both divergence and convergence. She also notes that the amount of effort can be affected by encouragement for convergence but not divergence. There were several limitations to the study, including the fact that only one examiner completed all assessment and was unmasked to the study group. Also, there was a wide age range, but was skewed toward a younger population. Finally, some participants had undergone prior orthoptic evaluations. Regardless of the limitations, the author finds that standardizing vergence testing will allow greater accuracy for future studies.

**Children’s Accommodation to a Variety of Targets – A Pilot Study**
Prior studies show a disparity between the accommodative response and target demand may exist. The accommodative response can be affected by spatial frequency, cognitive demand, contrast, blur and/or proximity clues. The authors sought to establish a normative database of accommodation responses at 1/3 meter to targets with varying complexity and cognitive demand. To complete this study, a remote haploscopic photorefractor was used while presenting 7 different targets at 1/3 meter to 24 children, 18 of whom were 6-7 years old and 6 of whom were 10-11 years old. The authors found that text was found to elicit a significantly higher accommodation response than drawings, cartoons, or individual letters. The text size did not influence the accommodation. The authors conclude that children accommodate as much as necessary to make the target clear, and thus more demanding tasks such as reading elicit a greater accommodative response.

4. VISION IMPAIRMENT


In this longitudinal cohort study, the authors evaluated childhood visual function in the United Kingdom between 1961 and 1986. Of note, the authors used harmonized data sets from the British 1946, 1958, and 1970 national birth cohorts. Complete data was available for 14,283 cohorts at age 15 or 16 years in 1961, 1974, and 1986, respectively. Results indicated that the proportion of children with bilateral normal vision decreased by 1.3% in 1974 and 1.7% in 1986. The risk of overall of impaired vision increased by 1.20 times and the risk of visual impairment/severe visual impairment/blindness by 1.75 times during this period. The authors report that girls were consistently at increased risk of all vision impairment categories. Higher social position at birth and in childhood were associated with reduced risk of visual impairment/severe visual impairment/blindness and unilateral impairment, respectively. In summary, this study provides evidence of temporal decline in childhood visual function between 1961 and 1986. The authors noted a contribution of sociodemographic status to the cohort effect that may be antecedent of the current picture of childhood blindness. At the same time, early-life social position may also have contributed to the current social patterning in visual function in older adults in the United Kingdom. In summary, the authors point out that their findings highlight the potential value of targeting children in national ophthalmic public policies tackling inequalities.
New trends in childhood vision impairment in a developed country.
Pham, C., Sheth, S. J., Keeffe, J. E. and Carden, S. M. J AAPOS. 2017 Dec; 21(6):496-498.
The Education Vision Assessment Clinic (EVAC) is a unique statewide service that reviews school children 4-18 years of age with low vision in Victoria, Australia, to determine their eligibility for educational support. The purpose of this retrospective study was to identify causes of vision impairment in students in Victoria using data from the EVAC. Participants were identified through the EVAC schedule of medical appointments. Medical records were reviewed for clinical and demographic information, including diagnosis of vision impairment and best-corrected visual acuity and/or visual fields. A total of 543 students were included in the study, 355 (65%) were eligible for educational assistance. Of those, 249 (70%) had best-corrected visual acuity between 20/60 and 20/200 and/or a field of vision of <20 degrees to 10 degrees, and 106 (30%) had a best-corrected visual acuity worse than 20/200 and/or a field of vision of <10 degrees. Common causes of vision impairment were retinal dystrophies (24%), optic nerve pathology (14%), albinism (14%), and infantile motor nystagmus (10%). The authors conclude that treatable and potentially preventable causes of vision impairment, such as retinopathy of prematurity and cataract, caused <10% of vision impairment cases in Victorian school children. Analysis of demographic trends is essential to supporting efforts to ensure that students with low vision, from any socioeconomic background, receive specialist teaching services. The trends presented in this Australian study contrast with previous American epidemiological studies that demonstrated slightly different causes of childhood blindness in the United States, which cortical visual impairment, optic nerve hypoplasia, and retinopathy of prematurity.

Reading difficulties and the pediatric ophthalmologist.
This article is part of symposium on childhood reading difficulties. Approximately 20% of children have dyslexia, a language-based reading disability. A variation in language processing in the brain leads to a deficit in phonological (auditory) processing, which leads to problems in learning to read, write, and spell. Myths continue to exist regarding dyslexia and vision, and although eye and vision problems may coexist with dyslexia, they are not more prevalent than in the general population. Rarely vision problems may make reading at near very difficult and may masquerade as a learning problem or attention deficit disorder/attention deficit hyperactivity disorder. The pediatric ophthalmologist can play a valuable role in determining whether any eye or vision problems exist that might interfere with learning or reading. Treatments to improve these eye conditions may help make reading more comfortable, but they are not a therapy for coexisting dyslexia. The use of vision therapy has never been shown scientifically to be effective and may prevent the application of effective interventions during the critical period of development when reading disorders can best be remediated. The pediatric ophthalmologist should educate parents about reading and dyslexia and provide
prompt referral to professionals who have expertise in evaluating and treating learning disabilities. This comprehensive review discusses different aspects of dyslexia, its signs and its management. Early diagnosis is emphasized for better prognosis.

**Audible Image Description as an Accommodation in Statewide Assessments for Students with Visual and Print Disabilities**


Image description has been identified as an accommodation for presentations in the classroom setting, but has been approved by only a few U.S. states for use in high-stakes assessments. This study examined the use of audible image description as an assessment accommodation for students with visual and print disabilities by investigating student comprehension under multiple conditions. Students in 3 western states in grades 3 – 8 who had visual (n=117) or print (n=178) disabilities participated in an abbreviated test constructed of retired assessment questions in English language arts, mathematics, and science, under conditions with and without standardized descriptions of graphic images. A within-subjects block design was used to collect and compare comprehension data under conditions where audible image description was used and not used in an abbreviated test. Students who read braille were more likely to respond correctly under the audible image description condition, and students with visual and print disabilities who used print were equally likely to respond correctly regardless of condition.

One limitation of this study is that the total number of braille readers was only 28. It is possible that replicating the study on a larger scale could yield different results. Also, the test was administered in the November – February time frame and thus some students may not yet have been exposed to the concepts prior to testing. Nevertheless, as agencies take steps to include image descriptions in their assessment accommodations, the authors suggest that teachers might want to develop a standard method for describing images and familiarize their braille readers by including the strategy in instruction and classroom tests.

**Bridging the Gap Between Physical Therapy and Orientation and Mobility in Schools: Using a Collaborative Team Approach for Students with Visual Impairments**


This paper explores transdisciplinary collaboration and role-release strategies that would allow physical therapists and orientation and mobility (O&M) specialists to more effectively support students with visual impairments and additional disabilities with their expanded core curriculum (ECC) goals. The public and spe-
cialized school special education documentation for 20 school-age students was retrospectively examined. The authors sought to understand current practice patterns of both O&M and physical therapy professionals who work with students who are visually impaired with additional disabilities, and they suggest ways in which educational team members from both disciplines can work together toward common goals for their students. They emphasize the importance of a collaborative approach, but admit that a lack of support individually, interpersonally, and organizationally may make successful implementation difficult, along with added time constraints, professionals' attitudes toward sharing skills and knowledge, lack of communication between team members, and insufficient implementation training. Study limitations include a small number of subjects and no interaction with students or teachers.

**Implementation of Unified English Braille by Teachers of Students with Visual Impairments in the United States**


141 teachers of students with visual impairments in the United States completed an online survey during spring 2016 regarding their experiences about the implementation of Unified English Braille (UEB). Although most respondents knew if their state had a UEB transition plan, few participated in its development. Half attended workshops to learn about word-based UEB, but few attended workshops about math-based UEB. The teachers generally believed that their students would be successful in transitioning to word-based UEB, but were less certain about the transition to math-based UEB. Urgent issues that were identified by the teachers that participated in the survey included the need for additional clarification on the relationship between math-based UEB and the Nemeth Braille Code for Mathematics and Science Notation, an increased capacity of math-based UEB training, and clear instruction for high-stakes testing. Although this study may be subject to response bias due to its voluntary survey design, the authors argue that as UEB is implemented and the Nemeth code maintained as well, future studies, workshops, and resources are needed to ensure that braille users have the knowledge and materials needed to be literate in all aspects of UEB.

**Effects of Contrast Sensitivity on Colour Vision Testing**

Anvesh Annadanam, Jiawei Zhaoa, Jiangxia Wangb, and Allen O. Eghrari *Neuroophth.* Aug 2017; 41(4): 182-186

This study analyses how contrast sensitivity loss affects color vision (CV) testing. Eleven participants were scored while cycling through randomly arranged pictures of CV tests with varying levels of contrast changes applied. Hardy-Rand-Rittler (HRR) scores declined significantly at each successive decrease in con-
Bilateral childhood visual impairment: child and parent concerns.

The purpose of this observational descriptive study was to identify specific health-related quality of life and visual function concerns affecting children with bilateral visual impairment as expressed by the children or one of their parents (proxy) and concerns affecting the parents themselves. A total of 37 children <16 years of age with visual impairment (visual acuity worse than 20/70 in the better eye) and one parent for each child were prospectively enrolled. Semi-structured individual interviews were performed with children 5-15 years of age (n = 16) and with one parent for each child (ages 0-15 years, N = 37). Interview transcripts were analyzed using NVivo software. Categories of concern were identified from both child and parent interviews, from which broad themes were identified. The frequencies of the themes and specific categories of concerns were calculated. Regarding the child's experience, categories of concern were grouped into 6 themes: visual function (expressed by 13 of 16 children [81%] and 33 of 37 parents [89%]), treatment (63% and 54%), emotions (50% and 68%), social (50% and 70%), physical discomfort (50% and 22%), and worry (38% and 8%). Concerns expressed regarding the parents' own experience were grouped into 5 themes: worry (100%), compensate-adjust for condition (89%), treatment (84%), emotions (81%), and affects family (46%). The authors conclude that individual interviews in their cohort of patients identified a wide spectrum of concerns in children with visual impairment and their parents, affecting functional, emotional, social and physical domains. These specific concerns will be used to develop patient-derived questionnaires for quantifying the effects of visual impairment on children and parents in everyday life.
A detailed description of the questions used in the interviews, patient characteristics and detailed concerns are presented in the article.

Visual Function 20 Years After Childhood Hemispherectomy for Intractable Epilepsy.

Hemispherectomy for intractable epilepsy has been performed for over 85 years. While motor, speech, cognitive, language, and behavioral outcomes have all been studied, the long term visual consequences of childhood hemispherectomy...
have not been well described. This is a case series of six adults who had a childhood hemispherectomy with a mean post operative period of 21.5 years. The authors compared visual acuity, visual field height, global RNFL thickness and prVEP amplitude by full and half field stimulation in each eye. All participants had the expected homonymous hemianopia and additionally had the residual field constricted when compared to normative data. The midline field crossed into the blind hemifield in 11 of 12 eyes and was confirmed by VEP. The height of the visual field was smaller in the eye contralateral to the side of the surgery compared to the ipsilateral eye and the authors hypothesized that this might be because of the greater representation of macular function on the contralateral cortex, because of tropic preservation of the macular ganglion cells across the vertical raphe, or because of strabismic amblyopia. Four of the 6 patients had a divergent strabismus and none had strabismus surgery. This is thought to be due to the potentially advantageous nature of exotropia in enlarging the visual field with the sacrifice of binocularity. The authors highlight the limitations being the small number of patients in the study and the bias of left hemispherectomies. Additionally not all patients had monitoring in all modalities.

**Visual discrimination training improves Humphrey perimetry in chronic cortically induced blindness**


This study employed the use of visual discrimination training in an attempt to improve visual fields in the blind hemifield of patients with homonymous hemianopia. The authors found that visual discrimination training in patients improved visual field area on average 92 degrees² more than untrained individuals. It is proposed in this study that visual discrimination training is able to reduce the size of visual field defects in patients with hemifield defects from cortical lesions. The amount of training received was proportional to the effect seen. It is unclear how this training improves patients’ performance on visual field testing. The authors propose that this training may be more dependent on koniocellular response, which is thought to be more involved in the extrageniculostriate pathway.

**Visual Impairment in Preschool Children in the United States: Demographic and Geographic Variations From 2015 to 2060**


This was a prevalence study to examine what the projected prevalence of visual impairment (VI) would be for children in 2060. According to the authors, 26% of school-age children will have visual impairment in 2060, 69% resulting from uncorrected refractive error and 25% of children with bilateral refractive amblyopia. The authors evaluated states such as California, Texas, and Florida, which they predict will have the largest increase in VI for children between 3 to 5 years old. In addition, the authors evaluated demographic variables, such as race, ethnicity in the context of VI in preschool children. In summary, vision screening for refrac-
tive error will continue to help prevent VI in preschool-age children, especially among children from minority populations.

**Oral Braille Reading Decoding Strategies of Middle School Students Who Are Blind or Have Low Vision**


In addition to learning letters, sounds, grammar, and spelling, braille readers must learn nearly 200 contractions and composition signs and the rules for using such symbols. This study was conducted as collaborative action research involving two teachers of students with visual impairments (TVIs) that teach at a residential school for students with visual impairments, and one university professor. Over an 8 week period, 3 middle school students participated in lessons focused on oral reading of braille with their TVIs 2 – 3 times per week. During the lessons, the teachers documented decoding errors, supported students in the use of decoding strategies, and provided further literacy instruction as needed. Over the course of the study, the TVIs utilized the data that they collected to reflect upon and adjust their instructional practices. The nature of word errors varied greatly among the students. The decoding strategies used were most often text-based, but reader-based strategies were employed as well. Throughout the study, both TVIs gained insight to inform their own instruction and also to guide the practice of others. The authors conclude that the analysis of decoding errors and strategies should be utilized in designing individualized reading instruction. They suggest that future research should focus more specifically on the types of errors that students make while reading, and should consider whether decoding and instructional strategies have a positive impact on reading.

**The Influence of Need-Supportive Teacher Behavior on the Motivation of Students with Congenital Deafblindness**


Research has indicated that need-supportive learning environments (in which teachers provide structure, autonomy support, and involvement to support their students’ psychological needs for competence, autonomy, and relatedness) positively influence students’ motivation. This study aimed to explore whether teachers of students with congenital deafblindness provide such an environment and how they adjust their need-supportive teaching to these students. An analysis of teacher-student interactions was conducted using a multiple-case-study design. Videos of interactions of 4 teacher-student pairs were analyzed from the perspective of self-determination theory. The results suggested that successful need support for this group requires careful adjustments for each individual student, and only if the provision of structure, autonomy support, and involvement is tai-
lored to the student can a positive influence on motivation be noticed. It was also found that teachers provide more structure and involvement than autonomy support. Although this was a small study, the results suggest that need-supportive teaching is important in the education of students with congenital deafblindness. Video analysis enabled the demonstration of teaching strategies that led to greater student motivation, and practical insights were gained that teachers can use to create need-supportive learning environments for these students.

**Insights into the Feelings, Thoughts, and Behaviors of Children with Visual Impairments: A Focus Group Study Prior to Adapting a Cognitive Behavior Therapy-Based Anxiety Intervention**


Anxiety is the most common psychological problem reported among children with visual impairments. Although cognitive behavior therapy interventions have proven successful in treating childhood anxiety, it is unclear whether they are suitable and accessible for children with visual impairments. This study aimed to determine if and how traditional cognitive behavior therapy-based interventions could be adapted for use with this population. 16 children with visual impairments (aged 9 – 13 years) attending two special schools in the Western Cape, South Africa, participated in 2 focus group interviews. Three primary themes emerged from the focus group data: 1) difficulties encountered by children with visual impairments, 2) existing coping strategies, and 3) insight into the concepts of feelings, thoughts, and behaviors (central to cognitive behavior therapy). The study was limited by a small sample size. In addition, older children were more confident in talking and sometimes talked over the younger children. However, these results provide practitioners with guidelines to consider when using or adapting therapeutic techniques such as cognitive behavior therapy for children with visual impairments.

**Adaptation of a Developmental Test to Accommodate Young Children with Low Vision**


This study analyzed the effects of accommodations for children with low vision in the Griffiths Mental Development Scales Extended Revised (GMDS-ER). 25 children with low vision and chronological ages between 28 – 76 months were assessed in two phases: first, the Griffiths Scales were administered according to the procedures described in the manual, and 2 – 4 weeks later a second assessment was performed with the same instrument that had been adapted for low vision. There were significant improvements of scores in the subscales of lo-
comotor, language, and performance, as well as in the full scale with the use of item accommodations for children with low vision. A combination of accommodations including materials, administration conditions, and success criteria generated the best results. This study was limited by a small sample size. Also, lack of a control group assessed twice with the standard instrument made it difficult to rule out the influence of maturation or familiarity with the instrument. The type of visual impairment and presence of developmental delays was also not controlled. Nevertheless, the authors encourage test developers and test users to consider accommodations for young children with low vision to more precisely describe the developmental level and adjust interventions to each child’s abilities. A more accurate developmental assessment of a child’s competencies and difficulties may also be useful in determining eligibility criteria for special education services.

**Infant viewing of social scenes is under genetic control and is atypical in autism**


Social visual engagement is pathognomonically impaired in autistic children. Evidence shows that autism is among the most highly heritable neuropsychiatric conditions. This study examined concordance patterns in how children visually engage in social interactions. Preferential attention and the timing, direction, and targeting of individual eye movements are strongly influenced by genetic factors. The authors found a high monozygotic twin-twin concordance in eye-tracking experiments (0.75-0.98) versus dizygotic twin-twin concordance (0.00-0.60). Monozygotic twins also have greater probability of shifting their eyes at the same moment in time and in same direction. The characteristics that are most highly inheritable, preferential attention to eye and mouth regions of the face, are decreased in children with autism (P<0.0001). According to the authors the findings underscore the notion that social visual engagement constitutes a neurodevelopmental endophenotype, for autistic children ad population-wide variation in goal-directed seeking and valuation of social information.

**International practice in care provision for post-stroke visual impairment**


Visual impairment after stroke occurs in more than half of patients due to ocular and cortical damage. The authors sought to gain a consensus on what the visual complaints were and how they were identified, treated and followed by orthoptists. An online 30 question survey was administered to orthoptists contacted via the International Orthoptic Association during a 3 month period. 134 individuals from 16 countries completed the survey. The majority (87%) routinely assessed stroke survivors, relying on the use of Snellen charts, cover testing, stereopsis,
fusional abilities, and visual fields to complete their assessment. The most common issues were reading difficulty, visual field changes or blurred vision. The most common interventions were vision advice, functional advice, reading strategies, prisms to treat diplopia, monocular patching and refraction. The average follow up period was less than 3 months. The authors believe these results may guide the development of a core set of outcome measures to assess visual function in stroke survivors.

**Are all children with visual impairment known to the eye clinic?**

There is evidence that children with special needs are more likely to have visual issues, and in the UK there is a widespread program of vision screening in schools. However, the screening is not fully developed in special needs schools and prevalence data in some studies relied upon parental reporting. This study obtained outpatient records for all children at local special schools in Bradford, England, and performed visual assessments on site by an orthoptist or pediatric ophthalmologist. Referrals were made to the hospital eye service if they identified significant refractive error, severe visual impairment, or decreased acuity with unreliable refraction. The hospital eye service repeated acuity assessments, refraction, and performed fundus examination. 157 children were assessed, 31% of which had significant refractive error. 6 children had severe visual impairment (VA <3/60). The authors conclude that children with special needs can have undiagnosed visual impairment, and that visual screening/assessments done in-school can be valuable. Efforts to ensure follow-up to referred specialists (as there was a high proportion in the study who did not attend their eye clinic referral) should be explored.

**5. NEURO-OPHTHALMOLOGY**

**Accuracy of Diagnostic Imaging Modalities for Classifying Pediatric Eyes as Papilledema Versus Pseudopapilledema**

The authors conducted a prospective observational study comparing diagnostic imaging modalities for classifying papilledema (PE) or pseudopapilledema (PPE) in pediatric eyes. Classification of PE and PPE were based on clinical diagnosis with aide of imaging modalities. Not all children had MRI or lumbar puncture. Nineteen children between the ages of 5 and 18 years were recruited from pediatric and neuro-ophthalmology clinics from Sept 2015 to February 2017. Five children (10 eyes) with PE, 11 children (19 eyes) with PPE owing to suspected buried optic disc drusen (ODD), and 3 children (6 eyes) with PPE owing to superficial ODD were included. All subjects underwent imaging with B-scan ultrasonography, fundus photography, autofluorescence, fluorescein angiography (FA),
optical coherence tomography (OCT) of the retinal nerve fiber layer (RNFL), and volumetric OCT scans through the optic nerve head with standard spectral-domain (SD OCT) and enhanced depth imaging (EDI OCT) settings. Images were read by 3 masked neuro-opthalmologists, and the final image interpretation was based on 2 of 3 reads. Image interpretations were compared with clinical diagnosis to calculate accuracy and misinterpretation rates of each imaging modality. Fluorescein angiography had the highest accuracy (97%, 34 of 35 eyes, 95% confidence interval 92%-100%) for classifying an eye as PE or PPE. FA of eyes with PE showed leakage of the optic nerve, whereas eyes with suspected buried ODD demonstrated no hyperfluorescence, and eyes with superficial ODD showed nodular staining. Other modalities had substantial likelihood (30%-70%) of misinterpretation of PE as PPE. The authors concluded that the best imaging technique for correctly classifying pediatric eyes as PPE or PE is FA. Other imaging modalities, if used in isolation, are more likely to lead to misinterpretation of PE as PPE, which could potentially result in failure to identify a life-threatening disorder causing elevated intracranial pressure and papilledema. It is important to note that the authors used intravenous fluorescein administration in all patients included in this study. Oral FA may have less sensitivity.

Visual and ocular motor outcomes in children with posterior fossa tumors.

The aim of this retrospective study was to describe the clinical characteristics and visual and ocular motor outcomes of pediatric patients treated for tumors of the posterior cranial fossa. The medical records of all patients with posterior fossa tumors evaluated by the ophthalmology services at two large tertiary care academic hospitals between 2005 and 2011 were reviewed retrospectively. A total of 139 patients were included. Visual outcomes were categorized as "good" (bilateral acuity of 20/20-20/40) in 101 patients (72.7%), "fair" (<20/40-20/200 in one or both eyes) in 12 patients (8.6%), or "poor" (<20/200 in one or both eyes) in 9 patients (6.5%). Thirteen patients (9.4%) had optic atrophy on their post-treatment examination. Patients with medulloblastoma and ependymoma had a significantly greater risk of a poor or fair visual outcome than those with juvenile pilocytic astrocytoma (JPA) (both P < 0.05), independent of age and sex. Thirty-two patients (23.0%) developed nystagmus, and 59 patients (42.4%) developed strabismus. Twenty-four patients (17.3%) underwent eye muscle surgery for persistent strabismus. The authors concluded that the majority of patients had good visual outcomes, although ocular motor abnormalities were common. Tumor type was a significant risk factor for permanent vision loss. While JPA tends to be a slow-growing tumor that is often fully resectable without the need for adjuvant treatment, ependymoma and medulloblastoma have much more aggressive growth patterns. This relatively large cohort of patients gives us an insight to the visual prognosis of these tumors.
Pupillary measurements and anisocoria in Chinese preschoolers 3-4 years of age screened using the plusoptiX A12C.

Causes of anisocoria range from physiologic to life threatening. According to previous reports, approximately 15%-20% of normal individuals have physiologic anisocoria. Portable infrared pupillometers can objectively measure pupil size and pupillary reflexes. This analysis is part of the ongoing prospective population-based Yuhuatai Pediatric Eye Disease Study (YPEDS). The purpose of this cross-sectional, population-based study conducted in Chinese children aged 3-4 years in Nanjing, China, was to evaluate the distribution of the pupil diameter and distance and the incidence of anisocoria in this age group. The assessment was conducted using the Plusoptix photo screening tool without cycloplegia. Additional assessments were conducted, including light reaction test, re-evaluation for anisocoria (in dim and bright light), swinging-flashlight test, and cocaine test, if necessary. A total of 1,818 children were screened. The pupil diameters of both eyes of each individual were highly correlated (5.9 +/- 0.7 mm in both eyes; P < 0.0001; r = 0.93). The mean interpupillary distance was 50.1 +/- 3.1 mm. The pupil diameters (6.0 mm in boys; 5.8 mm in girls) and interpupillary distance (50.6 mm in boys; 49.5 mm in girls) were correlated with sex (all P < 0.0001) but not age (P = 0.22; P = 0.68). General anisocoria of 0.5-0.9 mm in 7.8% of children and 1.0-1.2 mm in 0.4% of children was found. No child was diagnosed with pathological anisocoria, craniofacial trauma, or congenital malformation syndrome. The authors conclude that the Plusoptix photo screener is a useful tool for obtaining pupillary measurements and detecting anisocoria in a screening setting. Despite some limitations of the study such as a high dropout rate of almost 20%, the study demonstrates the advantages of using photo screeners, such as the Plusoptix A12C, MTI, and iScreen, which can combine the screening of amblyopia risk factors with the detection of anisocoria, requiring minimal cooperation from children. However, the variability of the measurements provided by the Plusoptix make it only applicable in screening setting rather than in the clinical setting.

Increased Mortality and Comorbidity Associated With Leber’s Hereditary Optic Neuropathy: A Nationwide Cohort Study.

Leber’s hereditary optic neuropathy (LHON) is a mitochondrial genetic disease in which optic neuropathy is considered a key feature. Several other manifestations of LHON have been reported; however, little is known of their incidence and the life expectancy in LHON patients.
This study, based on Danish nationwide health registries, included 141 patients diagnosed with LHON and 297 unaffected family members in the maternal line. The incidence of comorbidities and mortality for patients with LHON and unaffected family members was compared with that in the general population. Having LHON was associated with an almost 2-fold risk of mortality with a rate ratio (RR) of 1.95 (95% confidence interval [CI]: 1.47-2.59; P < 0.001). The incidence of several diseases was increased for LHON patients, but not for family members. The incidence of stroke was 5.73 per 1000 patient-years for LHON patients compared to 2.33 for the general population, and the RR was 2.38 (95% CI: 1.58-3.58; P < 0.001). The incidence of demyelinating disorders was 2.24 compared to 0.21 for the general population; RR was 12.89 (95% CI: 6.70-24.77; P < 0.001). A 4-fold risk of dementia was seen for LHON patients (RR: 4.26, 95% CI: 1.91-9.48; P < 0.001), incidence 1.45 for LHON and 0.37 for the general population. Moreover, LHON patients had an increased risk of epilepsy, atherosclerosis, nerve symptoms, neuropathy, and alcohol-related disorders. The manifestation of LHON was associated with increased mortality and increased incidence of several disorders including stroke, demyelinating disorder, dementia, and epilepsy.

**No evidence of disease activity is associated with reduced rate of axonal retinal atrophy in MS**

This longitudinal cohort study evaluated retinal nerve fiber layer (RNFL) thickness in patients with multiple sclerosis. Patients were evaluated with OCT, VEP, disability scores at onset and at 2 years, and with annual MRI. The authors controlled for baseline disability score, RNFL thickness, disease duration, and MS subtype. Patients who developed optic neuritis after the initial evaluation were excluding from analysis. Patients with disease activity had a -2.83 micron RNFL thickness decrease compared to patients with no evidence of disease activity with a -0.93 micron decrease. This study would benefit from a control group without MS to define physiologic RNFL thinning. Further study of the use of OCT in evaluation and prediction of disease activity and severity is needed.

**Optic nerve head edema among patients presenting to the emergency department**

The authors performed a cross-sectional analysis of patients who had optic nerve head edema (ONHE) in the prospective Fundus Photography vs Ophthalmoscopy Trial Outcomes in the Emergency Department (FOTO-ED) study. Nonmydriatic fundus photographs were performed in all patients presenting to the emergency room with headache, neurologic deficit, vision loss, or elevated blood
pressure. Comparisons of patients with ONHE and without ONHE were performed. One in 38 patients (2.6%) of patients presenting to the emergency room with headache, neurologic deficit, vision loss, or elevated blood pressure had ONHE. Final diagnoses for these patients were IIH (19/37), CSF shunt malfunction/infection (3/37), optic neuritis (3/37), brain tumor (2), cerebral venous sinus thrombosis (2), malignant hypertension (2), non-arteritic anterior ischemic optic neuropathy (2), cerebral infarction (1), meningitis (1), neurosarcoidosis (1), and retinopathy (1). A life-threatening diagnosis was made in 8 (22%) patients. Patients with ONHE were more likely to be admitted, stay longer in the hospital, undergo brain imaging, more likely to have abnormal brain imaging, and were more likely to be referred to other physicians, and more likely to be evaluated by neuro-ophthalmology. The authors estimate that of the >3 million patients to come to the ER for headache, 90,000 would have ONHE. The authors suggest that more widespread routine use of non-mydriatic fundus photography in the emergency room will make it easier for non-ophthalmologists to evaluate the fundus for ONHE.

Optical coherence tomography identifies outer retina thinning in frontotemporal degeneration

This is a cross-sectional study evaluating SD-OCT of the macula in patients with frontotemporal dementia (FTD). The authors propose that photoreceptor abnormalities may be present in patients with FTD tauopathy since tau is a microtubule-associated protein. Patients with Alzheimer’s disease (AD) were excluded from the FTD group by evaluating CSF for tau β-amyloid. Patients with AD have previously been demonstrated to have inner retinal thinning. The control patients included in this study had significant demographic differences to the patient group, however when age, sex, and race matched, the authors found that patients with FTD did have thinner outer retinal layers compared to controls. The authors propose that outer retinal thickness may be used as a biomarker for FTD.

Population-based study of ischemic stroke risk after trauma in children and young adults

This study evaluated the epidemiology of ischemic stroke following trauma in a population-based longitudinal cohort study. The authors identified cases of ischemic stroke in the pediatric population within four weeks of trauma, and compared them to 3 controls per case. After adjusting for demographics and trauma severity, head and neck injuries were found to have an odds ratio of ischemic stroke of 4.1 and 5.6 respectively. The authors conclude that stroke risk is ele-
vated for 2 weeks after trauma. This article is important for the practicing ophthalmologist as we often see children and young adults following head and neck injuries with various traumatic injuries. The ophthalmologist may see these children with transient vision loss or Horner syndrome following trauma due to carotid dissection.

**Oral fluoroquinolones and risk of secondary pseudotumor cerebri syndrome**

This is a case-control study where cases were identified in a database. These cases had received a new ICD-9 code of pseudotumor cerebri syndrome after receiving a prescription for a fluoroquinolone. Also required for cases were CPT codes for an MRI or CT of the brain and lumbar puncture within 15 days of the ICD-9 code for pseudotumor cerebri syndrome. Ten controls were chosen for each case that were matched by age, sex, etc. The authors found an increased risk of pseudotumor cerebri syndrome in patients who received fluoroquinolones with a relative risk of 5.62 for patients receiving fluoroquinolones within 15 days, and 4.02 for within 30 days. The authors estimate that approximately 30% of cases of pseudotumor cerebri syndrome may be attributed to fluoroquinolone use. One weakness of this study is its dependence upon diagnostic codes. A strength is its large sample size.

**Prognostic relevance of MOG antibodies in children with an acquired demyelinating syndrome**

This study evaluates the prognostic implications of a positive MOG antibody in children with demyelinating disease. Anti-MOG antibodies have been found in acute disseminated encephalomyelitis (ADEM), aquaporin-4 antibody negative neuromyelitis spectrum disorder (NMOSD), recurrent optic neuritis, transverse myelitis, and multiphasic acute disseminated encephalomyelitis (MDEM). This study looked at the prevalence and predictive value of a positive MOG antibody in children with clinical and MRI features at onset and at 2 years. Patients with MOG antibodies were confirmed to tend to have a non-MS like course. Recurrent demyelination was associated with female sex, MOG antibody positivity, and older age. 31% (65/210) children with an acquired demyelinating syndrome had a positive MOG antibody. 34/60 children initially diagnosed with ADEM had a positive MOG antibody. 40/65 (61%) of children with a positive MOG antibody had a monophasic disease course. Persistent elevation of MOG antibody titers was associated with disease recurrence. This is an important study that can help with the prognosis and outcome of demyelinating presentation in children with MOG antibody positivity.
Optic Nerve Hypoplasia Is A Pervasive Subcortical Pathology of Visual System in Neonates

Optic nerve hypoplasia (ONH) is the most common cause of childhood congenital blindness in developed nations and its prevalence is growing, yet the fundamental pathobiology of ONH remains unknown. The objective of this study was to employ a ‘face validated’ murine model to determine the timing of onset and the pathologic characteristics of ONH. Based on the robust linkage between X-linked CASK haploinsufficiency and clinically diagnosed ONH, the authors hypothesized that heterozygous deletion of CASK (CASK\(^{+/-}\)) in rodents would produce an optic nerve pathology closely recapitulating ONH. They analyzed the entire subcortical visual system in female CASK\(^{+/-}\) mice using immunohistochemistry, anterograde axonal tracing, toluidine blue staining, transmission electron microscopy, and serial block-face scanning electron microscopy. CASK haploinsufficiency in mice phenocopied human ONH with complete penetrance, thus satisfying the ‘face validity’. The optic nerve in CASK\(^{+/-}\) mice was not only thin, but also comprised of atrophic retinal axons and displayed reactive astrogliosis. Myelination of the optic nerve axons remained unchanged. There was a significant decrease in retinal ganglion cell (RGC) numbers and perturbation in retina-thalamic connectivity. This mouse model was used to define the onset and progression of ONH pathology, demonstrating for the first time that optic nerve defects arise neonatally in CASK\(^{+/-}\) mice. Optic nerve hypoplasia is a complex neuropathology of the subcortical visual system involving RGC loss, axonopathy, and synaptopathy and originates at a developmental stage in mice that corresponds to the late third trimester development in humans. This mouse model may be useful for testing therapeutic interventions in the future. In addition this study provides some evidence that ONH and optic nerve atrophy may have similar pathology, just differing in timing. A better understanding of ONH may also help unlock the pathophysiology of other neurodevelopmental disorders, such as autism.

Increased Mortality and Comorbidity Associated With Leber’s Hereditary Optic Neuropathy: A Nationwide Cohort Study

This study aimed to determine the incidence of comorbidities associated with Leber’s hereditary optic neuropathy (LHON), a mitochondrial disease genetic disease, as well as life expectancy in these patients. The study was based on Danish nationwide health registries, and included 141 patients diagnosed with LHON and 297 unaffected family members in the maternal line. Having LHON was associated with an almost 2-fold risk of mortality with a rate ratio (RR) of 1.95 (P < 0.001). The incidence of stroke was 5.73 per 1000 patient-years for
LHON patients compared to 2.33 for the general population, and the RR was 2.38 (P < 0.001). The incidence of demyelinating disorders was 2.24 compared to 0.21 for the general population; RR was 12.89 (P < 0.001). A 4-fold risk of dementia was seen for LHON patients (RR: 4.26; P < 0.001), incidence 1.45 for LHON and 0.37 for the general population. In addition, LHON patients had an increased risk of epilepsy, atherosclerosis, nerve symptoms, neuropathy, and alcohol-related disorders (RR 7.53 for alcohol-related disorders). This study is limited by its retrospective nature; for example, no data on smoking habits or body mass index were available, and hence the analysis could not be controlled for these confounding factors. Additionally, the diagnosis of comorbidities relied on registered diagnoses at a hospital, which comes with obvious limitations. In addition, causality between LHON and comorbidities has yet to be resolved.

Multiple Sclerosis.

A review of multiple sclerosis (MS) is helpful to the pediatric ophthalmology/strabismus specialist, who treats patients with strabismus resulting from brainstem involvement and pediatric patients with optic neuritis. This review covers the pathology, epidemiology, pathogenesis, magnetic resonance imaging (MRI) findings, and therapies, and herein are summarized a few relevant points. Epidemiological risk factors for MS include female gender, an affected first-degree relative, temperate climate, tobacco exposure, obesity, mononucleosis and the HLA DRB1*1501 haplotype. Brain MRI findings can precede neurological findings. Healthy individuals who undergo brain MRI for other reasons and are found to have MRI findings consistent with MS have a 50% likelihood of actually developing MS, and new MRI lesions are an order of magnitude more frequent than clinical relapses in patients with MS. Retinal ganglion cell axon loss results in easily detectible retinal nerve fiber layer thinning on optical coherence tomography, which tracks with MRI changes in the brain and can predict the evolution of disability at the cohort level. As of December 2015, the FDA has approved 15 medications for modifying the course of multiple sclerosis: 5 preparations of interferon beta, 2 preparations of glatiramer acetate, 4 monoclonal antibodies, the chemotherapy agent mitoxantrone, and the small molecule oral agents fingolimod, dimethyl fumarate, and teriflunomide. These therapies reduce, to various extents, the likelihood of development of new white matter lesions, relapses, and stepwise accumulation of disability. There is a general approach to treating early and escalating treatment with a goal of “no evidence of disease activity,” which means no new lesions on MRI, clinical relapse, disability progression, or tissue atrophy.

Leber hereditary optic neuropathy: bridging the translational gap
Leber hereditary optic neuropathy (LHON) is the most common primary mitochondrial DNA (mtDNA) genetic disorder. Occurs in 1 in 30-50,000 in Northern European population with slight predilection for males. Acute cases have a rapidly evolving central scotoma and in 25% of cases both eyes are affected simultaneously. In unilateral cases the fellow eye is usually involved within 3-6 months. Clinically discs are hyperemic with peripapillary telangiectasias and vascular tortuosity with pseudoedema secondary to RNFL swelling. When the swelling subsides, optic atrophy sets in with RNFL thinning over 6-12 months. Prior to onset of swelling there are changes in ganglion cell layer thickness in the macula. Increased peripapillary RNFL thickness and decrease in mean deviation on HVF were observed 4-6 months prior to onset of subjective visual loss. These parameters may be useful in identifying LHON carriers at high risk of impending visual deterioration and may allow early intervention to be instituted to slow or prevent vision loss with future therapies. Patients with childhood LHON only make up 10% of patients but carry a better visual prognosis than adult forms with 3 subtypes: classic acute in 2/3 of cases, slowly progressive, and insidious/subclinical. Childhood onset is a positive prognostic factor. LHON has variable penetrance with male carrier at 50% risk of vision loss compared to 10% female. Smoking and alcohol consumption is a major risk factor due to the impact on mitochondrial function and there may be an estrogen related hormonal protective mechanism due to their neuroprotective effect under stress. Treatment options are limited including idebenone which is a synthetic analogue to ubiquinone and may be partially effective in acute stage. Improved mitochondrial biogenesis may be a compensatory mechanism that could be used and boosting levels of NAD+ with vitamin B3 may help. Gene therapy is now in clinical trials and may be of value in the future. Currently there are some studies looking at mitochondrial replacement techniques in the embryos of affected mothers but the full extent of the effects may not be known for a long time. In conclusion this article is a review describing the disease and current diagnostic approaches and prognosis as well as possible therapeutic regimens that may be available in the future.

Childhood-onset Leber hereditary optic neuropathy

Leber hereditary optic neuropathy (LHON) is a mitochondrial disorder causing acute or subacute loss of vision in young men, with peak onset of visual loss at 20-30 years of age. Childhood onset is rare, with less than 10% of patients diagnosed at age 12 or younger. This study aimed to describe the clinical and genetic
characteristics of childhood onset LHON in a UK cohort of 27 patients as well as 69 patients from a literature review. The two groups had similar clinical and molecular profiles, so their data was combined. The authors found that the childhood cohort had comparable distributions of the three major LHON mutations. The male to female ratio (1.8) was less than that seen in adults. Acute pattern of vision loss was the most common presentation, although over a third had slow or subclinical onset. The insidious/subclinical group did occur with all three major mtDNA mutations. Rates of spontaneous visual recovery were similar to that of adults, and was more common in certain mutations, with those having the m.3460G>A mutation having a better visual prognosis. Overall 39% of patients achieved BCVA ≥ 0.5 in at least one eye, and 19% had BCVA <0.05 in their better eye. The authors conclude that the childhood onset cohort had a more varied clinical evolution and favorable visual prognosis than classical adult LHON, and that children do not always have an acute or subacute presentation.

First Pediatric Patient With Neuromyelitis Optica and Sjögren Syndrome Successfully Treated With Tocilizumab
Achille Marino MD, Sona Narula MD and Melissa A. Lerman MD, PhD, MSCE. *Pediatric Neurology*, 2017-08-01, Volume 73, Pages e5-e6

The authors describe treatment of Neuromyelitis Optica and Sjögren syndrome with tocilizumab (a humanized monoclonal antibody to the interleukin (IL)-6 receptor). They discuss that IL-6 could promote anti-aquaporin 4 production and an important role in the immunopathogenesis of NMO. In this study, remission on tocilizumab was maintained after B-cell repopulation, not seen with other common forms of treatment. This is an important development in the treatment of NMO and Sjogren Syndrome.

Opsoclonus-Myoclonus Syndrome: A New Era of Improved Prognosis?
Armine Galstyan MD, Colin Wilbur MD, FRCPC, Kathryn Selby MBChB, FRCPC and Juliette Hukin MBBS, FRCPC. *Pediatric Neurology*, 2017-07-01, Volume 72, Pages 65-69

This retrospective review evaluates the records of twelve children diagnosed with opsoclonus-myoclonus syndrome at BC Children's Hospital. It specifically evaluates multimodal immunotherapy and treatment with a combination of corticosteroids, intravenous immunoglobulin (IVIG), and an additional immunosuppressant agent. At median follow-up of three years from diagnosis, the majority of participants had few neurological abnormalities; better than previous reports with treatments. Since there were some patients who improved and some who did not do as well with less aggressive treatment, the authors concluded that further studies are necessary to determine optimal treatment approach.
Simultaneous Mouth Opening Facilitates Funduscopy in Young Children  
Imad T. Jarjour MD. Pediatric Neurology, 2017-05-01, Volume 70, Pages e1-e1,

This short article describes a neurologists practice of having children “open their mouth widely and say “ah” during ophthalmoscopy” to increase the likelihood of visualizing the optic disc more than 80% of the time. The author continues by saying that he has “the parent or caregiver stand three to four feet in front of the child and make faces helps to distract the child”. He finds this technique helpful in older children with photophobia and feels that it makes eye closure somewhat more difficult when the mouth is wide open simultaneously. The technique may not be effective in children with neurodevelopmental disabilities, such as untreated attention-deficit disorder, intellectual disability, and autism.

Medically unexplained visual loss in children and young people: an observational single site study of incidence and outcomes.


Medically unexplained visual loss (MUVL) describes visual loss or visual symptoms in the absence of any medically detectable eye, visual pathway, or brain condition. It is classified as a conversion disorder, a functional neurological symptom disorder resulting in loss of function. The reported prevalence in pediatric patients is 1-9%; girls are more commonly affected; most common age 9.0-13.4 years. Complaints include deterioration of visual acuity, visual field defects, and double vision. Psychological stressors such as family problems, problems at school, or bullying are reported in 40–90% of the cases, and more likely to report symptoms such as depression and attention deficit hyperactivity disorder. Screening for and detecting mental health problems in children with MUVL may facilitate access to appropriate services. Review of all clinical information of all consecutive patients younger than 16 year-olds who presented to Moorfields Eye Hospital over a 12-month period and were diagnosed with MUVL or suspected MUVL with a minimum follow up of 3 months. Children were considered as having fully recovered if they felt the eye problems had completely resolved and visual acuity was at least 0.1 logMAR in the initially affected eye. Eighty-five cases were included in the analysis. The estimated annual incidence was 3.5% worse in the winter months. Median age at presentation was 9 years and 63% were girls. Patients were first time seen within 1 week of symptoms. The mean follow up was 1.2 months. The most common investigation involved ocular motility, refractive errors and peripheral vision. None of the children seen were referred for psychological assessment or intervention. Bilateral involvement was reported in 64%. Past ocular history was found in 36% including glasses; most common complaints included decreased visual acuity (68%), painful eyes (24%), photop-
sia or perception of phosphenes (19%), and diplopia (19%). Complete loss of vision (13%), photophobia (9%), visual field loss (7%), and swollen lids (7%). Ocular symptoms were associated with non-ocular symptoms in 35% of all cases, headache being the most common complaint (93%). Half of the patients had other non-ocular health problems including allergies, asthma, and hypothyroidism. Thirty-three per cent of all children had a history of psychiatric disorders or showed signs of psychiatric disorders, 28% reported stressful live events and 24% reported recent injuries.

The reported incidence of 3.5% of MUVL in children is higher than previously reported. This study also reports that not all patients fully recover, 3 months after presentation, 87% of those children who had at least 3 months of follow-up still experienced vision problems. Several questions are raised by the authors including further research to establish any seasonal variation, and the real impact of psychiatric consultation addressing psychological issues. Authors conclude that a comprehensive multidisciplinary assessment of these children should include ophthalmological and medical history, a mental health review, family history, and social and educational history.

Magnetic resonance imaging findings in children with spasmus nutans.

Spasmus nutans (SN) is a rare pediatric ophthalmologic syndrome characterized by nystagmus, head bobbing, and abnormal head positioning. Historically, SN has been associated with underlying optic pathway gliomas (OPG); however, evidence of this association is based primarily on a small number of isolated case reports. Prior retrospective analyses have found the rate of OPG to be <2%, but these studies only intermittently used neuroimaging with computed tomography, which has limited sensitivity for detection of small lesions in the optic pathway. The purpose of this multicenter retrospective study was to investigate the association of SN with intracranial abnormalities, particularly OPG, using magnetic resonance imaging of the brain and orbits. Neuroradiology databases at three institutions spanning January 2010 to May 2016 were queried for examinations ordered for evaluation of SN; MRI examinations of the brain and/or orbits were included and evaluated for OPG and other structural abnormalities by one experienced fellowship-trained neuroradiologist. A total of 40 patients with eligible MRI examinations were identified. None had optic nerve pathway gliomas. Two children had optic nerve hypoplasia; no other patients had optic pathway abnormalities. None had intracranial or orbital masses. MRI examinations were normal in 25 (63%) patients. The intracranial abnormalities that were found in 15 patients included: midline abnormalities involving the corpus callosum, periventricular leukomalacia and ventriculomegaly. Medical records were reviewed to confirm a diagnosis of SN, presence of other underlying neurological disease, or pre-existing
diagnoses, but were only available in 31 cases. Ophthalmology examination was performed in 13 subjects. Hence, misdiagnosis cannot be entirely ruled out. Despite its retrospective design and limited availability to prior medical information, this series represents the largest collection of MRI examinations for SN in the literature to date and shows no association between OPG and SN. The authors’ conclude that children presenting with SN, but with no other findings suggesting OPG or neurological abnormalities, neuroimaging may not be required. However, we would just like to point out that yet a substantial number of patients in this cohort had some form of intracranial abnormalities that were demonstrated on the MRI.


Clinical diagnosis has been supplemented by neuroimaging advances, genetic discoveries, and molecular research to generate new neurobiological discoveries pertaining to early maldevelopment of ocular motor control systems. In this focused review, the author examined recent paradigm shifts that have transformed our understanding of pediatric ocular motor disease at the prenuclear and infranuclear levels. The pathogenesis of complex ocular motor disorders, such as paradoxical pupillary constriction to darkness, benign tonic upgaze of infancy, congenital fibrosis syndrome, and the constellation of unique eye movements that accompany Joubert syndrome, are elucidated. Please refer to this formidable lecture in the journal.

Diagnostic algorithm for relapsing acquired demyelinating syndromes in children

This article proposes an algorithm for classifying the pediatric relapsing demyelinating syndromes, multiple sclerosis (MS) and neuromyelitis spectrum disorder (NMO-SD). 110 children with relapsing demyelination were included. A panel diagnosed 56% with MS, 25% with NMO-SD, 13% with multiphasic disseminated encephalomyelitis, and 6% with recurrent optic neuritis. The authors propose that first an MRI brain and spine should be performed, and if the findings are typical or suggestive of MS, to apply the McDonald diagnostic criteria. If not typical or suggestive of MS, but the MRI and clinical findings are more suggestive of NMOSD, aquaporin-4 antibodies should be performed. In AQP-4 negative cases, MOG antibody should be tested. If the MRI is not typical for MS or NMOSD, but suggestive of ADEM, MOG antibody should be tested. The remaining cases are antibody negative relapsing demyelinating syndromes if other diseases are
eliminated as possibilities. Overall 83% of the patients with non-MS relapsing demyelinating syndrome had an antibody associated disease. The authors suggest in the next set of diagnostic criteria that anti-MOG antibody disease be included as a distinct entity from other relapsing demyelinating syndromes.

A multi-institutional study of brainstem gliomas in children with neurofibromatosis type 1

This retrospective cross-sectional study performed at 4 centers evaluated 133 children with NF1 and brainstem gliomas. The purpose of this study was to characterize the presentation and symptomatology of patients with NF1 and brainstem gliomas. Average age of presentation was 7.2yrs, which is older than NF1 associated optic pathway gliomas (4.2 yrs). 54% were asymptomatic at diagnosis. Most tumors (80%) were confined to one area of the brainstem, with 14% in the pons, 36% in the midbrain, and 30% in the medulla. This is in contrast to sporadic gliomas, which tend to involve the pons most commonly. Treatment was performed in 12% of the asymptomatic patients, and 74% of the symptomatic patients. One third of the patients who received tumor-directed therapy required further treatment.

Monophasic demyelination reduces brain growth in children

This study evaluated how single events of demyelination affects the growth of the brain of pediatric patients. Subgroups analyzed included patients with ADEM (18), non-ADEM patients with T2 lesions on MRI (33), and non-ADEM patients without T2 lesions on MRI at onset (32, 15 of whom had isolated optic neuritis). The results demonstrated for all demyelination, whether isolated optic neuritis, ADEM, or non-ADEM with or without T2 lesions, all patients had reduced white matter and grey matter growth. ADEM had the most significant effect on brain growth. This study demonstrates that the pediatric central nervous system is vulnerable to even a monophasic demyelinating event.

Clinical implications of the melanopsin-based non-image-forming visual system

In this important review the authors discuss the roles of the melanopin system in various physiologic systems and disease states. They also discuss recent advances in our understanding of the physiologic responses of ipRGCs (intrinsically photosensitive retinal ganglion cells). The ipRGCs roles in the pupillary light re-
flex, circadian rhythms, and neonatal light avoidance are discussed. The proposed roles of ipRGCs in seasonal affective disorder, sleep dysregulation in aging, photophobia in migraine are also discussed. Also discussed are the sparing of ipRGCs in diseases such as dominant optic atrophy and Leber hereditary optic neuropathy resulting in sparing of light perception and the pupillary light response, and the destruction of ipRGCs in glaucoma, leading to a dysfunctional pupillary light response and circadian rhythm disruption. Potential targets and strategies for treatment of disease states relating to the non-image-based visual system may soon be found.

Evaluation of Optical Coherence Tomography to Detect Elevated Intracranial Pressure in Children
Jordan W. Swanson, Tomas S. Aleman, Wen Xu, Gui-Shuang Ying et al.

The authors evaluated the peripapillary retina from spectral domain optical coherence tomography (SD-OCT) in 79 children with elevated intracranial pressure to determine if retinal measurements could be an effective surrogate for invasive intracranial pressure measurement. From 2014 to 2015, the cross-sectional study included three cohorts: patients with craniosynostosis, a positive control cohort of patients with hydrocephalus, and a negative control cohort of healthy patients undergoing minor procedures. In summary, noninvasive measurements of the peripapillary retina by SD-OCT were correlated with invasively measured intracranial pressure. In this way, SD-OCT measurements show promise as a noninvasive surrogate to measure intracranial pressure in children, especially children under 5 years old.

Ocular Motor Function in Children with Spastic Hemiplegia Evaluated by the Ocular Motor Score

Children with neurologic disorders commonly have ocular motility abnormalities. The authors sought to assess the ocular motor function in children with spastic hemiplegia using the Ocular Motor Score (OMS). They looked at 34 children with a median age of 11 years (range 7-17 years) that were divided in three groups based on the neurologic condition. Each child underwent the OMS protocol which consists of 15 subtests with both static and dynamic components. All children had a significant difference in the static and dynamic OMS scores and all had saccadic dysfunction, dysmetric smooth pursuits and pathological OKN. The highest median score was seen in the group with a brain malformation. The authors suggest that the OMS protocol is easy to use and provides an overview of the patient’s ocular motor function. It also has a high inter-observer and intra-observer agreement, which can aid in the follow up of these patients.
Ganglion Cell Complex Loss in Chiasmal Compression by Brain Tumors


Twenty-three patients with chiasmal compression and age matched controls were imaged with Cirrus high-definition optical coherence tomography macula cube protocol, retinal nerve fiber layer protocol and automated,30-2, Humphrey)visual fields. Ganglion cell complex thinning demonstrated in macula cube protocol corresponded to visual field defects and mean deviation correlated more with ganglion cell complex rather than nerve fiber layer thinning. Binasal ganglion cell complex loss was typical for patients with chiasmal lesions.Postoperatively, visual filed loss mean deviation improved in 7 of 8 patients with persistent nasal ganglion cell complex thinning and six patients had loss of ganglion cell complex in spite of normal visual fields. The authors concluded that ganglion cell complex thinning may be detected before loss of retinal nerve fiber layer in some patients with chiasmal lesions and after decompression, many patients demonstrated improvement in visual field even with persistent ganglion cell complex loss. Patients with less ganglion cell loss before decompression had better postoperative visual fields. Macula cube ganglion cell analysis may be a particularly sensitive method to monitor patients with chiasmal lesions.

Optic gliomas in Neurofibromatosis Type 1


The purpose of this study is to report the incidence, presentation and outcome of optic nerve gliomas in children with neurofibromatosis type I (NF-1) in Southern California Kaiser Permanente. Out of 708 patients younger than 21 years of age who were diagnosed with NF-1, only 30(4.2%) had an optic nerve glioma. The average age of diagnosis was 5 years, ranging from 18 months to 12 years. Half of the patients who were diagnosed as having optic nerve glioma, presented with symptoms. Symptomatic patients were diagnosed later than asymptomatic patients through routine screening.63% of the gliomas were bilateral, 23% right-sided and 13 % left-sided. Fifty-three percent of the optic glioma patients were involving the optic chiasm. The authors conclude that annual ophthalmologic examination and screening of all children diagnosed with NF-1 is very importance for early detection of optic nerve gliomas.

Idiopathic Intracranial Hypertension

Diagnostic criteria in pediatric intracranial hypertension
The modified Dandy criteria and the newer diagnostic criteria for pseudotumor cerebri syndrome (PTCS) are both used to diagnose intracranial hypertension (IH). In comparison to the modified Dandy criteria, the PTCS criteria stratify the IH diagnosis into definite, probable, and suggested categories, exclude clinical symptoms, and use radiologic evidence for diagnosis. There is a lack of consensus on which criteria should be used in the pediatric population. The purpose of this retrospective study was to compare the diagnostic criteria for PTCS to the modified Dandy criteria and to identify limitations within both sets of criteria, by retrospectively applying the diagnostic criteria for PTCS to 50 patients originally diagnosed with IH under the modified Dandy criteria. Of the 50 patients, 31 (62%) met diagnostic criteria for definite PTCS, 10 (20%) met criteria for probable PTCS, and 9 patients (18%) failed to meet sufficient PTCS criteria for diagnosis, despite an elevated opening pressure of >28 cmH2O. The reason these patient failed to meet them PTCS criteria was because they lacked both papilledema and abducens nerve palsy. The authors conclude that although the PTCS criteria uses objective data to make the IH diagnosis, the subjective symptoms are useful indicators of disease in this group of patients. They also emphasized that distinguishing probable from definite IH may not have clinical relevance, because both groups were treated similarly. The absence of radiographic evidence of IH should not preclude a diagnosis of the condition, as it was present in a minority of patients included in this study.

Despite its retrospective nature, it is a very interesting report. It highlights some of the difficulties in making the diagnosis of IH in children. It makes the point that the new diagnostic criteria for PTCS may under diagnose IH and that a combination of both diagnostic criteria may generate a set of guidelines that increases the sensitivity for diagnosing IH. It also emphasizes the need for further research to clarify the disease process in patients, who present with signs and symptoms of elevated intracranial pressure but lack ocular pathology, the intracranial hypertension without papilledema variant.

**Perimetry**

**Optic Nerve Imaging**

Optical coherence tomography detection of characteristic retinal nerve fiber layer thinning in nasal hypoplasia of the optic disc.


Nasal hypoplasia of the optic disc (NHOD) is a congenital anomaly characterized by hypoplasia of the nasal portion of the optic disc with thinning of the retinal nerve fiber layer (RNFL). Visual symptoms include sector visual field defects
emerging from the blind spots and extending to the temporal periphery, but pa-
tients might not be aware of their visual field defects unless they are tested. Au-
thors initially looked at the records of all patients who presented to neuro-
ophthalmology unit with temporal visual field defects. The medical records of five
patients (eight eyes) with NHOD were reviewed. All patients underwent complete
ocular examinations, including measurement of the best-corrected visual acuity
(BCVA) and intraocular pressure (IOP), Goldmann perimetry, slit-lamp biomi-
croscopy, and dilated fundus examinations. The patients' color fundus photo-
graphs and spectral-domain OCT images. All patients were female (mean age,
38.8 ± 10.4 years). Two patients had unilateral involvement, and three were af-
acted bilaterally The BCVA at the initial visit was 1.2 in six eyes and 1.5 in two
eyes. The mean RNFL thicknesses of the temporal, superior, nasal, and inferior
quadrants were 90.3 ± 12.6, 103.1 ± 16.6, 34.8 ± 4.1, and 112.8 ± 11.2 microns,
respectively. All 8 eyes were below 1% level RNFL nasal quadrant thickness.
But also the superior (especially) and inferior quadrants were compromised (be-
low 5% level). The mean ratio of the disc- macula distance to the disc diameter
(DM/DD) was 3.1 ± 0.5. Optic disc tilt was assessed using the disc ovality ratio
of the minimal to maximal DD; the mean disc ovality ratio of the minimal to max-
imal DD was 0.81 ± 0.07. Hypoplasia of the optic nerve varies in appearance,
ranging from nearly total aplasia to subtle segmental hypoplasia. Segmental hy-
poplasia results in normal visual acuities and sector visual field defects corre-
sponding to the hypoplastic areas of the optic disc. the actual prevalence of
NHOD might be much higher because patients might be unaware of their visual
field defects unless they are tested and because the nasal rim of the optic nerve
is difficult to evaluate owing to the emergence of large retinal vessels. Segmental
optic nerve hypoplasia is thought to be associated with small optic discs and tilt-
ed discs. A DM/DD ratio of 3.0 or higher has been reported to predict the pres-
ence of optic disc hypoplasia in patients with good visual acuities. In the current
study the mean DM/DD ratio was 3.1, and five of the eight eyes with NHOD had
a DM/DD ratio exceeding 3.0.

Optic disc ovality has been used as an index to evaluate optic disc tilt, and a disc
ovality ratio of 0.8 or lower has been considered significant. In the current study,
the mean disc ovality ratio was 0.81, and six of the eight eyes with NHOD had
disc ovality ratio of 0.8 or lower. These results suggested that small optic discs
and tilted discs also might be associated with NHOD.

**Congenital Anomalies of the optic disc: insights from optical coherence tomography imaging**

Karen W. Jeng-Miller, Dean M. Cestari, and Eric D. Gaier


Congenital anomalies can appear similar on fundoscopic examination and OCT elucidates subtleties to accurately diagnose the abnormality. Optic disc pit (ODP)
is a cavitary lesion of the optic nerve that is predominantly unilateral with a normal sized optic nerve and a round or oval depression usually temporally in the optic nerve. Visual acuity is often normal and 30-45% of patients have maculopathy defined by schisis and fluid collection. OCT reveals cystic outer retinal edema with a schisis cavity and outer layer detachment from RPE. There is a membrane spanning the optic disc cup in patients without maculopathy which is absent in patients that have it. SS-OCT has a demonstrated that congenital ODP has a defect of the lamina cribrosa in that area and that vitreous adhesions are stronger in eyes with ODP compared to normal which directly results in maculopathy. Optic nerve coloboma (ONC) funduscopically appear as large excavations of the optic nerve usually in the inferior aspect of the nerve head and may be uni or bilateral. May be associated with CHARGE. On OCT there is retinochoroidal-scleral excavation with sclera immediately beneath the retina corresponding to adjacent choroidal coloboma. Similar to ODP’s, schisis overlies the area of excavation with herniated retinal tissue. In addition, the presence of a membrane over the optic cup in both ODP and ONC without schisis suggests a protective role of the membrane against the development of maculopathy. Furthermore, this may argue for ODP and ONC as existing on a spectrum distinct form morning glory. Morning glory disc anomaly (MGDA) is a sporadic congenital anomaly with conical excavated optic disc and central glial tuft with retinal vessels exiting in a radial fashion. More common in women (2:1) and whites. OCT shows an increased cup diameter with sparse neuroretinal rim, increased RNFL thickness and reduced macular thickness. Temporal RNFL thickness is greater than inferior unlike normal distribution. OCT further supports the hypothesis that there is an initial neuroectodermal dysgenesis followed by a secondary postnatal mesenchymal abnormality. Optic nerve hypoplasia appears as an abnormally small optic nerve which is most often bilateral but can be unilateral as well. Appears to have a double ring sign and may be associated with septo-optic dysplasia which warrants further workup. OCT of the macula demonstrates thinning of both the inner and outer retinal layer of the nerve fiber layers with the degree of changes in the ganglion cell layer thickness correlating with visual function. The authors review the fundoscopic findings in congenital anomalies of the optic nerve as well as the OCT findings which help to differentiate them as well as to account for some of the associated symptoms and visual issues.

**Myasthenia Gravis**

**Optic Neuritis**

**Other**

The Eye Drop Preservative Benzalkonium Chloride Potently Induces Mitochondrial Dysfunction and Preferentially Affects LHON Mutant Cells
Benzalkonium chloride (BAK) is the most commonly used eye drop preservative and has been associated with toxic effects such as “dry eye” and trabecular meshwork degeneration, but the underlying biochemical mechanism of ocular toxicity by BAK is unclear. This study looked at mitochondrial O₂ consumption rates of human corneal epithelial primary cells (HCEP), osteosarcoma cybrid cells carrying healthy (control) or Leber hereditary optic neuropathy (LHON) mutant mtDNA [11778(G>A)], before and after acute treatment with BAK. Mitochondrial adenosine triphosphate (ATP) synthesis and cell viability were also measured in the BAK-treated control: LHON mutant and human-derived trabecular meshwork cells (HTM3). BAK inhibited mitochondrial ATP (IC₅₀, 5.3 µM) and O₂ consumption (IC₅₀, 10.9 µM) in a concentration-dependent manner, by directly targeting mitochondrial complex I. At its pharmaceutical concentrations (107–667 µM), BAK inhibited mitochondrial function >90%. In addition, BAK elicited concentration-dependent cytotoxicity to cybrid cells (IC₅₀, 22.8 µM) and induced apoptosis in HTM3 cells at similar concentrations. Furthermore, BAK directly inhibits mitochondrial O₂ consumption in HCEP cells (IC₅₀, 3.8 µM) at 50-fold lower concentrations than used in eye drops, and that cells bearing mitochondrial blindness (LHON) mutations are further sensitized to BAK’s mitotoxic effect. BAK in topically applied eye drops has been reported to reach the optic nerve of rodents and the anterior chamber of human eyes, causing trabecular meshwork damage. The data suggests that BAK-containing eye drops should be avoided in patients with mitochondrial deficiency, including LHON patients and carriers; autosomal dominant optic atrophy (ADOA); myoclonic epilepsy with ragged-red fibers; mitochondrial encephalopathy, lactic acidosis and stroke-like episodes (MELAS); and neuropathy, ataxia and retinitis pigmentosa. Since some primary open-angle glaucoma have a complex I deficiency, eye drops containing BAK should be administered with caution and careful monitoring in these patients. This study is important in further elucidating the mechanism of BAK toxicity and showing us that such a commonly used preservative can be potentially dangerous in some patients.

6. NYSTAGMUS

Magnetic Oculomotor Prosthetics for Acquired Nystagmus

The authors have devised a novel magnetic prosthesis to dampen the oscillation in acquired nystagmus patients. Acquired nystagmus is often resistant to pharmacotherapy. Although heterogeneous in its neural cause, its expression is unified at the effector—the eye muscles themselves—where physical damping of the oscillation offers an alternative approach. Because direct surgical fixation would immobilize the globe, action at a distance is required to dampen the oscillation at the point of fixation, allowing unhindered gaze shifts at other times. The device is a 2-part, titanium-encased, rare-earth magnet powered to dampen nystagmus
without interfering with the larger forces involved in saccade. Implementing this idea magnetically allows for unhindered gaze shifts at other times. A 49-year-old man with longstanding, medication-resistant, upbeat nystagmus resulting from a paraneoplastic syndrome caused by stage 2A, grade I, nodular sclerosing Hodgkin’s lymphoma requested for a novel therapy and underwent this procedure. The smaller magnet (the ocular component) was sutured to the undersurface of the inferior rectus, centered approximately 10 mm behind the muscle insertion. The larger magnet was placed alongside the ocular magnet, and the eye was aligned to primary position, allowing an estimate for the optimal position of the orbital magnet; this position was maintained while medical-grade cyanoacrylate glue was run into the gap between the orbital floor and magnet base. Outcomes evaluated include comparing visual functions and high-resolution oculography before and after implantation and monitoring the patient for more than 4 years after surgery. The patient reported a clinically significant improvement of 1 line of Snellen acuity (from 6/9 bilaterally to 6/6 on the left and 6/5-2 on the right), reflecting an objectively measured reduction in the amplitude, drift velocity, frequency, and intensity of the nystagmus. These improvements were maintained throughout a follow-up of 4 years and enabled him to return to paid employment. This work opens a new field of implantable therapeutic devices—oculomotor prosthetics—designed to modify eye movements dynamically by physical means in cases where a purely neural approach is ineffective.

Non-sedated handheld electroretinogram as a screening test of retinal dysfunction in pediatric patients with nystagmus.
The purpose of this prospective cross-sectional study was to assess the feasibility, sensitivity, and specificity of non-sedated handheld cone flicker electroretinogram (ERG) as a screening tool to detect retinal dysfunction in children with nystagmus. A total of 71 pediatric patients were enrolled and placed into three age-matched groups: normal, nystagmus with a retinal dystrophy, and nystagmus without a retinal dystrophy. Unsedated 30 Hz cone flicker ERG responses were obtained using a handheld device (RE-Teval) from both eyes of each patient using skin electrode sensors after pupillary dilation. Amplitudes and implicit times were successfully obtained in 65 (92%): 31 (mean age +/- SD, 5.6 +/- 2.7 years; range, 1-12 years) without nystagmus and 34 with nystagmus. Nystagmus patients were grouped by those with (n = 15; mean age, 8.5 +/- 4.5 [range, 2-17 years) and without (n = 19; mean age, 4.3 +/- 3.0 [range, 6 months-10 years]) a retinal dystrophy. The patients with retinal dystrophies had significantly smaller amplitudes and prolonged or non-measurable implicit times than the other two groups (P < 0.001). A 100% specificity and 93% sensitivity for retinal dystrophies was achieved with a cut-off of 2.54 mV amplitude, and 94.7% specificity and 93% sensitivity was achieved with a cut-off of 5mV. The authors conclude that unsedated handheld cone flicker ERG is a feasible screening test that effectively detects retinal dysfunction in children with
nystagmus. In conjunction with clinical findings, the test helps reduce the need for sedated ERG in children. The authors acknowledge some limitations related to this device including: no established normative data for different age groups and gender, and that it tests for cone function and can miss rod-based retinal abnormalities such as congenital stationary night blindness (CSNB). Despite these limitations, we felt that this well-designed study highlights the advantages of the cone flicker ERG as a screening method, which is a highly reproducible and easily-obtained test that can be acquired within a few seconds and does not require dark adaptation.

Incidence and Types of Pediatric Nystagmus

This is a retrospective study over 30 years of children diagnosed with nystagmus in Olmsted County with the purpose of reporting the incidence, subtypes, and clinical characteristics of pediatric nystagmus. The authors found the incidence of 6.72 per 100,000 patients and that most patients were diagnosed with infantile nystagmus (87.3%). The birth prevalence of nystagmus was 1 in 821 live births. The most common types of nystagmus diagnosed were those associated with eye disease (retina/nerve) (32%), idiopathic (31%), and manifest latent or latent (24%). A small percentage (2.8%) of cases were associated with CNS tumor (pilocytic astrocytomas - both cases were acquired unilateral nystagmus), chiari malformation, or medications (carbamazepine and phenytoin). A large percentage (43.6%) of patients also had developmental delay and strabismus (35%). 14% of patients carried a diagnosis of amblyopia. Importantly, 80% of patients had 20/40 or better vision at presentation in at least one eye. The limitations of this paper were nicely outlined by the authors and mostly due to the retrospective nature of the study and the lack of diversity in the patient population.

Assisting the Person with Nystagmus Beyond the Office: Infantile Nystagmus Syndrome
Parkinson, Joan American Orthoptic Journal 2017; 67: 43-51

Infantile nystagmus syndrome (INS) has many challenges beyond the clinical examination. Patients have everyday developmental, educational, and psychosocial challenges that need to addressed. This required cooperation between the clinicians, educators, support services, and families for optimal adaptation. Children with INS and associated afferent visual sensory loss have a greater psychosocial need. The author discusses the role of the Atlantic Provinces Special Education Authority (APSEA) which provides low vision services in Atlantic Canada. In developmental stage 1, 3-6 months, patients present with nystagmus and require a full ophthalmic examination and electrodiagnostic testing, ERG and VEP. Early testing is beneficial in that sedation can typically be avoided. A referral is then made to APSEA and the initial meeting addresses the family impact of caring for a low vision child. During development stage 2, 6 months to 3 years,
the goal is to assist visual development by optimizing visual acuity, correcting strabismus, and encouraging binocularity. APSEA makes regular home visits encouraging visual stimulation, physical activity, mobility. The 3rd developmental stage, 4-5 years of age, involves transition to formal education. The role of the clinician involves stereopsis, color vision, and visual field testing. These results assist the APSEA in advising the classroom teacher as to the child’s capabilities. Self-esteem can be boosted with visual aids such as tablets. During stage 4, age 6-10, the clinicians repeats color vision, stereopsis, and visual field testing. A nystagmogram can be useful in guiding extraocular muscle surgery for null points and compensatory head postures. The psychosocial impact becomes greater during this stage due to the scrutiny of peers. From age 11-18, stage 5, optimizing visual acuity for social, academic, and potential careers in the goal. Contact lenses help with cosmetic concerns, and improve vision by aligning the visual axis and the optical axis of the lenses. Addressing ability or inability to drive has a major impact on quality of life. A visual field is difficult to perform on a patient with nystagmus due to unsteady fixation and compensatory head posture.

**Nystagmus with Strabismus**
Merril, Kimberly S. *American Orthoptic Journal* 2017; 67: 36-38

Strabismus has been reported in 16% to 51% of patients with congenital nystagmus. It occurs less frequently in patients with infantile nystagmus syndrome (INS, 16-18.5%) versus anterior visual pathway disorders such as optic nerve hypoplasia (up to 85%). Albinism is frequently associated with strabismus and retinal dystrophies less so. Nystagmus blockage syndrome is a variable esotropia with infantile nystagmus, it is believed that convergence dampens nystagmus. As neutralization is attempted with prisms the angle increases. Ciancia syndrome is defined as latent nystagmus (that increases in abduction), alternate head posture (fixating with adducted eye), pseudo-abduction deficit with large-angle esotropia. The esotropia in both nystagmus blockage syndrome and Ciancia syndrome is treated surgically. Strabismus measurements in patients with nystagmus are difficult and often inaccurate based on corneal light reflexes. Patients with albinism and aniridia often have a positive angle kappa making corneal light reflexes underestimate esoptropia and overestimate exoptropia.

**Nonsurgical and Orthoptic Management of Nystagmus**

Optimal treatment of nystagmus depends on a number of factors including visual acuity at distance and near, severity of refractive error, visual system deficits, binocularity, nystagmus characteristics, and presence of null point. Visual acuity testing should be performed in different positions of gaze to determine if a null point is present and if the visual acuity improves in that gaze. It also should be checked at near to determine if convergence dampens the nystagmus therefore improving vision. If amblyopia is present it should be treated with occlusion, atropine penalization, or Bangerter filters. Refractive errors should be corrected to
improve vision. Over-minus lenses can aid in dampening nystagmus in patients who have convergence dampening by overstimulating accommodative convergence. Contact lenses allow patients to look through the central axis of the lenses in patients with anomalous head postures therefore improving vision. Prisms (base toward the direction of the head turn, tilt, or chin position) are used to correct the compensatory head posture and aid in titration of surgical numbers. Base-out prisms (artificial divergence) assist patients whose nystagmus dampens with convergence. Surgery can be performed in these patients to induce an intermittent exotropia which produces a convergence response therefore dampening the nystagmus and improving vision and oscillopsia.

Examining Children with Nystagmus: Pearls for Success
Fray, Katherine J. American Orthoptic Journal 2017; 67: 22-26

Patience and time are key to obtaining a proper diagnosis and treatment plan in patients with nystagmus. Take a thorough history including family history, birth history, onset of nystagmus, parent’s perception of child’s vision, etc. An external examination should include head posture, which can be measured with a goniometer or version prisms, describe the nystagmus: unilateral or bilateral, conjugate or dissociated, pendular versus jerk, horizontal, vertical or torsional, direction, amplitude, frequency, null point. Observe eye movements for 10 minutes. Look for abnormalities in ocular structures. Determine visual function by OKN, visual acuity (binocular and monocular), stereopsis, strabismus, papillary reaction, color vision, contrast sensitivity, visual field testing, and a dilated fundus examination.

A Sheep in Wolves’ Clothing? Nystagmoid Eye Movements

Nystagmoid eye movements are a class of eye movements not initiated by a slow phase, unlike nystagmus. These include saccadic intrusions such as square wave jerks or ocular flutter/opsoclonus, voluntary nystagmus, superior oblique myokymia, The Heimann-Bielschowsky phenomenon, and sensory intermittent exotropia. Saccadic intrusions are thought to be a dysfunction of omnipause neurons in the PPRF. Square wave jerks are horizontal back-to-back saccades interrupting fixation that are seen in normal patients at a rate of 4-6 per minute. They are considered pathologic if occurring greater than 15 per minute, and are seen in patients with basal ganglia and cerebellar disease. Ocular flutter (horizontal) and opsoclonus (multiplanar) are saccadic oscillations with no intersaccadic interval that cause decreased vision and oscillopsia. These are seen in paraneoplastic syndromes, parainfectious brainstem encephalitis, and may be drug-induced. Voluntary nystagmus is a horizontal saccadic oscillation that can be purposely initiated. Superior oblique myokymia is an intermittent, high frequency monocular microtremor. Patients have episodes of vertical and torsional diplopia with oscillopsia. Can be treated with carbamazepine, gabapentin, and surgery. Heimann-Bielschowky phenomenon is a monocular, irregular, small
amplitude vertical oscillation in a poorly seeing eye. The authors propose that sensory intermittent exotropia is a nystagmoid movement.

The Red Flag: When Pediatric Nystagmus is a Harbinger of Life-Threatening Disease
Chilakapati, Madhuri; Edmond, Jane American Orthoptic Journal 2017; 67: 31-35

Childhood nystagmus can be divided into two groups: infantile and acquired. Infantile has an onset by 2-4 months of age and includes congenital infantile nystagmus, sensory nystagmus, and manifest latent nystagmus. Acquired nystagmus usually presents after 4-6 months of age and often requires diagnostic imaging and further medical work-up. Spasmus Nutans (SN) is a triad of characteristics including nystagmus, head oscillations, and torticollis. The nystagmus is described as shimmery due to its small-amplitude and high-frequency, it is usually horizontal and asymmetric. SN may be associated with suprasellar tumors, most commonly gliomas involving the chiasm and hypothalamus. Opsoclonus and ocular flutter are nystagmoid oscillations with no intersaccadic interval. They may be associated with opsoclonus-myoclonus syndrome (OMS) which has features of opsoclonus, myoclonus/ataxia, behavioral change, and/or sleep disturbance and is a paraneoplastic syndrome associated with neuroblastoma. Downbeat nystagmus is associated with cervicomедullary junction pathology such as Chiari malformations. Convergence retraction nystagmus characterized by retraction of the eyes into the orbit induced by attempted convergence or up-gaze and is a feature of Parinaud syndrome (dorsal midbrain syndrome). See-saw nystagmus is a dysconjugate nystagmus with alternating pattern of one eye elevating and intorting while the other depresses and extorts. It has been associated with achiasmia, Joubert syndrome, albinism, septo-optic dysplasia, and parasellar tumors. Neurodegenerative disease can occasionally present as nystagmus. Other neurological signs such as developmental delay, hypotonia, and ataxia often develop and are progressive.

Nystagmus in Infancy and Childhood: Clinical and Eye Movement Characteristics

Infantile Nystagmus Syndrome (INS) most commonly has both slow and fast phases, but can be pendular; most commonly horizontal and increases in eccentric gaze, becoming right-beating in right gaze and left-beating in left gaze. INS is also characterized by remaining horizontal in up-gaze, increasing in intensity with fixation, having a null point, dampening with convergence, anomalous head position, strabismus, and need for spectacles. INS is often associated with visual sensory defects such as albinism, achromatopsia, aniridia, congenital retinal dysmatures and degenerations, visual cortex anomalies, and congenital cataracts, glaucoma, and corneal disease. An anomalous head position is used to place the eyes closest to the null point to improve foveation, especially when fixating on a distant target. Oscillopsia is rarely a complaint in children with nystagmus pre-
sent within the first decade of life. INS patients can have a form of acquired periodic alternating nystagmus referred to as Infantile (a)periodic alternating nystagmus (IPAN). IPAN has a null point that shifts positions and is asymmetric. Fusional maldevelopment nystagmus syndrome (FMNS) (formerly called latent nystagmus) is a benign, binocular horizontal oscillation of infantile onset. It is often associated with manifest strabismus. FMNS is a constant nystagmus that increases in intensity by monocular occlusion and minimizes when the fixating eye is in adduction. FMNS decreases in intensity with successful treatment of associated strabismus and amblyopia. Spasmus Nutans Syndrome (SNS) refers to triad of nystagmus, head nodding, and torticollis. SNS has a typical onset of 6-12 months of age, and becomes clinically silent within 1-2 years of onset. Nystagmus in SNS is high-amplitude, high-frequency, asymmetric and typically horizontal. The head nodding is compensatory for the nystagmus to slow the waveform and improve foveation. SNS can be a sign of a suprasellar tumor therefore MR is recommended.

Eye movement recordings can be used to aid in diagnosis of nystagmus, saccadic intrusions, and oscillations, they can also be used to direct treatment.

**What Causes Nystagmus?**


Nystagmus is an involuntary oscillation of the eyes initiated by a slow phase. The slow drift is followed by a fast phase, jerk nystagmus, or a slow phase, pendular nystagmus. Saccadic intrusions, square wave jerks, ocular flutter, and opsoclonus have an initial fast-phase away from fixation. Pathologic nystagmus develops when there is a deficiency in the vestibulo-ocular and optokinetic reflexes. Three systems help maintain fixation and prevent unwanted eye movements, visual input, the gaze-holding system, and the vestibular system. Disorders of the visual pathway lead to large amplitude jerk nystagmus; the two most common forms are idiopathic infantile nystagmus (IIN) and fusion maldevelopment nystagmus (FMN, or latent nystagmus). A “leaky” neural integrator system can lead to nystagmus in eccentric gaze and can play a part in IIN. Vestibular nystagmus can involve abnormalities in the peripheral or central portions of the system. Both types manifest in a “saw-tooth” pattern nystagmus. Peripheral lesions result in a slow drift toward affected side followed by beat away from affected side. Central causes of vestibular nystagmus may manifest as vertical nystagmus; upbeat is correlated with brainstem lesions and downbeat correlated to cranio cervical junction or cerebellar flocculus. Pendular nystagmus is a special form of nystagmus that lacks a fast phase. Spasmus Nutans (SN) is a form of childhood nystagmus with small-amplitude, high-frequency (shimmering) nystagmus. SN has a clinical triad of shimmering nystagmus, head nodding, and anomalous head posture.

**Soft Contact Lenses to Optimize Vision in Adults with Idiopathic Infantile Nystagmus: A Pilot Parallel Randomized Controlled Trial.**
Infantile nystagmus syndrome (INS) is commonly associated with reduced visual acuity. This may impact quality of life, as patients may not meet visual standards for activities such as driving. There is no gold standard for the treatment of INS. The authors hypothesize that contact lenses may damp ocular oscillations, allow fixation through the optimal optical area even with an anomalous head position, and provide superior optical correction throughout the visual field. In this randomized control trial, the authors compared ocular movement in visual acuity in corrective soft contact lens with plano soft contact lenses in adults with INS. Twenty-seven of the 38 enrolled patients completed the study (16/19 plano CL, 11/19 corrective CL). Overall the contact lenses were well tolerated with no adverse events. They found that there was no significant difference in visual acuity between the plano and corrective CL. On the other hand, there was an improvement in most nystagmus parameters in both the plano and corrective CL groups. Specifically the plano CL group had a significant difference in the mean amplitude and the corrective CL had significant differences in velocity and expanded nystagmus acuity function. The data suggests a beneficial effect of CLs in damping the nystagmus which improves visual function more than refractive correction alone. However, a large RCT is required to provide a safe evidence-based option for treatment in people of all ages, including children and women of childbearing age.

**Effect of Gabapentin/Memantine on the Infantile Nystagmus Syndrome in the Zebrafish Model: Implications for the Therapy of Ocular Motor Diseases**


This study employed the zebrafish infantile nystagmus syndrome (INS) model *belladonna (bel)* to conduct an in-depth study of how gabapentin and memantine interventions alleviate INS signs. In addition, the influence of both medications on ocular motor functions in healthy zebrafish was also studied to determine possible iatrogenic effects. Ocular motor function and INS characteristics were assessed by eliciting optokinetic response, spontaneous nystagmus, and spontaneous saccades in light and in dark, in 5- to 6-day postfertilization *bel* larvae and heterozygous siblings. Single larvae were recorded before and after a 1-hour drug treatment (200 mM gabapentin/0.2 mM memantine). Both interventions significantly reduced nystagmus intensity (gabapentin: 59.98%, memantine: 39.59%). However, while the application of gabapentin affected all tested ocular motor functions, memantine specifically reduced nystagmus amplitude and intensity, and thus left controls completely unaffected. Finally, both drug treatments resulted in specific changes in nystagmus waveform and velocity. This study provides deeper insight into gabapentin and memantine treatment effect in the zebrafish INS model, and suggests fewer ocular motor side effects.
with memantine. Although this study was very small, it did show that zebrafish appears to be a good pharmacologic animal model for treating nystagmus and ocular motor disease, with potential to serve as a basis for future large-scale drug screenings.

7. PREMATURITY.

Ophthalmic Features of Premature Infants

Retinal vascular changes in preterm infants: heart and lung diseases and plus disease.

Plus disease, diagnosed on the basis of increased venular dilation and arteriolar tortuosity at the posterior pole, is a recognized feature of increasing severity of ROP and one of the main indicators for treatment. Retinal vascular tortuosity in arterial and venous vessels has also been described in congenital heart disease (CHD) in almost 20% of infants. The purpose of this retrospective study was to determine whether CHD, lung disease (pulmonary hypertension [PH] and bronchopulmonary dysplasia [BPD]), and ROP with plus disease are distinguishable on the basis of retinal vessel morphology. Qualitative vascular findings were validated using computer-based software to analyze 25 representative images, each corresponding to one infant's eye. Vessel diameter (d) and tortuosity index (TI) were measured. A total of 106 infants (mean gestational age, 30.5 +/- 2.22 weeks) were included. Ophthalmologic evaluation of preterm infants with CHD and lung diseases showed vascular tortuosity without vasodilation at the posterior pole as well as in the periphery. Their results indicated statistically significant increased venular diameter in plus disease compared to the diameter in the other groups. Vascular tortuosity showed a significant difference between plus disease and lung diseases; however, there was no difference with CHD. The authors conclude that the patterns of retinal vascular tortuosity may be unique to different systemic congestive conditions. The authors acknowledge the limitations of the study including its retrospective, the possible selection bias created by the image selection method and its small sample size.

Changes in Relative Positions of Choroidal Versus Retinal Vessels in Preterm Infants

This study is a secondary analysis of prospectively collected data as part of the Imaging and Informatics for ROP (i-ROP) study. The purpose of this study was to
characterize a novel finding that relative positions of choroidal and retinal vessels change over time in preterm infants and to identify factors associated with this finding using quantitative analysis. Fundus images were obtained prospectively through a retinopathy of prematurity (ROP) cohort study. Images were excluded if choroidal vessels could not be identified. Changes in relative position of characteristic choroidal landmarks with respect to retinal vessels between two time points 5 to 7 weeks apart were measured. Univariate and multivariate regression analyses were performed to identify associated factors with the amount of change. The discovery and replication cohorts included 45 and 58 patients, respectively. Ninety-two of them (89%) were non-Hispanic Caucasians. Changes in relative position of choroidal versus retinal vessels were detected in all eyes of the discovery and replication cohorts (mean amount = 0.42 ± 0.12 and 0.35 ± 0.12 mm, respectively). On combined multiple regression analysis of the two cohorts, type 1 ROP, higher postmenstrual age at the first time point, and shorter distance from optic disc to choroidal landmark were significantly associated with less change in relative position. Choroidal vessels grow anteriorly with respect to retinal vessels at posterior pole in preterm infants, suggesting relatively faster peripheral growth of choroidal versus retinal vessels. Eyes with severe ROP showed less difference in growth, which might represent alterations in choroidal development due to advanced ROP. These findings may contribute to better understanding about the physiology of choroidal development and involvement in ROP. Limitations of this study include unclear accuracy of measurements performed on fundus images and selection bias in including lighter pigmented eyes with higher quality images.

Central Macular Thickness in 6.5-year-old Children born Extremely Preterm is Strongly Associated with Gestational Age Even When Adjusted for Risk Factors


This population-based study assessed macular thickness in 6.5-year-old children born extremely preterm (EPT) in comparison to children born at term, and investigated risk factors associated with macular thickness in the preterm group. 134 children born before 27 weeks gestational age (mean gestational age 25 weeks) and 145 age-matched control subjects born at term underwent macular assessment with OCT, and the results were compared with neonatal risk factors and sex. The mean central macular thickness was significantly increased in the EPT group (right eyes 282 um, left eyes 283 um) compared to the control group (right eyes 249 um, left eyes 248 um). A multiple linear mixed model analysis of the EPT group revealed gestational age, ROP, and male gender as important risk factors for increased macular thickness. The macular thickness decreased by 3.9 um per gestational week when adjusted for ROP and sex.

Unlike prior investigations, this study included a large number of EPT children and focused exclusively on this group. However, 65 of the original 199 children in
the EPT cohort dropped out, and the dropout group contained some of the most immature (GA 22 weeks) children, and also some with previously treated ROP. The difference in GA between the preterm group and the preterm dropout group was statistically significant and might have affected results. Nevertheless, this study demonstrates that EPT birth is an important risk factor for a thick central macula, a sign of macular immaturity. Other risk factors are low GA, previous ROP (regardless of stage or treatment), and male gender. Further studies are needed to explore functional outcomes related to these structural abnormalities.

Optical Coherence Tomography Angiography of the Fovea in Children Born Preterm


This cross-sectional observational comparative case series compared the foveal avascular zone (FAZ) area measured by OCT angiography in children born preterm to age-matched controls. 43 eyes of 26 children (28 eyes of 15 former preterm infants and 15 eyes of 11 former term infants) between the ages of 4 and 12 years old were included. OCT angiography with a scan size 3 x 3 was performed for all eyes, FAZ area was measured, and inner and outer retinal thicknesses were measured. A distinct FAZ was absent in 12 eyes (42.8%) of preterm children but was present in 100% of control eyes. The FAZ area was significantly correlated with gestational age and birth weight. The GA was less than 29 weeks and birth weight less than 1,480 grams in eyes with no distinct FAZ. Mean central foveal vessel density in the superficial capillary plexus was 41.8% in the preterm group and 32.8% in the control group. In all eyes, a negative correlation was found between the central foveal density and GA and birth weight. On SD-OCT examination, the foveal depression was absent and the inner retinal layers were preserved in all eyes with absent FAZ. In all eyes, a significant negative correlation was found between the inner retinal thickness and GA and BW. 10 eyes of 6 preterm children had a history of laser therapy for ROP. A distinct FAZ was absent in 6 eyes (60%) with ROP with history of laser, and 6 eyes (33.3%) with preterm birth without laser therapy. Eyes with a history of laser had a higher inner retinal thickness and central foveal vessel density and smaller FAZ compared to eyes with preterm birth without laser therapy.

This study had a small sample size and limited age range at the time of OCTA imaging. However, the identification of an abnormal web-like foveal microvasculature comprising the FAZ in eyes with history of preterm birth is novel. This study expands knowledge of foveal abnormalities in ROP, and confirms that a small or absent FAZ seems to be a distinct sign of prematurity.

Electrophysiological changes in 12-year-old children born MLP: reduced VEP amplitude in MLP children

Moderate to late preterm infants (MLP) are at increased risk of morbidity and mortality than term infants. Previous studies in preterm and IGUR infants have shown abnormal responses on ERG and VEP testing, as well as abnormal macula morphology and thickness. This study aimed to investigate electrophysical changes in MLP children (without previous ROP) at age 12, when the visual system is believed to be mature. 22 MLP children and 21 controls were included in the study. OCT, pattern reversal VEP, and full-field ERG were obtained. The results showed a trend for thinner RNFL in the MLP group. Visual evoked potential amplitudes were lower in the MLP group, but latencies were similar. No ff-ERG differences were found. Therefore, the authors conclude that MLP children may have affected visual evoked potentials without significant retinal structural changes. This may imply differences in the optic tract or visual cortex, although the significance of the reduced VEP amplitudes is not fully understood.

**Anterior Chamber Angle and Anterior Segment Structure in Children With Early Stages of Retinopathy of Prematurity.**

Premature infants have steeper corneas, more shallow anterior chambers and shorter axial lengths than their full term counterparts. As the degree of retinopathy of prematurity (ROP) increases, so do these differences. Additionally infants treated for ROP have thicker lenses than those who did not require treatment. All of these changes add to an increased risk of narrow angle glaucoma in these patients. Acute angle closure glaucoma has even been reported after dilation in a child with regressed ROP. This study was a prospective cross-sectional study of 54 eyes of 29 preterm infants now at school age to compare the structural differences in the anterior chamber angle (ACA) in children with or without ROP. The authors compared patients who had ROP requiring and receiving laser treatment to age-matched full term control children by evaluating the ACA structures with gonioscopy. The authors found that the children with a history of ROP treatment had a narrower ACA, steeper iris curvature, and a more anteriorly inserted iris than their full term counterparts. Additionally, the eyes treated for ROP had steeper corneas, more shallow anterior chambers, thicker lenses, and higher refractive errors. The axial lengths in the two groups were not different. The authors also found a high rate of poor corrected distance vision highlighting the importance of amblyopia treatment in children who were treated for ROP. The authors highlight the limitations starting with the difficulty to find age-matched control for patients with and without ROP treatment. Additionally, gonioscopy evaluation has some subjectivity and different observers may report different findings. The authors concluded that the eyes that had ROP treatment had many structural risk factors for glaucoma but that further research was needed to determine if these differences in the structure actually increases the risk of glaucoma.
Reduction of Rod and Cone Function in 6.5-Year-Old Children Born Extremely Preterm

This was a subcohort study from 2010 to 2014 of the Extremely Preterm Infants in Sweden Study and included children born at term and children born <27 weeks’ gestational age. The children were examined at 6.5-years old at the Uppsala Health Care region with a full field electroretinograph (ff ERG), bilateral, using a DTL electrode with 30Hz flicker and single-cone flash. Adequate ff ERG recordings were obtained in 52 preterm children and 45 term children. No association was noted between gestational age or retinopathy or prematurity in the preterm children. The authors found that both rod and cone function were reduced in extremely preterm children as compared to children born at term. This electrophysiology study suggests that being born extremely preterm is a reason for retinal dysfunction and contribute to amblyopia.

**Prematurity and Outcomes**

**Association of Maternal Preeclampsia With Infant Risk of Premature Birth and Retinopathy of Prematurity**

In this cohort study, there was a 2.5-fold increased risk of infants developing ROP. In the preterm cohort with very low birth weights, preeclampsia was inversely associated with the development of all ROP. The authors did a retrospective review of 290,992 live births within the intermountain Healthcare System in Utah from 1/1/2001 through 12/31/2010. In the full cohort, 51% of the infants were male and the mean gestational age was 38.38 weeks. In the P-VLBW cohort, 55% were male and the mean gestational age was 26.87 weeks. In summary, although the authors report conflicting associations in the full and P-VLBW cohorts, the authors note that the association of a reduced risk of ROP among the P-VLBW subcohort may reflect biases from restricting the cohort to prematurity, because prematurity was an outcome of preeclampsia.

ROP and Telemedicine/Screening
Toward Achieving 100% Adherence for Retinopathy of Prematurity Screening Guidelines.

The purpose of this data analysis was to report on the use of a cloud-based electronic medical record (ROP Check; glacier medical software, Anchorage, AK) designed to provide American Academy of Pediatrics (AAP) guideline-adherent retinopathy of prematurity (ROP) care through the scheduling and documenting of ROP examinations. Three thousand one hundred fifty five patients from a de-identified dataset from thirteen neonatal intensive care units were analyzed. All newborns with a gestational age of 22 to 30 weeks (N = 2,278) were entered with a documented ROP examination. Of those, 98% and 97.4% completed their initial and follow-up examinations, respectively, within AAP guidelines. All but 1 of 145 initial treatments were completed within AAP guidelines after a decision for treatment was made. Of 369 newborns older than 30 weeks' gestational age and with a birth weight of less than 1,500 grams, none progressed to treatment; four patients had stage 2 or 3 ROP. Of 508 newborns with a gestational age of 31 to 32 weeks and a birth weight of more than 1,500 grams who were entered to identify unstable newborns, 34% did not need examinations; of those who were examined, one progressed to treatment. Fourteen percent of patients were observed as outpatients before retinal maturity and 12% missed some or all outpatient appointments. A decision was made to treat at the first examination for 2 (10%) newborns with a gestational age of 22 weeks and 2 (2%) newborns with a gestational age of 23 weeks. Each patient was within the AAP guidelines for initial treatment. The authors conclude that a computerized system specifically designed with process improvement and error-free delivery of ROP care as a focus can improve adherence to AAP guidelines and achieve superior results.

Retinopathy of prematurity: screening and treatment in Costa Rica

A nationwide ROP screening program was started in Costa Rica in 1982, with a database developed in 2004. This paper reports the incidence and outcomes of the ROP program there and compares the results with other countries. The authors performed a retrospective chart review of all preterm infants meeting ROP screening criteria (≤34 weeks GA, BW ≤1750g, or at risk) in the system from January 2010-December 2014. This included 3018 preterm infants, 585 of which had ROP. 90 patients (15.4%) required laser treatments. Of these 53% had BW <1000g. The highest percentage of infants requiring laser treatment were born between 26 and 29 weeks. Aggressive posterior disease was found in nine patients. Two infants suffered severe visual impairment. The authors note that babies born in Latin American countries may develop ROP with increased GA and
BW compared to the United States, which is why the screening criteria are expanded compared to the US. They note four infants requiring treatment that would have been missed if they had used the US screening criteria, and one would have been missed if using the UK criteria. Therefore, the authors state that the current screening parameters used in Costa Rica are appropriate.

Validation of WINROP for detecting retinopathy of prematurity in a North American cohort of preterm infants. 


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WINROP (weight, insulin-like growth factor 1, neonatal, and retinopathy of prematurity) is a web-based retinopathy of prematurity (ROP) risk algorithm that uses postnatal weight gain as a surrogate of insulin-like growth factor-1 (IGF-1) to predict the risk of severe ROP in premature infants. The purpose of this retrospective study was to validate the web-based algorithm WINROP in detecting severe (type 1 or type 2) ROP in a cohort of infants from two centers in Colorado. The records of consecutive infants who underwent ROP examinations between 2008 and 2011 were reviewed retrospectively. Infants were classified into categories of "alarm" (at risk for developing severe ROP) and "no alarm" (minimal risk for severe ROP). Excluded were infants, who did not meet the inclusion criteria for the WINROP algorithm: (1) gestational age at delivery >32 weeks’ gestation, (2) missing weekly weight measurements, and (3) a weight gain of more than 450 g per week. Out of a total of 563 infants only 483 met the WINROP criteria and were included in the study. Alarm occurred in 241 neonates (50%), with the median time from birth to alarm of 2 weeks. The authors found that WINROP had a sensitivity of 81.8% (95% CI, 67.3%-91.8%) and specificity of 53.3% (95% CI, 48.5%-58.0%) for identifying infants with severe ROP. Eight of the 44 infants with severe ROP were not detected (5 with type 1 and 3 with type 2). Of these 8 infants, 7 (88%) had birth weight in excess of the 70th percentile. With additional weight data entry, sensitivity of WINROP rose to 88.6%. The authors conclude that very preterm infants (gestational age of ≤27 weeks) with relatively high birth weight for gestational age may not be detected by WINROP as high risk for developing severe ROP.

The low specificity of the current screening protocol for ROP has prompted many groups to investigate other screening algorithms for ROP. This is yet another study trying to validate the suggested alternatives to the current national screening criteria. The article includes a nice summary of previous validation studies of this algorithm.

Colorado Retinopathy of Prematurity Screening Algorithm (COPROP): a validation study at a tertiary care center.

The Colorado Retinopathy of Prematurity Screening Algorithm (CO-ROP) recommends screening for infants meeting the following criteria for retinopathy of prematurity (ROP): gestational age \(\leq 30\) weeks, birth weight of \(\leq 1500\) g, and net weight gain of \(\leq 650\) g between birth and 4 weeks of age. The purpose of this retrospective study was to evaluate the validity of CO-ROP in a tertiary referral county hospital. CO-ROP was compared against a total of 374 consecutive newborns, who were screened for ROP using national screening guidelines at one center during 5 years. Sensitivities and specificities for identifying ROP were calculated. In this cohort, 29 (7.8\%) developed type 1 ROP and 12 (3.2\%) developed type 2 ROP. The CO-ROP model would have decreased the number of infants screened by 34\% compared to current national screening criteria. CO-ROP had sensitivity of 93.1\% (95\% CI, 77.2-99.1) and 92.7\% (95\% CI, 61.5-99.8) for identifying type 1 and type 2 ROP, respectively. Of 29 patients who developed type 1 ROP, 2 were not identified using CO-ROP. The authors concluded that the CO-ROP model significantly reduced the total number of newborns screened for ROP, but failed to detect 2 infants with type 1 ROP, suggesting the need for further modification of the algorithm. The authors suggest adding the diagnosis of sepsis as another criterion for screening together with the CO-ROP criteria. In their cohort this would have increased the sensitivity for identifying type 1 ROP from 93.1\% to 100\%, and the number of infants requiring screening would have been reduced by 32.1\% as opposed to 34.2\% by CO-ROP criteria alone.

The study’s population was primarily composed of Hispanic and black infants and hence the results may not be generalizable to other populations.

**Intraocular Hemorrhages and Retinopathy of Prematurity in the Telemedicine Approaches to Evaluating Acute-Phase Retinopathy of Prematurity (e-ROP) Study.**


In this study, the authors evaluated whether clinical characteristics of intraocular hemorrhage (IOH) can potentially be used for prediction of disease severity and to improve sensitivity of a telemedicine system to detect referral-warranted retinopathy of prematurity (RW-ROP). RW ROP is defined as presence of zone I ROP, stage 3 ROP or plus disease. However early stage 3 retinopathy (especially in zone I) and evolving plus disease may be difficult to detect with certainty and the exact border between zone I and zone II can be difficult to capture with photos. However, IOH is easier to detect and recognize in photos. For that reason, this study describes the clinical characteristics of IOHs in infants to evaluate their potential use for prediction of disease severity. Preterm infants with birth weight (BW) \(\leq 1250\) g underwent serial digital retinal imaging in both eyes starting at 32 weeks’ postmenstrual age. Non-physician trained readers (TRs) evaluated all image sets from eyes that ever had IOHs documented on image evaluation or eye examination for the presence, location, type, area, and relation of the IOH to...
the junction between vascularized and avascular retina. Associations of IOH with demographic and neonatal factors, and with the presence and severity of retinopathy of prematurity (ROP) were investigated by univariate and multivariate analyses. Sensitivity and specificity of identifying RW-ROP were calculated with and without incorporating hemorrhage into the standardized grading protocol. Among 1239 infants (mean [standard deviation] BW = 864 [212] g; gestational age [GA] = 27 [2.2] weeks) who underwent an average of 3.2 imaging sessions, 22% had an IOH in an eye on at least 1 of the e-ROP visits. Classification of IOH was preretinal (57%), blot (57%), dot (38%), flame-shaped (16%), and vitreous (8%); most IOHs were unilateral (70%). The IOH resolved in 35% of eyes by the next imaging session and in the majority (76%) of cases by 8 weeks after initial detection. Presence of IOH was inversely associated with BW and GA and significantly associated (P < 0.0001) with the presence and severity of ROP (BW and GA adjusted odds ratios [ORs] of 2.46 for any ROP, 2.88 for stage 3, and 3.19 for RW-ROP). Incorporating IOH into the grading protocol minimally altered the sensitivity of the system (94% vs. 95%). Approximately 1 in 5 preterm infants examined had IOHs, generally unilateral. The presence of hemorrhage was directly correlated with both presence and severity of ROP and inversely correlated with BW and GA, although including hemorrhage in the grading algorithm only minimally improved the sensitivity of the telemedicine system to detect RW-ROP.

Assessment of a Tele-education System to Enhance Retinopathy of Prematurity Training by International Ophthalmologists-in-Training in Mexico

An increase in the incidence of ROP, termed the “third epidemic,” has uniquely occurred in middle-income countries. A lack of standardization for ROP education within both high- and middle-income countries has resulted in significant differences in the accuracy of ROP diagnosis. The Global Education Network for ROP is a multi-institutional collaboration interested in developing innovative ways to educate and increase the workforce for ROP. This is a prospective study offering web-based learning to medical trainees in Mexico to improve diagnostic competency in ROP by ophthalmologists-in-training. Fifty-eight ophthalmology residents and fellows from a training program in Mexico consented to participate. Twenty-nine of 58 trainees (50%) were randomized to the educational intervention (pretest, ROP tutorial, ROP educational chapters, and posttest), and 29 trainees were randomized to a control group (pretest and posttest only). A secure web-based educational system was created using clinical cases (20 pretest, 20 posttest, and 25 training chapter–based) developed from a repository of over 2500 unique image sets of ROP. For each image set used, a reference standard ROP diagnosis was established by combining the clinical diagnosis by indirect ophthalmoscope examination and image-based diagnosis by multiple experts.
Trainees were presented with image-based clinical cases of ROP during a pre-test, posttest, and training chapters. The accuracy of ROP diagnosis (e.g., plus disease, zone, stage, category) was determined using sensitivity and specificity calculations from the pretest and posttest results of the educational intervention group versus control group. The unweighted kappa statistic was used to analyze the intrgrader agreement for ROP diagnosis by the ophthalmologists-in-training during the pretest and posttest for both groups. Trainees completing the tele-education system had statistically significant improvements ($P < 0.01$) in the accuracy of ROP diagnosis for plus disease, zone, stage, category, and aggressive posterior ROP (AP-ROP). Compared with the control group, trainees who completed the ROP tele-education system performed better on the posttest for accurately diagnosing plus disease (67% vs. 48%; $P = 0.04$) and the presence of ROP (96% vs. 91%; $P < 0.01$). The specificity for diagnosing AP-ROP (94% vs. 78%; $P < 0.01$), type 2 ROP or worse (92% vs. 84%; $P = 0.04$), and ROP requiring treatment (89% vs. 79%; $P < 0.01$) was better for the trainees completing the tele-education system compared with the control group. Intrgrader agreement improved for identification of plus disease, zone, stage, and category of ROP after completion of the educational intervention. The authors concluded that this system has the potential to increase competency in ROP diagnosis and management for ophthalmologists-in-training from middle-income nations.

**ROP and imaging**

Computer-assisted quantification of pre-plus and plus disease in images obtained using Pictor versus video indirect ophthalmoscopy: a pilot study.

Subjectivity in the diagnosis of plus disease in retinopathy of prematurity has prompted the creation of computer programs to objectively measure vascular characteristics. ROPtool is a semi-automated computer program that analyzes retinal vascular dilation and tortuosity. The purpose of this retrospective study was to explore its ability to trace images taken with a FDA-approved, portable, handheld noncontact digital fundus camera (Pictor). The study was conducted as part of a much larger study evaluating the feasibility of using Pictor as an ROP screening tool. The ROPtool analysis of Pictor still images acquired by non-ophthalmologists was compared to video indirect ophthalmoscopy (VIO) still images acquired by ophthalmologists. The authors conclude that ROPtool could trace Pictor images better than VIO images. The study showed that Pictor images are highly traceable by the ROPtool. However, it did not show that it is non-inferior to RetCam images in the setup of ROP.
Macular morphology following unilateral bevacizumab injection for retinopathy of prematurity: an OCT study.
Clark, A., Wright, T., Isaac, M., Westall, C., Mireskandari, K. and Tehrani, N. N.

This retrospective case series assessed the influence of unilateral intravitreal bevacizumab (IVB) for unilateral type 1 retinopathy of prematurity (ROP) on macular thickness and foveal development. Seven infants with unilateral type 1 ROP were treated with intravitreal bevacizumab 0.625 mg/0.025 ml in one eye only. To determine whether macular thickness and foveal structural development were affected by treatment, spectral domain optical coherence tomography was performed on both treated and untreated eyes. The mean gestational age of infants was 25.3 +/- 0.3 weeks; the mean birth weight, 776 +/- 17.6 g. Treatment was given at a mean postmenstrual age of 37.2 +/- 0.4 weeks. Foveal development was normal in 3 (43%) treated versus 5 (71%) untreated eyes. The mean central foveal thickness for treated and untreated eyes was 270.1 mum +/- 19.6 and 253.0 mum +/- 27.2 respectively (P = 0.15). There was small but nonsignificant difference in foveal development and thickness in eyes treated with intravitreal bevacizumab compared to fellow eyes. Despite the obvious limitations of this small retrospective study it generates important data to test the hypothesis that foveal thickness is greater in unilateral type 1 ROP eyes treated with IVB compared to untreated fellow eyes. Unfortunately, we cannot establish from the data presented in this paper whether the differences in foveal development and thickness in treated eyes reflect IVB treatment or ROP severity, since OCT images were not preformed prior to treatment.

Sayman Muslubas, I., Karacorlu, M., Hocaoglu, M., Arf, S. and Ozdemir, H.

The purpose of this cross-sectional observational study was to evaluate the outcomes of transscleral diode laser photocoagulation in the eyes of children with a history of threshold retinopathy of prematurity (ROP) and compare them with the eyes of children with no or subthreshold ROP and normal term infants using spectral-domain optical coherence tomography (SD-OCT). Three groups of children aged 4 to 10 years were included as follows: 45 patients with regressed ROP who had not received any treatment (group 1), 48 patients with a history of zone 2 threshold ROP who had been treated with transscleral diode laser (group 2), and 56 age-matched healthy full-term children (group 3). Visual acuity, refractive error, and measurement of retinal and choroidal thickness by SD-OCT were compared between groups retrospectively. The mean gestational age (GA) and birthweight (BW) were 31 weeks and 1,409 grams in group 1, 28.7 weeks and
1,274.5 grams in group 2, and 38.4 weeks and 3,285 grams in group 3, respectively. All three groups were significantly different by GA and birth weight. Foveal depression was absent in 16% of group 1 and 63% of group 2 eyes and non in controls (p<0.001). BCVA was also significantly reduced in both group 1 and 2 (0.1±0.1 and 0.2±0.1, respectively) compared to controls 0.03±0.04 (p<0.001). The spherical equivalent in group 2 post laser was significantly reduced (1.9 ± 2.5) compared to 0.4 ± 2.1 and 0.3 ± 0.9 in group 1 and 3, respectively. In contrast, there were no significant differences among any of the choroidal parameters in all of the groups. Neither macular nor choroidal thickness correlated with visual acuity. The authors conclude that although retinal structural changes were observed in patients with a history of ROP, especially in patients treated with laser, no significant difference was found in choroidal thickness between groups. These structural abnormalities may be related to both severity of ROP and laser treatment. This study validates previous observations.

Comparison of strategies for grading retinal images of premature infants for referral warranted retinopathy of prematurity
JAAPOS Apr 2017; 21(2): 141-145.

The use of telemedicine in retinopathy of prematurity (ROP) is increasing worldwide to identify at risk premature infants, but implementing it can be challenging. The purpose of this retrospective study was to determine the accuracy of identifying referral-warranted retinopathy of prematurity (RW-ROP, defined as any zone I ROP, stage 3 or worse, or plus disease) from retinal image sets using three grading protocols: a single optic disk-centered image, a set of 3 horizontal images, and a 5-image set. In this secondary analysis of images from the e-ROP study, a weighted sample of 250 image sets from 250 infants (125 with RW-ROP and 125 without RW-ROP) was randomly selected. The sensitivities and specificities for detecting RW-ROP and its components from a single disk center image, along with nasal and temporal retinal images, were calculated and compared with the e-ROP grading of RW-ROP of all 5 retinal images (disk center and nasal, temporal, superior, and inferior retinal images). The retinal images were obtained by non-physicians, who were highly trained and underwent an extensive certification process. These selected image sets were independently graded by 2 of 3 trained non-physician readers using the same standard grading protocol. RW-ROP was identified with a sensitivity of 11.2% (95% CI, 6.79%-17.9%) using a single disk center image, with a sensitivity of 70.4% (95% CI, 61.9%-77.9%) using 3 horizontal images, and a statistically higher sensitivity of 82.4% (95% CI, 75.0%-89.0%) using all 5 images (P = 0.002). The specificities were 100%, 86.4%, and 90.4%, respectively. For grading using 3 horizontal images, sensitivity was 14.3% for plus disease, 25% for zone I ROP, and 71.2% for stage 3 or worse compared to 40.8%, 50%, and 79.8% for grading using 5-image sets, respectively. The authors conclude that both a single, disk-centered, posterior pole
image and 3 horizontal images were less effective than a 5-image set in determining the presence of RW-ROP on qualitative grading by trained readers. It seems that even with the 5-image set the sensitivities were not as high as would have been warranted.

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

**Follow-up to Age 4 Years of Treatment of Type 1 Retinopathy of Prematurity Intravitreal Bevacizumab Injection versus Laser: Fluorescein Angiographic Findings.**

This is a single-center, randomized controlled trial looking at the structural outcome at age 4 years of eyes treated with intravitreal injection of bevacizumab (IVB) with fellow eyes treated with conventional laser photoablation in type 1 ROP. The study was conducted at the Catholic University in Rome, from September 1, 2009, to March 31, 2012.. Structural outcome at age 4 years was assessed using fluorescein angiography (FA). In each of 21 infants (42 eyes), 1 eye was randomized to receive an intravitreal injection of 0.5 mg bevacizumab; the fellow eye underwent conventional laser photoablation. Digital retinal imaging and FA were performed at an average of 4 years after treatment in follow-up after these studies performed at treatment and 9 months. FAs were examined by 2 experts to document retinal and choroidal findings. Among the 20 IVB-treated eyes available at 4 years of age, all showed abnormalities at the periphery (avascular area, vessel leakage, shunts, abnormal vessel branching, and tangles) or the posterior pole (hyperfluorescent lesions, absence of foveal avascular zone). These lesions were not observed in the majority of the laser-treated eyes. Among the 19 laser-treated eyes, leakage was noted in 1 eye, shunts and tangles were noted in 3 eyes, and macular abnormalities were noted in 3 eyes. The authors concluded that FA has shown potentially serious and long-term ocular effects that are present more commonly after treatment with bevacizumab for acute-phase ROP than after laser.

**Effect of intravitreal aflibercept on central retinal arterial blood flow in type 1 retinopathy of prematurity**


The authors used color Doppler imaging to prospectively evaluate central retinal artery blood flow changes in infants receiving intravitreal aflibercept for treatment of type 1 retinopathy of prematurity. They measured the peak systolic velocity, end diastolic velocity, pulsatility index, and resistivity index of the central retinal artery before injection and 1 hour, 1 week, and 1 month after injection. Twenty-nine eyes of 15 infants were included in this study, and all eyes had complete re-
gression of ROP after treatment. The authors found that vascular resistance increases and ocular blood flow decreases, and that changes in hemodynamic parameters may remain for a month after intravitreal aflibercept. The effects of anti-VEGF treatment on developing eyes of premature infants are not known, and this article is important because it demonstrates that ocular blood flow is affected. Long-term effects on visual function are unknown.

Low-dose ranibizumab as primary treatment of posterior type I retinopathy of prematurity

Bevacizumab is the most commonly studied intravitreal anti-VEGF therapy for ROP. However, ranibizumab is being evaluated in an increasing number of studies. Intravitreal ranibizumab has been shown to have a lower serum concentration than bevacizumab, which may be associated with a lower risk of systemic effects. The authors of this study conducted a retrospective case series study of infants receiving low dose ranibizumab (0.2mg in 0.02ml). 42 eyes of 21 infants were included in the study. Mean GA was 24.6 weeks, and mean birth weight was 613g. Anatomic outcome was deemed favorable in all eyes. 12 eyes (6 infants) received supplementation laser at a mean PMA of 72.0 weeks, done for failure of vascularization to proceed beyond zone II. No cases required treatment for disease progression or reactivation. VA was measured in 28 eyes and mean was 0.94 logMAR (by Teller Acuity. Mean spherical equivalent was +1.00. There were no reported ocular or systemic complications. The authors concluded that a single intravitreal injection of ranibizumab was safe and effective. Note that like many other studies, this paper was not designed to evaluate long-term systemic safety.

Ultra-low-dose intravitreal bevacizumab for the treatment of retinopathy of prematurity: a case series

There are significant concerns about the effect of VEGF suppression in early human development, particularly on neurological development. Lower doses of anti-VEGF are being studied to lessen the systemic concerns when treating retinopathy of prematurity. The authors of this study performed a retrospective review of infants receiving 0.16mg in 0.025ml of bevacizumab for ROP in England. 29 eyes (15 infants) were included. Mean GA was 23.9 weeks, and mean BW was 596.3g. Mean postmenstrual age at treatment was 34.1 weeks. Follow-up was for a mean of 9.4 months. All cases showed early improvement in plus disease and retinopathy within 48 hours of injection. Success was defined as complete regression of retinopathy and vascularization into or laser treatment of zone 3. Initial success was achieved in 23/29 eyes, and secondary success (additional treatment required) in 27/29 eyes. 6/29 eyes underwent additional treatment at a mean of 9.8 weeks after first injection (mean 44 weeks PMA). There were no
recorded ocular adverse events. Two infants died during follow-up, both due to respiratory disease. While this study was not designed to address systemic effects, overall the authors conclude this low dose of bevacizumab is effective for ROP without adverse ocular outcomes.

Anti-Vascular Endothelial Growth Factor Therapy for Primary Treatment of Type 1 Retinopathy of Prematurity: A Report by the American Academy of Ophthalmology.

This is a systemic review of available research for clinical efficacy and safety of anti-VEGF agents for the treatment of ROP compared with laser photocoagulation therapy. A literature search of the PubMed and Cochrane Library databases was conducted on September 6, 2016, with no date restrictions and limited to articles published in English. This search yielded 311 citations, of which 37 were deemed clinically relevant for full-text review. Thirteen of these were selected for inclusion in this assessment. The panel methodologist assigned ratings to the selected articles according to the level of evidence. Of the 13 citations, 6 articles on 5 randomized clinical trials provided level II evidence supporting the use of anti-VEGF agents, either as monotherapy or in combination with laser therapy. The primary outcome for these articles included recurrence of ROP and the need for retreatment (3 articles), retinal structure (2 articles), and refractive outcome (1 article). Seven articles were comparative case series that provided level III evidence. The primary outcomes included the effects of anti-VEGF treatment on development of peripheral retinal vessels (1 article), refractive outcomes (1 article), or both structural and refractive or visual outcomes (5 articles). Current level II and III evidence indicates that intravitreal anti-VEGF therapy is as effective as laser photocoagulation for achieving regression of acute ROP. Although there are distinct ocular advantages to anti-VEGF pharmacotherapy for some cases (such as eyes with zone I disease or aggressive posterior ROP), the disadvantages are that the ROP recurrence rate is higher, and vigilant and extended follow-up is needed because retinal vascularization is usually incomplete. After intravitreal injection, bevacizumab can be detected in serum within 1 day, and serum VEGF levels are suppressed for at least 8 to 12 weeks. Intravitreal ranibizumab also can lower serum levels of VEGF by 1 day after treatment, but this effect is short-lived and serum VEGF levels recover to baseline within 1 week of treatment. The effects of lowering systemic VEGF levels on the developing organ systems of premature infants are unknown, and there are limited long-term data on potential systemic and neurodevelopmental effects after anti-VEGF use for ROP treatment. Still, evidence is lacking on the long-term safety of anti-VEGF agents, the best anti-VEGF agent to use for ROP treatment, the optimal dose for each agent, and the potential long-term side-effects. Anti-VEGF agents should be used judiciously and with awareness of the known and unknown or potential side effects.
Ranibizumab Injection as Primary Treatment in Patients with Retinopathy of Prematurity: Anatomic Outcomes and Influencing Factors.

This is a study evaluating the anatomical outcome after using ranibizumab as the primary treatment modality for ROP in Xinhua Hospital, affiliated with Shanghai Jiao Tong University School of Medicine. In a retrospective study, a total of 283 eyes of 145 patients with type 1 ROP were treated with 0.25 mg/0.025 mL of (half of the dose administered in adults) ranibizumab (IVR) as primary treatment between January 2012 to August 2015. Children were admitted to NICU for the injection and were kept there for 2 weeks following the injection. Weekly eye exams were conducted and a minimum of 6 months of follow-up was required. Initial response to IVR was conducted 1 week after the injection and the eyes were classified as positive or negative/no response. The positive response group was defined as follows: ridge and venous dilation and arteriolar tortuosity of the posterior retinal vessels (plus disease) regressed after IVR, and retinal vessels continued to develop into the peripheral area. The negative/no response group was defined as follows: ROP worsened after IVR and developed into Stage 4A, 4B, or 5, or plus disease and ridge did not show any change one week after IVR. The positive response group was subdivided into 2 groups: regression without reactivation and regression with reactivation. The regression without reactivation subgroup was defined as plus disease, ridge regressed after IVR without recurrence, and flat retina achieved at the last visit. The regression with reactivation subgroup was defined as eyes with reoccurrence of plus disease or ridge during follow-up. The study investigators chose to apply laser treatment in the regression with reactivation subgroup to reduce the burden of long-term follow-up. There were a total of 266 eyes (94.0%) in the positive response group and 17 eyes (6.0%) in the negative/no response group after IVR. Among the positive response group, 139 eyes (48.6%) were in the regression without reactivation subgroup, and 127 eyes (44.9%) were in the regression with reactivation subgroup. A total of 152 eyes received additional laser or surgical treatment. At the last visit, 278 eyes (98.2%) had attached retinas, and 5 eyes (1.8%) had retinal detachment. A classification tree model showed that for patients with gestational age (GA) ≤29.5 weeks, the possibility of experiencing reactivation after IVR is higher than that of those with GA >29.5 weeks (61.6% vs. 29.6%). Moreover, for patients with GA ≤29.5 weeks, those diagnosed with zone II stage 2+ ROP have a lower possibility of experiencing reactivation than other patients (37.9% vs. 80%). The authors concluded that IVR is effective in treating ROP as a first line therapy. However, more than half of the babies in the cohort required additional treatment with laser or surgery. The authors did not adequately address systemic side effects of the drug. The only comment regarding this was that there was no complication described by the neonatal intensivists during the 2 week stay in the NICU after the IVR injection.
Histopathologic Characterization of the Expression of Vascular Endothelial Growth Factor in a Case of Retinopathy of Prematurity Treated with Ranibizumab.

Retinopathy of prematurity is sometimes treated with anti vascular endothelial growth factor (VEGF) agents, however there is no documentation of the expression of VEGF in eyes treated with an anti-VEGF agent. Here the authors present an observational case series of histologic retinal findings in four patients who died. Case 1 was a baby who was treated with ranibizumab. Case 2 had ROP without treatment. Case 3 was a premature baby without ROP and the fourth case was a baby without prematurity or ROP. The authors found less VEGF staining in the retina of the eye treated with anti-VEGF than the cases with ROP not treated with anti-VEGF agent. However VEGF was not completely eliminated by the injection, supporting the idea that anti-VEGF treatment can suppress without completely blocking the drive for vascularization of the immature retina.

Serum Vascular Endothelial Growth Factor After Bevacizumab or Ranibizumab Treatment for Retinopathy of Prematurity

This study investigated systemic VEGF levels after intravitreal injections of bevacizumab (IVB) or ranibizumab (IVR) in 10 patients with Type 1 ROP. Serum samples were collected before and up to 12 weeks after anti-VEGF treatment. In patients receiving IVB only, the median serum VEGF level decreased significantly at 2 weeks, 4 weeks, and 8 weeks after injection. In patients receiving IVR only, there was no significant difference in the serum VEGF level between baseline and up to 8 weeks post-injection. All eyes had complete resolution of abnormal neovascularization after IVB or IVR. This study was limited by a small number of patients and blood samples. In addition, the treatment choice was not random as the choice of IVB or IVR treatment was made by the parents. Nevertheless, the authors conclude that IVB, but not IVR, for Type 1 ROP causes significant serum VEGF suppression and should therefore be used with caution in the treatment of ROP.

Comparison of Intravitreal Injection of Ranibizumab Versus Laser Therapy for Zone II Treatment-Requiring Retinopathy of Prematurity
This prospective, randomized, controlled single-center study compared the efficacy of intravitreal injection of ranibizumab (IVR) monotherapy and laser therapy for Zone II treatment-requiring ROP. 100 eyes of 50 ethnic Han Chinese infants with Zone II Stage 2 or 3 ROP with plus disease were randomly assigned to receive IVR monotherapy or laser therapy. Infants were followed for at least 6 months, and all eyes that developed recurrence of ROP underwent crossover retreatment. At the last follow-up, 26 eyes of 13 infants in the IVR group developed recurrence, versus 2 eyes of 1 infant in the laser therapy group. Study limitations include a relatively small sample size and short follow-up. In addition, all infants in this study were of Han nationality, and differences in results may be influenced by different racial backgrounds. Also, anterior and posterior Zone II treatment-requiring ROP differs in behavior and treatment response, and the eyes were not stratified in this study. The authors conclude, however, that although IVR leads to prompt regression of neovascularization and promotes peripheral retinal vascularization, the effect for Zone II ROP is not as durable as conventional laser therapy and IVR is not recommended as a single-dose monotherapy for Zone II treatment-requiring ROP in this population.

Roles of cytokines and treatment algorithms in retinopathy of prematurity

ROP varies throughout the world and may be due to differences in genotype, resources for prenatal and perinatal care and the number of trained experts to diagnose and treat ROP. Evidence for the use of intravitreal bevacizumab (IVB) is being collected but the level of evidence is low. Currently used doses of IVB reduces blood cytokines and VEGF for 2 months according to some studies, which is longer and lower than using ranibizumab. Recurrences after 0.625 mg IVB is estimated at <10% for aggressive posterior ROP and usually show up within a year but there are studies to suggest that longer follow up is necessary. In addition, there is some evidence that there is impairment in neurodevelopment with IVB but that myopia is lessened in eyes treated with IVB than traditional laser. Larger randomized studies and longer follow up are needed to obtain the evidence of these trends. The use of lower oxygen saturation targets to reduce ROP risk is of concern because of reports of increase in mortality, however there is also concern that higher oxygen saturation targets may increase the development of severe ROP. Because of the dearth of well controlled studies and the significant variability in the study groups, it is important to assess whether studies used any ROP vs. severe ROP to evaluate the outcomes. In addition, the gestational ages and birth weights studied must be determined and the perinatal resources and genetic influences must be considered.

At this time, while there are current clinical trials ongoing, the current recommendation from the AAP and AAO should still apply in the treatment of Type 1 ROP.
Treatment of type I ROP with intravitreal bevacizumab or laser photocoagulation according to retinal zone

Retinopathy of prematurity (ROP) is commonly treated today with anti-VEGF intravitreal injections. One of the proposed benefits of anti-VEGF treatments is that it allows further retinal vascularization while vitreoretinal proliferations are regression. The BEAT-ROP trial demonstrated fewer recurrences and fewer unfavorable structural outcomes in cases treated with intravitreal bevacizumab (IVB) vs laser in zone I disease. There was also lower incidence of high myopia in these eyes. In this study the authors retrospectively reviewed 54 consecutive cases of very low birth weight infants with type I ROP that were treated with IVB or laser. 33 infants had posterior ROP (Zone 1 or posterior zone II), of which 28 were treated with IVB and 5 with laser. 21 infants had peripheral zone II disease, of which 9 were treated with IVB and 12 with laser. Time to regression was shorter in infants with posterior ROP treated with IVB. This difference compared to laser was only seen in cases with posterior ROP. 7 infants (12%) had recurrence at a median of 12.7 weeks after treatment. The zone of ROP did not impact recurrence rate. No recurrences were seen in laser treated eyes. Infants treated with IVB in posterior zone had lower spherical equivalent refractive error (+0.37D) at 12-15 months compared to cases in peripheral zone II (+3.0D). Spherical equivalent was also lower in laser treated eyes in peripheral zone II compared to IVB cases. Retinal vascularization was deemed incomplete in all cases of posterior ROP, but funduscopy showed a structurally normal fovea in 95% of eyes. In conclusion, the authors found that IVB led to faster regression compared to laser in posterior zone disease. 78% of patients (either treatment) had age appropriate refractive errors, but was significantly lower in posterior ROP than peripheral zone II.

ROP Epidemiology and Outcomes

Paul Sternberg, Alia K Durrani Am J Ophthalomol February 2018;186:xxiii-xxxii

This is a literature review that reviews and summarizes the evolving concepts in the clinical management of retinopathy of prematurity while also providing a personal perspective on its management today and future directions of treatment. The authors perform a literature review on studies that evaluate the use of anti-VEGF treatment for ROP. Although initial treatment strategies focused on ablative therapy for threshold ROP, earlier treatment for type 1 or pre–threshold dis-
ease has been found to decrease unfavorable visual and structural outcomes. Vascular endothelial growth factor has emerged as a significant contributor to retinal-vascular diseases in the previous 2 decades. The potential role of anti-VEGF treatment for type 1 ROP has become a focus in recent years, but the protracted recurrence of disease and unknown adverse ocular and systemic effects have caused concern from some clinicians. In addition, the use of telemedicine technologies may provide the ability to screen remote areas with a shortage of ROP providers, thereby reducing the burden of disease. The authors conclude that the diagnosis and management of ROP has changed over the past 40 years; the role of anti-VEGF therapy remains to be established in current treatment strategies. Screening for initial disease and progression will likely be impacted by the increasing prevalence of telemedicine and relative shortage of clinicians.

**International variations and trends in the treatment for retinopathy of prematurity**

The purpose of this study was to compare ROP incidence and treatment in very preterm infants within the networks of the iNeo (International Network for Evaluating Outcomes) consortium. The iNeo comprises 10 population based national neonatal networks from 11 countries. Infants born between 24 and 27+6 weeks and weighing <1500g were retrospectively examined. 48,087 were included. 81.8% survived to 32 postmenstrual age, and 95% of survivors were screened for ROP. ROP rates range rates were wide, from 25.2% in Switzerland to 91.0% in Japan. Overall 24.9% received treatment (range 4.3% to 30.4%). Overall the rate of ROP treatment declined significantly from 2007 to 2013. Japan has been shown to have higher amounts of ventilation days and oxygen treatment (at least compared to Canada), which could contribute to the increased risk of ROP found. The diagnosis and treatment criteria may also be different in Japan. All of the networks did show variation in treatment criteria. Adoption of common definitions of pathology could help to understand the differences in outcomes, and further study is warranted.

**Is artificial reproductive technology a risk factor for retinopathy of prematurity independent of the generation of multiple births?**

There is some debate regarding whether artificial reproductive technology (ART) constitutes an independent risk factor for retinopathy of prematurity (ROP). The purpose of this retrospective study was to evaluate whether ART constitutes a risk factor for ROP independent of the generation of multiple births. A retrospective audit was performed of all multiple birth babies
admitted to a tertiary neonatal unit who met the UK ROP screening criteria (<32 weeks gestational age [GA] and/or <1,501 g birthweight [BW]). A total of 205 babies were included, of whom 87.3% were twins. A total of 39.5% were born following ART. A total of 30.5% of the non-ART group developed ROP vs 34% of the ART group (p = 0.837). Stage 3 ROP developed in 5.1% of non-ART babies and 6% of ART babies. A total of 8.5% of non-ART babies and 10% of ART babies required treatment for ROP. Logistic regression demonstrated that ART was not independently associated with development of ROP. The authors conclude that artificial reproductive technology multiple birth babies make up a considerable proportion of the ROP screening burden and their number is likely to increase as ART is increasingly available and utilized. No significant difference between the numbers of babies developing ROP in the ART vs non-ART groups was found, but the numbers were small. They state that the estimated odds of developing ROP are slightly higher in the ART babies and that they cannot rule out a possible association, but looking at the results the calculated OR was 1.173 with a confidence interval of 0.524-2.627. This means that this cohort did not demonstrate an association between ART and the development of ROP.

**Plus Disease in Retinopathy of Prematurity: Diagnostic Trends in 2016 Versus 2007.**

Plus disease in Retinopathy of Prematurity (ROP) is a very important prognostic indicator in determining the need for treatment of this potentially blinding disease. Plus disease is defined as retinal venous dilation and arterial tortuosity in the posterior pole and a standard photograph selected in the 1980s is used for comparison. Because of this, there is a strong subjective component to the definition of pre-plus and plus disease. The author's sought to determine if ROP experts in 2016 would judge plus disease differently than the ROP experts in 2007 with the hypothesis that there is a trend towards diagnosing plus disease at an earlier level of disease in more recent years. This was a prospective study and part of the Imaging and Informatics in ROP multicenter cohort study group. A set of 34 retinal images that had been evaluated in 2007 by 22 experts were then evaluated by a contemporary group of 13 experts. The authors found that the average severity score for each image was higher for 30/34 (88%) of the images in 2016 when compared to 2007 and that more images were characterized as plus disease in the more contemporary analysis. They conclusion of the paper was that experts are diagnosing plus and pre-plus disease at earlier stages of disease severity in 2016 compared to 2007, which has implications for patient care, teaching and research. The authors suggest that moving to a computer based image analysis could limit the subjectivity of describing plus disease in ROP.
Validation of the Children’s Hospital of Philadelphia Retinopathy of Prematurity (CHOP ROP) Model

This multicenter cohort study sought to validate the CHOP ROP model’s sensitivity for treatment-needed ROP. In 30 hospitals in North America between 2006 and 2012, this study was a secondary analysis of data from the Postnatal Growth and Retinopathy of Prematurity (G-ROP) Study. Patients included 7483 premature infants at risk for ROP with a known ROP outcome. The median birth weight (BW) was 1070 grams, median gestational age (GA) was 28 weeks. This study noted that the CHOP ROP model showed high but not 100% sensitivity and the CHOP ROP model may be better suited to reduce the number of examination frequency. With a modified ROP screening schedule, the number of examinations among infants with GA exceeding 27 weeks could be reduced by 28.4%. In the future, the CHOP ROP model may be appropriate to use if expanded beyond 30 hospitals, with close collaboration between NICU staff, neonatologist and pediatric ophthalmologist.

Postnatal Serum Insulin-like Growth Factor I and Retinopathy of Prematurity

This prospective cohort study sought to determine the relationship between postnatal serum IGF-1 levels and severe ROP in a racially diverse U.S. cohort. 74 infants (20 white, 45 black, 2 Asian, and 7 other or unidentified) with birth weight <1,251 grams and a known ROP outcome were enrolled. Weekly postnatal filter paper blood spot IGF-1 assays were measured through 42 weeks postmenstrual age. During postmenstrual age weeks 28 – 33, mean IGF-1 was 20.0 ng/mL for no ROP, 18.0 for Stage 1 or 2, and 17.0 for Stage 3 (p=0.003). Adjustment for birth weight and gestational age showed similar results. These findings of an association between lower postnatal serum IGF-1 levels and the subsequent development of increasingly severe ROP in a racially diverse cohort of U.S. infants are consistent with the association between IGF-1 and ROP reported by investigators in Europe and with studies of postnatal weight gain as a predictor of the development of severe ROP. These results support potential clinical applications such as exogenous postnatal IG-1 supplementation to prevent or reduce the severity of ROP, and risk prediction using growth-based models to improve ROP screening efficiency. Although these results cannot be generalized to countries with developing neonatal care systems where older GA infants develop severe ROP and IGF-1 may play less of a role in ROP pathogenesis, similar studies may help to clarify disease pathogenesis in world regions where growth-based models perform less well and oxygen supplementation plays a more dominant role.
ROP screening guidelines exist in order to catch cases of this potentially blinding condition while at the same time limiting unneeded exams and cost. The authors aimed to investigate ROP screening compliance in Hong Kong compared to international recommendations. They conducted a retrospective review of 611 infants that were screened at a single tertiary hospital, 9 of which were excluded due to incomplete data. Screening was performed according to the Royal College of Ophthalmologists ROP screening guide. All babies <32 weeks GA or <1501g were screened, with first exam at 31 weeks GA or 4 weeks postnatal age, whichever is later. 2 infants exceeded criteria for screening. Mean birth weight of the children screened was 1.27kg and mean GA was 29 weeks. Of the 602 cases, 75.8% were screened during recommend guidelines, 15.6% were early, and 5.8% were late. 170 infants developed ROP, with 23 (3.8%) developing type I requiring treatment. Mean GA of infants requiring treatment was 26 weeks and mean birth weight 0.88kg. Of the 35 cases that were screened late, 5 developed ROP requiring treatment. These children were screened 1 week later than recommended due to systemic condition causing deferring of exam. ROP treatment was not delayed in these cases. When using the American Academy of Pediatrics 2006 guidelines (<=1500g, GA 30 weeks or less, or selected larger babies with unstable clinical course), 15.4% of the infants exceeded the criteria. Of those, 3 (0.5%) developed ROP, but none progressing to type 1 requiring treatment. In summary, the authors noted reasons for late screening included interhospital transfers and unstable critical condition, but there were no delayed treatment cases. The UK guidelines seemed applicable and safe for this Asian population, and the AAP guidelines may also be safe and cost-effective in Hong Kong, although the study was done at one center and may not be generalizable to the entire population.

**ROP - Other Topics**

**The inner retinal structures of the eyes of children with a history of retinopathy of prematurity**


The eyes of preterm children have more highly curved corneas, shallower anterior chambers, thicker lenses, and shorter axial lengths (ALs) than those of full-
term children; these differences become more significant as the severity of ROP increases. Preterm children with or without a history of ROP have a thinner retinal nerve fiber layer (RNFL) than full-term children. Glaucoma is a progressive optic neuropathy characterized by RNFL thinning and it is recognized as an important cause of visual decline in children with severe ROP after surgery. Myopia, especially high is strongly associated with glaucoma. The mechanical stretching of the ocular structure alone or insufficient ocular perfusion in people with myopia can lead to RNFL damage. An analysis of the ganglion cell layer (GCL) might be a powerful predictor to diagnose and monitor glaucoma. The present study performed detailed measurements of the optic nerve head (ONH) and inner retinal structures (including the peripapillary RNFL and mGCC). This study recruited two cohorts of children: children with a history of treatment-requiring ROP. The second cohort consisted of age-matched healthy controls born at > 37 weeks; Birth weight > 2500 g and they did not present with any ocular disease except refractive errors. ROP grade was categorized by the maximal severity in the acute stage. Patients were excluded if they had stage 4 or 5 ROP and had undergone vitrectomy or scleral buckling. Patients with residual retinal sequelae of ROP, including retinal detachment or macular dragging or fold, were also excluded. To measure the ONH, RNFL, and mGCC, the standard glaucoma module was used. The peripapillary RNFL thickness was measured at a diameter of 3.45 mm around the center of the optic disc. The mGCC consists of three layers: the RNFL, the GCL, and the IPL. The mGCC scan covered a $7 \times 7$ mm area in the macula and was centered 1 mm temporal to the fovea to improve coverage of the temporal macula. Four types of data (average, superior, inferior thicknesses, and superior-inferior difference) were used to analyze the mGCC. The mGCC global loss volume (GLV) and focal loss volume (FLV) metrics are designed to detect patterns of loss. The GLV detects diffuse loss, and the FLV detects localized loss over the mGCC map. A total of 41 eyes of 21 preterm children and 34 control eyes of 17 full-term children were included in this study. The mean GA of children in the ROP group was $26.2 \pm 2.1$ weeks (range, 23–36 weeks) and $39.0 \pm 1.7$ weeks (range, 37–41 weeks) in the control group ($P < 0.001$). The mean BW of the children in the ROP group was $919.4 \pm 260.8$ g (range, 552–1530 g) and $3195.9 \pm 384.3$ g (range, 2500–3878 g) in the control group ($P < 0.001$). The mean age (years) at examination was $9.6 \pm 2.5$ in the ROP group and $8.4 \pm 1.7$ in control group ($P = 0.14$).

In the ROP group, all of the eyes (100%) were zone 2 ROP. Six eyes (14.6%) were stage 2 ROP plus disease, and 35 eyes (85.4%) were stage 3 ROP plus disease. A total of 37 (90.2%) eyes were treated with diode laser photoagulation, and 4 eyes (9.8%) were treated with diode laser photoagulation and IVB. A significant greater spherical equivalent was seen in the ROP cohort. (Myopia 4.6 vs 0.4 D). Other analysis revealed similarity in average AL between the two cohorts, significantly shallower ACDs and thicker LTs in the ROP cohort, and no differences in the vitreous depth, baseline intraocular pressure, central corneal thickness. The average RNFL thickness of children with ROP did not significantly
differ from that of full-term children (108.4 ± 16.0 μm and 109.5 ± 12.1 μm, respectively, P = 0.91). The peaks near the superior and inferior sectors showed a temporal deviation in the ROP group, which means that the superotemporal and inferotemporal sectors were thicker, and the superonasal and inferonasal sectors were thinner. The average, superior, and inferior mGCC thicknesses were all thicker in children with a history of ROP than healthy children. mGCC difference between the superior and inferior areas was similar across these two groups (P = 0.20). The spherical powers, cylindrical powers, and spherical equivalent in all patients were positively correlated with RNFL thickness. The AL in all patients was negatively correlated with RNFL thickness. The ACD in all patients was not correlated with RNFL thickness. There was no significant correlation between mGCC thickness and spherical powers, cylindrical powers, spherical equivalent, AL, or ACD among all patients. Preterm children with a history of ROP have poorer best-corrected visual acuity, shallower ACD, greater LT, changes in peripapillary RNFL distribution, and greater mGCC thickness with increased mGCC-FLV compared with full-term children. Inner retina in children with a history of ROP was thicker and had a different distribution pattern than those of full-term children. The temporal RNFL thickening in children with a history of ROP was related to the disrupted development of the inner retina rather than the temporal shift of RNFL peaks in axial myopia observed in full-term children.

An international comparison of retinopathy of prematurity grading performance within the Benefits of Oxygen Saturation Targeting II trials.


Variation in the rates of severe ROP between clinical centers have been attributed in part to observer bias. A number of studies have demonstrated inter-observer variation when grading ROP using retina images. This study aimed to determine whether international variation in the interpretation of images and subsequent treatment decisions was present. Nine readers from Australia, two from New Zealand, and seven from UK who participated in the BOOST II trials were used. The median (range) number of years’ experience of the readers in performing clinical ROP screening examinations was 25 (14–26) for the UK group, 15 (3.5–40) for ANZ, and 21 (10–38) for the international reference group. Each reader assessed 48 eye examinations. Seventeen of the 42 (40.5%) image sets were obtained at the time when a decision to treat was made, or immediately prior to treatment. Thirteen of the 42 (31.0%) image sets were from infants who did not require treatment at the time of imaging, but who were subsequently treated. Twelve of the 42 (28.6%) image sets were from infants who were not treated for
ROP at any time. Of the 42 eye examinations reviewed the mean (SD) number of examinations per reader judged as ‘plus’ disease was 14.1 (6.23) for UK readers, 8.5 (3.24) for ANZ readers, and 13.2 (6.31) for the international readers (Table 1). The difference between UK and ANZ readers was significant (t-test $P = 0.021$, mean difference $= 5.69$, 95% CI $= 0.98–10.40$). Examinations per reader classified as stage 2 was higher in the ANZ group than in the UK group ($t$-test, $P = 0.026$, mean difference $= 7.47$, 95% CI $= 1.00–13.94$). For stage 3 there were no significant differences between the groups. The proportion of eye examinations read as each zone was not significantly different between any pair of groups. Agreement was highest within the ANZ group for all measures, with ‘moderate’ agreement for treatment decisions and for plus disease categories. Agreement was ‘fair’ for treatment decisions within the UK group. Agreement was poor for most measures within the INT group. UK ophthalmologists demonstrated a lower threshold to treat than Australian and New Zealand ophthalmologists. UK ophthalmologists graded more images as plus disease, and more images as treatment-requiring. There were no significant differences in grading stage 3 disease or ROP zone. The UK ophthalmologists had more inter-observer variation than the Australian and New Zealand ophthalmologists. Intra-observer consistency appeared to be good among all ophthalmologists. The international reference ophthalmologists graded in a similar way to the UK ophthalmologists. It is likely that variation in treatment rates between countries was due to international variation in ROP grading and treatment decisions.

**Fetal hemoglobin, blood transfusion, and retinopathy of prematurity in very preterm infants: a pilot prospective cohort study.**


Neonates have a predominance of fetal hemoglobin (HbF) at birth. HbF has a greater affinity for oxygen compared to HbA, shifting the hemoglobin–oxygen dissociation curve to the left, causing preferential fetal oxygen binding in utero. HbF preponderance postnatally in very preterm infants leads to greater difficulty unloading oxygen to the tissues. Oxygen–hemoglobin dissociation curve is shifted to the right in preterm infants after blood transfusion. Authors hypothesized that as the HbF : HbA ratio decreases with blood transfusion, more oxygen is made available to the developing retina contributing to ROP development. The purpose of this study is to explore whether there might be an association between either initial %HbF (on admission after birth) and/or the mean inpatient HbF% (during their hospital admission), with the development of ROP in very preterm infants. Prospective cohort study across two tertiary neonatal intensive care units in Bristol, UK. All inborn infants within 24 h of birth born less than 32 weeks of gestation or less than 1501 g were eligible for inclusion. With informed parental consent, all routine EDTA samples taken during the baby’s admission
were analyzed for HbF%, HbA%, and HbF : A ratio. A total of 42 infants were recruited between January 2012 and November 2013. No infants were excluded from the study. Six infants died before ROP screening and 24 infants received a transfusion of red blood cells (RBCs) during their admission. Infants who developed ROP were more likely than infants who did not develop ROP to be from multiple births (P = 0.027), more preterm (P<0.001), of lower birth weight (P = 0.007), to have had more transfusions (P<0.001), larger volumes infused (P<0.001), and to have spent longer on ventilators (P<0.001) and continuous positive airway pressure (P = 0.028). A total of 14 infants developed ROP. On admission, non-ROP infants had higher initial hemoglobin levels compared to infants who developed ROP (P = 0.009). Infants who developed ROP had significantly lower (P = 0.0001) mean %HbF during their admission compared to those infants who did not develop ROP. There was no evidence that initial HbF% was associated with increasing risk of ROP grade (P >0.05). There was strong evidence for an association between mean %HbF and increasing risk of ROP grade in both the unadjusted (P<0.001) and the adjusted (birth weight, gestation at birth, and volume of transfusion) analyses (P = 0.034). It is possible that HbF is a protective factor against ROP, and that transfusion of adult (HbA) blood may play a part in ROP development by suddenly making more oxygen available to the developing retina and downregulating VEGF.

Systemic Inflammation-Associated Proteins and Retinopathy of Prematurity in Infants Born Before the 28th Week of Gestation

This study was performed as part of the ELGAN study. The purpose of this study was to assess the association between systemic levels of inflammation-associated proteins and severe retinopathy of prematurity (ROP) in extremely preterm infants. Whole blood was collected on filter paper on postnatal days 1, 7, 14, 21, and 28 from 1205 infants born before the 28th week of gestation, and the concentrations of 27 inflammation-associated, angiogenic, and neurotrophic proteins were measured. The odds ratios with 95% confidence intervals were calculated for the association between top quartile concentrations of each protein and prethreshold ROP. During the first three weeks after birth, high concentrations of VEGF-R1, myeloperoxidase (MPO), IL-8, intercellular adhesion molecule (ICAM)-1, matrix metalloproteinase 9, erythropoietin, TNF-a, and basic fibroblast growth factor were associated with an increased risk for prethreshold ROP. On day 28, high levels of serum amyloid A, MPO, IL-6, TNF-a, TNF-R1/-R2, IL-8, and ICAM-1 were associated with an increased risk. Top quartile concentrations of the proinflammatory cytokines TNF-a and IL-6 were associated with increased risks of ROP when levels of neuroprotective proteins and growth factors, including BDNF, insulin-like growth factor 1, IGFBP-1, VEGFR-1 and -2, ANG-1 and PlGF, were not in the top quartile. In contrast, high concentrations of NT-4 and BDNF appeared protective only in infants without elevated inflammatory media-
tors. Systemic inflammation during the first postnatal month was associated with an increased risk of prethreshold ROP. Elevated concentrations of growth factors, angiogenic proteins, and neurotrophins appeared to modulate this risk, and were capable of reducing the risk even in the absence of systemic inflammation. Due to the blood-retinal barrier, concentrations of cytokines and growth factors in blood do not necessarily reflect levels in the retina and vitreous. It would be interesting also to look at levels during phase 2 of ROP, which was not looked at in this study. This study adds to our knowledge of the complex etiology of ROP development, and appears to be the first study with such a wide variety of systemic biomarkers in a large cohort of extremely low gestational age newborns.

**The Cutting Edge of Retinopathy of Prematurity Care: Expanding the Boundaries of Diagnosis and Treatment**


Despite progress in ROP management, ROP remains a major global issue as industrialized nations now treat profoundly premature infants with posterior and aggressive disease, and middle-income nations are experiencing ROP epidemics. This literature review with 176 references discusses the latest advances and controversies in the diagnosis and care of infants with ROP. Remote digital imaging may address the decreasing ratio of ROP providers to premature infants while improving patient care. Widefield angiography, OCT, and the Wnt signaling pathway have provided new insights into ROP pathogenesis. Anti-VEGF treatment is increasing in popularity, but information is lacking to guide dosing, and unpredictable reactivation, persistent vascular abnormalities, the “crunch” phenomenon, and unknown effects of systemic VEGF suppression are unresolved concerns. Neurodevelopmental delay has been raised as a potential consequence, but current evidence is weak. Vitrectomy is the preferred treatment for Stages 4 and 5, and illumination techniques, ab interno incision, plasmin-assisted vitrectomy, staged surgery in the setting of corneal clouding, and immediate sequential bilateral vitreoretinal surgery are discussed. This review is a useful summary as clinicians expand the boundaries of their abilities to manage ROP globally.

**Comparative systems pharmacology of HIF stabilization in the prevention of retinopathy of prematurity**


Retinopathy of prematurity (ROP) causes 100,000 new cases of childhood blindness each year. ROP is initiated by oxygen supplementation necessary to pre-
vent neonatal death. We used organ systems pharmacology to define the transcriptomes of mice that were cured of oxygen-induced retinopathy (OIR, ROP model) by hypoxia-inducible factor (HIF) stabilization via HIF prolyl hydroxylase inhibition using the isoquinolone Roxadustat or the 2-oxoglutarate analog dimethyloxalylglycine (DMOG). Although both molecules conferred a protective phenotype, gene expression analysis by RNA sequencing found that Roxadustat can prevent OIR by two pathways: direct retinal HIF stabilization and induction of aerobic glycolysis or indirect hepatic HIF-1 stabilization and increased serum angiokines. As predicted by pathway analysis, Roxadustat rescued the hepatic HIF-1 knockout mouse from retinal oxygen toxicity, whereas DMOG could not. The simplicity of systemic treatment that targets both the liver and the eye provides a rationale for protecting the severely premature infant from oxygen toxicity.

Pharmacological activation of the hypoxia-inducible factor (HIF) pathway can prevent experimental oxygen-induced retinopathy and thus has the potential to prevent blindness in 100,000 children annually. Comprehensive analysis of liver and retinal transcriptomes after HIF stabilization demonstrates that select small molecules, given systemically, protect the retina by two pathways: stimulating the liver to secrete angiogenic hepatokines or locally stimulating retinal protection. These findings support a low dose, intermittent systemic approach for preventing oxygen induced injury to premature infants.

**Investigation of the effect of hemoglobin F and A levels on development of retinopathy of prematurity.**


The purpose of this prospective study was to investigate the effect of hemoglobin F (HbF) and hemoglobin A (HbA) levels on development of retinopathy of prematurity (ROP) in premature infants. Blood samples were collected from the side of the heel of 49 premature infants (mean gestational age 30.9±2.7 weeks, range 25-35 weeks; mean birth weight, 1542±582 g, range 520-3240 g) at postnatal months 0, 1, 2, and 3. HbF and HbA levels were measured in all samples and analyzed statistically. Furthermore, correlation analysis was performed regarding development of ROP, blood transfusion, and HbF and HbA levels. Stage 1 ROP or worse developed in 26 (53%) infants. Mean HbF levels were lower at postnatal months 1 and 2 in premature infants with ROP compared to those without ROP (P = 0.013 and 0.02, respectively); while mean HbA levels were higher in the infants with ROP verses infants without ROP (P = 0.034 and 0.029, respectively). Since blood transfusion can affect Hb distribution, analysis of covariance ANCOVA correcting for presence of transfusion as a possible co-factor was performed. This eliminated the difference between the means of Hb variants in the infants with and without ROP (P = 0.572 and 0.486). The authors conclude that blood transfusion can significantly altered the levels of HbF and HbA in premature infants. An increased prevalence of ROP was found in the transfused infants, but this could have been related to the significantly lower birth weight of
this group. No direct effect on development of ROP related to Hb variants could be demonstrated in this cohort.

9. STRABISMUS

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

Strabismus and binocular diplopia due to advanced glaucomatous visual field loss.

The purpose of this observational case series was to describe patients with glaucoma whose strabismus and binocular diplopia were due to advanced visual field loss and inability to maintain sensory and motor fusion. Specific characteristics of the strabismus associated with advanced glaucomatous visual field loss were a subjective floating second image and marked variability of the prism and alternate cover measurements. Measured hypertropia changed in magnitude over a few seconds or a few minutes (even in 1 patient to a hypotropia), which distinguishes this specific type of strabismus from other types of comitant or incomitant strabismus associated with glaucoma. Although visual acuity was 20/400 or better in both eyes in all patients, there was advanced visual field loss in at least one eye. All patients responded poorly to prism, but their symptoms improved with a Bangerter filter applied to the spectacle lens or a MIN occlusion lens to further blur the worse-seeing eye. The authors conclude that variable strabismus associated with advanced glaucomatous visual field loss appears to be a distinct clinical entity that should be distinguished from other types of strabismus associated with glaucoma. Management of this specific type of strabismus is limited by inadequate visual field to fuse, analogous to hemifield slide, and therefore prism and/or strabismus surgery is unlikely to be successful. Primary treatment options include optical blur with Bangerter filters or a MIN occlusion lens although some patients prefer to ignore the second image. Although variability of diplopia and strabismus can be seen in myasthenia gravis, which was considered in one of the patients presented, the rapid changes in alignment over a period of seconds was more consistent with diplopia and strabismus associated with advanced glaucomatous visual field loss. This condition is somewhat analogous to other conditions, where advanced visual field loss is a barrier to fusion, where overlapping of visual fields is insufficient to maintain stable single vision, such as in chiasmal lesions, which has been termed hemifield slide. This very interesting report also includes a comprehensive discussion on the possible obstacles to fusion in these patients.
Convergence Insufficiency Symptom Survey scores for required reading versus leisure reading in school-age children.

This cross-sectional study compared the Convergence Insufficiency Symptom Survey scores for required reading for school versus scores for leisure reading. It was performed at a single private practice, where a 100 children with normal binocular vision were surveyed using modified survey questions specifying either required reading or leisure reading as the near visual activity. The survey’s instructions were modified to control for possible symptoms caused by prolonged reading, a modification designed to minimize the influence of sustained reading that may cause fatigue in all children regardless of their near visual skills. The study found that the average score for the required reading survey was significantly higher than for the leisure reading survey (14.4 ±9.1 vs 9.8 ±6.9 [P = 0.005]). Scores for the leisure reading survey highly correlated (R²= 0.95) with each child’s self-reported reading speed. The authors conclude that the Convergence Insufficiency Symptom Survey scores vary greatly depending on the type of near activity being surveyed and thus do not accurately isolate and reflect near visual ability. They suggested that beginning each survey with the question about self-rated reading speed could eliminate the need for additional questions, if a child self-rates his or her reading speed as average or better. Despite the slightly cumbersome presentation of the results, it is a well-designed study. Those using this survey to monitor improvement of CI treatment, should take notice of its variable results.

Two Orthoptic Treatment in Dragged-Fovea Diplopia Syndrome

Binocular diplopia can be a rare complaint secondary to retinal diseases such as epiretinal membranes (ERMs). ERMs are fibrocellular tissue that exerts traction on the inner retinal surface leading to progressive distortion. Patients report blurred vision micropsia, macropsia, metamorphopsia, scotomas, and monocular or binocular diplopia. Dragged foveal diplopia syndrome is a condition caused by foveal displacement due to macular traction resulting in binocular diplopia. Retinal diplopia does not benefit from prism therapy. The authors present two patients with dragged foveal diplopia syndrome. Patient one experienced vertical binocular comitant diplopia at distances greater than 1 meter that resolved with monocular occlusion. An ERM was present and confirmed on OCT and FA. The patient had a concomitant hypertropia, when the angle was neutralized the diplopia remained. The patient was treated with penalization with a small round opaque tape placed centrally on his left lens. Patient two complained of binocular vertical diplopia beyond 2 meters. Fundus examination revealed an right ERM confirmed by Oct and FA. He had a right hypertropia of 3 prism diopters
which could not be neutralized with base-down prisms. The patient was treated with optical penalization with monovision contact lenses successfully.

Convergence Accommodation in orthoptic practice
Anna M. Horwood PhD Br Ir Orthopt J 2016; 13: 2-8

Orthoptists are very familiar with accommodation driving convergence and its role in strabismus. This study looks at the inverse relationship: convergence leading to accommodation (CA/A). Disparity leads to convergence leading to convergence-accommodation and blur leads to accommodation leading to accommodative-convergence. The lab measured accommodation and convergence concurrently on a haploscopic photorefractor measuring both AC/A and CA/A. The authors state that the majority of individuals image disparity is more of a driving factor than blur thus the CA/A ratio is more clinically relevant. The exception is patients with accommodative esotropia. Binocular accommodation is much better than monocular accommodation in the majority of patients therefore encouraging binularity with orthoptic exercises helps both convergence and accommodation. Exotropes do not use accommodation to control near deviations they use convergence secondary to disparity. This may explain why minus lenses only temporarily control exotropia because the basic divergent angle and excessive convergence demand remain the same. The authors recommend continuing to evaluate AC/A ratios but to understand that convergence accommodation should be considered more in orthoptic practices.

Causes of Diplopia in Patients With Epiretinal Membranes.

Patients with epiretinal membrane can suffer from both monocular and binocular diplopia. The monocular double vision is thought to be due to the abnormal retina causing decreased vision, metamorphopsia, and aniseikonia. Binocular misregistration and rivalry is thought to cause binocular diplopia in these patients. The authors performed a retrospective observational case series of 50 patients with ERM, 25 of whom had symptoms of diplopia with the goal of better describing the causes of diplopia in this patient population. Eleven of the 25 patients had retinal misregistration as the only cause of the diplopia, 7 patients had strabismus, 1 patient had refractive error causing monocular diplopia, 2 patients had both retinal misregistration and strabismus and for 4 patients the cause of the double vision was not determined. Interestingly 15 of the 25 patients without double vision (60%) had evidence of misregistration on optotype frame test and or synaptophore. The authors hypothesize that some level of retinal misregistration can be tolerated before the patient experiences diplopia. The authors point out that about a third of symptomatic patients had treatable causes of their diplopia such as strabismus or refractive error. The study was limited by its retrospective design and small sample size.
An Optimal Measurement of Fixation Disparity Using Ogle’s Apparatus

Fixation disparity is defined as a small ocular misalignment that is not measurable with cover testing. This finding is important because it can result in asthenopia that cannot be alleviated with prisms or strabismus surgery. Ogle’s apparatus is the only instrument that can measure fixation disparity in a dynamic manner. The authors analyzed 26 participants in regards to point zero, motor fusion amplitude, esodisparity, exodisparity and asthenopic symptoms. They found that there was a significant difference in exodisparity but no relationship between asthenopic symptoms and abnormal fixation disparity curves. The authors recommend the most reliable procedure when using Ogle’s apparatus to measure fixation disparity is to use prisms of ascending strength combined with moving the line from divergent.

Strabismus in children with white matter damage of immaturity: MRI correlation.

Premature infants are vulnerable to damage to the periventricular area of the brain from a variety of causes, including ischemia, hemorrhage, periventricular leukomalacia (PVL), and diffuse white matter injury. White matter injury, or white matter damage of immaturity (WMDI) can be associated with spastic diplegia, cognitive delays, and visual impairment. Visual impairments reported included reduced visual acuity, reduced visual field, delayed visual maturation, and others. The association of white matter damage and strabismus has been known, but the authors of this study evaluated the prevalence and characteristics of strabismus based on the severity of WMDI. Patients with diagnosed WMDI who had brain MRI and ocular examinations were retrospectively reviewed. 73 patients were identified, with median GA at birth of 31.4 weeks. 76.7% had significant refractive errors, but this was not correlated with the grade of WMDI. 38 children (52.1%) had strabismus, the prevalence of which increased with the stage of WMDI. All had horizontal strabismus, nearly equally split between exotropia and esotropia. 13 also had vertical strabismus. Constant strabismus was associated with higher grades of WMDI. The authors note that although their patients most likely had more severe disease and visual acuity was not assessed with this study, the degree of WMDI can have prognostic value for the occurrence of strabismus and constant tropia, and strabismus can be a sign of cerebral dysfunction in these children.

Anatomy
Neuroanatomical Structures in Human Extraocular Muscles and Their Potential Implication in the Development of Oculomotor Disorders.
Ala Paduca, Jan Richard Bruenech JPOS. 2018;55(1):14-22

The potential role of sensory feedback from human extraocular muscles has been subjected to considerable speculation in the ophthalmic literature. Extraocular muscles pull against a fairly even load and do not initiate a stretch reflex, even when the eyes are directed toward the boundaries of their respective field of action. These unique working conditions and physiological properties have led to the notion that the sensory signal arising from receptors in extraocular muscles differs from the conventional proprioceptive signal arising from their somatic counterparts. The interest in the receptors at the myotendinous junction of human extraocular muscles has been renewed due to their alleged role in the development of binocular vision and their potential implication in the etiology of binocular vision anomalies. The idea that extraocular muscles provide knowledge of eye position and whether this function can be affected by surgical intervention has initiated several clinical and neuroanatomical studies. Many of these studies support this concept and suggest that surgical procedures that impose only minimal interference with the proprioceptive signal will give a better postoperative result. However, other studies contradict this view because the afferent capacity of the receptors can be questioned and some uncertainties remain. The purpose of this study was to review the related literature and discuss the possible role of ocular proprioceptors in relation to binocular vision and the development of eye motility disorders.

Postoperative change in lateral rectus muscle insertion measured by anterior segment optical coherence tomography.

AS-OCT can be used to image the structure of the horizontal rectus muscles, and shows good agreement with intraoperative measurements. AS-OCT could accurately detect rectus muscle insertions. The purpose of this study were to investigate the longitudinal change in LR muscle insertion after strabismus surgery, and to determine the effect of insertion movement on the angle of deviation. The caliper function of the AS OCT was used to measure the Spur-LR distance. Two blinded independent examiners performed the measurements. All measurements were repeated 1 month later and postoperatively at months 1, 3 and 6. There was a stability in the insertion of the lateral rectus muscle and a negative correlation between the lateral rectus muscle and the alignment. AS-OCT can determine the position of the muscle. Authors conclude that no movement of the muscles were seen postoperatively.

Development of a simple computerized torsion test to quantify
subjective ocular torsion.

Kim YD, Yang HK, Hwang J-M. *Eye* (2017) 31, 1562–1568

Cyclodeviation, torsional diplopia has been recognized in 13% patients with strabismus and cyclodeviation, and this cannot be corrected with prisms. Therefore, the documentation and diagnosis of cyclodeviation is essential in the management of strabismus. Subjective ocular torsion could be measured using the double Maddox-rod test (DMRT), Lancaster red–green test (LRGT), unmounted double Bagolini lenses, the torsionometer and synoptophore. In the present study, authors developed a novel subjective torsion test designed using Microsoft Office PowerPoint for the individual assessment of subjective ocular torsion using red and green filters and validated the reliability and accuracy of the test compared with those of the DMRT and LRGT. A total of 30 patients with cyclovertical strabismus and 30 controls without any strabismus were included in this retrospective study. All subjects underwent our newly developed computerized torsion test (CTT), DMRT, and LRGT in random order on the same day. The CTT evaluated torsional cyclodeviation using two different colored lines: red and cyan. The cyan line was made with an equal proportion of blue and green. Cyan targets were used instead of green because only cyan was completely filtered using a green filter. The red line was invisible when viewed through the red filter, and the cyan line was invisible when viewed through the green filter. Every slide was constructed with five concentric circles, a red line and a cyan line horizontally passing through the circles. The concentric circles were used as a fixation target. Two parallel horizontal lines were demonstrated in the first slide: an upper red line and a lower cyan line. If the subject noted that the upper red line was tilted (torsion in the left eye) in the first slide, the instructor pressed the right arrow key to go to the next slides, and the upper line (red line) was gradually slanted from $-30^\circ$ to $+30^\circ$ by $1^\circ$ intervals on each slide. If the subject noted the lower cyan line to be tilted (torsion in the right eye) in the first slide, then the instructor pressed the end key to go to the last slide and then pressed the left arrow key to perform the test with the upper line (cyan line) gradually slanted from $-30^\circ$ to $+30^\circ$ by $1^\circ$ interval on each slide. Thirty patients with cyclovertical strabismus (16 men, 14 women; age range, 5–70 years; mean age, 46.8 ± 18.4 years) and 30 controls (10 men, 20 women; age range, 31–74 years; mean age, 46.7 ± 13.0 years) participated in this study. CTT showed better reliability than the DMRT. Paired t-tests revealed significant differences between the DMRT and CTT values in the strabismus group ($P = 0.001$), but not in the control group ($P = 0.42$). DMRT values were smaller than the CTT values when the mean value for both tests was less than $2^\circ$, and larger than the CTT values when the mean value for both tests was between $2^\circ$ and $5^\circ$. The overall sensitivity of the LRGT was 32.1%. Compared with the DMRT as a gold standard, the sensitivity of the LRGT was 40.0% and specificity was 87.5%. Compared with the CTT as a gold standard, the values were 39.1% and 100%, respectively. CTT had better reproducibility and higher sensitivity than the DMRT.

The main advantages of the CTT over the DMRT are its higher reliability and easy operation.
Cyclocheck: a new web-based software for the assessment of objective cyclodeviation.

Examination of cyclodeviation is usually limited to use of the Maddox double rod test, Bagolini striated glasses, and the synoptophore. These tests, however, yield subjective results that may be inconsistent. The goal of this study was to present a novel, free, web-based software tool (www.cyclocheck.com) for the assessment of objective cyclodeviation, based on measuring the disk-foveal angle (DFA) and to evaluate reproducibility of the results. Digital fundus photographs of both eyes of all study subjects were obtained using DRS CenterVue non-mydriatic fundus camera. Four separate measurements were made for each eye, and the DFA was calculated using Cyclocheck software independently by two observers to determine reproducibility and repeatability of the technique. A total of 32 subjects (mean age, 34.4; range, 12-83) were enrolled: 18 were orthophoric; 14, strabismic. The interclass correlation coefficient (ICC) for the intraobserver repeatability for one observer was 0.979 (95% CI, 0.970-0.985; P < 0.0005) and for the other was 0.988 (95% CI, 0.983-0.991; P < 0.0005). The ICC for the interobserver agreement was 0.994 (95% CI, 0.992-0.996; P < 0.0005), indicating high reproducibility of the measurements. The authors conclude that the Cyclocheck can assess ocular torsion quickly and easily and that it provides reliable and reproducible measurements of the DFA and thus objective cyclodeviation in both orthophoric and strabismic subjects. A small group of patients with strabismus was assessed in using this technique, this technique’s clinical relevance is not completely clear from this report.

The accuracy of wide-field ultrasound biomicroscopy in localizing extraocular rectus muscle insertions in strabismus reoperations.

The purpose of this cross-sectional study was to compare the accuracy of widefield ultrasound biomicroscopy (UBM) with intraoperative measurements of the distance between rectus muscle insertions and the corneal limbus in strabismus reoperations. Subjects with a history of horizontal rectus muscle surgery who required further surgery on horizontal rectus muscle(s) were recruited prospectively. All widefield UBM measurements were carried out under topical anesthesia using a 50 MHz linear probe without immersion cup and external caliper. The insertion angle distance was measured using the caliper tool of the UBM device; the actual muscle insertion distance from the limbus was considered to be the measured dis-
tance plus 1 mm. The results of UBM and were compared to the intraoperative surgical measurements. A total of 28 subjects were recruited, and 53 horizontal muscles (30 medial rectus, and 23 lateral rectus muscles) were included. The longest distance of the muscle insertion from limbus detectable on UBM was 13 mm for the medial rectus muscle and 15 mm for the lateral rectus muscle. In 38 muscles (71.7%) UBM and surgical measurements were within 1 mm of each other. Only in 1 muscle (1.9%) was the difference between measurements >2 mm (2.3 mm). The intraclass correlation coefficient was 0.87, demonstrating excellent agreement between measurements. Using the Bland-Altman analysis when a difference of ±2mm was used as a clinically acceptable result, better agreement was demonstrated between measurements of medial rectus muscles in consecutive exotropia cases. The authors concluded that good agreement between intraoperative measurement of muscle insertion-limbus distance and widefield UBM measurements can be achieved. This study basically validated previous reports.

Anterior Segment Optical Coherence Tomography of Previously Operated Extraocular Muscles

Strabismus surgery performed on previously operated extraocular muscles (EOMs) can be unpredictable. A number of modalities have been used to determine the position of the EOMs pre- and intra-operatively to aid in surgical plan and decrease exploration. These modalities include computed tomography (CT), magnetic resonance imaging (MRI), B-scan ultrasonography (US), and ultrasound biomicroscopy (UBM). The authors use the Heidelberg anterior segment optical coherence tomography (AS-OCT) to localize the EOMs. The study imaged the horizontal muscles of patients which have previously undergone strabismus surgery. The lateral rectus insertion was imaged with the eye in adduction and the medial rectus insertion was imaged with the eye in abduction. The EOM insertion-limbus distance was measured using digital calipers using chord length in the AS-OCT software by a pediatric ophthalmologist not performing the re-operation. This value was compared to the measurement obtained by the surgeon with handheld calipers using arc length. Chord length and arc length were compared by calculating a Bland-Altman plot and intraclass correlation coefficients. The muscle insertion could be identified in 6 of 10 previously operated muscles and 4 of 4 unoperated muscles on AS-OCT. The difference between the AS-OCT and intraoperative measurements of limbus to insertion distance in previously operated muscles was <1mm in 3 of 6 and <1.5 mm in 6 of 6, it was <1 mm in 4 of 4 unoperated muscles. In a few eyes the insertion was not identifiable on AS-OCT but the presence of the muscle belly was identified providing valuable information for the surgeon. The limitations of determining EOM insertion on AS-OCT include ambiguous transition between muscle tendon to sclera
or Tenon’s capsule, inability to image oblique muscles or posterior portions of the EOMs, and poor image quality through scar tissue.

The role of imaging in strabismus


The authors discuss a review of the use of imaging in evaluating the EOMs in particular for the purposes of surgical planning. MRI can be useful to evaluate the function of a muscle as well as its thickness with respect to inflammation. In addition, the location of pulleys has been found to be relatively consistent across individuals so that MRI can identify misplacement of pulleys which may cause redirection of EOM force. MRI may also help to differentiate conditions such as sagging eye and heavy eye syndrome which clinically may appear similar but on imaging have different angles between the superior and lateral rectus that are diagnostic. This modality has also revealed that muscle contraction may be compartmentalized and that normal ocular motility may involve muscles thought uninvolved due to the compartmentalized contraction and action of those muscles. This may explain the variance in motility within similar types of strabismus. MRI is limited however by the lack of established protocols for more sensitive analysis of the above, which may vary by institution and at this time are largely unavailable to most clinicians. UBM can detect the muscle insertions which may be useful for surgical planning in reoperations but its accuracy declines with distance from the limbus and therefore this may limit its use. Wide field UBM has the ability to scan larger areas and thus may be a better modality for direct ultrasound measurement of the insertion. Lastly, anterior segment OCT has the advantage of being non-contact, readily obtained in the office and easier to get on younger patients. AS-OCT measurements were shown to capture muscle insertions as far back as 13.5 mm from the limbus although does not have as large a field as wide-field UBM. AS-OCT may be a useful tool for planning re-operations especially in young patients.

Cortical Visual Connections via the Corpus Callosum are Asymmetrical in Human Infantile Esotropia.


Hemi-decussation and interhemispheric connections are important in binocularity. Diffusion tensor imaging (DTI) has been used to map the fibers between the hemispheres in humans with normal binocularity. The authors in this study use DTI to examine the distribution of callosal neurons in each hemisphere in 4 adult
patients with infantile esotropia and 9 adult control patients. DTI analysis showed that both the right and the left visual areas showed more callosal fibers in individuals with infantile esotropia. All subjects with infantile esotropia showed an asymmetrical distribution of callosal fibers between the two hemispheres with many fibers terminating near the tips of the occipital cortices. Normal subjects tended to show fibers terminating on the medial aspect of the calcarine sulcus of both hemispheres. This strongly suggests that interhemispheric pathways are involved in human binocular development.

The enlarged extraocular muscle: to relax, reflect or refer?

Extraocular muscle enlargement (EOME) is most commonly associated with thyroid eye disease, but there are other more rare non-thyroid-related extraocular muscle enlargement conditions. The incidence is usually less than 5%. And the most common condition related is inflammation. The underlying diagnosis associated with NTR-EOME is usually made on the basis of orbital imaging. The aim of this study is to report the results of patients with NTR-EOME and the systematic use of imaging. A retrospective consecutive case series review January 2007 and January 2015. Out of 593 orbital scans, 116(20%) showed EOM enlargement. All patients underwent a complete ocular and systemic evaluation. Further systemic imaging was usually limited to the NTR-EOME group and sometimes helped in determining the most suitable diagnostic biopsy site. Patients were classified as inflammatory, infective, primary tumor, metastatic tumor, vascular, or other. Mean age at presentation was 59.3 years. There was a slight female preponderance (5:6). Majority of cases (87%) were associated with an underlying systemic neoplastic process. The most common primary or locally invasive tumor was lymphoma, most of them involved either the superior rectus or the lateral rectus (2:5) and rarely the inferior rectus. Adenocarcinoma from various sources was the most common metastatic tumor followed by carcinoid tumor. There were few cases of presumed paraneoplastic syndrome associated with breast carcinoma and thyroid papillary carcinoma. All cases involved predominant enlargement of a single rectus muscle. The most commonly involved EOM was the SR (50%) followed by the lateral rectus (25%). All cases of SR enlargement were associated with an underlying neoplastic cause. All patients exhibited diffuse muscle belly enlargement with no obvious discerning features apparent between the different underlying diagnoses. Mean follow-up was 3.2 years; 25% died within 3 years of follow up from time of presentation due to disseminated systemic malignancy. Patients with an isolated, enlarged extraocular muscle on CT scan, normal thyroid function tests, and no clinical findings, suggestive of thyroid eye disease can be classified as NTR-EOME. Neoplastic involvement of the extraocular muscles may be caused by local infiltration by adjacent tumors, including primary orbital tumors and secondary neoplasms from periorbital sites, or by metastases from distant sites. Tumors primarily involving extraocular muscles are extremely rare. Extraocular muscle lymphoma predominantly involves the SR. Previous publications have reported that most patients
with metastasis to the orbit have the primary source of the tumor at the moment of diagnosis. However, these authors only found 20% of patients with metastasis presenting with history of the primary tumor. Regarding infections, the medial rectus is more frequently involved in infectious cases due to its close proximity to the ethmoid sinus. In the authors experience cases should be viewed with a high index of clinical suspicion for systemic neoplasia, especially when the SR is involved. Systemic imaging should be considered in all cases of isolated NTR-EOME as this diagnosis can be associated with significant mortality (25%).

**Agreement between Three Optical Coherence Tomography Devices to Assess the Insertion Distance and Thickness of Horizontal Rectus Muscles.**

The purpose of this study is to assess the agreement between two different spectral domain (SD-OCT) and one swept source OCT (SS-OCT) optical coherence tomography device in order to measure the insertion distance and the thickness of the horizontal rectus muscles. Seventy eyes from 35 patients were studied. Three OCT devices- Spectralis (Heidelberg Engineering Inc., Heidelberg, Germany), Cirrus 5000 (Carl Zeiss Meditec, Dublin, CA), and Triton (Topcon, Inc., Tokyo, Japan)-were used to measure the limbus insertion distance, and the thickness of the lateral rectus and medial rectus muscles. The intraclass correlation coefficient (ICC) was calculated to determine the reproducibility and the agreement between the three methods. The study showed that the thickness could be measured in 75% or more patients with spectralis, 74% or more with cirrus, and 78% or more with Triton. The agreement of the insertion distance measurements between the three devices ranged from an ICC of 0.629 or greater to 0.887; for the muscle thickness, the ICC ranged form 0.495 or greater to 0.854. The best agreement existed between the Spectralis and Topcon devices for insertion distance and for muscle thickness. The reproducibility of the device was good and was higher for insertion distance (ICC>/=0.880) than for muscle thickness (ICC>/=0.763). The highest reproducibility values were obtained with Triton. This is the first study to assess the limbus insertion distance and the thickness of the horizontal rectus muscles with SS-OCT and to compare these parameters between one SS-OCT and two SD-OCT devices. The excellent reproducibility observed in the current study highlights the reliability of the limbus insertion distance and muscle thickness measurements in a clinical setting, using a device readily available in clinical practice. The ability of the OCT to accurately image the extraocular muscles could be useful in the preoperative evaluation of patients with strabismus, especially in cases of slipped or lost muscles, or in reoperations.
Combination of anterior segment optical coherence tomography modalities to improve accuracy of rectus muscle insertion location

Anterior segment optical coherence tomography (AS-OCT) is useful for locating the extraocular muscle insertion prior to strabismus surgery; however, its accuracy decreases in reoperations. This masked retrospective study investigated whether a combination of AS-OCT modalities improves accuracy. The distance between the corneoscleral limbus and extraocular muscle insertion was measured with AS-OCT, first using the standard grayscale modality alone and then refined with the color modality. The AS-OCT measurement was considered accurate when within 1.00 mm of the intraoperative caliper measurement. A total of 139 AS-OCT images were analyzed from 74 patients (mean age, 52 years), including 60 medial rectus (19 reoperations), 61 lateral rectus (11 reoperations), 10 superior rectus, and 8 inferior rectus muscles. Compared to grayscale alone, the combination grayscale/color modalities improved AS-OCT accuracy from 77% to 87% (P = 0.03), reflecting an increase from 83% to 94% (P = 0.01) in primary surgeries and from 53% to 60% (P = 0.60) in reoperations. The authors conclude that the use of color in combination with the grayscale AS-OCT improves the accuracy in determining the extraocular muscle insertion location compared to the grayscale modality alone. However, its accuracy within 1.00 mm is lower in reoperation cases than in primary procedures. This is a short report and the study has some obvious limitations, due to its retrospective nature, but it introduces another technique to improve accuracy of extraocular muscle detection pre-operatively. Determining muscle location can be clinically useful when planning for strabismus surgery.

Magnetic resonance imaging in dissociated strabismus complex demonstrates generalized hypertrophy of rectus extraocular muscles.

Dissociated strabismus complex (DSC) is an enigmatic form of strabismus that includes dissociated vertical deviation (DVD) and dissociated horizontal deviation (DHD). DSC includes various combinations of sursumduction, excycloduction, and abduction not conforming to Hering's law. In this cross-sectional observational study magnetic resonance imaging (MRI) was employed to evaluate the extraocular muscles in DSC. The study included five patients with DSC with a mean age of 25 years (range, 12-42 years), and 15 age-matched, orthotropic control subjects. All patients had DVD; 4 also had DHD. High-resolution, surface coil MRI was employed with thin, 2 mm slices and central target fixation. Volumes of the rectus and superior oblique muscles in the region 12 mm posterior to 4 mm anterior to the globe-optic nerve junction were measured in quasi-coronal
planes in central gaze. Patients with DSC had no structural abnormalities of rectus muscles or rectus pulleys or the superior oblique muscle but exhibited modest, statistically significant increased volume of all rectus muscles ranging from 20% for medial rectus to 9% for lateral rectus $(P < 0.05)$. The authors conclude that in their cohort of patients a modest generalized enlargement of all rectus muscles was demonstrated. DSC is associated with generalized rectus extraocular muscle hypertrophy in the absence of other orbital abnormalities.

**Accuracy of Optical Coherence Tomography Measurements of Rectus Muscle Insertions in Adult Patients Undergoing Strabismus Surgery.**


Prior strabismus surgery can make locating the insertion of the muscle quite difficult. Pediatric ophthalmologists have looked for multiple ways to preoperatively determine where the muscles are located. This paper aimed to assess the accuracy of anterior segment optical coherence tomography (AS-OCT) in measuring the distance of the extraocular muscle insertion from the limbus. The authors performed a reliability analysis using 74 adults scheduled for strabismus surgery. They used AS-OCT to measure the distance from the limbus to the muscle insertion. The position of the muscle was then measured intraoperatively and success was defined as 1 mm or less difference between the AS-OCT measurement and the intraoperative measurement. 144 muscles were analyzed in the data set and 31 of the 33 reoperated muscles were successfully imaged by AS-OCT. AS-OCT measurements were accurate in 77% of all muscles. In the eyes without previous surgery, 83% of the muscles were accurately identified and among those with previous strabismus surgery thus number dropped to 58%. However if you changed the definition of success rates to within 2 mm of the surgical measurements, then this goes up to 93.5% (29/31 eyes). There are three previous studies, but only 2/3 included muscles that previously had surgery. The authors conclude that AS-OCT can be a powerful tool in my patients with previous strabismus, but its accuracy is limited in patients with reoperation.

**Strabismus – Cranial Nerve palsy**

**Early Onset Sixth-Nerve palsy with Eccentric Fixation**


Congenital sixth nerve palsy has a reported incidence of 6 in 110 in a series of all sixth-nerve palsies. The most common etiologies of sixth nerve palsy are vascular, neoplasm, trauma, post-viral, inflammatory, idiopathic, and congenital. Sixth-nerve palsies are the second most common palsy presenting in childhood. Eccentric fixation is a complication of long-standing strabismus and leads to denser
amblyopia. The authors report 4 children with early-onset sixth-nerve palsy with associated eccentric fixation. It is difficult to distinguish between an early-onset sixth nerve palsy and Duane syndrome. Palpebral fissure changes are associated with Duane syndrome and larger angle esotropia is associated with sixth-nerve palsy. All four patients had dense amblyopia in the esotropic eye, had large angle strabismus (35-60 prism diopters), eccentric fixation contributing to the poor vision, and 3 of 4 patients did not have a face turn. Eccentric fixation is an adaptive state where the patient uses an extrafoveal area to fixate when viewing monocularly with their amblyopic eye. Eccentric fixation is found in 22% of patients with strabismic amblyopia. Eccentric fixation can be diagnosed by monocular corneal light reflex, visuoscope, or ophthalmoscope with fixation target. Treatment of eccentric fixation includes occlusive therapy (conventional), inverse occlusive therapy of the amblyopic eye, and red-filter occlusive therapy. All four patients underwent extraocular muscle surgery, the most effective of which was vertical muscle transposition.

**Neurological Imaging in Acquired Cranial Nerve Palsy: Ophthalmologists vs. Neurologists**

The availability of magnetic resonance imaging has increased the number of patients who undergo neurologic imaging, however this has the effect of raising health care costs. Neurologists and ophthalmologists differ in their guidelines to obtain neuroimaging in patients with cranial nerve palsies. The authors performed a PubMed literature search of all case series published between 2000-2015, yielding 10 case series that were subsequently analyzed. They found that all 3 neurologists invariably opt for an MRI, whereas only 2 of the 7 ophthalmologists always recommend an MRI. However they did agree that patients with a third nerve palsy should have an MRI, however this was not true for patients with fourth and sixth nerve palsies. That being said, the authors note that age is a factor and that they would recommend all patients under 50 years old with a sixth nerve palsy undergo an MRI. This study is limited by the small number of specialists in each field and likely omitted studies focusing on treatment and/or case presentations. Further studies were recommended using a larger and more diverse group of patients and specialists.

**Strabismus – Childhood XT and ET**

In children with intermittent exotropia, a worsening of control is considered an indicator for surgical intervention. The term control refers to the proportion of time that the deviation is manifest and ease of re-fusion after dissociation. The goal of this prospective, non-interventional case series was to assess the level of control in intermittent exotropia by applying the office-based 6-point control scale to far-distance testing. A total of 52 children with intermittent exotropia were enrolled. Control of exodeviation was assessed at indoor distance (ID) of 3 m and near distance of 33 cm using the office-based 6-point control scale, which was additionally applied to indoor far distance (IFD) fixation of 30 m and outdoor far distance (OFD) fixation of 50 m. In all 52 patients, the level of control at OFD fixation was either worse than (31%) or the same as (70%) the level of control at IFD fixation and the level of control at IFD fixation was worse than (64%) or the same as (35%) the level of control at ID fixation. The level of control at OFD fixation was worse than (69%) or the same as (31%) the level of control at ID fixation for all 52 patients. The differences between mean control scores of OFD and IFD fixation (P = 0.002), IFD and ID fixation (P < 0.001), OFD and ID fixation (P < 0.001) were statistically significant. The authors conclude that the outdoor and indoor far distance control scores can increase the sensitivity of the office-based 6-point control scale. Not sure that the best statistical test was chosen for comparison, possibly repeated measures ANOVA would have been preferable. The clinical implications of these results are yet to be determined.

Relationship among clinical factors in childhood intermittent exotropia

Intermittent exotropia (IXT) patients are treated using surgical interventions and nonsurgical interventions, such as part-time occlusion, fusional vergence exercises, and over minus lenses. Nevertheless, the relative effectiveness of such treatments has not been rigorously studied, and the natural history of IXT is unknown. The authors are attempting to address some of these issues through two randomized clinical trials—one comparing part-time patching to observation, continuing with a natural history component, and a second study evaluating the effectiveness of bilateral lateral rectus recession versus monocular unilateral lateral rectus recession with medial rectus resection for the treatment of IXT. The goal of this preliminary study was to determine the relationships between stereoacuity, control of exotropia, and angle of deviation in children with intermittent exotropia (IXT). Data collected for 652 participants 3 to <11 years of age with IXT meeting eligibility criteria for enrollment into one of the aforementioned clinical trials, were used to evaluate relationships between stereoacuity, control, and angle of deviation at enrollment. Any level of stereoacuity and
angle of deviation could be accompanied by any level of control. Worse
distance exotropia control was weakly associated with poorer distance ste-
reoacuity (R = 0.26; 99% CI, 0.17-0.36) and larger angles of deviation at dis-
tance (R = 0.27; 99% CI, 0.17-0.36). Worse near exotropia control was weak-
ly associated with poorer near stereoacuity (R = 0.17; 99% CI, 0.07-0.27)
and moderately associated with larger angles of deviation at near (R = 0.37;
99% CI, 0.28-0.45). There was no association between stereoacuity and an-
gle of deviation at distance (R = 0.07; 99% CI, -0.03 to 0.17) or at near (R =
0.02; 99% CI, -0.08 to 0.12). However, the odds of being monofixational at
distance, compared with being bifoveal, were greater when distance con-
trol was worse (OR 5 1.49; 99% CI, 1.24-1.80). A similar relationship was
observed at near (OR 5 1.42; 99% CI, 1.16-1.73). Some limitations with the
measurement of some of the parameters (Only a single measurement of
exodeviation control was obtained at each fixation distance) were acknowl-
edged. The authors conclude that weak and moderate associations were
found between stereoacuity, control, and angle of deviation; a child may
exhibit any combination of stereoacuity, control, and angle of deviation.
The specific roles of control, stereoacuity, and angle of deviation in the di-
agnosis, management, and pathogenesis of IXT are unclear, and each ap-
pears to yield somewhat independent information.

**Everyday Exotropia: Learning from the Littlest**
Intermittent exotropia, X(T), is one of the most common types of childhood stra-
bismus. Seventy percent of exodeviations occur in otherwise healthy children
and the remaining 30% are associated with ocular or systemic conditions. Inter-
mittent exotropia has an incidence of 1% in the general population and has a typ-
ical onset before 5 years of age. The etiology and underlying mechanisms of
common exotropia has baffled the pediatric ophthalmic world. The author per-
formed a retrospective chart review of patients with exodeviation to identify the
subset of patient with early onset exotropia. 470 patients were identified be-
tween 6 months and 15 years of age that met inclusion criteria: no prior surgical
treatment, no significant amblyopia, anisometropia, or ametropia, no paralytic or
restrictive strabismus, no ocular, neurological, or craniofacial disease, and no
prematurity. 39 of the 470 patients identified were diagnosed less than 1 year of
age. 35 of these 39 patients had X(T) and 4 had constant infantile XT. These
two groups were compared and an earlier onset was reported in the XT group
with a greater deviation size, both at near and distance, compared to the X(T)
group. The XT group had no measurable stereopsis despite surgical correction
while the majority of X(T) patients had measurable stereopsis. Intermittent exo-
tropia tends to present later to pediatric ophthalmologists due to the intermittency
and remarkably better control at near. The study also showed a high incidence,
4 of 4 patients, of dissociated vertical deviation (DVD) in the XT group. The rela-
tionship between infantile XT and early onset X(T) remains intriguing, and per-
haps finding a correlation can assist in successful treatment of exodeviations.
Incomitance and Eye Dominance in Intermittent Exotropia

The purpose of this study was to determine if the deviation angle changes in subjects with intermittent exotropia as they alternate fixation between the right and left eye in primary gaze. In this prospective observational cohort study, 37 subjects (median age 30 years; range, 7-65) with intermittent exotropia were tested for evidence of incomitance. The position of each eye was recorded with a video tracker during fixation on a small central target. A cover–uncover test was performed by occluding one eye with a shutter that passed infrared light, allowing continuous tracking of both eyes. The deviation angle was measured during periods of right eye and left eye fixation. Incomitance was assessed as a function of eye preference, fixation stability, and exotropia variability. The mean exotropia was 18.28° ± 8.1°. A difference between right exotropia and left exotropia was detectable in 16/37 subjects. Allowing for potential tracking error, the incomitance had a mean amplitude of 1.7°. It was not related to a difference in accommodative effort, eye preference, fixation stability, or variability in deviation. Comitance is regarded as a feature that distinguishes typical strabismus from paralytic or restrictive processes. Unexpectedly, eye tracking during the cover–uncover test showed that incomitance is present in approximately 40% of subjects with intermittent exotropia. It averages 10% of the exotropia, and can equal up to 5°. The authors concluded that when substantial, it may be worth considering when planning surgical correction, for example performing asymmetric lateral rectus resections. It is unclear how the measurements of deviation angle with the machine used in the study correlates with clinical tests using prisms. Also, the authors describe the use of cover-uncover; however the alternate prism cover test is generally used in the measurement of strabismus when planning for surgery. This needs to be studied further in a clinically relevant manner before considering adjusting surgical treatment plans.

A high prevalence of exotropia in Patients with Duane Retraction Syndrome in a Tertiary Eye care center in South India.
Manjushree Bhate, Virender Sachdeva, Ramesh Kekunnaya

The purpose of this study is to determine the prevalence and clinical characteristics of patients with exotropic Duane retraction syndrome in a tertiary eye care center. In this retrospective chart review, 140 patients were included. The age at presentation, gender, laterality, manifest primary position, abnormal head posture, ocular motility overshoots as well as the presence of other ocular or systemic abnormalities and amblyopia have been studied. Abnormal head posture was present in 72% and upshoot in 18.6% of patients. Unilateral type I Duane retraction syndrome accounted for 84.2%, type II for 5%,
and type III for 7.1%, whereas 3.6% had Duane retraction syndrome and bilateral exotropia. Although, this is a first study that exclusively reports the clinical characteristics of patients with Duane retraction syndrome and exotropia it lacks data regarding strabismus measurements, documentation of degree of amblyopia, ocular systemic manifestations and refractive error. The study reports a much greater incidence of associated overshoots and face turn to the opposite side which the authors attribute to a tight/short lateral rectus muscle.

Stereopsis in patients with refractive accommodative esotropia.

The purpose of this retrospective study was to investigate the factors associated with stereopsis in patients with refractive accommodative esotropia. The medical records of patients with refractive accommodative esotropia in a single center were analyzed retrospectively. Refractive accommodative esotropia as a residual esotropia <10D after full hyperopic correction. Age, sex, cycloplegic refractive error, presence of amblyopia, angle of deviation, and stereoaucity and fusional ability were evaluated. Patients were divided into good stereopsis (40-100 arcsec) and poor stereopsis (>100 arcsec) groups. A total of 85 patients were included, 31 (36.5%) in the good stereopsis group. The initial mean cycloplegic refraction were 3.61±1.86D in the good stereopsis group and 4.55±1.62D in the poor stereopsis group (P=0.016). Differences in the cycloplegic refraction between both eyes were 0.40±0.45 D in the good stereopsis group and 0.77±0.85 D in the poor stereopsis group (P=0.025). The final angles of deviation with correction were 0.4±1.0 PD at distance and 1.8±2.6 PD at near fixation in the good stereopsis group and 0.9±1.4 PD and 2.6±3.0 PD, respectively, in the poor stereopsis group (P=0.001 and <0.001, respectively). Patients with suppression at distance were more common in the poor stereopsis group (P=0.007). Those with orthotropia both at distance and near had better stereopsis than those with residual esotropia (P<0.001). The initial deviations without correction were 17.1±9.4 PD at distance and 19.1±9.5 PD at near in patients with orthotropia and 23.8±12.2 PD and 28.4±11.8 PD, respectively, in patients with residual esotropia (P=0.009 and P=0.001, respectively). Patients with >4 PD of deviation at distance or >5 PD of deviation at near with full correction had only gross or nil stereopsis. The authors conclude that a smaller initial refraction, a smaller differences in refraction between both eyes, a smaller final deviation angle, and fusional ability were associated with better stereopsis in patients with refractive accommodative esotropia. Good stereopsis may be only achievable with a misalignment of ≤4 PD at distance and ≤5 PD at near fixation. The poor prognostic factors for stereopsis were more hyperopic refraction and anisometropia at initial visit.

In the discussion, the authors also highlight that of the orthophoric patients only 48% had stereoaucity of 100 arcsec or better. This result sug-
gests that the presence of motor fusion does not always indicate the presence of high-grade stereopsis and that other factors may also be associated with good stereopsis.

**Duane syndrome with prominent oculo-auricular phenomenon.**

Duane syndrome is a congenital cranial dysinnervation disorder involving absent or anomalous innervation of the lateral and medial rectus muscles that is sometimes associated with other manifestations of dysinnervation. The authors describe a patient with right esotropic Duane syndrome with a long-standing retro-auricular tugging sensation in right gaze who was noted to have prominent ipsilateral oculo-auricular phenomenon, representing either abnormal enhancement of existing innervation or an uncommon dysinnervation. After successful strabismus surgery the tugging sensation improved but the phenomenon could still be elicited. The phenomenon is nicely demonstrated in a supplementary video.

**Capturing the Moment of Fusion Loss in Intermittent Exotropia.**

This is a study to better understand the mechanisms of intermittent exotropia and to characterize how the outward rotation of the deviating globe should be classified among the repertoire of eye movements made by primates. Intermittent exotropia (IXT) is characterized by interruption of fusion that triggers two sensory adaptations: 1. peripheral temporal retina suppression, and 2. shifting of the image falling on the deviated eye’s retina to avoid visual confusion. In this study, the authors compared eye position and peak velocity measured during spontaneous loss of fusion, shutter-induced loss of fusion, and recovery of fusion. The position of each eye was recorded with a video eye tracker under infrared illumination while fixating on a small central near target. Thirteen patients with typical IXT were recruited for the study. In 10 of 13 subjects, the eye movement made after spontaneous loss of fusion was indistinguishable from that induced by covering 1 eye. It reached 90% of full amplitude in a mean of 1.75 seconds. Peak velocity of the deviating eye’s movement was highly correlated for spontaneous and shutter-induced events. Peak velocity was also proportional to exotropia amplitude. Recovery of fusion was more rapid than loss of fusion, and often was accompanied by interjection of a disconjugate saccade. The authors concluded that loss of fusion in IXT is not influenced by visual feedback. Excessive divergence tone may be responsible, but breakdown of alignment occurs via a unique, pathological type of eye movement that differs from a normal, physiological divergence eye movement. The findings in the eye movement recordings are typical of clinical observations of IXT patients.

**Intermittent exotropia with a positive Bielschowsky head-tilt test**
Intermittent exotropia (IXT) can be frequently associated with vertical deviations and also with a positive Bielschowsky head-tilt test (BHTT). There can be a simulated superior oblique palsy due to pseudo inferior oblique overaction, which may be difficult to distinguish. Concomitant vertical deviations have been shown in reports to improve after horizontal surgery alone. The authors aimed to examine cases of IXT with and without a positive BHTT, but without true superior oblique palsy. They retrospectively reviewed 118 patients with IXT. 50 of these patients had hypertropia on head tilt. 101 of the patients underwent surgery, of which 41 had a positive BHTT. The time from onset of IXT was significantly longer in patients with positive BHTT. Risk factors for a positive BHTT, other than time from onset, were angle of distance exodeviation, suppression, and worse near stereoaucity. After surgery, the number of positive BHTT patients decreased in both groups that underwent horizontal muscle surgery and horizontal plus inferior oblique weakening surgery. The authors suggest using caution regarding unnecessary cyclovertical muscle surgery when treating IXT when associated positive BHTT, as the positive test can resolve after horizontal surgery alone.

Proposing a new scoring system in intermittent exotropia: towards a better assessment of control

To properly manage children with intermittent exotropia (IXT), assessing the severity and progression of the disease is critical. Two common scoring systems, the Newcastle Control Score and the Mayo Clinic Office-based Scale have made positive impacts on patient assessment. However, some weaknesses of these systems include using subjecting home data and the time required for observation. The authors developed a new scoring system, LACTOSE (Look and Cover, then Ten seconds of Observation Scale for Exotropia) and tested the reliability and validity of the system. The scale is scored 0 to 4 for distance and near (with total score range 0 to 8), and involves scoring the patient based on regaining alignment after periods of looking, covering the eyes, and the observing again. The scoring system was performed on 235 patients with IXT. Inter-rater and test-retest reliability was assessed on 10 patients using video-recorded data. 10 trained raters scored the patients for inter-rater data, and 2 sets of scores by the same rater (face-to-face and video recording) were used for test-retest data. Mean scores for the entire cohort were 2.9 distance, 1.6 near, and 4.5 combined. Inter-rater reliability was considered good (intraclass correlation coefficient 0.729 distance, 0.818 near) and test-retest reliability excellent (0.849 distance, 0.727 near). The age of onset was negatively correlated with score, and amount of exotropia positively correlated. Stereo testing did not show a significant correlation with the overall score. The authors conclude that the scoring system demonstrated ease of use, requires only 1 minute to complete, and was valid and reliable.
They do concede the reliability data was done on a small sample size, and some scoring was based on video recording.

**Binocular Summation and Control of Intermittent Exotropia**
Fatma Yulek, Federico G. Velez, Sherwin J. Isenberg, Joseph L. Demer et al

The management of intermittent exotropia is controversial, as there is little consensus on treatment and outcome measures. As patients with strabismus demonstrate subnormal binocular summation, the authors postulate that lower binocular summation may result in poorer control of intermittent exotropia. The authors performed a prospective study of 34 patients with an average age of 19 years (range: 3.5-69 years) examining the binocular summation score, vision, and stereopsis in patients with intermittent exotropia. The authors found that the binocular summation scores of strabismus patients were lower than normal controls. In addition, the binocular summation scores were significantly lower in patients with worse control scores, indicating a positive relationship between the control of intermittent exotropia and the binocular summation. The authors conclude that lower binocular summation in patients with higher control scores may suggest that decreased binocular summation is associated with less control in intermittent exotropia.

**Strabismus – Convergence / Divergence insufficiency**

Pediatric ophthalmology and childhood reading difficulties: Convergence insufficiency: relationship to reading and academic performance.

This article is part of a symposium on childhood reading difficulties. Patients with convergence insufficiency (CI) are often symptomatic during activities that require near fixation, such as reading. Indeed, CI has been associated with reading impairment and poor academic performance. However, these associations do not prove a causal relationship between these conditions. The current evidence regarding the relationship between CI and its treatment, reading ability, and academic performance is discussed in this review. The convergence insufficiency treatment trial (CITT) study group has performed multiple investigations examining the effectiveness of various treatment regimens on the symptoms and signs of CI. Some limitations with the Convergence Insufficiency Symptom Survey (CISS) and the low positive predictive value of this survey were raised and discussed in this comprehensive review.
Effect of Induced Vertical Disparity on Horizontal Fusional Reserves.

Horizontal fusional vergence is important for binocularity. Deterioration of horizontal fusion reserves have a considerable effect on task performance. Small magnitude vertical deviations can compromise horizontal fusional vergence, however restoration of fusion can be achieved with the correction of vertical deviation despite a horizontal deviation. The authors sought to investigate the effect of induced vertical disparity by prism on horizontal fusional reserves at near. They performed a prospective study of 170 patients examining the positive (PFR) and negative fusional reserves (NFR) before inducing 0.5 PD and 1.0 PD vertical disparities. They found that inducing vertical disparity reduces horizontal fusional reserves at near and the NFR was more affected than PFR. Also, the standard deviations of measurements with vertical prism were higher than without prism, indicating the horizontal fusional reserves with the prism are more variable than without the prism. Based on these observations, the authors conclude that small vertical deviations need to be corrected in patients with mainly horizontal phorias. These deviations can be treated with prism correction to provide symptomatic improvement.

*Strabismus* – Acquired

Long-term Surgical Outcomes for Vertical Deviations in Thyroid Eye Disease

Strabismus surgery in patients with thyroid eye disease (TED) can be unpredictable. Even the use of adjustable sutures, muscle slippage and post-operative drift result in reoperation rates that are as high as 40%. The authors performed a retrospective review of 42 adult patients with TED who underwent adjustable suture strabismus surgery for a vertical deviation who had at least 1 year of follow-up. Post-operatively the deviations decreased from a mean of 21.5 PD to 4.4 PD at 3 months and 3.8 PD at 1 year. Over half of the patients (57%) had a vertical deviation <5 PD at the 1 year follow-up. However, there was a trend toward increasing overcorrection with time (5 patients at 3 weeks, 7 patients at 3 months, and 8 patients at 1 year), although this was not statistically significant. Eight patients (19%) required treatment for overcorrection (surgery, botulinum toxin injection, prism, steroids). The re-operation rate during the study period was 9.5% and all repeat surgeries were due to late overcorrection. Interestingly, the authors found that patients who developed overcorrection started with a statistically significant lower amount of immediate undercorrection in post-adjustment than patients with larger residual deviations. Therefore the authors suggest that aiming
for undercorrection immediately post adjustment would yield better long-term results by taking into account the expected amount of postoperative drift.

**Strabismus – Misc**

**Strabismus Incidence in a Danish Population-Based Cohort of Children**

This Danish-based population cohort study of 96,842 children between 1996 and 2008 identified 1309 cases of strabismus with a cumulative incidence of 2.56% at 7 years. Of note, this population of children is predominantly white with a boy-girl ratio of 51:49. The overall incidence of strabismus was similar among boys and girls. The four major strabismus subtypes were: partially accommodative esotropia (19.3%), congenital esotropia (16.5%), exotropia (13.8%), and fully accommodative esotropia (13.5%). The median age for the detection of these four subtypes was 0, 32.0, 26.1, and 16.6 months, respectively. In summary, this national, population-based cohort study provides cumulative incidence of strabismus consistent with those reported in smaller European and American cohorts. However, this Danish cohort reports a higher esotropia:exotropia ratio as well as patterns of incidence by age as compared to other research, implying differences in the underlying etiology for different strabismus subtypes.

**Strabismus Measurements with Novel Video Goggles.**

In this report, the authors describe a novel portable strabismus video goggle to measure strabismus. They assessed its performance compared to the standard Hess screen test. The authors studied 41 adults and children aged ≥ 6 years with ocular misalignment due to congenital or acquired paralytic or comitant strabismus and 17 healthy volunteers. All participants underwent measurement using the video goggles and a Hess screen test with ocular deviation measured on a 9-point target grid located at 0±15° horizontal and vertical eccentricity. The goggle has a head-fixed laser target display and LCD shutters for binocular dissociation. Each LCD shutter occlusion was 2 seconds long and 3 cycles of alternate eye occlusion were performed at each gaze position. The data from eye movement recording was then displayed in the same format as the Hess test. Agreement between the two tests was quantified using the intraclass correlation coefficient (ICC). Secondary outcomes were the utility of the goggles in patients with visual suppression and in children. There was good agreement between the strabismus video goggles and the Hess screen test in the measurements of horizontal and vertical deviation (ICC horizontal 0.83, 95% confidence interval [0.77, 0.88], vertical 0.76, 95% confidence interval [0.68, 0.82]). Both methods repro-
duced the characteristic strabismus patterns in the 9-point grid. The new device is simple, fast (recording time of about 2 minutes) and accurate in measuring ocular deviations, and the results are closely correlated with those obtained using the conventional Hess screen test. It can even be used in patients with visual suppression who are not suitable for the Hess screen test. The youngest patient tested in this study was 6 years of age.

Role of magnetic resonance imaging in heavy eye syndrome.


Highly myopic patients can develop a form of strabismus named myopic strabismus fixus or ‘heavy eye’. These patients classically present a progressive esotropia and often hypotropia with limited abduction and elevation. MRI has become an important tool in examining patients with ocular motor disorders. The purpose of this study is to evaluate the importance of performing MRI before surgery in highly myopic patients. Authors reviewed the MRI records of patients with Myopic Strabismus Fixus who underwent strabismus surgery. The dislocation angle was measured using the area centroids of the lateral rectus muscle and the superior rectus muscle globe. A total of 54 patients (65 eyes), 42 females and 12 males, were enrolled. Their mean age was 52.3 ± 13.4 years, going from 31 to 80 years. Most patients 43/54 had unilateral strabismus. Mean distance esotropia was 49.2 ± 14.4 prism diopters (PD) and the mean hypotropia was 4.3 ± 4.4 DP. Mean axial length was 30.5+/-3 mm. All subjects exhibited severe superotemporal globe prolapse. The mean angle of dislocation was 167.5 ± 12.9°. The LR–SR band was thinned in 56 orbits and ruptured in 8. Muscle displacement and thinning /rupture of the LR –SR is common to all patients with heavy eye syndrome

Rectus muscle excyclorotation and V-pattern strabismus: a quantitative appraisal of clinical relevance in syndrome craniosynostosis


V-pattern strabismus in patients with syndromic craniosynostosis may be due to a variety of causes. This was a retrospective cohort study comparing the severity of V-pattern with the degree of excyclorotation of rectus muscles in patients with Apert, Crouzon, or Pfeiffer syndrome. 28 patients were included for analysis. The patients had available CT of the orbits for review, with views sufficient to measure cyclorotation and trajectory of the rectus muscles. The patients were placed into one of four V-pattern severity groups, based on change in horizontal misalignment from downgaze to upgaze. Results showed an increasing severity of V-pattern strabismus correlated with greater excyclorotation. Also, the severity of V-pattern was highly associated with Apert syndrome. Apert patients were more
likely to have moderate to severe or “seesaw” V-pattern, whereas Crouzon or Pfeiffer syndrome patients were more likely to have mild or moderate V-pattern. This is likely due to the complex orbital differences between these syndromes.

**Abnormal fixational eye movements in strabismus**

Prior studies have reported greater fixation instability in patients with amblyopia as well as strabismus. In particular patients with strabismus can have disconjugate horizontal saccades. This study examined the stability of eye position during fixation with strabismus in order to correlate the severity of the instability with strabismus angle and vision. They recorded movements in 13 patients with strabismus and 16 controls using a high-resolution video eye tracker. The authors found that patients with strabismus had greater fixation instability in the deviating eye, higher intersaccadic drift velocity and greater disconjugacy in fixational saccades. Patients with small-angle strabismus and preserved binocular vision had better fixational stability than those with large-angle strabismus and absent stereopsis. Therefore they conclude that strabismus alone is sufficient to disrupt the fixational stability even in the absence of amblyopia and latent nystagmus, and fixational instability could be a screening tool to diagnose strabismus.

**Knobby Eye Syndrome.**

Heavy eye syndrome is characterized by limited abduction and supraduction in high myopes, associated with axial myopia with non-uniform staphylomas. The abnormal shape of the globe results in shifting of the pulley system and changing the vector forces of the extraocular muscles. This study used high-resolution MRI to evaluate the globe shape in 21 patients with high axial myopia and identify equatorial staphylomas that can alter the extraocular muscle course, leading to strabismus. Ten eyes of 7 patients were spherical, whereas the other 14 patients had abnormalities in one or both globes. Eleven eyes had diffuse posterior, 12 eyes had equatorial, and 4 eyes had combined posterior and equatorial staphylomas. The author concludes that irregular equatorial or posterior staphylomata were commonly encountered in strabismic axial high myopes. Prior to MRI, these staphylomata were often unsuspected by both the patients and the strabismus surgeons, and could possibly complicate strabismus surgery. These irregularly shaped staphylomas probably influence ocular motility. Therefore the possibility of knobby eye syndrome should be considered when evaluating myopic strabismus patients, especially in elderly pseudophakic patients who may have been myopic prior to cataract surgery.

**Long-term Surgical Outcomes in the Sagging Eye Syndrome.**
Sagging eye syndrome is due to degeneration of the connective tissues supporting the extraocular muscles, elongation of the muscles and anomalies in the pulley positions. The lateral rectus is the most affected of all the muscles. In order to compare the various procedures to treat this form of strabismus, the authors performed a retrospective chart review of consecutive patients who underwent strabismus surgery for small angle horizontal or vertical strabismus over a ten year period. Of the 103 cases included, 93 underwent surgery. 84 used prisms prior to surgery. Except for imbrication of the LR muscle to the SR muscle combined with superior LR transposition, all other procedures had a recurrence rates between 14 and 25%. The average age of the 15 patients with recurrences was 72 ± 7.5 years (five males), significantly higher than the 72 patients who maintained orthotropia at 66 ± 12 years (p = 0.02). The authors conclude that the recurrence of post-operative diplopia in patients with SES was due to progression of the age-related dehiscence of orbital connective tissue, not surgical overcorrection or undercorrection. This is supported by the fact that there were no cases of surgical overcorrection, only undercorrection which manifested as symptomatic diplopia over a period of time. They recommend that counseling patients that strabismus surgery can provide relief from diplopia for an interval of time but the diplopia and strabismus may recur.

**Magnetic resonance imaging of the functional anatomy of the superior oblique muscle in patients with primary superior oblique overaction.**


In general the diagnosis of oblique muscle dysfunction is based on clinical findings. However many other conditions can mimic oblique muscle dysfunction. Non invasive imaging such as magnetic resonance imaging (MRI) permits addressing the functional anatomy of the extraocular muscles. The aim of this study was to quantitatively determine the morphology and contractility of the SO muscle in patients with primary superior oblique overaction. A prospective observational study on 12 patients with a clinical diagnosis of PSOOA and 10 healthy orthotropic volunteers. PSOOA was diagnosed when the following clinical findings were present: an overdepression of the ipsilateral (affected) eye in adduction and was always associated with an ‘A’ pattern; ipsilateral hypotropia increasing in infra-adduction and the difference in the vertical deviation with head tilting was minimal. Generally, if SO overaction is bilateral and symmetric, there will be no hypertropia in the primary position, but an ‘A’ pattern is typically present. If the SO overaction is unilateral, there may be a degree of hypertropia in the primary position. Subjects were excluded if they could not cooperate for MRI exam, or if they had a history of prior strabismus surgery. In the primary position, the greatest SO cross-sections occurred about midorbit, 6 mm posterior to the globe-optic nerve junction. In down gaze, the SO cross-sectional area increased, and the plane in which the maximum cross-sectional area observed was more posterior.
The maximum cross-sectional area of SO muscle on the ipsilesional was not different than on the contralesional side. However the maximum contractility of SO muscle in the ipsilesional side was significantly more than on the contralesional side in patients and in control subjects. Authors did not observe that the SO in particular was not hypertrophic in primary position but had significantly more contractile change. This may indicate abnormal innervation resulting in increased muscle stimulation or changes in muscle fiber composition.

Comparison of subjective and Objective Techniques of Strabismus Measurements in Adults with Normal Retinal Correspondence.
Derek P. Bitner, Ore- Ofe O. Adesina, Kai Ding, Bradley K. Farris et al.
*Journal of Pediatric Ophthalmology & Strabismus* July/August 2017; 54(4): 216-220

Accurate measurement of strabismus is vital to proper diagnosis and treatment. There are subjective and objective techniques that can be used. The authors of this study hypothesized that subjective measurement techniques would measure larger deviations than objective ones. Seventy-three consecutive patients with manifest strabismus in primary gaze were included in this prospective study. The patients' deviation was measured first by an attending physician using the alternate prism cover test (APCT) and then by another attending physician using the red glass test (RGT). In this test, the patient had a red filter placed over one eye and is asked to describe the location of a single red light and a single white light while the observer adds prism until the two lights overlap. Like the APCT, the RGT measures the total (manifest plus latent) deviation by disrupting fusional mechanisms via stark color differences between the eyes. Objective mean deviations were 9.1 (distance horizontal), 5.1 (distance vertical), 10.0 (near horizontal), and 2.6 (near vertical) prism diopters (PD). Subjective mean deviations were 10.2 (distance horizontal), 6.8 (distance vertical), 12.2 (near horizontal), and 3.2 (near vertical) PD. Subjective measurements were larger by a statistically significant margin and were more likely to show the presence of a vertical deviation not measured objectively (19 occurrences vs 2 at near, \( P = .008 \); 15 occurrences vs 0 at distance, \( P = .004 \)). The measured deviations were within 5 PD horizontally and 3 PD vertically most of the time (range: 66.7% to 83.6%). The authors conclude that the red glass test was more likely to measure a larger deviation at distance and at near and to identify a vertical deviation not seen objectively at both distance and near. The mean difference between the tests was usually not large enough to affect surgical treatment, but could potentially result in different amounts of prescribed prism for patients treated optically. Although this is a good study, it also has several limitations: both types of measurement were performed by the same strabismologists, which could lead to potential examiner bias, although similar results were obtained by both examiners. Also, although attempts were made to eliminate patients with abnormal retinal correspondence using the results of other sensory testing, there was not a single standardized protocol for
identifying and excluding patients. Finally the reproducibility of the measurements was not evaluated.

**Changing strabismus Surgery Distribution at Shanxi Province Eye Hospital in Central China.**
Jun Hong Li, Wen Fang Xie, Jiao Ni Tian, Li Jun Zhang et al

The purpose of this study is to investigate whether there has been a change in the trend of strabismus surgery in a provincial eye hospital in the central part of China over the past decade. In this retrospective analysis of data, 12327 patients received strabismus surgery at the hospital from 2005 to 2014. Over this period of time, the number of surgeries increased steadily. Constant exotropia was the most common type of strabismus and superior oblique palsy was the most common type of paralytic strabismus. The study showed that the amount of strabismus surgery has increased over the past decade.

**Rate of strabismus detection on Digital Photographs Increases by Using Off-center Near target**
Ron Maor, Joanna Holland, Vijay Tailor, Marina Banteka et al

The purpose of this study is to increase the detection rate of strabismus on digital photographs, with the ultimate aim of developing a new automated strabismus detection algorithm. In this prospective case series, the authors acquired digital face photographs of 409 children with latent or manifest strabismus, using a 14-million-pixel camera with CCD image sensor. Images were taken at a distance of 40 to 70 cm in primary position, with camera lens as fixation target and in slight off-center fixation, and using a novel target of small light emitting diodes mounted onto the camera case. The location of the corneal light reflection was manually calculated in relation to the center of the pupil in both eyes and ocular deviation as the difference in corneal light reflection location between the two eyes. In orthotropia, the expected deviation is zero. The study showed that manual measurement of corneal reflection location on digital photographs acquired with off-center fixation onto an accommodative target has good sensitivity to detect manifest strabismus. The downside of this study is that the manual measurements are observer dependent and time-consuming. The next step would be to develop and implement an automated image processing, measurements, and calculation algorithm.

**The frequency and causes of abnormal head position based on an ophthalmology clinic's findings: is it overlooked?**
The aim of this retrospective study was to determine the frequency of abnormal head position (AHP) and identify the underlying causes in patients, who presented to a general ophthalmology clinic. Included in the study 2,710 consecutive patients (1,492 female and 1,218 male) with a mean age of 14.62±17.45 years (range 6 months-91 years), who presented with a variety of ophthalmologic symptoms during a 6-month period to a single center. The medical record of each patient was reviewed including the ophthalmologic evaluation. Among the 2,710 patients, 30 (1.1%) (7 female and 23 male) had AHP. In total, 24 (80%) of the patients with AHP were aged 16 years or younger. The initial complaint in the patients with AHP was ocular misalignment in 18 (60%) patients, AHP in 4 (13.3%), abnormal ocular movements in 4 (13.3%), double vision in 3 (10%), and droopy eyelid in 1 (3.3%). Comitant strabismus, nystagmus, and Duane syndrome were the most common causes of AHP. Other diagnoses included fourth nerve palsy, sixth nerve palsy, Brown syndrome, congenital muscular torticollis, ptosis, and blowout orbital fracture. The authors conclude that in this cohort the leading underlying causes of AHP are ocular and treatable. Of note, in only a minority of these patients AHP was the initial presenting complaint. They emphasize that clinicians must be aware that observation of any abnormal head position should prompt additional investigation. The sample size in this cohort is quite small compared to previous publications. Our general impression was that this paper was aimed for the general comprehensive ophthalmologist, raising awareness among general ophthalmologists to this presentation.

**Strabismus and mental disorders among Israeli adolescents.**

The psychological and social implications of strabismus, such as low self-esteem and social phobia, even in the absence of a visual impairment, should not be underestimated. The purpose of this retrospective case-control study was to assess the association between strabismus and mental disorders in adolescents. A total of 662,641 Israeli teenagers (mean age 17.3 ± 0.53 years, a male predominance [59%]) that underwent medical evaluation by the Israel Defense Force as part of the pre-conscription assessment between 2005 and 2013, were included in the study. The association between common mental disorders (anxiety disorder, mood disorder, adjustment disorder, and attention deficit hyperactivity disorder [ADHD]) and either uncorrected strabismus or corrected strabismus was examined. The uncorrected strabismus group in this study included subjects that either did not undergo corrective surgery or had a past unsuccessful correction, who had impaired vision and depth perception at the time of assessment. A total of 1,598 subjects (0.24%) had strabismus. Of those, 952 (60%) underwent successful correction and 646 (40%) did not undergo successful correction. A significant association was found between uncorrected strabismus and anxiety disorders (OR = 1.91; 95% CI = 1.02-3.57; P = 0.047) and between corrected strabismus and ADHD (OR = 2.62; 95% CI = 1.18-5.87; P = 0.03). The uncorrected strabis-
mus group had lower scores on the intelligence scale compared to the corrected strabismus group and the non-strabismic group (prime cognitive status score was 46.4 ± 20.09, P<0.0001). Uncorrected strabismus was assessed as a risk factor for the development of several mental disorders but was not significantly associated with any of the mental disorders that were assessed. However, a nearly significant association with anxiety disorder was observed (OR = 2.978; 95% CI, 1.013-8.754; P = 0.06). The authors concluded that in their cohort of patients uncorrected strabismus was not associated with mental disorders examined in this study. The study’s main weakness is that its definitions of strabismus and strabismus correction are not fully acceptable by pediatric ophthalmologists. It is possible that if the authors had defined strabismus undercorrection differently they would have arrived at a much more significant associations with the variety of mental disorders that were examined.

Strabismus Measurements in Adults Before and After Pupil Dilation.

The accuracy of preoperative strabismus measurements is important in planning surgery and various studies have looked at the variability of these measurements between examiners and length of dissociation in the office. Accommodation can be affected by cycloplegic medications and thus strabismus measurements are typically performed before dilation, but waiting to perform these measurements prior to dilation can add complexity to the workflow in the office. The authors hypothesized that due to the lack of strong accommodative amplitudes in adult patients and the weaker cycloplegic effects of the dilating drops used in adults that the pre and post dilation strabismus measurements would be unchanged in adults. This study was a prospective cohort study of 55 patient aged 18 and older with strabismus to determine the effect of dilating drops on strabismus measurements. The patients had a full sensory motor exam by a certified orthoptist before and after dilation with the second exam done by a masked, and different orthoptist. The primary outcome was the mean difference in the angle of both horizontal and vertical deviation. The authors found that the horizontal measurements changed and average of 0.5 prism diopters (PD) at distance and 1.67 prism diopters at near and 0.05 PD at near with a +3.00 add. The vertical deviation was 0.18 PD at distance 0.57 PD at near and 0.47 PD at near with an add. They concluded that pupil dilation did not meaningfully change the strabismus measurements in adults with the exception of mild variability at near in younger patients, which was eliminated by using a +3.00 lens at near to measure. By dilating adult patients prior to examination by the ophthalmologist, clinic workflow could be improved.

A Case Report of Drug-Induced Myopathy Involving Extraocular Muscles after Combination Therapy with Tremelimumab and Durvalumab for Non-Small Cell Lung Cancer
Recently developed anti-tumor therapies targeting immune checkpoints include tremelimumab and durvalumab. These agents have incompletely characterized side effect profiles. The authors report a 68-year-old man treated for non-small cell lung cancer (NSCLC) with a combination of tremelimumab and durvalumab. After treatment he developed diplopia, ptosis, fatigue, weakness, and an inflammatory myopathy affecting the extraocular muscles requiring hospitalization. Electromyography (EMG) testing and muscle biopsy suggested inflammatory myopathy without sign of myasthenia. Within 1 month of withdrawal of cancer therapies and initiation of oral steroid therapy, ocular and systemic symptoms had resolved. This notable adverse effect has not been previously described for these drugs administered singly or in combination, and ophthalmologists should be aware of this presentation in patients treated with these agents. This case illustrates the importance of systemic evaluation in new onset cases of adult strabismus.

A review of Cochrane systematic reviews of interventions relevant to orthoptic practice

Twenty-seven reviews with direct relevance to orthoptic practice were found in the 2016 Cochrane Library database. Four reviews were related to refractive error, twelve were related to strabismus, eight were related to amblyopia and nine were related to low vision, with some overlap between subjects. In amblyopia, both conventional occlusion and atropine have proven effective in the treatment of amblyopia. The authors found that there are very limited (if any) robust clinical trials in the areas of refractive errors, strabismus and low vision. The authors conclude there is a need for high quality randomized controlled trials of inventions for strabismus, ocular motility disorders, amblyopia, low vision, refractive error and stroke-related visual impairment to improve the evidence base in orthoptic practice.

2016 International Orthoptic Congress Burian Lecture: Folklore or Evidence?

Intermittent misalignments are normal in infants and should be resolved by 12-16 weeks of life. However, when they do not resolve, it is possible that abnormal accommodation and convergence may be at fault. The author constructed an infant vision laboratory with a remote haploscopic autorefractor (PlusoptiX SO4 photo-refractor in PowerRef II mode) to capture objective, continuous and simultaneous vergence. They conducted studies on adults, orthoptics and optometry students,
and full-term and premature infants. They found that in normal circumstances, disparity drove most of the vergence and accommodation responses (via the CA/C linkage). The vergence and accommodation driven by response to blur (the AC/A linkage) and proximal/looming cues were much less important. Thus for most people the CA/C relationship matters much more than the AC/A relationship. The author then applied this concept to eye exercises and found the most effective exercise to improve both convergence and accommodation responses was convergence exercises concentrating on resolving disparity, independent of blur.

Comparison of Naso-temporal Asymmetry During Monocular Smooth Pursuit, Optokinetic Nystagmus, and Ocular Following Response in Strabismic Monkeys

An intact visual-oculomotor system maintains a relatively stable image of the object of interest on the fovea during self or object movement. In infantile strabismus, both humans and monkeys exhibit asymmetric naso-temporal responses to motion stimuli. The authors used two rhesus monkey who had four months of disrupted binocular vision with contact lenses or Fresnel prisms for the first four months of life. They were then allowed to grow under unrestricted conditions until four years of age. Tracking was tested under monocular viewing conditions with optokinetic nystagmus (OKN), smooth pursuit (SP), and ocular following response (OFR) stimuli. The authors found the nasalward movement had a statistically significant differences with all three stimuli, with a larger steady state gain with OKN, high velocity gain with OFR, and larger gain and acceleration with SP. The authors conclude that loss of binocular connections from cortical areas to brainstem areas results in asymmetric responses to monocular stimuli; therefore, disruption of binocularity in and disruption of signaling to brainstem areas important for visual tracking, such as the nucleus of the optic tract, can lead to similar nasal-temporal asymmetry during OKN, OFR, and SP.

The Prevalence of Strabismus, Heterophorias, and Their Associated Factors in Underserved Rural Areas of Iran

The prevalence of strabismus in the underserved rural areas of Iran is unknown. As economic constraints limit access to eye care, this knowledge is important to guide resource allocation. The authors performed a cross-sectional study with randomized multistage cluster sampling in subjects >1 year old from two randomly selected districts in the north and southwest of Iran to study the visual acuity, refraction, and covering testing results. They analyzed 3248 patients with a mean age of 37.4 years evenly distributed in gender and geographic origin. The preva-
lence of tropia was 4.3% overall, and was higher in older populations (7.45% in adults 60-70 years old). Exotropia was more common in all age groups except children <5 years. The authors note that the prevalence of exotropia was higher than other published studies and attribute this to the inclusion of adults in the study population. There were no significant relationships between tropias and sex or geography. The authors conclude that the prevalence of exotropia was higher than esotropia, similar to other studies performed in Asia; however, the comparability of this study was limited by the age-related inclusion criteria.

**Choroidal Thickness in Strabismus and Amblyopia Cases**


The choroid is important in the thermoregulation and growth of the eyes, thus playing a significant role in emmetropization. Prior studies have shown that choroidal thickness can differ with refractive error, but these studies have not looked at patients with strabismus. To investigate the effects of hyperopia, anisometropic amblyopia, and horizontal strabismus on choroidal thickness, the authors measured the choroidal thickness with the spectral domain OCT enhanced depth imaging program in a prospective, cross-sectional, comparative study of 120 children (<16 years old). The authors found the choroidal thickness was thicker in amblyopic eyes of anisometric patients compared to fellow and control eyes, however the thickness was similar between eyes in patients with strabismus. This study also found a statistically significant negative correlation between visual acuity and choroidal thickness, which contrasts to prior studies that suggest better visual acuity is associated with a thicker choroid. In addition, hyperopic patients had thicker choroids than the control group, but the difference was not statistically significant. Of note, the authors did not include a myopia group in any of the analyses. The authors conclude that anisometropic amblyopia is associated with a thicker choroid, however there are no differences in choroidal thickness in patients with horizontal strabismus.

**10. STRABISMUS SURGERY**

**Factors Associated With Failure of Adult Strabismus-20 Questionnaire Scores to Improve Following Strabismus Surgery**

Sarah R. Hatt, David A. Leske, Kemuel L. Philbrick et al


This was a prospective observational case series of 276 adults with strabismus surgery, between 7/2012 and 8/2016 to assess for the psychosocial and functional outcomes of strabismus surgery, pre-operatively and at 6-weeks post-operatively. All participants completed the Adult Strabismus-20 (AS-20), a health-
related quality of life (HRQOL) questionnaire regarding psychosocial and functional outcomes related to strabismus surgery. Participants also completed: a self-report depression scale (CESD-R) and a Type-D Scale personality questionnaire. Of the 276 participants, the median age was 57 years (range of 18-91 years) and 55% women and 96% white. Results indicated that a failure for improvement in the AS-20 score post-operatively was associated with post-operative diplopia, increased depression symptoms, type-D personality, and visually obtrusive anomalous appearance. In summary, continued study of HRQOL is important to achieve a better understanding of the well-being of our strabismus surgery patients.

**Impact of Strabismus Surgery Suture Course for First- and Second-Year Ophthalmology Residents**

Aldo Vagge, Kammi Gunton, Bruce Schnall *J of Pediatric Ophthal & Strabismus. November/December 2017; 54(6): 339-345*

This prospective cohort pilot study evaluates the effectiveness of an eye muscle surgery course on first–and second year postgraduate ophthalmology residents. A total of 12 residents, 8 (67%) first-year and 4 (33%) second-year, participated in a 2-hour strabismus surgery course at Wills Eye Hospital. The course consisted of a didactic session followed by a wet laboratory session. The wet laboratory session simulated strabismus surgery using a model constructed of chicken breast followed by partial-thickness scleral suture passes in pig eye. A structured self-assessment evaluation form and a questionnaire in the validated Ophthalmology Surgical competency assessment rubric approved by the international council of Ophthalmology (ICO-OSCAR: strabismus) were used to assess the effectiveness of the course. Following the course, most of the residents felt less anxious (67%) and all of them responded that the course was helpful or somewhat helpful in preparation for strabismus surgery. Regarding the distribution of ratings on questions of subjective experience, knowledge of steps, and understanding of potential complications, the residents gave significantly higher ratings after the course ($P<.029$). The change in the modified ICO-OSCAR: strabismus assessment’s mean score was statistically significant before and after training ($P=.038$). The authors conclude that a strabismus course might be helpful in preparing the residents for strabismus surgery. The study is limited though by the very small number of participants.

**Role of botulinum toxin A in treatment of intractable diplopia.**


The goal of this retrospective study was to evaluate the effect of botulinum toxin A (BTXA) in patients with intractable diplopia related to intracranial problems or long-term interruption of fusion due to cataract or uncorrected aphakia and to identify the group of resistant cases who have no potential to fuse the two images. The medical records of patients over a period of 20
years were reviewed retrospectively to identify those who underwent BTXA treatment for intractable diplopia. All cases had horizontal and/or vertical deviations. The diagnostic criterion was persistent diplopia despite neutralization of the deviation by prisms or synoptophore. BTXA was injected into the appropriate extraocular muscle to control the deviation in the identified patients. A total of 22 patients were identified: 13 developed intractable diplopia following head trauma, intracranial surgery, or stroke; 9 had a history of binocular sensory deprivation due to traumatic cataract or uncorrected aphakia. The duration of sensory deprivation ranged from 2 to 41 years. BTXA was injected into the appropriate extraocular muscle(s). Diplopia resolved completely in 14 patients, resolved incompletely with short-term single vision in 3 cases, and persisted in 5 patients despite correction of the deviation by BTXA. The authors conclude that BTXA offers the advantage of a temporary decrease of the deviation that allows the visual system to recover fusion under real-life conditions. Permanent treatment with surgical correction of the deviation should be reserved for those who achieve fusion during the orthotropic period provided by BTXA. Despite its limitations due to its retrospective nature, small sample size and diverse group of patients, this study introduces an interesting concept regarding the benefit of BTXA in these challenging cases.


Effective strabismus surgery often depends on securely attaching extraocular muscle to the globe with suture using a spatulated ophthalmic needle. The purpose of the experimental study was to investigate the tensile properties of several components used to secure extraocular muscle to sclera in strabismus surgery to determine potential failure points. A digital force gauge was used to measure the tensile strength of intact and damaged 6-0 Vicryl suture (Ethicon, Somerville, NJ), as well as threads tied in a 2-1-1 or 2-1-1-1 surgeon’s knot configuration. Human sclera was used to test the resistance to drag of knotted and unknotted 6-0 Vicryl suture thread through partial thickness sclera. The study found that the mean tensile strength of 6-0 Vicryl suture was 623.5 g, but it was markedly reduced by damage from the needle (P < 0.0001) or ophthalmic needle holder (P < 0.0001). The mean force necessary to break both the 2-1-1 knots and the 2-1-1-1 knots was similar (307.6 g vs 292.8 g, respectively, P = 0.84). Drag through a 2 mm scleral tunnel was 4.6 g, compared to 13.6 g for a 4 mm tunnel (P = 0.011). The force required to pull a knotted suture through a 4 mm scleral tunnel was 254 g for a 2-1-1 knot and 367 g for a 2-1-1-1 knot (P < 0.015). The author concluded that although 6-0 Vicryl possesses adequate tensile strength for muscle fixation, thread damage from a needle or a needle holder may cause serious losses in tensile strength. Knot-breaking strength is not significantly increased by adding a fourth throw.
Frictional forces of the scleral tunnel are not sufficient to provide muscle stabilization, but the presence of a knot can provide substantial resistance to suture slip into the scleral tunnel. This paper is a part of a triad of studies published on this subject. Despite the limited number of experiments performed in each phase, this study looks at some fundamental steps that are acceptable in strabismus surgery and re-examines them.

Securing extraocular muscles in strabismus surgery: biomechanical analysis of knot-tying technique.

The safe and precise reattachment of extraocular muscles requires a technical approach that minimizes any opportunity for the muscle to slip intraoperatively or postoperatively while minimizing surgical risk. The capacity of the first knot throw to hold a muscle in place until the second throw is tightened is a key measure of its ability to provide optimal muscle stabilization. This experimental study looked at the tensile properties of different knot configurations and tying techniques of 6-0 polyglactin 910 suture in the human sclera by using a precision digital force gauge. It found that the mean tensile strengths of the first knot throw formed with either one, two, or three loops, with widely separated scleral tunnels, were relatively weak measuring 5 g, 10 g, or 27 g, respectively. When the scleral tunnels were closely spaced in a "cross-swords" fashion, the mean strength of a first throw made with two loops increased to 385 g. If a first throw with two conventional loops was cinched against one of the scleral tunnels or a reversed first loop is used, the mean tensile strength increased to 112 g and 381 g, respectively, even with widely spaced scleral tunnels. The author suggested that proper cinching and reverse orientation of the first knot throw can improve the tensile strength of the knot, even with short, widely spaced scleral tunnels. This study also confirmed that the crossed swords technique significantly improves the stability of the first knot throw compared to widely spaced tunnels.

This paper is a part of a triad of studies published on this subject. Despite the limited number of experiments performed in each phase, this study looks at some fundamental steps that are acceptable in strabismus surgery and re-examines them.

Securing extraocular muscles in strabismus surgery: biomechanical analysis of muscle imbrication.

This experimental study was performed to quantitatively evaluate the tensile strength of extraocular muscle imbrication as it relates to the positioning of the imbricating suture. The study was conducted in a controlled
fashion using fresh ex vivo pig eyes with extraocular muscles attached and a precision digital force gauge. The results of the study suggest that imbrications performed 0.5 mm or less from the cut muscle edge or 0.5 mm or less from the lateral margin may be prone to tensile failure. The study is an animal model of muscle imbrication and as such cannot be used as a translational work, but rather as an indication regarding secure surgical muscle imbrication.

A controlled study of the role of cryopreserved amniotic membrane transplant during strabismus reoperations.

The purpose of this small prospective study was to evaluate the effects of using cryopreserved human amniotic membrane (AM) transplant during strabismus reoperations. A total of 30 patients with persistent strabismus, who required repeated strabismus surgery, were included in this prospective study. Patients were divided into two groups of 15 patients each. The AM group underwent strabismus reoperation with wrapping of the muscles with cryopreserved amniotic membrane. Controls underwent strabismus reoperation without an AM wrap. Final follow-up visit was scheduled between 3 and 12 months postoperatively. Three patients were excluded in the AM group due to incomplete follow-up. Surgical success was defined as ≤ 10 PD of horizontal tropia and ≤ 4 PD of vertical tropia post-operatively, with no limitation of ductions exceeding -1. A cosmetically acceptable outcome was defined as a tropia of ≤ 15 PD. A successful outcome was achieved in 7 patients in each group (58% and 47% in groups AM and C, resp.; P = 0.63). A cosmetically acceptable outcome was achieved in 10 patients in the AM group (83.3%) and 12 (80%) in the control group (P = 0.48). The mean ocular deviation angles improved to 8.7± 12 PD in the AM group and 12.3 ± 17.4Delta in the control group (P = 0.63). The authors concluded that the amniotic membrane wrap of the extraocular muscles during strabismus reoperations was of limited clinical benefit. They attributed this to surgical technique and to the presence of other causes of failure rather than adhesions.
The concept is very interesting, but the results disappointing. The study is limited mainly by its small sample size and short follow-up.

A double-masked randomized trial of postoperative local anesthetic for pain control in pediatric strabismus surgery

The purpose of this prospective double-masked, randomized clinical trial was to determine whether sub-Tenon’s bupivacaine 0.75% or topical lidocaine ophthalmic gel 3.5% administered at the end of pediatric strabismus surgery reduces
postoperative pain and to what extent. Recruited to the study were 50 children (<8 years of age) undergoing strabismus surgery. Subjects were randomly assigned to one of three treatments given at the conclusion of surgery: topical lidocaine gel and sub-Tenon's (balanced salt solution) placebo (n = 16), topical placebo (hypromellose) and sub-Tenon's bupivacaine 0.75% (n = 17), or topical and sub-Tenon's placebo (n = 17). Pain was otherwise managed systemically in the usual fashion by the masked anesthesia team and assessed at regular postoperative intervals by a masked observer using an objective, validated pain scale. Average pain in the first 30 minutes was 6.57, 6.36, and 6.58 in the lidocaine, bupivacaine, and placebo groups, respectively, and was only significantly lower (P=0.016) for bupivacaine vs placebo. The bupivacaine group had significantly lower scores for pain after 30 minutes, total pain, and peak pain compared to the lidocaine group, despite similar pain score in the first 30 minutes. The total average fentanyl use was similar for each group (bupivacaine, 1.65±0.61 mcg/kg; lidocaine, 1.78±0.66 mcg/kg; control, 1.60±0.77 mcg/kg). The average time to discharge was also very similar in the three groups (bupivacaine, 106±16 minutes; lidocaine, 107±25 minutes; control, 106±21 minutes). The authors conclude that sub-Tenon's bupivacaine may reduce postoperative pain in children undergoing strabismus surgery. 

Although it is a well-designed study, one of its pitfalls was that there were fewer bilateral cases in the bupivacaine group compared to the other groups and upon reanalysis of the bilateral cases only, the results were no longer favorable for the bupivacaine group. It is also not clear from the study design how much of the pain relief was attributed to the anesthetic team proactive post-operative care. Because of the relatively small sample size, a few confounding variables may have affected the results.

Reduced surgical success rate of rectus muscle plication compared to resection.

Alkharashi, M. and D. G. Hunter JAPOS June 2017; 21(3): 201-204.

This retrospective study evaluated the surgical success of rectus muscle plication compared to resection and compared the short- and long-term changes in ocular alignment after both procedures. The medical records of all patients, who underwent a rectus muscle tightening procedure (resection or plication) at a single institution over a 5-year period by a single surgeon were reviewed retrospectively. Binocular alignment was recorded before and immediately after surgery and again at 6-12 weeks and final follow-up visit. Primary outcome was surgical success rate, defined as distance alignment of less or equal to 10 PD for horizontal and less or equal to 6 PD for vertical strabismus. Secondary outcomes were reoperation rate and postoperative alignment drift. A total of 72 surgeries were identified for inclusion: 48 resections and 24 plications. Surgical success was significantly higher in the resection group than in the plication group (89% vs 58%; P = 0.005) at both 6-12 weeks' follow-up (P = 0.005) and at mean final follow-up of 19 ± 13 months (range, 3-56 months [n = 48]; P = 0.03). Reoperations were performed in 3 patients in the plication group (12.5%), all for undercorrec-
tion; there were no reoperations in the resection group (P = 0.03). The authors conclude that despite the potential advantages of rectus muscle plication over resection, in their experience, patients treated with plication had lower surgical success rates and a higher reoperation rate. They suggested that surgeons should monitor their long-term results before considering plication as their procedure of choice over resection.

The technique used in this study is not comparable to previous more favorable reports on plications. This study is limited by its retrospective nature, which may have biased patient selection. Both groups are very diverse and statistically different by age. The plication group was older and that may have also affected the results.

Superior and Lateral Rectus Myopexy for Acquired Adult Distance Esotropia: A “One Size Fits All” Surgery

Aging and atrophy cause degradation of the lateral rectus-superior rectus band, shifting the lateral rectus down. This leads to age-related distance esotropia, a benign but important cause of diplopia in the adult population. The authors performed a retrospective review of 18 patients who underwent a bilateral superior rectus and lateral rectus myopexy during a 5 year period. All patients were myopic (18/18), the majority had diplopia (16/18) and many were female (14/18). The preoperative distance deviation averaged 24.3 PD and the near deviation averaged 15.7 PD. After a follow up period of average 17 months, all patients had a deviation less than 4 PD and diplopia resolved in all patients. None of the patients had an overcorrection. The authors conclude that a bilateral myopexy of the superior and lateral rectus muscles is an effective treatment for age-related distance esotropia.

Decreased Binocular Summation in Strabismic Amblyopes and Effect of Strabismus Surgery
Melinda Y. Chang, Joseph L. Demer, Sherwin J. Isenberg, Federico G. Velez et al

Binocular summation is diminished in patients with strabismus, but is postulated to improve after strabismus surgery in some patients. The authors performed a prospective study examining the binocular summation of 15 patients with strabismic amblyopia who underwent strabismus surgery, and compared the results to 30 age-matched normal and 30 non-amblyopic strabismus patients. The binocular summation was tested pre-operatively and within three months post-operatively, and was calculated by subtracting the number of ETDRS chart letters of the better eye from the binocular score. Of the 11 strabismic amblyopes
and 22 matched strabismic controls who completed the study, the authors found binocular summation was lower in amblyopic and non-amblyopic strabismus patients. They also found that the lower pre-operative binocular summation in strabismic amblyopia and strabismic controls was similar and did not change significantly after surgery. In the few patients who did improve, the improved binocular summation was associated with older onset and larger pre-operative angle of strabismus. Three strabismic amblyopes (3 of 11) had worse binocular summation after surgery; however, there were no common patient characteristics. The authors conclude that further investigations in larger groups of patients should be conducted to validate these results.

**Horizontal muscle surgeries**

**Reduction of Consecutive Esotropia Using Modified Contralateral Recession and Resection for Recurrent Intermittent Exotropia.**


The purpose of this study is to compare the surgical outcomes of modified (surgical dose reduction by 5 PD compared to conventional surgical dose) and conventional contralateral lateral rectus recession and medial rectus resection for exotropia after unilateral lateral rectus recession and medial rectus resection. A total of 36 patients were included in this retrospective study. As a primary surgery for exotropia, all patients underwent unilateral lateral rectus recession and medial rectus resection on the non-dominant eye. Patients were subsequently assigned to either conventional contralateral lateral rectus recession and medial rectus resection (surgical dosages based on Wright's surgical table) (n = 19; conventional group) or modified contralateral lateral rectus recession and medial rectus resection (surgical dosages reduced by 5 prism diopters on Wright's surgical table) (n = 17; modified group) for recurrent exotropia. Surgical success rates were evaluated. Reoperation or prism glasses prescription rates due to consecutive esotropia were evaluated. The mean follow-up durations after reoperation were 25.8 and 24.0 months in the conventional and modified groups, respectively. The surgical success rates were 73.7% and 82.4% (P = .538) and the recurrence rates were 0% and 17.6% (P = .059) respectively. The reoperation or prism glasses prescription rates due to consecutive esotropia were 26.3% and 0%, respectively (P = .025). The authors state that in their study on patients with recurrent exotropia, conventional contralateral lateral rectus recession and medial rectus resection showed a significantly higher rate of overcorrection in the early and late postoperative periods. Therefore, the surgical dosage for contralateral lateral rectus recession and medial rectus resection in recurrent exotropia should be reduced. A novel modification for contralateral lateral rectus recession and medial rectus resection in recurrent exotropia after unilateral lateral rectus recession and
medial rectus resection might be useful to reduce the rate of consecutive esotropia after a secondary operation for patients with recurrent exotropia.

To reduce consecutive esotropia after surgery for recurrent exotropia after previous unilateral lateral rectus recession and medial rectus resection, surgical dosages reduced by 5 PD from the conventional surgical table are highly recommended, per the authors of the article.

Surgical Outcome of Intermittent Exotropia With Improvement in Control Grade Subsequent to Part-time Occlusion Therapy.

In this study the authors evaluated the effect of improved control with part-time occlusion therapy on the final postoperative outcome in patients with intermittent exotropia. Control of intermittent exotropia was graded as good, fair, or poor in 89 consecutive patients with intermittent exotropia during their first visit. The patients were reevaluated after part-time preoperative occlusion therapy and divided into two groups (improvement and no improvement) according to whether they showed improvement in control grade. The surgical success rate was compared retrospectively between the two groups. The mean angle of deviation on the first visit was 27.61 ± 5.40 prism diopters (PD) at distance and 29.82 ± 5.28 PD at near. There were significant improvements in the angles of deviation for distance (26.17 ± 5.09 PD) and near (27.26 ± 5.56 PD) after part-time occlusion (both P < .001). The 49 patients who had a significantly improved control grade had a significantly better surgical success rate (77.6%) than the 40 patients who did not (50%; P = .007). The final success rate of surgery was better in the improvement group than in the no improvement group (77.6% vs 50.0%), without any other contributing factors that might have caused a statistically significant difference between the two groups. This suggests that patients with intermittent exotropia who achieve improved control with part-time occlusion therapy could expect better surgical outcomes than their counterparts who did not. There are some limitations to this study. First, its retrospective nature meant that it was difficult to confirm the exact degree of compliance with occlusion therapy. Second, the sample size was relatively small, and the larger size of the improvement group might have led to an overestimation of the success rate in this group. Third, it was not possible to perform fusion and stereoacuity tests at distance or near, so we could not determine the relationship between control, fusion, and stereoacuity. Fourth, the follow-up period was only 1 year, so a study incorporating a longer follow-up evaluation might be necessary in the future.

The authors conclude that improving the control grade of intermittent exotropia through the implementation of part-time preoperative occlusion therapy may lead to a better surgical success rate than that achieved by surgery alone. Part-time occlusion therapy improves the control grade,
which affects the surgical outcome in addition to decreasing the angles of deviation for distance and near.

**Medial rectus Bridge Faden Operations in Accommodative and Partially Accommodative Esotropia With Convergence Excess.**

The purpose of this retrospective chart review was to compare the surgical outcomes of bilateral bridge Faden operation on the medial rectus muscle with or without recession in the treatment of accommodative and partially accommodative esotropia with convergence excess. One hundred three patients participated in the study: Fifty-one patients underwent the bridge Faden operation on both medial rectus muscles with recession (recession group) and 52 patients underwent the bridge Faden operation on both medial rectus muscles without recession (no recession group). The mean preoperative amount of esotropia at near was 43.51 ± 7.00 and 24.24 ± 3.56 prism diopters (PD) for the recession and no recession groups, respectively. The mean preoperative amount of esotropia at distance was 26.63 ± 6.86 and 9.22 ± 2.09 PD for both groups, respectively. The mean preoperative near–distance disparity was 17.14 ± 3.00 and 14.05 ± 4.14 PD for both groups, respectively. In both groups, there was a statistically significant difference in the near and distance deviations and the near–distance disparity between preoperative and postoperative values (*P* < .05). Postoperatively, there was no significant difference between 1 month, 6 months, and 1 year and between 6 months and 1 year (*P* > .05). The authors of the study concluded that the bridge faden operation on both medial recti muscles with or without recession was a successful procedure in the treatment of accommodative and partially accommodative esotropia with convergence excess. The study is limited though by its retrospective nature and the small sample of patients.

**Clinical features and Surgical Outcome of Triad Exotropia**

This retrospective chart review describes the surgical outcomes and clinical features of A pattern exotropia combined with dissociated vertical deviation (DVD) and superior oblique overaction. The patients (n=40) who participated in the study were divided into two groups: in the first group, only horizontal muscle surgery was performed and in the second group, horizontal muscle surgery was combined with bilateral superior oblique weakening surgery. Surgeries consisted of lateral rectus recession alone in the first group. In the second group, lateral rectus recession was combined with downward transposition when superior oblique overaction was less than +2. The apparent (+3) superior oblique overaction was corrected with superior oblique posterior four-fifths tenotomy. Superior rectus recession was also performed based on the amount of DVD presents preoperatively. Surgical success was defined as exodeviation less than 10 PD or
esodeviation less than 5 PD at the final visit without abnormal head position, diplopia, reading difficulty, large angle DVD, or reoperation in the entire follow-up period. The study showed that at the final visit, the horizontal angle deviation was not significantly different between the groups. The success rates were 57.1% and 80% in the horizontal muscle surgery alone and combined surgery groups, respectively and the difference was statistically significant ($P = .04$). The study has several limitations including her small sample size, her retrospective nature, the limited follow-up period and the fact that the surgical techniques used were variable.

Lateral rectus muscle resection following maximal recession of the medial rectus muscle in thyroid eye disease

Rectus muscle restriction is a common finding in thyroid eye disease (TED). Typically, restricted muscles are recessed to address strabismus and diplopia. However, some patients have residual strabismus following maximal recession of a restricted muscle. The purpose of this retrospective study was to report outcomes following resection of the lateral rectus muscle after maximal recession of the medial rectus muscle in patients with TED. The medical records of patients with TED who underwent lateral rectus resection between 1998 and 2015 were reviewed. Information regarding thyroid disease history and surgical treatment, including history of orbital decompressions, rectus muscle recessions, rectus muscle resections, and pre- and postoperative alignment was collected. Adjustable suture was used in all cases. Success was defined as a postoperative orthotropia with $\leq 2$ PD of phoria at distance and a phoria at near. A total of 11 patients were included. All 11 patients had a history of orbital decompression. Of these, 10 (91%) required postoperative adjustment. A successful outcome was achieved in 10 cases (91%). The authors conclude that lateral rectus muscle resection to address residual esotropia and diplopia was effective at reducing residual esotropia following medial rectus recession in their study cohort. Although the results presented with this adjustable technique are very promising, the follow-up period for all patients was short (2 months).

Factors associated with atypical postoperative drift following surgery for consecutive exotropia.

The aim of this retrospective study was to evaluate the associations of clinical and surgical factors with atypical postoperative drift following surgery for consecutive exotropia. A total of 66 patients with consecutive exotropia ($\geq 10$PD at distance), after previous surgery for esotropia were retrospectively identified. All patients underwent unilateral lateral rectus recession (on adjustable suture) with medial rectus advancement and/or resection.
Immediate postoperative target angle was 4-10 PD of esotropia at distance, anticipating mild postoperative exodrift. Actual postoperative drift was calculated as change in distance deviation from immediately post-adjustment to 6 weeks. Typical drift was defined as 0-9 PD of exodrift. Excessive exodrift was defined as ≥10 PD. Esodrift was defined as 1 PD or more. Univariate and multiple logistic regression analyses were performed to evaluate for associations with a wide range of clinical and surgical factors. Overall there was a median exodrift (4 PD, quartiles 0 PD-10 PD). Of the 66 patients, 18 (27%) showed excessive exodrift; 15 (23%), esodrift. In multiple logistic analyses, larger preoperative distance exodeviation was associated with excessive exodrift (P = 0.01), and non-normal medial rectus attachment status (abnormal [stretched scar, pseudo-tendon], attached to pulley, or behind pulley) was associated with esodrift (P = 0.02). The authors conclude that approximately half of patients show atypical drift following unilateral surgery for consecutive exotropia, with larger preoperative distance exodeviation associated with exodrift and non-normal medial rectus muscle status with esodrift. Knowing these associations may help when counseling patients regarding surgical outcomes. The fact that a surgically-induced larger-angle esotropia immediately postoperatively does not appear to be protective against excessive exodrift suggests other, as yet unidentified, treatment strategies are needed to correct this tendency to exodrift. This study from an experienced surgeon is comparative to previous reports.

Long-term evaluation of two reoperation groups for intermittent exotropia.
Lee, J. Y., Lee, G. I., Park, K. A. and Oh, S. Y.

The aim of this retrospective study was to evaluate the effect of initial postoperative deviation on subsequent reoperation in patients with intermittent exotropia and to compare the clinical factors and surgical outcomes between two surgical failure groups, recurrent intermittent exotropia patients and consecutive esotropia patients. The medical records of patients who underwent reoperation after failed primary surgery for intermittent exotropia at a single center were reviewed retrospectively. Various clinical factors were compared between these two groups, including age at surgery, interval between surgeries, stereoacuity, spherical equivalent, office control, surgical type, presence of neurologic disease, amblyopia and other strabismus, and postoperative angles of deviation. A total of 139 patients met inclusion criteria of 3,406 patients who underwent surgery for intermittent exotropia; 125 (3.8%) underwent reoperation for recurrent intermittent exotropia; 14 (0.4%), for consecutive esotropia. On postoperative day 1 the intermittent exotropia group showed esodeviation at distance fixation of 2±4PD; the esotropia group, esodeviation of 5±4 PD. The intermittent exotropia group showed a significant progression of exodeviation from 2 months postoperatively (all P < 0.005). In the esotropia group, the
amount of esodeviation significantly improved in postoperative months 2 and 6 (P = 0.024 and 0.013) then further worsened after 6 months. The interval between the first and second surgeries was 64 ±28 months in the exotropia group and 55 ±36 months in the esotropia group, a significant difference (P = 0.003). The authors conclude that initial postoperative overcorrection following primary surgery for intermittent exotropia may not predict long-term success. Careful monitoring for consecutive esotropia is needed 6 months postoperatively, and annual check-ups are recommended for all patients with under- and overcorrections for a period of at least 5 years after surgery. It seems from the report that the authors selected to reveal only part of their analysis regarding the characteristics of each group. We were curious to know what parameters were related to failure of both groups.

**Postoperative esotropia: initial overcorrection or consecutive esotropia?**

The authors conducted a retrospective study of patients undergoing surgery for intermittent exotropia to determine how much time needed to pass before an “initial overcorrection” could be labeled “consecutive esotropia. In other words, when do overcorrections stop improving? They included fifty consecutive patients with postoperative esotropia ≥6 prism diopters at 1 week following exotropia surgery, managed with nonsurgical management, who were followed after surgery for at least 6 months. Thirty-two of 50 patients had resolution of esotropia by one month. Patients without resolution by one month were older (p=0.006), had a larger preoperative deviation at distance (p = 0.015), and were more likely to have a concomitant vertical deviation (p = 0.019). The authors concluded that when initial postoperative esotropia persists for more than 1 month, it should be regarded as consecutive esotropia, and that more postoperative attention should be given to patients who are older and/or have a larger preoperative deviation or concurrent vertical deviation. A limitation of this study is that patients who did not follow-up for 6 months were excluded, and these patients may differ from those who did follow-up, which would make results less generalizable.

**Early postoperative overcorrection in recurrent exotropia**

Recurrent exotropia is common after surgery for intermittent exotropia. There are various surgical options for recurrent exotropia. This study intended to evaluate the early postoperative outcomes after surgery for recurrent exotropia. The authors performed a retrospective review of 106 patients, mean age 11.8 years. The mean interval from previous surgery was 5.9 years. The mean preoperative angle was 22.9 PD. On post-operative day one, the majority of patients (77.4%) were orthotropic (defined as orthotropia or <5PD exo). 18.9% were overcorrected
(≥ 2PD esodeviation), and 3.8% were undercorrected (≤5 PD exo). Surgical success at final follow-up was higher in the overcorrection group compared to the orthotropic and undercorrected groups. Final deviation was 2.1 PD in the overcorrection group, compared to 6.0 in the orthotropic and 16.3 in the undercorrection groups. Regression analysis found that only the post-operative day 1 measurements were a reliable predictor of long-term success. Therefore initial overcorrection is a good predictor of ultimate success in treatment of recurrent exotropia.

The role of rectus muscle myectomy in the management of large-angle strabismus for Graves’ ophthalmopathy.


Graves’ disease infiltration of lymphocytes and fibroblasts within the extraocular muscles may result in fibrosis and restrictive strabismus. Weakening procedures of restrictive muscles are the procedure of choice in strabismic Graves’ disease patients. Undercorrections are common in patients with severe restrictions and large deviations. Authors report 47 consecutive patients with large angle strabismus who underwent rectus muscle myectomy. Muscles were cut at a distance 10 mm or more from the muscle insertions. The anterior muscle segment was extirpated. The posterior muscle retracted free. All surgeries were performed by the same surgeon. Large-angle strabismus was defined as more than 25 prism diopters (PD), median age of 56.7 years. None of the patients received prior orbital decompression. All patients had at least 3 months of ocular motility stability. Mean time period between the initial clinic visit and the first surgery was 6.69 ± 3.74 months. Mean postoperative follow up ranged from 8.4 to 79.7 months). 89.4% of patients received single-muscle myectomy. Four patients (8.5%) received myectomy of two muscles and one (2.1%), three muscles. Fourteen patients (29.8%) had more than 40 PD of deviation.Postoperatively, 78.7% of patients reported no diplopia within central 30° field and in reading position. The mean correction of deviation with a single-muscle myectomy was 34.3 ± 7.7 PD, ranging from 26 to 60 PD. All three groups of muscles (IR, MR and SR) had similar postoperative correction after myectomy. No differences in exophthalmos were seen (Preoperative 17.7 ± 2.1 mm vs. postoperative 17.4 ± 1.9 mm). Authors suggest that an advantage of the procedure is the possibility of performing the surgery in patients with a very limited space. Markedly enlarged muscles in Graves’ disease may not retract posteriorly to a more relaxed position.

Authors conclude that patients undergoing myectomy showed improved movement and less incomitance and no diplopia in central 30° field and reading position. The paper lacks validation to demonstrate such an improvement. There is no binocular single vision field to confirm such a gain
or perhaps severe limitation for a functional binocular patient to have only 15 degrees of single vision in some gazes away from the central primary position. No data is presented to confirm lateral or vertical incomitance. The scan presented for one patient with severely enlarged vertical rectus muscles who underwent inferior rectus myectomy and resulted in a severe overcorrection perhaps demonstrates that this uncontrolled procedure can result in severe overcorrection in patients with severely enlarged and restricted antagonist muscles. Finally, some patients who required exploration of previously myectomized muscles demonstrated that muscles were inserted 8-10 mm posterior to the insertion. Now those muscles have been resected 10 mm. an experienced strabismus surgeon can recess a muscle 8-10 mm posterior to the insertion especially after the tight muscle has been disinserted from the sclera.

**Patient characteristics and Surgical Approach Impacting Simultaneous to Alternate Prism Cover Test Disparity After Exotropia Surgery: A Quantitative Look at the Difference in Motor Outcomes.**


The simultaneous prism cover test (SPCT) and alternate prism and cover test (APCT) provide different, but equally valuable information regarding residual postoperative misalignment after surgery for exotropia. The SPCT measures manifest deviation, whereas the APCT measures total deviation including intermittent and latent components. The purpose of this study is to investigate the disparity between simultaneous prism and cover test (SPCT) and alternate prism and cover test (APCT) outcomes after exotropia surgery, and to identify characteristics associated with significant disparity between them. The authors hypothesized that intermittency of deviation and absence of medial rectus resection in the surgical plan might be associated with a greater postoperative SPCT-APCT disparity. A retrospective review of sensorimotor history and postoperative outcomes of patients treated for exotropia with strabismus surgery was performed. Two hundred seventy-four and 319 patients had both measurements recorded at distance and near, respectively. Correlation between the SPCT and APCT and range of APCT when the SPCT measurement was zero were determined. Patient characteristics studied for association with a difference between the SPCT and APCT exceeding known APCT test–retest variability included age, visual acuity, fusion, intermittency, pattern, preoperative and postoperative angle, and treatment with or without medial rectus resection. SPCT and APCT outcomes were strongly correlated (\( P < .001 \)), significantly different (\( P < .001 \)), and linearly related. The percentage of patients who were orthotropic (SPCT = 0) was 76% at distance and 80% at near. Misalignment of 10 prism diopters (PD) or less by the APCT was present in 92% of orthotropic patients at distance and 84% at near. Surgery without medial rectus resection (\( P = .015 \)), larger preoperative angle (\( P = .003 \)), intermittent exotropia (\( P = .028 \)), and postoperative exotropia rather
than esotropia ($P < .001$) were associated with a significant SPCT–APCT difference. The authors conclude that although a greater postoperative SPCT–APCT disparity was confirmed for patients with intermittent exotropia, it also independently associated with a larger preoperative deviation and surgery without medial rectus resection. Performing medial rectus resection, a surgeon’s prerogative, provides more apparently consistent postoperative alignment characterized by less SPCT–APCT disparity. This is the most clinically significant outcome of the study.

Surgical Treatment of Adult-Onset Esotropia: Characteristics and Outcomes.

This is a retrospective case study of patients who developed esotropia at or after the age of 18 years and underwent surgical treatment. The purpose of the study was to describe the characteristics of strabismus, surgical management, and outcomes of these patients. Preoperatively, all patients (n=244) with esotropia experienced diplopia except from the ones with sensory esotropia (n=4). The four most common causes were: cranial nerve VI palsy (36%), thyroid eye disease (18%), age-related distance esotropia (15%), and decompensated latent esodeviations (13%). A variety of surgical procedures were used with adjustable sutures being used in 79%. Approximately 80% of patients at 2 month follow-up were aligned within 10 PD, and 72% experienced resolution of diplopia. Success rates were significantly higher in patients with adjustable sutures and reoperation rates were low overall (15%-highest in cranial nerve VI palsy and lowest in age-related distance esotropia). Dose-response calculations showed a non-significantly smaller effect per millimeter of recession and resection in cranial nerve VI palsy and age-related distance esotropia. The authors conclude that a variety of surgical approaches in combination with adjustable sutures provide a good rate of diplopia resolution in patients with adult onset esotropia. The study is limited by its retrospective nature and the limited follow-up time.

To what extent may Botulinum toxin type A injections be an alternative choice to surgery in infantile esotropia?

The purpose of this retrospective case series was to evaluate the results of a single injection of botulinum toxin A in infantile esotropia as an alternative choice to surgery. Enrolled in the study were 65 consecutive pediatric patients (mean age 15, range 9 to 26 months) with infantile esotropia, who underwent botulinum toxin A injection in both medial recti. Clinical data was collected, including measurement of pre- and post-operative angle of deviation, visual acuity, stereoscopy and side effects. All patients had a minimum of 24 months follow-up period. Success was defined as a post-
operative stable deviation ≤ 8 PD. It was obtained in 33 cases (50.7%). Excellent result -2 PD to +4 PD was obtained in 17 children (26%). Additional surgery was required in 32 cases for a residual angle (albeit smaller angle than the initial deviation) or recurrent deviation and/or DVD (49.2%). A complication of ptosis of variable duration (1 to 3 months) was recorded in twenty-eight children (43%). The authors state this did not affect patients visual acuity, but do not give information on patients’ visual acuity. The authors conclude that Botulinum toxin A reduces the tonic spastic motor component of strabismus and, should additional surgery be required, allows the procedure to be carried out on a smaller angle. A reduction in the maximum angle of deviation is thus achieved sooner, and allows the development of anomalous binocularity in a stable microtropia. Despite some obvious limitations in the study design, it does show some benefits to the use of botox in infantile esotropia. Unfortunately, the authors did not share a dose-effect relationship. The methods section does not specify if the same dose was used for all patients or if the amount of botox A toxin was modified according to the size of measured pre-operative deviation.


Wright central plication is a minimally invasive tightening procedure described for the first time by Wright and colleagues in 2012. The purpose of this retrospective study was to compare outcomes of lateral rectus central plication (LRCP) to medial rectus recession (MRR) in the treatment of adult divergence insufficiency esotropia (ADIE). ADIE also called sagging eye syndrome was defined as esotropia (ET) that is at least 10 PD greater at distance than at near. A retrospective chart review of 30 consecutive patients with ADIE, who underwent either LRCP or MRR between 2010 and 2015 was performed. Inclusion criteria included age ≥45 years, LRCP or MRR surgery fixed suture technique, esotropia (ET) at least 10Δ greater at distance than at near, subjective diplopia at distance, fusion at near fixation, follow-up of at least 6 months. Primary outcome was postoperative single binocular vision. Secondary outcome was postoperative deviation of <5 PD. A total of 28 patients (15 females) met inclusion criteria: 15 had LRCP and 13 MRR. Both groups were quite similar by several parameters including, age (mean age ±SD was 68.92±8.07 years in the central plication group versus 64.38 ±12.33 years in the recession group [P =0.26]). Primary outcome of no diplopia was not significantly different between LRCP and MRR group having a success rate of 93.3% versus 92.3%, respectively (P ≥ 0.01). Secondary outcome of a deviation of ≤5 PD at distance was better in the LRCP group than the MRR group (15/15 vs 11/13 [P ≥ 0.01]). One patient in LRCP group had an early overcorrection corrected by in-office suture lysis. The authors conclude that both procedures had excellent primary out-
comes eliminating diplopia in over 90% of cases. The LRCP group had statistically better postoperative alignment of <5 PD. The authors claim that The Wright LRCP has the advantage of being minimally invasive, semi-reversible, vessel sparing, and can be done with topical anesthesia. The study introduces the LRCP as another option for alleviating distance diplopia with patients with age-related divergence insufficiency. It has its obvious limitations, including its retrospective nature and small sample size.

Botulinum toxin as an adjunct to monocular recession-resection surgery for large-angle sensory strabismus.

This retrospective case series evaluated the results of using intraoperative botulinum toxin A (BTA) as an adjunct to monocular recession-resection surgery in the management of large-angle sensory strabismus. The study included 13 patients (mean age, 31.04 ±18.5 years) that were diagnosed with sensory large-angle strabismus, who underwent monocular recession-resection surgery combined with 5 units of BTA injection into the recessed muscle of the nonfixating eye. They all had best-corrected Snellen visual acuity in one eye of less than 20/100, horizontal deviation of at least 50D, and follow-up of at least 12 months. Surgical outcome was considered successful if the final deviation was within 10 PD. Included were eight patients with exotropia and 5 with esotropia. The mean follow-up period was 52.77 ± 10.9 months. The mean preoperative deviation was 66 PD ± 16 PD in the esodeviation group and 56 PD ± 5 PD in the exodeviation group. The final postoperative mean deviation was 6 PD ± 7 PD in the esodeviation group and 6 PD ± 8 PD in the exodeviation group. Successful final outcome was achieved in seven patients (87.5%) in the exodeviaton group and also in four patients (80%) in the esodeviation group. Postoperatively 4 patients (30%) developed mild ptosis caused by leakage of BTA into the superior levator muscle. The authors conclude that adjunctive usage of BTA with conventional surgery appears to enhance surgical outcomes by increasing the amount of expected correction. The combined use of BTA with monocular recession-resection rectus muscle surgery may be a good alternative in the treatment of large-angle sensory strabismus. Apart from its retrospective nature this study was also limited by its small sample size and lack of controls.

A chronicle of surgical thinking and doing for exotropia: innovations and rediscoveries.
This historical review unfolds the evolution of theories and practices concerning surgery for exotropia over the last approximately 200 years. Major ophthalmology texts and relevant references were reviewed to discover experience and thinking concerning the causes of comitant intermittent and constant exotropia and corrective surgical approaches, but the author selected to highlight certain aspects and it does not reflect all contributions. The concept that excessive divergence is the cause of comitant exotropia has given way to one recognizing that this disorder is a position of rest modified by convergence. Several procedures practiced at former times have regained popularity. The author concludes that the history of progress in surgery for exotropia is mixed. Although some procedures now employed are new, others currently in favor had been well known and formerly utilized by ophthalmologists for many decades. These should be regarded as rediscoveries or revivals rather than as novel. This review also suggests a need to address how to better report retrospective studies. It raises many controversies regarding different aspects of exotropia surgery and best treatment options in strabismus surgery in general such as: measurements issues, “dissociated strabismus complex,” monocular versus binocular surgery, single muscle surgery, role of imaging, etc. It seems that some of the topics chosen reflect the author's preferences and not all are directly related to exotropia, but it is an excellent introduction to understanding present practices. The reference includes some seminal papers in strabismus surgery.

A retrospective evaluation of bilateral medial rectus recession for management of accommodative esotropia according to prism-adapted motor response preoperatively.

The prism adaptation test (PAT) is a preoperative tool that may fine-tune surgical dosage and reduce under- and overcorrection in pediatric partially accommodative esotropia; however, it is resource intensive and the benefits are uncertain. PAT involves correction of esodeviation with prisms, with subsequent assessment for and quantification of change in angle of esodeviation, thereby augmenting the surgical target angle in a subset of patients. The purpose of this retrospective study was to evaluated PAT response and postoperative outcomes in a cohort of 28 children with partially accommodative esotropia, (defined as esodeviation in hyperopic patients that persisted despite full hyperopic correction), who underwent bilateral medial rectus recession and found that 36% of patients showed a requirement for increase of prism dosage to retain orthotropia during PAT. A prism builder was defined as requiring $\geq 5$ PD increase in base-out prism during PAT, and a non-builder experienced a reduction or $< 5$ PD increase in base-out prism requirement. These prism builders did better than those whose deviation was stable, with postoperative rate of motor success (de-
fined as ≤10 PD esotropia) of 100% versus 56%. The authors conclude that PAT may be a useful positive prognostic test, and it also identifies a substantial patient population who may avoid undercorrection, the prism builders. However, this cohort may do better postoperatively regardless of the target angle for surgery. Additional randomized studies are required to demonstrate definitive benefit of PAT. Identification of the builder phenotype prior to commencing adaptation may reduce the workload involved in the PAT technique.

Variability of preoperative measurements in intermittent exotropia and its effect on surgical outcome.
Kim, W. J. and M. M. Kim JAAPOS June 2017; 21(3): 210-214.

The purpose of this retrospective study was to investigate the variability of preoperative measurements in patients with intermittent exotropia and to compare surgical outcomes according to the variability. A total of 344 patients, who underwent unilateral lateral rectus recession and medial rectus resection and had 24 months' postoperative follow-up were enrolled. Patients were divided into three groups according to variability, which was defined as the largest angle minus the smallest angle ever measured during the preoperative visits; group C (n=128; mean age 6.9 ± 3.2 years) comprised patients with consistent exodeviation; group VL (n=155; mean age 7.6 ± 4.5 years), patients with less variability (<10 PD); and group VM (n=61; mean age 7.6 ± 4.0 years), patients with more variability (≥10 PD). Surgical outcomes of the three groups were compared. The largest variability was 20 PD and 62.8% (216/344, group VL + group VM) of the patients showed variable angles of deviation during the preoperative measurements. Longitudinal data is also presented showing that postoperative exodeviation increased in all groups over the 24-month follow-up; however, the postoperative exodeviation of group VM was lower than that of both groups C and VL (repeated-measure ANOVA, P = 0.032). There was a trend toward decreased rates of reoperation from group VM compared with groups VL and C (linear by linear association, P = 0.004). The authors conclude that in their cohort of patients more than half of patients with intermittent exotropia showed variable angles of deviation during the preoperative measurements. The surgical outcomes were better in those with variable preoperative measurements than in those with consistent preoperative measurements.

Despite its retrospective nature, the study reports on a relatively large cohort of patients, all operated on by a single surgeon. One hypothesis that is raised by the authors in the discussion to explain their surprising result is that the higher variability of preoperative angle in the VM might originated from better fusional control potential, which leads to a favorable surgical outcome. Unfortunately fusional status and stereo-acuity were not available for analysis.

Bilateral medial rectus resection for primary large-angle exotropia.
Surgical treatments for large-angle exotropia include bilateral lateral rectus resection, recession-resection procedures, and three- and four-muscle surgery. Undercorrection and limitation of abduction are common complications of these procedures. This retrospective study evaluated the results of bilateral medial rectus resection as a first procedure for primary large-angle exotropia. The medical records of 64 patients, who underwent bilateral medial rectus resection for angles equal to or greater than 60 PD (range 60 PD-140 PD) with a minimum follow-up period of 6 months were reviewed. The amount of resection ranged from 8 mm to 12 mm according to the preoperative angle (a surgical table is presented in the article). Success was defined as a final outcome within the range of 8 PD of esotropia to 10 PD of exotropia. The overall success rate was 77%, with no significant difference in success rate between subgroups of smaller and larger angles. In five patients with an angle greater than 120 PD success was achieved only in 40%. Limitation of abduction was seen in the first postoperative week. At 6 months' follow-up 64% of eyes had no limitation of abduction. At 6 months' follow-up 64% of eyes had no limitation of abduction. The author concludes that in his patient cohort, bilateral medial rectus resection successfully corrected large-angle exotropia of up to 140 PD, with results comparable to three- and four-muscle procedures. The author claims that this technique has the advantage of not causing significant abduction deficits, even with resections up to 12 mm.

It seems that despite this statement, approximately a third of the patients continued to experience an abduction deficit at the end of the follow-up period. Not included in the results is level of incomitance. There are obvious limitations to this study, including its retrospective nature, lack of controls, and the relatively short follow-up period of 6 months. However, the overall success rate described for this technique is quite high. The discussion includes a good summary of other techniques and reports on surgical treatments for large-angle exotropia.

Intraoperative Findings in Consecutive Exotropia with and without Adduction Deficit.

Consecutive exotropia has a reported incidence of up to 27% with long-term follow-up. Consecutive exotropia may be associated with limited adduction, which has been reported to be caused by 1 or more anatomic abnormalities of rectus muscles or their insertions. The authors studied the relative frequency of grades of adduction deficit and the relative frequency of abnormal anatomic findings. They conducted a retrospective review of patients undergoing surgery for consecutive exotropia of ≥10 PD, excluding paralytic or restrictive strabismus. Study period was between 1995 and 2016. All surgeries were performed by a single surgeon (J.M.H). Preoperative duction deficits were graded on a -5 (severe limitation) to 0 (normal) scale. Operative reports were reviewed to classify intraoperative factors: (1) medial rectus muscle attachment type (normal, ab-
normal [slipped or stretched scar], attached to pulley, behind pulley, or mixed [a tenuous normal attachment, but with muscle fibers also attached to the pulley or behind the pulley]), (2) medial rectus muscle distal fiber location (millimeters from original insertion), and (3) lateral rectus muscle tightness (normal, mild restriction, moderate restriction). The authors evaluated the relationship of graded adduction deficit to each intraoperative factor. Of the 143 eyes, 124 (87%) had an adduction deficit. Eyes with abnormal (n = 23), pulley (n = 9), behind pulley (n = 8), or mixed (n = 7) attachments had worse adduction deficits than normal attachments (n = 96; P < 0.02). There was a significant correlation between distal medial rectus muscle fiber location (0-19.5 mm recessed) and grade of adduction deficit (P < 0.0001). Eyes with mild or moderate lateral rectus muscle tightness on forced duction testing (n = 48/143 eyes) had worse adduction deficits than eyes without tightness (P < 0.001). Nevertheless, despite overall correlation, there was considerable individual variability. For example, for -1 and -2 adduction deficits, medial rectus muscle attachment could be at the pulley, behind the pulley, or include the pulley (19/87 eyes [22%]), and the lateral rectus muscle was tight in 36 of 87 eyes (41%). The authors concluded that adduction deficits are common in patients with consecutive exotropia. Overall, more severe preoperative adduction deficits are associated with medial rectus muscle insertion abnormalities and abnormal forced ductions, but frequently there are exceptions. Severe medial rectus muscle insertion abnormalities, including lost muscles, may be found despite mild preoperative adduction deficits. Hence, these findings suggest that severity of preoperative adduction deficit is a poor predictor of the medial rectus muscle attachment type and the location of the distal end of the medial rectus muscle fibers, especially in patients with mild to moderate deficits of adduction. The authors recommended that surgeons need to be prepared for any combination of medial rectus muscle and lateral rectus muscle findings. They also recommend addressing any lateral rectus muscle tightness at the time of the surgery in addition to advancing or resecting the medial rectus muscle.

**Comparison of Botulinum Toxin With Surgery for the Treatment of Acute-Onset Comitant Esotropia in Children.**


Acute comitant esotropia is currently treated with strabismus surgery, however there are multiple drawbacks to the surgery including more time with disturbed binocularity and longer general anesthesia. Botulinum toxin is an alternative treatment for this condition, but has not been compared to standard surgery for the treatment of strabismus in acute onset comitant esotropia in the pediatric patient. The authors sought to determine if Botulinum toxin is as effective of a treatment as strabismus surgery in acute onset comitant esotropia. A retrospective study of 16 patients who were treated with the chemodenervation and 33 patients were treated with strabismus surgery was performed. The authors defined success as a total horizontal deviation of 10 prism diopters or less and evidence of binocular single vision. Success rates were not statistically different at 6 or 18
months after follow up with 13/16 (81%) of patients in the chemodenervation and 20/33 (61%) of patients in the surgery group achieving surgical success at 6 months. Additionally, the total OR time was shorter and the overall cost was lower in the patients who had the Botulinum injections. The authors concluded that the chemodenervation was not inferior to strabismus surgery for acute onset comitant esotropia in children. The authors acknowledged the surprisingly low surgical rate of success in this study. Additionally they hypothesized that the lack of delay in treatment in the chemodenervation group could have contributed to the success in this group. The limitations of the study being the retrospective nature, small number of patients due to this being a rare condition were highlighted in the paper’s discussion. The authors concluded that botulium toxin was as effective as strabismus surgery in the treatment of acute comitant esotropia in children and should be considered an alternative to strabismus surgery in this condition.

Clinical profiles and surgical outcomes of adult esotropia

Adult patients with esotropia can have various etiologies for their strabismus, and surgical approaches are also variable. In an effort to evaluate the clinical features and surgical outcomes of adults with esotropia, the authors conducted a retrospective cohort study of patients >14 years of age who underwent strabismus surgery at a single center. For all surgeries, limbal incisions and adjustable suture techniques were used. Patients were classified as either childhood-onset esotropia (CET) or adult onset esophoria-tropia (EPT). Postoperative success was defined as within 12PD or orthotropia at distance and near. 73 patients were included, 35 in CET group and 38 in EPT group. Mean pre-operative deviation at distance was 30PD for CET group and 22PD for EPT group. At 2 weeks post-operative, success was found in 88% for CET and 97% for EPT, decreasing at 4-6 months to 71% and 80% respectively. The post-operative difference between the groups was not statistically significant. There were no complications noted. The patients in the EPT group were more likely to have myopia (69% vs 40%) and experience diplopia or asthenopia pre-operatively. The CET group was more likely to have hyperopia and amblyopia. Patients who had previous surgery or larger pre-operative misalignment were more likely to experience post-operative drift. In conclusion, this study demonstrates clinical differences between adults with differing etiologies of esotropia, and adjustable suture strabismus surgery is safe and effective. However, this was a retrospective study, 4-6 month follow-up was not as consistent as the 2-week mark, and defining success as 12PD was chosen due to a patient population with large deviations.

Outcome of two-muscle surgery for large-angle intermittent exotropia in children
Achieving surgical success for intermittent exotropia can sometimes be challenging, with success rates varying widely in the literature for the most common types of surgical intervention: bilateral lateral rectus recession (BLR) and unilateral recess-resect (RR). Some authors advocate 3 or 4 muscle surgery for large angles, whereas others state two muscle surgery can be successful. The authors of this study retrospectively reviewed 178 consecutive children with large angle (>=40 PD) or moderate angle (>=20 to <30) intermittent exotropia who underwent BLR or RR surgery. Surgery was done by one surgeon without adjustable sutures or hangback. Mean pre-op deviation in the large angle group was 44PD, and 26PD in the moderate angle group. Mean follow-up was similar in both groups at nearly 6 months. At final follow-up, mean distance exodeviation was 12.68 in the large angle group and 4.71 in the moderate angle group. Reoperation rates were 40% and 21.7% respectively for the large and moderate angle groups. Final success rates (between 10PD of exodeviation and 5PD of esodeviation at distance and near) were 45% and 79% respectively. The large angle group also had a larger surgical effect/dose (PD/mm), whether BLR or RR. The authors reported no significant adverse events, including no reports of limitation of abduction. The authors conclude that children with large angle intermittent exotropia have lower surgical success rates compared to moderate angle, despite a greater dose response. Note however this is retrospective review, and therefore did not quantify in-office control of intermittent exotropia, did not include patients with shorter than 6 months follow-up, and summed the amounts of recession and resection in the RR group when reporting dose-response.

**Vertical muscle surgeries**

**Inferior Oblique Belly Transposition for Small Angle Hypertropia With Inferior Oblique Overaction: A Pilot Study**


The purpose of this retrospective study is to evaluate the efficacy of transposition of the belly of the inferior oblique muscle in treating inferior oblique overaction with small angle hypertropia. Ten patients participated in the study. Transposition of the inferior oblique muscle belly consisted of suturing the entire body of the muscle to the sclera 5 mm posterior to the temporal insertion of the inferior rectus muscle. All patients had small hypertropias (< 5 prism diopters) in the primary gaze position with associated inferior oblique overaction. Deviations in both primary and lateral gazes, compensatory face turns or head tilts, and the degree of inferior oblique overaction were evaluated preoperatively and postoperatively. The study showed that 9 out of 10 patients had a complete resolution of inferior oblique overaction. In the remaining patient, the inferior oblique overaction improved from +3 to +1. None of the patients had any residual vertical deviation. There was elimination of compensatory head tilting in 5 patients and correction of
compensatory face turns in 4 patients. One patient with mild up drifting of the involved eye also improved after the procedure. All patients expressed subjective satisfaction with the surgical outcome. The authors conclude that transposition of the inferior oblique muscle belly effectively weakened mild to moderate inferior oblique overaction and corrected small primary position hypertropias. This procedure may be a useful addition to surgical treatment options in patients with small hypertropias associated with inferior oblique overaction.

Anterior and nasal transposition of inferior oblique muscle in cases of superior oblique palsy.
Saxena, R., Sharma, M., Singh, D. and Sharma, P. 

The purpose of this small retrospective case series was to report long-term outcome of inferior oblique anterior and nasal transposition in superior oblique palsy. The medical records of patients with superior oblique palsy who underwent inferior oblique anterior nasal transposition were reviewed retrospectively. One-year postoperative results were evaluated for alignment in primary gaze, contralateral gaze, and upgaze; reduction in inferior oblique overaction and changes in fundus torsion to assess long-term outcome of the procedure. A total of 12 patients were included. Three cases also underwent horizontal muscle surgery. Mean age at the time of surgery was 20.6 ±4.1 years. The median preoperative hypertropia was 21.5 PD (range, 12-36 PD), corrected to 4.5 PD (range, 2-10 PD) at 12 months postoperatively (P = 0.002). Median inferior oblique overaction decreased from +3 (range, +1 to +4) to 0 (range, -1 to +1). Preoperative fundus extorsion was 19.2 degrees ±6.7 degrees; postoperative, 0.58 degrees ±1.8 degrees (P < 0.001). No consecutive hypotropia or underaction in elevation was observed in 10/12 patients; 1 patient complained of torsional diplopia in upgaze. Extorsion was eliminated and head tilt improved in all patients. The authors conclude that inferior oblique anterior and nasal transposition resulted in good long-term outcomes in their cohort of patients with superior oblique palsy presenting with hypertropia, inferior oblique overaction, and extorsion in primary gaze. However, the study is limited by its small sample size and its retrospective nature. There are several surgical modalities that are suitable for this clinical situation; This study demonstrates that inferior oblique anterior and nasal transposition may be considered for managing superior oblique palsy with significant torsion.

Graded versus ungraded inferior oblique anterior transposition in patients with asymmetric dissociated vertical deviation.
The purpose of this randomized trial was to compare the surgical outcomes of graded versus ungraded IOAT in the treatment of patients with asymmetric DVD and bilateral inferior oblique overaction (IOOA). A total of 74 eyes of 37 patients with asymmetric DVD (interocular difference of ≥ 5 PD) and bilateral IOOA of > +1 were included in this randomized clinical trial. In the ungraded group (n = 18), both inferior oblique muscles were sutured at the inferior rectus level; in the graded group (n = 19), the inferior oblique muscles of eyes with more DVD were sutured at the level of the inferior rectus and inferior oblique muscles of eyes with less DVD were sutured 2 mm posterior to the level of the inferior rectus muscle. DVD was significantly reduced in each group (P < 0.001 for both). Although the postoperative mean difference of asymmetry of DVD was less in the ungraded group compared to the graded group (1.2 ±1.9 vs 3.2 ±1.2 [P = 0.001]), the absolute amounts of reduction of DVD asymmetry were similar (4.3 ±2.3 vs 4.4 ±3.1 [P = 0.78]). IOOA and V patterns were also reduced postoperatively. The authors conclude that both methods of IOAT were effective in reducing DVD, DVD asymmetry, IOOA, and V patterns. Although there are some limitations attributable to a difference in the groups’ baseline characteristics, with less preoperative DVD asymmetry in the ungraded group compared to the graded IOAT, this randomized study clarified this debatable subject to some extent. The report includes a detailed review on what has been published on the subject that is worth reading.

One- Versus Two-Muscle Surgery for Presumed Unilateral Fourth Nerve Palsy Associated With Moderate Angle Hyperdeviations

The purpose of this retrospective study was to compare diplopia and motor outcomes in patients with 1 or 2-muscle surgery for moderate angle (14-25 PD) hyperdeviation due to unilateral cranial nerve IV palsy. The authors reviewed the medical record of 73 patients aged 5-86 (28 patients with one muscle surgery) and defined motor success as orthotropia or 1-4 prism diopters of undercorrection at distance by prism alternate cover testing (PACT). Diplopia success was defined as no double or “rare” double vision without prism correction. The authors included both congenital and acquired causes of fourth nerve palsy, and excluded patients with more than 15 degrees of exocyclotorsion. The measurements to determine success were those taken at or around the 6 weeks post op examination and a secondary outcome was success at 1 year follow up. The authors found that the motor success rates were similar in the 1 muscle and 2 muscle groups but the 1 muscle group had more undercorrections and the 2 muscle group had more (symptomatic) overcorrections. The authors concluded that there was no clear advantage of 2-muscle surgery over 1-muscle surgery for either motor or diplopia outcomes in presumed unilateral fourth nerve palsy. The authors point out weaknesses of the paper including a somewhat arbitrary motor success goal and the lack of randomization. Additionally the lack of thorough
understanding of the surgeon’s decision making is a big weakness of this paper (i.e., did the superior oblique tendon demonstrate laxity, forced ductions, measurements in all fields of gaze).

**Inferior oblique Overaction: Anterior Transposition Versus Myectomy.**


The purpose of this study is to compare the efficacy of inferior oblique myectomy and anterior transposition for correcting inferior oblique overaction (IOOA). This study was conducted on 56 patients with IOOA who had either myectomy or anterior transposition of the inferior oblique muscle. The authors compared preoperative and postoperative inferior oblique grading (−4 to +4) as the main outcome measure and vertical and horizontal deviation, dissociated vertical deviation (DVD), and A- and V-pattern between the two surgical groups as secondary outcomes. A total of 99 eyes of 56 patients with a mean age of 5.9 ± 6.5 years were included (47 eyes in the myectomy group and 52 eyes in the anterior transposition group). There were no differences in preoperative best-corrected visual acuity, amblyopia, spherical equivalent, and primary versus secondary IOOA between the two groups. Both surgical procedures were effective in reducing IOOA and satisfactory results were similar between the two groups: 61.7% and 67.3% in the myectomy and anterior transposition groups, respectively (P = .56). After adjustment for the preoperative DVD, there was no statistically significant difference between the two groups postoperatively. The preoperative hypertropia was 6 to 14 and 6 to 18 prism diopters (PD) in the myectomy and anterior transposition groups, respectively. After surgery, no patient had a vertical deviation greater than 5 PD. The authors conclude that both surgical procedures can produce satisfactory and similar results regarding IOOA correction. Also, both surgical procedures can similarly correct accompanying hypertropia and DVD in primary position. The study is limited by its retrospective design and and dissimilar age distribution.

**Adjustable Bilateral Superior Oblique Tendon Advancement for Bilateral Fourth Nerve Palsy.**


Bilateral fourth nerve palsy can present with or without a vertical deviation, depending on the symmetry of the palsy. A torsional deviation can also exist. There are multiple surgical options for symmetric cases that present with purely torsional components and there are also multiple techniques for asymmetric cases to adjust both the torsion and the vertical deviation. In this study the authors report 15 cases with bilateral superior oblique palsies who had bilateral superior oblique tendon advancement on adjustable sutures to evaluate the utility of this
surgical technique. This was a retrospective interventional case series of 15 patients with either symmetric or asymmetric bilateral fourth nerve palsies aged 17-73. Eleven patients had symmetric palsy with less than 2 prism diopeters of vertical deviation in primary gaze and 4 patients had asymmetric palsies. Patients were evaluated preoperatively, pre- and post- adjustment, and also 6 weeks post operatively. The patients were marked at the 12 and 6 o’clock positions and then adjusted with a goal of 10 degrees of incyclotropia. Surgical procedure is described in detail in this paper and the adjustment was done 2-8 hours after surgery. 80% of patients needed adjustment in order to achieve the target alignment. At 6 weeks post operatively there was a mean excyclotorsion of 4 degrees with 13 patients having 5 degrees or less of torsion. Fourteen of the 15 patients had 2 prism diopeters or less of hypertropia. The authors concluded that adjustable bilateral superior oblique tendon advancement allows for independent control of adjusting the torsional and vertical components of the deviation in bilateral fourth nerve palsies. This paper is limited by the small number of patients and limited follow up time.

Inferior Rectus Transposition: A Novel Procedure for Abducens Palsy.

Loss of abduction due to abducens nerve palsy causes esotropia for which multiple different surgical procedures are advocated. Recently treatment with full tendon transposition of just the superior rectus muscle to the lateral rectus muscle has been advocated. However some authors have described intorsion or hypertropia in certain patients with this procedure. The authors of this study transposed only the inferior rectus in 5 patients with abducens palsy to determine if this procedure could be as beneficial as the superior rectus transposition but with less post operative vertical deviation or incyclotropia. This was a prospective interventional case series of five patients with complete sixth nerve palsy and resulting esotropia. The authors evaluated the changes in head position, eye movement, alignment and torsion pre and post operatively. The authors found a significant improvement in post operative eye alignment (average prep op alignment of 39 PD and average post op alignment of 12 PD) as well as head position. The limitations of this study include the very small sample size and short follow up period of 8 weeks. The authors suggest that this procedure may be best in patients who also have partial third nerve palsies or inferior oblique palsies who are at risk of post operative incyclotropia, and also perhaps in patients with a pre operative hypertropia. Of note there is a letter to the editor on this paper noting that this is perhaps not a novel technique and was previously described.
Outcomes After Superior Rectus Transposition and Medial Rectus Recession Versus Vertical Recti Transposition for Sixth Nerve Palsy.

Traditionally full tendon transposition of the superior and inferior rectus to the lateral rectus with or without medial rectus recession has been used for the treatment of esotropia and diplopia due to sixth nerve palsies without significant lateral rectus function. Recently, transposition of only the superior rectus has been advocated with the goal of reducing the number of muscles operated on and thus lower the risk of anterior segment ischemia. The purpose of this study is to compare outcomes in patients who had superior rectus transposition with medial rectus recession (SRT/MRc) with patients who had the more traditional superior and inferior rectus transposition (VRT). This was a consecutive retrospective interventional case series of 16 patients, 8 in each group (8 VRT and 8 SRT/MRc). The authors found that residual esotropia was similar in both groups, but more patients in the VRT group needed additional procedures than those in the SRT/MRc group (medial rectus recession of either or both eyes, botulinum toxin injections, lateral fixation of the lateral rectus). Of note, none of the patients in the SRT/MRc group had additional procedures but the mean follow up in this group was significantly shorter (6.2 months) than in the VRT group (17.3 months). There was no new persistent vertical deviation or torsional diplopia in either group. The authors concluded that final outcomes in the groups were similar and that the SRT/MRc group was less likely to need more surgery. The acknowledged the small sample size and some baseline differences between the two groups, most notably the follow up time.

Transposition surgeries

Double Augmented Vertical Rectus Transposition for Large-angle Esotropia Due to Sixth Nerve Palsy.

In this prospective interventional study, fifteen patients with non-resolving sixth nerve palsy underwent surgical correction with double augmented Hummelsheim procedure. Fourteen of the fifteen patients also received a bilateral medial rectus recession. Two patients with an associated vertical deviation had also an augmentation of one of the vertical muscles with a complete resolution of the vertical deviation. Only three of the fifteen patients had a postoperative deviation greater than 10 pd of which only one was fitted with prism for residual diplopia. Induced vertical deviation was observed in two of the patients. The authors recommend
this procedure in patients with a positive forced duction test in longstanding sixth nerve palsy. They also recommend a selective augmentation of one of the vertical muscles in cases with an associated vertical strabismus.

**Sutures / Adjustables**

**Adjustable Strabismus Surgery under Topical Anesthesia: Alignment in Supine vs Seated Position.**


Topical anesthesia allows adjustment in the operating room while the patient is still conscious. No prior studies have compared strabismus alignment before adjustment in the seated and decubitus positions while under topical anesthesia. The authors sought to compare the ocular deviations between the seated and decubitus positions as well as the post-operative alignment outcomes at 1 day, 1 month and 3 months. The authors performed a prospective observational study of 30 adult patients undergoing adjustable suture strabismus surgery comparing the alignment outcomes in a supine or decubitus position. Defined parameters for viewing target type and distance and for proceeding with adjustment were standardized. The diagnoses were diverse and consistent of sixth nerve palsy, esotropia in high myopes, and age-related strabismus among others. The most frequent procedure was a unilateral recession and resection. Intraoperative adjustment was performed in 12 (40%) cases. No statistically significant differences were found between ocular deviations in the seated or supine position in the operating room. No statistically significant differences were detected in the final deviation between patients who were adjusted and those who were not. None of the factors evaluated (age, gender, diplopia, number of muscles operated on, surgical adjustment, preoperative deviation, and intraoperative deviation in the seated and decubitus position) influenced surgical outcome. The intraoperative deviation was not a predictor of success and most patients had a favorable outcome at all of the post-operative visits.

**Sedated suture adjustment in children undergoing adjustable suture strabismus surgery.**

The purpose of this retrospective study was to evaluate anesthesia/procedure related adverse events, surgical outcomes, and safety of postoperative sedated suture adjustment after strabismus surgery in the post-anesthesia care unit (PACU). The authors reviewed the postoperative experience of all children ≤18 years of age undergoing adjustable suture strabismus surgery at Boston Children's Hospital over a 3-year period. Of 356 patients, 113 required suture ad-
justment in the PACU, including 24 adjusted, while awake (age 12-18 years) and 89 adjusted under sedation (age 1-18 years). For sedation, sequential boluses of propofol were administered until adjustment was complete. Complete data from the sedated adjustment was only available in 76 patients. The median initial bolus was 30 mg; the median total propofol rate was 273 mcg/kg/min. Only a single bolus of propofol was required by twelve patients (16%). Of remaining 64 patients, median time from initial to final propofol dose was 7 minutes. Median anesthesiologist time in the PACU was 13 minutes. In the sedated adjustment group, there were no clinically significant adverse events; no incidents of oculocardiac reflex occurred and no airway/ventilation issues were experienced. The pain score never exceeded 6 (of a possible 10). Median duration of PACU stay was shortest in the group not requiring adjustment. The overall surgical success rate was 72.6% for horizontal strabismus and 82.3% for vertical strabismus at the 2-month postoperative follow-up visit. The authors conclude that sedated suture adjustment allows for fine-tuning of postoperative binocular alignment in children and uncooperative adults. No adverse events were observed in this study group, but the procedure does increase the time patients spend in the hospital. They advocate using adjustable sutures in strabismus surgery in children with complex strabismus, reoperations, and other factors, where standard surgical tables do not apply. The authors share their experience with this well-established protocol for performing sedated sutures in children. However, the implementation of it necessitates full collaboration with nursing and anesthesia. It also requires the extra cost of the additional time in the PACU, anesthesiologist time, and surgeon time. It is pointed out that the lack of a control group in this retrospective study makes it difficult to determine how effective this technique is compared to non-adjusted surgery and whether it is cost-effective.

**Strabismus surgery - Misc**

**The efficacy of Bilateral lateral Rectus Recession According to Secondary Deviation Measurements in Unilateral Exotropic Duane Retraction Syndrome.**
Daphna Mexad-Koursh, Ari Leshno, Ainat Klein, Chaim Stolovich

The purpose of this retrospective chart review study is to evaluate the surgical results of asymmetric bilateral lateral rectus recession in exotropic Duane retraction syndrome with abnormal face turn toward the opposite side according to secondary deviation measurements. Seven cases of unilateral exotropic Duane retraction syndrome were reviewed. All cases had globe retraction on adduction and exotropia with limited adduction, five of which also had mild limitation of abduction. Four cases had upshoot/downshoot on adduction and all patients had face turn. The exotropia was always measured at the primary position using the alternate cover test while the prism bar was held in front of the healthy eye to detect the maximal secondary deviation. In all patients, an asymmetric bilateral lat-
eral rectus recession was performed using the fixed recession technique. The amount of recession of the lateral rectus muscle of the affected eye was determined according to the maximal deviation measured at distance fixation in the forced primary position. The lateral rectus muscle of the unaffected eye was recessed by 1 mm more than that of the affected eye. Y-splitting of the lateral rectus muscle was performed in all cases with upshoot or down-shoot. The average lateral rectus recession was 6.36 mm (range: 5.5 to 7.5 mm) in the affected eye and 7.36 mm (range: 6.5 to 8.5 mm) in the healthy eye. The mean follow-up period was 282 days. Mean exotropia in the forced primary position improved from 27.9 ± 5.7 prism diopters (PD) preoperatively to 7.9 ± 16.8 PD postoperatively (P = .025). Head position resolved completely in all but one case (P = .031). There were no significant changes in ductions. The authors conclude that asymmetric bilateral lateral rectus recession in exotropic Duane retraction syndrome with abnormal head turn posture successfully eliminates abnormal head turn posture and exotropia in most cases. The study is limited by its retrospective nature as well as the fact that there was no control group (symmetric surgical approach), and therefore it is unknown whether a symmetric approach would have given the same results.

Combined Surgery for Simultaneous Treatment of Congenital Ptosis and Coexisting Strabismus

The purpose of this retrospective analysis is to evaluate the clinical outcomes of single-stage surgery for treatment of patients with congenital ptosis and coexisting strabismus. Patients were treated with levator resection or frontalis suspension for ptosis based on their levator’s function and ocular muscle surgery for strabismus, performed as a single-stage procedure. Levator resection was performed in 9 patients (15 eyes) and frontalis muscle flap suspension was performed in 1 patient (2 eyes) with blepharophimosis. Seven patients (11 eyes) simultaneously underwent exotropia correction, and inferior oblique myectomy was performed in 3 patients (3 eyes) with congenital superior oblique palsy. Motility was evaluated 2 weeks postoperatively and an excellent outcome was defined as hypertropia of less than 5 PD, or exotropia of less than 8 PD. Optimal outcomes often classified as "good" or "successful" were defined by less than 1 mm of postoperative ptosis. All patients showed good results with respect to ptosis and all patients but one achieved excellent alignment. This study has several limitations: the sensory status of patients was not evaluated after surgery, the number of patients participating in the study was small and other types of complex strabismus, large deviation strabismus, and ptosis were not included in the study. The authors conclude that single-stage surgical correction for congenital ptosis and coexisting strabismus is a viable option for surgical managements of such patients as long as these patients have detailed preoperative ophthalmic examination coupled with appropriate surgical design.

The purpose of this cross-sectional study was to quantify the retinal vascular diameter changes before and after strabismus surgery, analyzing the potential hemodynamic changes that may occur in the retinal circulation. Consecutive patients who underwent strabismus surgery for horizontal strabismus were prospectively enrolled. Color fundus photographs were taken of each eye before and 1 day after surgery. The retinal vessel diameters were measured using computer-assisted quantitative assessment software. Several parameters were evaluated: the central retinal arteriolar equivalent (CRAE), central retinal venular equivalent (CRVE), and arteriovenous ratio (AVR) before and 1 day after surgery. We also analyzed those changes in different subgroups according to surgical protocols. A total of 217 eyes of 148 patients were included. Compared with the pre-op data, the mean CRAE significantly increased 1 day after surgery (P = 0.01), so did the AVR (P = 0.003). There was no significant difference with respect to CRVE (P = 0.43). Further subgroup analysis for one rectus surgery group showed significant increase of CRAE and AVR only in the medial rectus recession but not in the lateral rectus recession group. The authors concluded that strabismus surgery on horizontal rectus muscles may change retinal hemodynamics by increasing the arteriolar blood flow during the early postoperative period. This may occur due to increased blood flow demands of the anterior segment postoperatively. The authors suggest in their discussion that strabismus surgeons should consider retinal circulation status when planning strabismus surgeries, particularly for patients at risk of retinal vascular diseases, such as diabetic patients. We were not sure that this can be directly inferred from their results.


The aim of this prospective, randomized, paired-eye controlled study was to determine the efficacy of a biodegradable Ologen (Aeon Astron Europe BV, Leiden, The Netherlands) collagen matrix in reducing the blue color change due to exposed thinned sclera after strabismus surgery. Fourteen patients with intermittent exotropia undergoing symmetric bilateral lateral rectus recession surgery were included. In each patient, Ologen was implanted at the original rectus insertion site in one randomly selected eye; the other eye underwent conventional surgery. Ologen was inserted under the conjunctiva without suturing, covering the muscle insertion site. Conjunctival color change was analyzed using computer-based image analysis immediately and 1 week, 1 month, and 3 months postoperatively. Slit-lamp
photographs of each eye were evaluated using contrast limited adaptive histogram equalization (CLAHE), Canny edge, and the RGB (red-green-blue) model. Secondary outcomes were conjunctival and sclera thickness 3 months postoperatively determined by anterior segment optical coherence tomography. Immediately and 1 week postoperatively all color models showed no significant differences between Ologen-implanted and control eyes. Three months postoperatively, Ologen-implanted eyes exhibited significantly lower CLAHE ($P = 0.041$) and RGB model blue color ($P = 0.008$) values than control eyes. Canny edge ($P = 0.061$) and RGB model red color ($P = 0.152$) values did not differ between eyes. Conjunctival stroma and episcleral complex thickness was greater in Ologen-implanted eyes than in controls ($P = 0.001$). The authors conclude that the blue color change was significantly less noticeable in Ologen-implanted eyes than in controls 3 months post-operatively. Thus, Ologen implantation helps prevent visible blue sclera at the original rectus insertion site after lateral rectus recession. Safety issues were not examined despite previous reports of implant exposure and necrotizing scleritis.

A paired comparison study on refractive changes after strabismus surgery.
Leshno, A., Mezad-Koursh, D., Ziv-Baran, T. and Stolovitch, C. J AAPOS. 2017 Dec; 21(6):460-462.e1

The goal of this retrospective study was to quantify the refractive changes following horizontal lateral rectus recession and medial rectus resection surgery and to investigate the causes of these changes. The medical records of patients who underwent unilateral horizontal lateral rectus recession and medial rectus resection for exotropia by a single surgeon were reviewed retrospectively. Using vector analysis, refractive changes in operated eyes (cases) were compared to changes in the sound eyes (controls). The main outcome measures were differences in mean change of refractive parameters and the proportion of clinically significant changes. A total of 31 subjects (median age, 13.6 years; interquartile range, 8.8-19.8 years) were included. A significantly higher magnitude of refractive changes was observed in the operated eyes ($P = 0.001$). In addition, the proportion of cases with clinically significant change in sphere or cylinder was significantly higher in the operated eyes compared to the sound eyes (48% vs 10% [OR = 2.31, $P = 0.002$] and 32% vs 10% [OR = 5.0, $P = 0.039$], resp.). The authors conclude that horizontal strabismus surgery is associated with refractive changes that might be of clinical significance. They also recommend that pediatric ophthalmologists consider repeated refraction 1 month postoperatively. The result of this study strengthen the argument that significant changes in refraction after strabismus surgery should be anticipated, and that these changes are not merely physiological or time related. However, longer refractive follow-up was not available for this cohort of pa-
Surgical management of strabismus following choroidal melanoma plaque brachytherapy.
Alfreih, S. H., Pineles, S. L., McCannel, T. A., Prada, A. M. and Velez, F. G.

Intraoperative findings and surgical management of strabismus following plaque brachytherapy for ocular melanoma have not been well characterized in the literature. Therefore, the authors conducted this retrospective study to further characterize the intraoperative findings, surgical approach, and postoperative outcomes in these patients. Of the 461 patients who underwent plaque brachytherapy during the study period, 13 (2.8%) met inclusion criteria. In this patient cohort the majority of the patients 9/13 had relatively good vision in the affected eye (20/40 or better). Most patients (85%) presented with combined vertical and horizontal deviation. Four patients (30%) required muscle disinsertion at the time of plaque placement and presented with underaction of the disinserted muscle. Intraoperatively, all muscles directly adjacent to the treated area appeared macroscopically thicker than normal despite being functionally underacting. This was also confirmed by magnetic resonance imaging in one of the patients. Microscopic examination of muscles in 2 patients showed reactive enlargement of the muscle fibers, granulation tissue, and inflammation. The results in this patient cohort suggest that good anatomical outcome can be achieved in these patients. The authors conclude that the typical findings of persistent strabismus post brachytherapy include enlarged, underacting rectus muscles adjacent to the area of the plaque, restrictive connective tissue, and incomitant strabismus. Previously disinserted muscles may be found in abnormal locations. The authors emphasize that in their experience surgery requires exploration of the area adjacent to the plaque with release of scar tissue prior to strengthening the weak muscle on the area of the plaque combined with recession of the antagonist muscle. Some patients require surgery on the contralateral eye due to primary position orthophoria and lateral incomitance.

This interesting report sheds some understanding of the complexity of this rare type of strabismus from experienced surgeons.

Pharmacological management of a patient following strabismus surgery
Geraldine McBride Br Ir Orthopt J 2016; 13: 45-47

There are no formal guidelines for post-operative pharmacologic care of patients following strabismus surgery. Management can include antibiotic drops, steroid eye drops, or no pharmaceuticals. The author presents a case report of a single patient whom underwent bilateral medial rectus recessions and was treated with
The resurgence of botulinum toxin injection for strabismus in children

The authors present a review of the use of botulinum toxin (BT) in strabismus. Advantages to the use of BT include decreased anesthesia time and postoperative care unit time, decreased risk of overcorrection once it has worn off (within 3-6 months of injection), and preservation of muscle tissue for possible further surgery in the future, although repeated injections may cause atrophy of the muscle over time. Additionally, treatment may be undertaken sooner at about 3 months after onset with the possibility of earlier re-establishment of binocularity and decreased amblyopia risk. It has a relatively painless post-operative period and it is a less invasive procedure with a theoretical reduction in risk of endophthalmitis due to the lack of scleral passes. The disadvantages include an overall lower success rate, thus necessitating the identification of strabismus subtypes that have the highest potential for success. There is a lower rate of success in those patients that lack binocular potential and that have large angle infantile esotropia. Patient’s may also have a longer duration of post-operative overcorrection and higher incidence of transient ptosis and vertical deviations. The authors identify subsets of patients that they feel would have the most likely benefit from the use of BT. Acute onset comitant esotropia was studied and found that 81% of patients who received BT achieved alignment of 10 PD or less with no statistical significance in the success rate compared to surgery, and those patients were treated 3 months earlier. Patients with esotropia and greater risk of overcorrection such as partially accommodative esotropia and children with CP may also be considered as an alternative to surgery.

Autogenous Fascia Lata Graft Fixation to Treat Exotropia Resulting From Iatrogenic Medial Rectus Transection

This paper aimed to describe autogenous fascia lata graft fixation as a novel method to treat exotropia related to medial rectus (MR) muscle injury following functional endoscopic sinus surgery. Three consecutive patients with MR transection and exotropia after functional endoscopic sinus surgery were selected. Preoperative examination was performed; no MR function was noted for over 3 months after injury. CT and dynamic functional MRI were performed, where MR
transection and medial wall breach were noted. An autogenous fascia lata graft was harvested and fixated from the remaining periosteum of the posterior-most extent of the medial orbital wall and attached to the globe at the MR insertion. In addition, an ipsilateral lateral rectus muscle recession was performed. Results showed good alignment of the eyes in primary gaze and downgaze was achieved and remained so at the 3-month postoperative examinations, requiring minimal head turn or prism correction (<5 prism diopters) to control diplopia. Two patients required recession of the fascial graft for a minor overcorrection and have remained stable for over 6 months. In conclusion, severe exotropia secondary to MR damage following functional endoscopic sinus surgery is a known complication historically difficult to treat. Traditional surgical methods, including vertical muscle transposition, commonly result in complete recurrence of exotropia and increase risk of anterior ocular ischemia. Unlike simple nonabsorbable suture fixation, fascial grafts are completely biointegratable, do not result in significant inflammation, and are unlikely to rupture. Fascia lata graft fixation of the MR to the posterior orbital medial wall is a new and successful method to eliminate exotropia after MR injury.

Comparison of Minimally Invasive Strabismus Surgery (MISS) and Conventional Strabismus Surgery Using the Limbal Approach.

Poonam Gupta, Subhash Dadey, Kamlesh, Vishaal Bmbhawani

The purpose of this study is to compare minimally invasive strabismus surgery (miss) with conventional strabismus surgery for horizontal recti muscles in terms of functional outcome and complications. In this prospective study a total of 40 patients requiring surgery for horizontal muscles were divided into two groups: those undergoing MISS and those operated on using the conventional limbal technique. In MISS group, two small keyhole radial cuts were made superior and inferior to the insertion of the muscle margin. Keyhole cut size was almost 1 mm less than the amount of the muscle recessed or resected. The study showed that there was a significant difference in conjunctival swelling and redness in both groups on postoperative days 1 and 7 and week 3. However, by week 3 both groups had similar appearance. There were no statistically significant changes found for final alignment, or binocular single vision. The authors conclude that the small incision, minimal dissection technique is feasible. Although more technically challenging the MISS technique seems to be superior in the immediate postoperative period because there were fewer conjunctival and eyelid swelling complications. Nevertheless, there was an increase in the incidence of tears and extensions of incisions. Overall, long-term results didn’t differ between the two groups. The study is limited by the small number of subjects participating and by the fact that the scoring system used for conjunctival chemosis and redness is subjective.
Results of combined resection-recession on a single rectus muscle for incomitant deviations-an alternative to the posterior fixation suture.

In this retrospective case series the outcomes of combined resection and recession on previously unoperated single horizontal or vertical rectus muscles were analyzed. The patients included were consecutive adult patients with acquired incomitant deviations, minimal in primary gaze and maximal in an eccentric gaze position. The surgical technique used included recessions for the maximal deviations combined with smaller resections using hang-back, nonadjustable sutures. The primary outcome of the study was a decrease the incomitance by 50%. Other outcomes were expansion of the field of binocular single vision, and relieve diplopia. Pre- and postoperative incomitance was compared using the paired t test. A total of 16 adults were studied (mean age at surgery, 49.3 +/- 17.5 years), 12 with incomitant vertical deviations and 4 with incomitant horizontal deviations. Eight patients had preoperative deviations of <2Delta in primary gaze (mean, 9.2Delta +/- 10.5Delta; range, 1Delta-35Delta). The mean maximum eccentric gaze deviation was 21.4Delta +/- 9.9Delta (range, 10Delta-48Delta). Postoperatively, 12 patients (75%) had a decrease in incomitance of >50%, and all had expansion of the field of binocular single vision. Improvement in postoperative incomitance was highly statistically significant in the vertical incomitant group (P < 0.0001) but not statistically significant in the horizontal group (P = 0.39). The technique corrected downgaze deviations in 4 patients with canine tooth syndrome (93% +/- 3.3, P < 0.0001) without worsening the hypotropia in upgaze. The authors conclude that combined resection-recession single muscle surgery significantly reduces incomitance with minimal effect on primary gaze. It is most effective for treating vertical deviations worse on downgaze with primary gaze deviations of <2Delta and for canine tooth syndrome; the technique was less successful in reducing horizontal incomitance and in cases involving gaze palsies and nystagmus.

Despite the limitations of a retrospective study, this important work demonstrates the advantages of using combined resection-recession single muscle surgery in difficult incomitant cases mainly in vertical cases. It is possible that the results were not as impressive in horizontal cases because only four cases were included. The paper discusses different aspects of surgical planning and reviews previous publications on this technique, which the reader may find very useful.

Evaluating the impact of strabismus surgery on the association of musculoskeletal injuries, fractures, and falls with disorders of binocular vision in Medicare beneficiaries.
Disorders of binocular vision that are increasingly prevalent among aged, fee-for-service Medicare beneficiaries are associated with fractures, falls, and musculoskeletal injuries. The purpose of this retrospective study was to evaluate whether strabismus surgery influences the association of injuries in elderly patients (≤ 65 years) with disorders of binocular vision in a 5% random sample of Medicare fee-for-service claims data from 2010 to 2013. There were 22,237 Medicare beneficiaries with a claim that included a diagnosis of a disorder of binocular vision. Of these, the majority had strabismus (49.5%); amblyopia (9.14%), diplopia (53.5%), and nystagmus (2.72%) were also represented. There were 530 patients who underwent strabismus surgery. The unadjusted odds ratio for the association between undergoing strabismus surgery and any of the three musculoskeletal injuries defined above was 0.868 (95% CI, 0.725-1.040; P = 0.13), and the adjusted odds ratio was 1.004 (95% CI, 0.833-1.210; P = 0.97). This study did not reveal a difference in the subsequent risk of musculoskeletal injuries, fractures, or falls in Medicare beneficiaries who underwent strabismus surgery. The authors conclude that the failure to find an association could represent a true lack of correlation, selection bias, study design using administrative claims data, or a very small effect.

Strabismus surgery outcomes in eyes with glaucoma drainage devices.

The purpose of this retrospective case series was to evaluate the strabismus surgery outcomes in eyes with prior implantation of glaucoma drainage devices (GDD). The medical records of 16 patients (mean age at surgery was 58 years; range, 16-83 years), who underwent strabismus surgery for ocular misalignment that developed after implantation of a GDD over a 13-year period at a single institution were examined retrospectively. Patient characteristics, deviation types, preoperative measurements, surgical procedures, and postoperative measurements were analyzed. Of the 16 patients that were included, 14 had exotropia (34±16 PD) and 11 had vertical deviations (15±7 PD), of which 9 had concurrent exotropia and vertical deviations. Preoperatively, 9 patients had diplopia. Strabismus surgery was performed between 8 months and 4 years after GDD implantation. Twelve patients had a single unilateral GDD, two had 2 GDDs in the same eye, one had bilateral single GDDs, and one had 2 GDDs in one eye and 1 GDD in the other. Thirteen implants were superotemporal (ST), and 8 were inferonasal (IN). The surgical approach was tailored to address the deviation most noticeable to the patient: horizontal, vertical, or both if the vertical component could be addressed by horizontal muscle supra- or infra-placement. Three patients underwent simultaneous horizontal and vertical surgery. All patients underwent strabismus surgery on an eye with a GDD. Postoperative follow-up ranged from 2 days to 11 months. Surgical motor success (defined as horizontal deviation ≤10 PD, vertical ≤4 PD) was achieved in 42% of horizontal and 57% of vertical deviations. Postoperatively 74% of deviations decreased by ≥50% in magnitude. Di-
plopia resolved in 50% of patients who presented with preoperative diplopia. One patient had intraoperative bleb perforation, but none had postoperative hypotony at any follow-up visit. Only 2 (12.5%) required a second strabismus surgery. The authors conclude that strabismus surgery with preservation of the filtering bleb following implantation of a glaucoma drainage device is a low risk procedure that can improve ocular alignment and related symptoms, despite a low motor success rate by standard criteria. Despite the obvious limitations of this study due to its retrospective nature and limited follow-up, it highlights the feasibility of strabismus surgery in GDD patients and the acceptable improvement of ocular alignment in these patients.

**Pericardial patch graft repair of severe localized scleral thinning encountered during strabismus surgery**

This article presents a surgical technique using a pericardial patch for the permanent repair of severe scleral thinning encountered during strabismus surgery. In the present case scleral thinning resulted from buckle removal. Familiarity with this technique may prove important for the strabismus surgeon treating patients with scleral thinning. The pericardial graft was chosen over a scleral allograft as it has a thinner profile (400 mm vs 1 mm). The authors state that its multidirectional matrix lends stability and ease of suturing without notable risk of cheese-wiring. A demonstrative video is included.

**Autogenous Fascia Lata Graft Fixation to Treat Exotropia Resulting From Iatrogenic Medial Rectus Transection**

This paper described the use of autogenous fascia lata graft fixation as a novel method to treat exotropia related to medial rectus (MR) muscle injury following functional endoscopic sinus surgery. Three consecutive patients with MR transection and exotropia after functional endoscopic sinus surgery were selected. Preoperatively, no MR function was noted for over 3 months after injury. CT and dynamic functional MRI were performed, where MR transection and medial wall breach were noted. An autogenous fascia lata graft was harvested and fixated from the remaining periosteum of the posterior-most extent of the medial orbital wall and attached to the globe at the MR insertion. In addition, an ipsilateral lateral rectus muscle recession was performed. The authors noted that alignment of the eyes in primary gaze and downgaze was achieved and remained so at the 3-month postoperative examinations, with minimal head turn or prism correction (<5 prism diopters) necessary to control di-
plopia. Two patients required recession of the fascial graft for a minor overcorrection and have remained stable for over 6 months.

The authors suggested that the natural material doesn’t induce as much inflammation and is unlikely to rupture, rendering it superior to other materials previously used. They describe fascia lata graft fixation of the MR to the posterior orbital medial wall as a new and successful method to eliminate exotropia after MR injury and suggest the possibility of using this method to correct other forms of paralytic strabismus.

**Trends in pediatric strabismus surgery in the new millennium: influence of funding and perceived benefits of surgery**

Andrei-Alexandru Szigiato, Meggie Caldwell, Yvonne Buys, Kamiar Mireskandari


Studies have showed decreasing rates of strabismus surgery perhaps explained by improved surgical outcomes, treatment of refractive errors, and other reasons. It is not known how much funding has influenced strabismus surgery rates in a single-payer system such as in Ontario. Therefore, the authors intended to study the trends in pediatric strabismus surgery while considering changes in health care funding, physician payment, and the psychosocial benefits of strabismus surgery. They performed a retrospective review of strabismus surgeries done in Ontario from 2000 to 2013 as recorded in the database maintained by the Ontario Ministry of Health and Long Term Care. There is a single payer for all insured services in this region. Over this time, the number of high-volume pediatric strabismus surgeons (>=50 surgeries per year) increased 37.5% (from 8 to 11), and the number of low-volume surgeons decreased 61.8% (58 to 23). The proportion of strabismus surgeries performed by high-volume surgeons increased from 75.4% to 87.9%. 60.9% of surgeries were 2 muscle, 24.5% 3 muscle or more, and 14.6% single muscle. The number of all procedure increased from 46.9 per 100,000 to 62.93 per 100,000 (38.1% increase). Repeat surgeries increased from 10.9% of procedures to 28.5%, with the number of surgeons performing these increasing 76.9%. From 2000 to 2013, physician payment surpassed inflation for single muscle and repeat surgery only; however there has been no change in any procedure remuneration since 2008. In summary, there was an increase in the number of strabismus surgeries performed from 2000 to 2013. This followed a decline in the 1990’s, and health care reforms in Ontario with increased funding may be partly responsible for the increase in surgery. The results also suggest there may be increased referral patterns to subspecialists, as high-volume surgeons performed the majority of 3 muscle and repeat surgeries. Fewer surgeons may be performing just occasional strabismus surgery, and no early career surgeons were noted to be high-volume, suggesting a potential lack of new trainees pursuing the field. Finally, literature describing positive functional outcomes and quality of life improvement after strabismus surgery may also have contributed to increased rates of strabismus surgery.
11. **ANTERIOR SEGMENT**

**Visual Outcomes and Complications of Type I Boston Keratoprosthesis in Children: A Retrospective Multicenter Study and Literature Review**


Use of Boston type 1 keratoprosthesis (KPro) implantation in children is not well studied. In this retrospective case series, the authors examined the visual outcome, device retention and complications after using KPro in children 16 years or younger. Kpro surgeries were done by 3 surgeons at 3 ophthalmology centers in Canada between January 2010 and November 2014. The KPro was implanted in 11 eyes of 11 patients 0.9 to 15.5 years of age, with 6 being primary corneal procedures. Lensectomy and anterior vitrectomy were performed concurrently in phakic patients. In aphakic patients, anterior vitrectomy was performed as part of the procedure. Best-corrected visual acuity recorded before surgery ranged from 20/600 to light perception (LP), and vision in 2 eyes was fix and follow. All patients had been diagnosed with glaucoma and 6 eyes had glaucoma drainage devices (GDDs) inserted before KPro implantation. At last follow-up (mean, 41.8 months; range, 6.5-85.0 months), 2 eyes retained BCVA of 20/400 or better, whereas 5 eyes lost LP. The majority of patients did not improve and 55% did worse than at pre-op. Postoperative complications included retroprosthetic membrane (9 eyes), corneal melt (5 eyes), infectious keratitis (3 eyes), endophthalmitis (3 eyes), GDD erosion (2 eyes), and retinal detachment (5 eyes). The initial KPro was retained in 4 eyes (36.4%). Boston type 1 keratoprosthesis implantation in children is associated with a substantially higher rate of complications, higher chance of device failure, and worse visual outcomes than observed in adults. This is also true in comparison to the published pediatric PKP outcomes. The authors also describe their experience that PKP following K pro does not prevent vision loss. In view of these results, the authors do not recommend the use of the KPro in the pediatric population.

**Long-term outcomes of corneal cross-linking for keratoconus in pediatric patients.**


The aim of this retrospective study was to report the long-term outcomes of corneal cross-linking (CXL) in pediatric patients with bilateral progressive keratoconus. The medical records of consecutive pediatric patients with bilateral progressive keratoconus who underwent CXL at a single institution were reviewed. All eyes underwent CXL treatment in accordance
with the original Dresden protocol. Pre- and post-operative (at 1 year and >5 years after CXL) examinations included, corneal thickness (CT) at the thinnest point, corneal topographic evaluation (flat, steep meridian keratometry and maximum keratometry), with manifest refraction and corrected distance visual acuity. A total of 20 eyes of 10 patients were included. Mean age at time of CXL was 14.34 ±2.14 years (range, 10.49-17.09 years). Mean follow-up was 7.63 ±1.31 years (range, 5.41-9.34 years). No intra- or postoperative complications were observed. Stabilization of all topographic indices (steep K, flat K, Kmax, and topographic cylinder) was demonstrated throughout the follow-up period (compared to preoperative topographic indices [P < 0.05]). Mean corrected distance visual acuity improved to 0.14 ±0.16 logMAR at final follow-up from the preoperative values 0.28 ±0.17 logMAR (P > 0.05); none of the eyes lost corrected distance visual acuity lines. Manifest refraction and mean corneal pachymetry at the thinnest point remained stable throughout the follow-up (P >0.05). The authors concluded that in their case series CXL (Dresden protocol) for pediatric keratoconus halted disease progression and offered improved visual function up to 7.5 years after treatment. Previous reports had demonstrated satisfactory outcomes in stabilizing the disease and in eliminating the need for further corneal surgical interventions in pediatric keratoconus patients. Despite its small sample size and retrospective nature, this study demonstrates the long-term stability that is achieved with this procedure.

The Associations of Lens Power With Age and Axial Length in Healthy Chinese Children and Adolescents Aged 6 to 18 Years

This study investigated the relationship between lens power and age as well as the relationship between lens power and axial length (AL) in Chinese children and adolescents. The participants underwent a comprehensive ophthalmic examination that included AL, cycloplegic refraction, and Pentacam measurements. The crystalline lens power was calculated using Bennett's formula and then compared among the children of different age groups, refractive statuses, and AL categories. The association of lens power and AL was analyzed using multiple regression. A total of 1992 children and adolescents aged 6- to 18-years old were included. The difference in lens power was greater before 10-years of age, followed by a relatively smaller difference in children aged 10 to 14 years and the difference in lens power came to a near plateau in adolescents after 14-years old. The negative association between lens power and AL was found to be more evident in nonmyopes than in myopes irrespective of age (younger than 10 years: nonmyopes: β = -1.499, myopes: β = -0.872; older than 10 years: nonmyopes: β = -1.288, myopes: β = -0.390, all P < 0.001). The lens power in children and adolescents aged 6 to 18 years exhibited three stages. The association between lens power and AL differed between the nonmyopes and myopes. These findings suggested that less reduction in lens power might be associated with
both growing age and increasing AL in myopes. Since this was a cross-sectional
study, the causal effects of the associations observed (especially regarding the
relationship between lens power and AL) cannot be determined. In addition, this
study depends on the accuracy of the Bennett formula for calculating lens power
across a wide range of refractive errors. While it has been shown to have rea-
sonable agreement with phakometry lens power in emmetropic eyes, individual
differences of up to 3.5 D can occur, so this must be considered when evaluating
the results of this study.

Pediatric Corneal Cross-linking: Comparison of Visual and
Topographic Outcomes Between Conventional and Accelerated
Treatment
2017;183:11–16. November

There are several studies demonstrating that conventional corneal crosslinking
(CXL) in pediatric keratoconus (KC) can stabilize or promote regression of cor-
ea ectasia. However the accelerated crosslinking procedure, which takes less
time but uses a higher intensity (10 minutes, 10mW/cm²) has not been evaluated
in pediatric patients. This is a comparative, retrospective, consecutive case se-
ries of 78 eyes of 58 patients who had corneal crosslinking. The authors’ goals
were to compare visual and topographic outcomes after conventional and accel-
erated corneal crosslinking at 1 year in pediatric patients. Patients all had topo-
graphically proven progressive KC at the time of treatment. Treatment failure
was defined as an increase in the Kmax of more than one diopter during follow
up. Loss of more than 2 Snellen lines of best-corrected vision from baseline was
defied as an adverse event. 39 eyes had conventional CLX (c-CXL) and 39 eyes
had accelerated CXL (a-CXL). The authors found that after 1 year, no significant
differences between uncorrected visual acuity, best corrected visual acuity, to-
pography parameters, failure rates, and adverse events parameters between the
a-CXL and c-CXL groups. The authors concluded that accelerated protocol could
be considered an alternative to the conventional cross linking protocol in pediatric
patients.

Combined interface tattooing and fibrin glue-assisted sutureless
corneal resurfacing with donor lenticule obtained from small-
incision lenticule extraction for limbal dermoid.

This case series of three patients describes a new technique for treating limbal
dermoids. After excision of the dermoid in a plane minimally below surrounding
cornea and sclera (instead of excision to the full depth of the dermoid), 1) tattoo
pigment to match the iris color is applied to the corneal bed and 2) donor cornea
obtained via small-incision lenticule extraction (SMILE) is then glued onto the
corneoscleral defect. Three patients ages 18 months, 13 years and 25 years were treated. All had improvement in astigmatism postoperatively, and the authors report satisfactory cosmetic results. Critiques of this technique are 1) even though the cosmetic outcome appears excellent from a distance, the unusual appearance of pigmented cornea next to clear cornea may be noticeable at near, and 2) this technique requires a donor lenticule obtained from a center performing SMILE, and these lenticules are not yet available from eye banks.

PAX6 aniridia syndrome: clinics, genetics, and therapeutics


The authors discuss a review of aniridia and its ocular and systemic findings as well as treatment approaches. The authors specify that the condition be labeled “PAX6 aniridia syndrome” to encompass those disorders that fall into this category and may be phenotypically confused with other anterior segment dysgenesis syndromes. The syndrome incidence is 1:40000-96000 with no sex or ethnic preponderance. 2/3 of patients have an affected parent with AD expression. The condition may present as isolated ocular abnormalities such as iris anomalies, cataract, glaucoma, foveal hypoplasia and nystagmus. Iris anomalies vary in severity and cataracts occur in 70-85% by adulthood and is most commonly an anterior pyramidal opacity that is nonprogressive. Patient’s may have aniridia associated keratopathy which can present as a ring of avascular pannus and progress to complete opacification with tear film insufficiency, corneal erosion and ulceration typically by the fourth or fifth decade. Glaucoma occurs in 30-67% with some present in infancy due to goniodysgenesis but more often develops later due to tissue strands from the iris to angle wall leading to angle closure. Foveal hypoplasia is the most common retinal finding and patients may have pendular horizontal nystagmus and variable vision impairment. ERG patterns may be abnormal suggesting an associated retinal dystrophy. Patients also have an increased risk of retinal tears or detachments. Systemically, there may CNS abnormalities specifically of midline structures and developmental delay. WAGR syndrome (Wilms tumor, aniridia, GU abnormalities and retardation) is due to large deletions of 11p13 and is a continuous gene deletion. It is diagnosed by 2 or more features, with 50-70% developing a Wilms tumor often between 1-3 years of age. 60% have chronic kidney failure with focal segmental glomerulosclerosis. WAGRO is the above syndrome with early onset obesity. Aniridia is caused by a haploinsufficiency of the PAX6 gene meaning that loss of one copy leads to the condition. There are different possible mutations with intragenic loss-of-function mutations being 65% of mutations due to premature termination codons leading to classic aniridia. Missense mutations make up 20% with wider phenotypic variability. Genetic diagnosis is essential looking for mutations in WT1 which could lead to Wilms tumor. The
risk of Wilms tumor is low in familial cases. Renal ultrasound should be performed. If there is a large deletion in PAX6 and WT1 then patients should undergo systemic evaluation of renal and GU system every 3 months until 8. Management of aniridia may include low vision aids, and surgery to address iris hypoplasia with a current multi-center clinical trial of the custom-Flex iris prosthesis. Cataract surgery can be successful although zonular weakness may be present with respect to IOL placement. Glaucoma needs to be screened for every 6 months and mainstay of treatment is with topical medication except in cases of congenital glaucoma when angle surgery is indicated. Prophylactic goniotomy may be effective in eyes demonstrating progressive TM coverage by iris tissue extension. Early keratopathy is treated with lubricants followed by autologous serum and amniotic membranes in moderate cases and PK may be recommended in severe cases but should be accompanied by limbal stem cell transplant to extend the success rate. Keratoprosthesis may be an alternative. For the retina, Ataluren is now in phase 2 clinical trial aimed at patients with nonsense mutations in PAX6 and may lead to PTC suppression with inhibition of progression and possible reversal of ocular symptoms including retina. In conclusion, this is a comprehensive review of aniridia with discussion of signs, symptoms, genetics and treatment.

Pediatric Corneal Transplants


The authors present a review of the challenges and considerations for corneal transplantation in children. Challenges include ocular comorbidities such as cataract and glaucoma, timing of surgery with respect to amblyopia and visual development, reduced scleral rigidity and positive vitreous pressure. Additionally, children have higher rates of rejection than adults and may require multiple EUAs. The authors then discuss the different techniques. PKP tends to have better graft survival in older children. There are differing opinions as to optimal age of donor tissue based on endothelial cell count and transplant curvature differences. Optimal graft sizing tends to be oversized by 0.5-1.0mm leading to a deeper AC and easier wound closure but may induce myopia. In addition, a ring provides scleral support but there is a risk of scleral penetration. Post-op high dose steroids with the possible addition of topical or systemic cyclosporin and aggressive antibacterial prophylaxis is required. Congenital corneal opacities have poorer graft survival (56%) vs acquired (79%). Complications include rejection, glaucoma, infection, and phtisis. Visual acuity is better in acquired (71%) than congenital group(50%) with respect to post op vision. Amblyopia therapy is the main predictor of post-op visual improvement. DSAEK can be used in CHED, failed PKP, buphthalmos, etc and leads to rapid visual recovery which decreases amblyopia. It requires a smaller
wound, fewer sutures which leads to faster healing and early suture removal as well as less astigmatism. It is a closed technique leading to decreased risk of choroidal hemorrhage and possible lower rejection rates. Challenges include risk of AC collapse and iris prolapse because of decreased scleral rigidity and positive posterior pressure. Post-op positioning is more challenging which may lead to higher rate of rebubbling. Protection of the crystalline lens is challenging and endothelial stripping may be difficult. DALK is useful in children with endothelial sparing corneal disorders. Surgery is safer with lower risk of expulsive hemorrhage and lower rate of graft rejection. Keratoprosthesis is reserved for patients with multiple graft failures, congenital glaucoma etc. Does minimize the risk of amblyopia as visual axis is immediately clear with minimal refractive error, no risk of rejection, easier funduscopic view. Disadvantages include vigilant care, lifelong drops, replacing bandage CL. In children, high rates of retroprosthetic membrane and glaucoma is a concern. In conclusion, this article is a comprehensive review of the techniques available for corneal transplantation in the pediatric population with their attendant challenges overall as well as a discussion of the indication, and pros and cons of each technique.

**Paediatric infectious keratitis: a case series of 107 children presenting to a tertiary referral centre**

Children may account for 13% of all cases of microbial keratitis. However, the impact of the disease may be greater on children. The authors of this study performed a retrospective review of records at Bascom Palmer Eye Institute of all patients less than 18 years old with microbial keratitis between 1992 and 2015. 107 children were analyzed in the study. The mean age was 13 +/- 4.6 years old. Mean visual acuity at presentation was 20/160, although in nearly half of patients VA was 20/60 or better. VA was worse than 20/200 in 29.9%. Contact lens wear was associated in 77.6% of cases, followed by trauma at 8.4%. Cultures were obtained in 89 patients, and 74 organisms were isolated, comprising 17 species. *Pseudomonas aeruginosa* was most common (46.2%), followed by *Stenotrophomonas maltophilia* (19.2%) and *Fusarium* (13.5%). The most common treatment was combined fortified antibiotics (most common combination tobramycin and vancomycin). Single agent treatment was used in 30.8% of cases. Natamycin was the most common initial treatment for fungal keratitis. Mean VA improved from 20/160 to 20/50. No therapeutic penetrating keratoplasty was needed urgently, although two patients later underwent PK for visual rehabilitation. The study shows that corneal ulcers can lead to permanent visual impairment in children, but with prompt evaluation and treatment, an optimal outcome is possible.
Corneal collagen cross-linking in paediatric patients affected by keratoconus

Corneal collagen cross-linking (CXL) is becoming a standard treatment for people with progressive keratoconus (KCN). Its safety and efficacy has been demonstrated in the pediatric population. In this study, the authors conducted a prospective cohort study of children treated with CXL for advanced keratoconus. The study included 43 consecutive patients (52 eyes, with average age 14.63 years) with progressive KCN (defined as 1.5D increase in topography within 1 year or loss of BCVA by one line or more). Traditional corneal CXL was performed with 0.1% riboflavin soaking for 30 minutes and 30 minutes irradiation. After treatment, a significant decrease in maximum keratometry from 59.30 to 57.07 was found two years after treatment. BCVA improved from 0.17 to 0.15 LogMAR (but not statistically significant). The eyes with worse keratometry improved from 64.94D to 62.25D (p<0.001). Endothelial cell density was stable. One patient had progression after treatment, but was stabilized after re-treatment. Another patient underwent later deep anterior lamellar keratoplasty. All cases had mild corneal haze after treatment that resolved 6 to 12 months later. Based on these results the authors conclude the procedure is safe and effective in stabilizing KCN, particularly in advanced KCN with high initial keratometry readings.

Corneal Abnormalities in Congenital Aniridia: Congenital Central Corneal Opacity Versus Aniridia-associated Keratopathy

This retrospective cohort study looks at the incidence, clinical characteristics, and progression of corneal abnormalities in 275 eyes of 138 Korean patients between 1991-2016. The aim of the paper was to characterize and compare two types of corneal abnormalities: congenital central corneal opacity from birth (CCO) and aniridia-associated keratopathy (AKK). The AAK became prominent at a mean of 21.6 years of age, and the severity progressed with age. Glaucoma was significantly more prevalent in aniridia patients with CCO (74%), compared to those with AAK (37%) (P <.0003). Cataract frequently occurred in patients with AAK (78%), and the patients required surgery at an average age of 26.6 years. The logMAR visual acuity was worse in patients with CCO (2.04 ± 0.71) than in those with AAK (1.29 ± 0.62) (P < .0001). Penetrating keratoplasty was performed in 6 eyes with CCO, and the graft survival was 33.3% during mean 45 months of follow-up (range 14–79 months). Overall, the study found that 13% of the aniridia patients had CCO at birth, while 25% progressively developed clinically significant AAK with age. The visual outcome was worse in patients with CCO than in those with AAK. The authors note that their incidence of ker-
A New Viscous Cysteamine Eye Drops Treatment for Ophthalmic Cystinosis: An Open-Label Randomized Comparative Phase III Pivotal Study

The purpose of this study was to evaluate the efficacy of new viscous cysteamine hydrochloride (CH) eye drops (vCH 0.55%) compared to standard CH 0.10% drops in the treatment of ophthalmic cystinosis. This was an open-label, phase III, randomized, two-arm multicenter trial conducted at 2 centers in France. Cystinosis patients ≥2 years old were randomized to receive either vCH 0.55% (15 patients) or CH 0.10% (16 patients) drops, 4 times per day for 90 days in both eyes. The authors compared the superiority in reducing corneal cystine crystal density as assessed by in vivo confocal microscopy (IVCM), evaluated photophobia, corneal cystine crystal scores (CCCSs), and cystine crystal depth measured by optical coherence tomography. Safety objectives were to assess adverse events (AEs), local adverse drug reactions, and ocular safety parameters. The mean absolute change in IVCM total score at day 90 in the vCH 0.55% drops group (-4.6 ± 3.1) was significantly greater than and superior to the mean absolute change in the CH 0.10% drops group (-0.46 ± 3.38; P < 0.0001). Photophobia, CCCS, and corneal cystine crystal depth were significantly more improved in the vCH 0.55% drops group than in the CH 0.10% group. The most frequent local adverse drug reactions in both groups were stinging, burning, redness, and blurred vision, none of which resulted in discontinuation of treatment. vCH 0.55% was superior to treatment with CH 0.10% drops, and offer improved convenience and ease of storage. CH 0.10% drops typically require 6-12 times per day usage and refrigeration and storage in a dark environment to remain stable, whereas vCH 0.55% is stable for up to 7 days after opening at room temperature. This study is important in that the replacement of CH 0.10% with vCH 0.55% could be life-changing for children suffering from cystinosis.

Visual, Topographic, and Pachymetric Effects of Pediatric Corneal Collagen Cross-linking.

This study evaluates the effect of pediatric corneal cross-linking (CXL) on corrected distance visual acuity (CDVA), maximum keratometry (Kmax), and other parameters of the Scheimpflug imaging system at 2 years of follow-up. The records of twenty nine eyes of twenty nine patients who underwent unilateral CXL were retrospectively reviewed. Subjects were younger than 18 years, had topographic evidence of keratoconus as well as inferior-superior difference on
topographic map greater than 1.5, and thinnest corneal pachymetry of greater than 400 microns. Changes in Kmax, CDVA, anterior chamber depth, anterior chamber volume, anterior chamber angle, pupil center pachymetry, apical pachymetry, thinnest pachymetry, corneal volume, and topographic indices were analyzed at baseline and at 1 and 2 year of follow-up. The study showed that at 1 year of follow-up there was significant improvement in CDVA and Kmax. Between 1 and 2 years postoperatively, CDVA and Kmax continued to improve slightly but the change was not statistically significant. The authors conclude that although corneal collagen cross-linking provides excellent visual and topographical improvement in adult keratoconus there are conflicting data regarding the long-term efficacy of this procedure in pediatric patients. Although the study seemed to show an improvement in the VA, steepest keratometry and corneal irregularity at 2 years of follow-up, the efficacy of the procedure in the long run remains controversial.

Yuan Wu, Haili Li, Yun Tang, Xiaoming Yan Journal of Pediatric Ophthalmology & Strabismus. March/April 2017; 54:(2)78-83

This study evaluations in vivo the differences in meibomian gland morphology between children and adolescents. Sixty nine patients were included in the study, out of which thirty one(n=31) were children and thirty nine(n=39) were adolescents.Images of the meibomian glands were were obtained by infrared meibography and analyzed using ImageJ software. The number of meibomian gland ducts, meibomian gland loss, the relative width of the meibomian gland ducts and the percent area of the meibomian gland acini were compared between the two groups. The study showed that meibomian gland loss occurs in both age groups. The number of meibomian gland ducts, relative width of the meibomian gland ducts, and percent area of the meibomian gland acini in the upper eyelid were significantly greater in adolescents than in children. However no significant changes were found in the lower eyelid between the two groups. The authors conclude that meibography is a useful tool for the assessment of ocular surface disease in children and in adults although additional studies should be undertaken in order to evaluate the association between the meibomian gland changes and and meibomian gland dysfunction in children and adolescents.

Accelerated corneal crosslinking for treatment of progressive keratoconus in pediatric patients.

The purpose of this observational cross-sectional study was to evaluate the safety and efficacy of accelerated corneal crosslinking (CXL) in patients with progres-
sive keratoconus aged 18 years or less. A total of 28 eyes from 19 patients with progressive keratoconus aged 18 years or less were enrolled. The participants were divided into two groups according to corneal thickness (CT). Group 1 included 13 eyes of 8 patients with CT ≥ 450 µm; group 2 included 15 eyes of 11 patients with CT <450 µm. Each participant underwent accelerated CXL using 10-minute ultraviolet A irradiance at 9 mW/cm² for a total energy dose of 5.4 J/cm². The efficacy and safety of the procedure were assessed postoperatively at 1, 3, 6, and 12 months with Pentacam and visual acuity. Group 1 showed a statistically significant improvement in uncorrected visual acuity at 3 months postoperatively +0.12 logMAR (p = 0.003), while group 2 showed a statistically significant improvement in visual acuity at 1 month postoperatively +0.3 logMAR (p = 0.005). At 12 months postoperatively, there was an improvement in best-corrected visual acuity of +0.15 logMAR (p<0.001) and +0.22 logMAR (p = 0.005) of group 1 and group 2, respectively. All mean keratometric values including K1 and K2 dropped by at least 1 D or remained stable (≤1 D) in both groups after accelerated CXL treatment. The authors conclude that in their cohort of patients accelerated CXL treatment seems to be effective in slowing or halting the progression of keratoconus and that no permanent apparent complications were noted 6 months after the procedure. This study basically validates previous reports of this technique in individuals younger than 18 years of age.

A novel method for examining corneal endothelial cell morphology in infants.

Previous studies have suggested that central corneal endothelial cell density (ECD) decreases from 6,100 cells/mm2 in neonates to 3,100 cells/mm2 in 10-year-olds. Currently data on ECD in young children is sparse because of the difficulty of examining young children with clinic-based specular microscopes. The authors share their technique of imaging young children intraoperatively with the NIDEK CEM-530 noncontact specular microscope. Children were also imaged awake in clinic using a child-friendly technique. A total of 58 children were recruited (mean age, 5.50; range, 0.44-10.36). This small cohort displayed a linear decrease in ECD with age (r = -0.56, P < 0.001), a decrease of approximately 79 cells per year. Larger studies are needed to establish normative data of ECD in children of various age groups.

Amniotic membrane transplants in the pediatric population.

The purpose of this retrospective case series was to investigate the indications for and the efficacy of amniotic membrane transplantation (AMT) for the treatment of ocular disease in pediatric patients at a single institution. The medical records of patients <18 years of age who underwent AMT for
ocular disease between January 1, 2003, and September 1, 2015, were re-
viewed retrospectively. The primary outcome was achievement of a clinical
endpoint. Patients were determined to have reached a clinical endpoint if
there was resolution of the ocular condition being treated after AMT place-
ment, no additional surgery required for treatment of the ocular condition,
and no active disease at most recent follow-up. A total of 48 records were
reviewed. Of these, 32 patients (67%) received AMT for treatment of ocular
disease related to Stevens Johnson syndrome (SJS), 29 (94%) of whom
reached the clinical endpoint. The remaining 16 patients (33%) underwent
AMT for indications other than SJS, including difficult-to-treat corneal ep-i-
theial defects and ulcers, conjunctival reconstruction, and scarring after
strabismus surgery. Of these, 80% reached the clinical endpoint. There
were no adverse effects related to AMT in either group. The authors con-
cluded that in this series, AMT was used successfully and without compli-
cations. Despite the limitations of this study, inherit to it retrospective nature and
small sample size, it is the first study to investigate the indications of AMT
for ocular disease specifically in patients under 18 years of age.

Steroid-Sparing Effect of 0.1% Tacrolimus Eye Drop for Treat-
ment of Shield Ulcer and Corneal Epitheliopathy in Refracto-
yre Allergic Ocular Diseases
Mar;124(3):287-294

Topical calcineurin inhibitors were recently introduced to treat severe allergic
conjunctival diseases with remarkable success. The purpose of this study was to
determine whether topical tacrolimus alone or with adjuvant steroids can cure
corneal epitheliopathy and shield ulcers in patients with refractory allergic ocular
diseases. The authors retrospectively analyzed 791 cases followed at 330 oph-
thalmological institutions in Japan between 2008 and 2016. Inclusion criteria
were presence of corneal epitheliopathy or shield ulcers, persistent or relapsing
allergic conjunctivitis, and age < 40 years. The effectiveness of the treatment
was determined by a corneal epitheliopathy score during the 3-month follow-up
period. The clinical signs were rated on a 4-grade scale. Corneal epitheliopathy
with no corneal staining was graded as 0, and shield ulcers or plaques were
graded as 3, the highest grade. The effects of tacrolimus with and without topical
steroids on the epitheliopathy scores were assessed after adjustments for the
severity of the clinical signs and characteristics. Results show that adjusted
mean epitheliopathy score at the baseline was 1.73 (95% CI, 1.65-1.81) for pa-
tients treated with tacrolimus alone, and this was significantly reduced by -0.93
at 1 month. The reduction of the score by topical and oral steroids was -0.02 for
fluorometholone, 0.02 for betamethasone, and -0.02 for oral steroids, and these
reductions were not significant compared with the reduction effect of topi-
cal tacrolimus alone at -0.93. The 238 patients with shield ulcer (score 3) were analyzed with adjustments, and the mean epitheliopathy score at 1 month was reduced to 1.38 with tacrolimus alone (95% CI, 1.24-1.51), 1.41 (95% CI, 1.26-1.56) with adjuvant fluorometholone, and 1.46 (95% CI, 1.32-1.61) with adjuvant betamethasone. No significant difference was observed in the adjunctive topical steroids. The presence of severe palpebral conjunctival symptoms, including giant papillae, was a significant resisting factor for topical tacrolimus. This is an effective steroid-sparing agent to be used to treat allergic ocular disease that can be common in children. Tacrolimus is available only as dermatologic preparation in the US.

Safety and efficacy of Sequential Intracorneal Ring Segment Implantation and Cross-linking in Pediatric Keratoconus.

Keratoconus in children tends to be more severe than in adults, under diagnosed, and children tend to be less tolerant of conservative treatments such as contact lenses. Additionally treatments such as penetrating keratoplasty have a higher risk of failure in the pediatric population and long term data on cross linking alone is conflicting. The purpose of this study was to look at intracorneal ring segment (ICRS) implantation followed by corneal collagen cross-linking (CXL) 1 month later, to determine the safety and visual outcome of this treatment regimen for keratoconus in children. This was a retrospective interventional case series of 12 patients (17 eyes) ages 9-14 with keratoconus and poor corrected distance visual acuity. The ICRS were inserted under topical anesthesia after using the femtosecond laser to create a corneal tunnel. The cross-linking was performed 1 month later and the patient’s data was reviewed at 6 months, 1 year, 2 years and 4 years where data was available. Follow up times ranged from 6 months to 4 years. The 6-month best corrected distance visual acuity (CDVA) was significantly improved when compared to pre op. Additionally there was a significant flattening of the keratometry readings and a decreased in spherical equivalent after the ICRS insertion. The other follow up points demonstrated stability over time. There was one patient who had to have the ring segment removed after 2 years but otherwise there were no other surgical complications. The authors conclude that ICRS implantation followed by CXL was safe and effective for improving vision in pediatric keratoconus but few patients in this study were followed long enough to compare to other studies evaluating the treatment of pediatric keratoconus.

Anterior segment disorders - surgical procedures
Anterior segment disorders – nonsurgical management
**Anterior segment biometry and refraction**

**12. CATARACT**

**Cataract morphology and risk for glaucoma after cataract surgery in infants with unilateral congenital cataract**


This study examined the association between congenital cataract morphology and development of glaucoma. A prior observation by Parks et al. suggested that glaucoma was more likely to develop in patients with fetal nuclear cataracts. In this subanalysis of results from the infant aphakia treatment study, the authors examined whether there was a relationship between cataract morphology and the development of glaucoma, glaucoma suspect and no glaucoma. 83 patients with unilateral congenital cataract were included and were followed until 5 years of age. Videos obtained at the time of cataract extraction were used to classify cataract morphology as nuclear, persistent fetal vasculature (PFV, which included nuclear cataracts with PFV), cortical, posterior, absorbed and total. The most common cataract morphology was nuclear; 39 (47%) of 83 patients had nuclear cataracts. Glaucoma was present in 8 (21%) and glaucoma suspect in 5 (13%) of the 39 patients with nuclear cataracts. Similarly, glaucoma was present in 8 (18%) and glaucoma suspect in 7 (16%) of the 44 patients without nuclear cataracts. Thus, there was no evidence that nuclear cataracts were more commonly associated with glaucoma. A limitation of this study is that the Parks et al. observation about higher glaucoma risk was primarily in patients with bilateral nuclear cataracts, and thus not applicable to patients with unilateral nuclear cataracts.

**Globe Axial Length Growth at Age 5 Years in the Infant Aphakia Treatment Study.**


The authors conducted a comparative case series of infants with unilateral cataract enrolled in the IATS study. They compared the longitudinal axial length (AL) at baseline to age 5 years. AL were analyzed relative to treated versus fellow eye, visual outcome, and treatment modality (contact lens [CL] vs. intraocular lens [IOL]). Eyes with glaucoma or glaucoma suspect were excluded from primary analysis but reported separately. Seventy patients were eligible; however, AL data for both eyes were available for 64 patients at baseline and 69 patients at age 5 years. The AL was significantly different between treated and fellow eyes preoperatively (18.1 vs. 18.7 mm, P < 0.0001) and at the final follow-up (21.4 vs.
22.1 mm, P = 0.0004). The difference in AL growth between treated and fellow eyes was not significant (3.3 vs. 3.5 mm, P = 0.31). The change in AL in eyes was similar with both treatments (CL 3.2 mm and IOL 3.4 mm, P = 0.53) and did not correlate with visual outcomes (P = 0.85). Eyes receiving additional surgery to clear the visual axis opacification grew significantly more compared with eyes not receiving surgery to clear the visual axis (3.8 vs. 2.7 mm, P = 0.013). Patients with glaucoma showed significantly more eye growth (5.7 mm) than those without glaucoma (3.3 mm) and glaucoma suspects (4.3 mm). In conclusion, eyes treated for monocular cataract in infancy have axial growth similar to that of fellow eyes, despite having a shorter AL at the time of surgery. The change in AL in eyes was similar with both treatments (CL and IOL), did not correlate with visual outcomes, and was higher in eyes receiving additional surgery to clear the visual axis or eyes diagnosed with glaucoma.

Anisometropia at Age 5 Years After Unilateral Intraocular Lens Implantation During Infancy in the Infant Aphakia Treatment Study.

In children with unilateral aphakia, large myopic shifts can result in anisometropia that can impair binocularity and cause amblyopia. Generally ophthalmologists will undercorrect the refractive error in children when they place an intraocular lens in anticipation of this myopic shift. In the Infant Aphakia Treatment study (IATS), infants ages 1-6 months had an intraocular lens placed of +6 or +8 depending on age. The purpose of this study was to report the prevalence of anisometropia at 5 years after unilateral IOL placement in the IATS. This was a prospective randomized clinical trial of 57 infants who had unilateral cataract extraction with placement of intraocular lens. The authors evaluated the median refractive error in the treated and fellow eyes and found that the median anisometropia was -3.5 diopters (range -19.63 to +2.75). Patients with glaucoma in the treated eye had a larger degree of anisometropia. There were 3 patients who had IOL exchanges prior to the 5 year follow up who were excluded. The authors concluded that most pseudophakic eyes had significant anisometropia at the age of 5 years and this contributes to the challenges of IOL placement in infancy.

Diagnosed Cataracts in Patients with Cystic Fibrosis in a United States Administrative Database.

Cystic fibrosis (CF) is an autosomal recessive genetic disease impacting multiple organ systems and causing progressive lung dysfunction and early mortality. Treatment has focused on alleviating secondary symptoms of the disease; this approach, coupled with significant changes in care, has led to an increase in the median age of survival for persons with CF from 27 in 1985 to 39.3 in 2014. Re-
search suggests that patients with CF patients may have a higher prevalence of eye disorders, including cataract. The authors estimated the incidence and prevalence of diagnosed cataracts among patients with CF versus the general population (GP). Using a large US health insurance claims database, they identified a CF cohort and a GP cohort matched with respect to age, gender, and calendar year. The prevalence and incidence of diagnosed cataract (primary outcome) for both cohorts were calculated, as well as the incidence rate ratios (IRRs). The prevalence of diagnosed cataracts among patients with CF alive and enrolled in the health plan on August 31, 2012 was 4.8% versus 2.8% in the GP. The incidence in the CF cohort was higher than in the GP and increased with age in both cohorts. The adjusted IRR comparing the CF and GP cohorts was 1.5 (95% CI: 1.2–1.8). Overall, the study suggests that the risk of developing cataract was higher among patients with CF than among the GP.

**Visual outcomes of patients presenting with bilateral infantile cataracts and nystagmus**


The presence of manifest nystagmus in patients with infantile cataracts has been correlated with poorer visual outcomes after surgery, although good outcomes can still be achieved in some patients. The authors conducted a retrospective case study to evaluate outcomes after surgery of children with bilateral infantile cataracts who had preoperative nystagmus. 29 patients were initially found, but 13 were excluded due to other ocular conditions that could explain the nystagmus and 3 were excluded due to poor follow-up. Therefore 13 total patients were examined. The mean age of diagnoses of the cataracts was 8.1 months, and mean age of first surgery 8.5 months. Average time between surgery of the 2 eyes was 9.3 days. Mean follow-up was 54.3 months. 12/13 were left aphakic, with one receiving primary IOL at surgery at 42.2 months. Two later received secondary IOLs. At last follow-up, 5 of the 10 patients who performed objective visual acuity had BCVA 20/40 or greater in the better eye. 4 had BCVA 20/60 or better, and one had 20/125 in the better eye. 2 patients no longer had manifest nystagmus, and 3 had only latent nystagmus. 8/13 had strabismus and 2 developed aphakic glaucoma. In summary, despite all patients presenting after 10 weeks of age and with nystagmus, many achieved good visual acuity. However this was a small sample size, and 3 patients could not perform verbal recognition acuity due to age. Still, this suggests preoperative nystagmus does not prevent a good visual outcome after surgery.

**13. CATARACT SURGERY**

*Pediatric cataract surgery outcomes*
Surgical Outcome of Congenital Cataract in Eyes With Microcornea.


In this retrospective, interventional, comparative case series, the authors reviewed 47 eyes of 26 children with microcornea and congenital cataract who underwent lens aspiration with primary posterior capsulectomy and anterior vitrectomy between 2008 and 2014 with a minimum follow-up period of 6 months. Demographic profiles and systemic and ocular features were documented. Intraoperative and postoperative complications were studied separately for bilateral and unilateral cases. Patients were also divided into two groups on the basis of their ages at surgery (early surgery group: 3 months or younger; late surgery group: older than 3 months) and postoperative complications were compared. Visual outcome was analyzed in those with a follow-up period of more than 1 year. Early surgery was performed in 24 eyes of 13 patients (11 bilateral and 2 unilateral) and late surgery in 23 eyes of 13 patients (10 bilateral and 3 unilateral). Intraoperatively, all eyes had poor pupillary dilatation and 6 (12.8%) eyes needed iris hooks. Postoperatively, the most common early complication was transient corneal edema observed in 22 (46.8%) eyes (13 and 8 eyes in the early and late surgery groups, respectively). Late complications included visual axis opacification in 6 (12.76%) eyes (3 in each group), and secondary glaucoma in 5 (10.64%) eyes (2 and 3 eyes in the early and late surgery groups, respectively). Vision was normal for age in 18 (60%) of the bilateral cases with a follow-up period of more than 1 year. The study shows that we can expect favorable postoperative outcomes after early surgery for congenital cataract in microcornea. Meticulous surgery with adequate capsulectomy and complete anterior vitrectomy, as well as regular follow-up with early identification and timely judicious management of postoperative complications, especially visual axis opacification and glaucoma, is crucial for a successful outcome. Furthermore, good visual rehabilitation with the appropriate use of amblyopia therapy and vision stimulation maximizes the visual outcome for these children. Although this study has the limitations of being retrospective in design and having a relatively shorter follow-up period for some patients, it adds to the limited literature on cataract surgery in microcornea in the pediatric age group.

Retrospective Study of Visual Outcomes and Complications After Sutureless, Flapless, and Glueless Intrasceral Fixation of Posterior Chamber Intraocular Lens in Children and Young Adults.

The purpose of this retrospective study is to evaluate the visual outcomes and surgical complications after sutureless, flapless, and glueless intrascleral fixation of a posterior chamber intraocular lens (IOL) in patients between the age of 5 and 20 years old. Fifteen eyes of eleven patients were included in the study with a mean postoperative follow-up of six months. BCVA, UCVA, as well as early and late postoperative complications were the main outcomes. The study showed that there was a statistically significant change between the preoperative and postoperative UCVA (P < .001) as well as between the preoperative and postoperative BCVA (P < .001). Only two patients showed early postoperative complication (hyphema and vitreous hemorrhage which resolved by the last follow-up visit) and none of the patients showed late postoperative complications during the 6-month follow-up. The final visual acuity between the complication (n=2) and no complication (n=13) groups showed no statistically significant difference (P = .91). Although this study is limited by the retrospective nature and the very short follow-up, the authors conclude that this technique of scleral fixation of a three-piece IOL can improve visual acuity and doesn’t cause significant complications postoperatively.

Modified technique of endocapsular lens aspiration for severely subluxated lenses


Authors describe an endocapsular technique to remove the lens material in patients with subluxated lenses. Authors include patients between 5-15 years who underwent a standard surgical technique. An MVR was used to create two paracentesis and to open two small incisions on the lens capsule. A vitrector and an irrigation with a 27 gauge needle. The lens material was removed using the cut I/A vitrector. After the remaining capsules were also removed. An AC IOL was placed. Thirty-two eyes of 16 patients were included. Out of 16 patients, 9 patients (56.2%, 9/16) were diagnosed as having Marfan’s syndrome, 4 patients (25%, 4/16) had a marfanoid habitus, and 3 patients (18.7%, 3/16) had bilateral microspherophakia with anterior subluxation of lens.

The mean age was 9.375 ± 3.16 years (range 5–15 years). All surgeries were uneventful. ACIOL were inserted safely in 22 eyes and 10 eyes were left aphakic. Out of these 10 eyes, 8 eyes had a large W–W diameter (412.5 mm) in which the ACIOL if placed may be small for the eye resulting in undue mobility. The rest of the 2 eyes of the same patient had microspherophakia out of which one eye had an anterior dislocated lens with pupillary block glaucoma (IOP = 30 mm Hg) and corneal edema (CCT = 640 μm), The mean endothelial cell loss at 3 months

\[ \text{compared to pre-operative levels was 269.6 \pm 151 cells/mm}^2 \text{ amounting to 7.1% endothelial cell loss over 3 months which was statistically significant (P = 0.001).} \]

The mean CCT at 1 week, 1 month, and 3 months post-surgery were 525.3 ± 39.61 μm, 526.8 ± 39.43 μm, and 526.5 ± 39.17 μm. The modified technique of endocapsular lens aspiration provides for a simple and effective way of removal
of the lens-capsular bag complex through small incisions on the cornea

**Outcome of various hydrophobic acrylic intraocular lens implantations in children with congenital cataract**


The authors retrospectively compared rates of visual axis opacification after cataract surgery, primary posterior capsulotomy, anterior vitrectomy, and implantation of different intraocular lenses in children aged less than 2 years. They included only children with a minimum follow-up of 1 year, and they excluded microphthalmos, persistent fetal vasculature, traumatic cataract, aphakia, secondary IOLs, or coexisting ocular disease.

A total of 257 eyes of 159 children were included, and the mean age at the time of surgery was 12 months (range 6-23 months). Twenty-nine eyes of 16 children received an SA60 AT IOL (AcrySof, Alcon, Fort Worth, TX); 75 eyes of 45 children received Hoya IOL (Hoya-PS AF-1 Series, Model PC-60AD, Hoya, Japan), 70 eyes of 46 patients received Sensar (Abbott Medical Optics Inc., Santa Ana, CA, USA), and 83 eyes of 52 children received MA60AC (AcrySof). At a mean follow-up of 18 months, 22% of the children required surgery for visual axis obscuration. By multiple regression analysis, the rate of visual axis obscuration was affected by the rate of perioperative complications (p = 0.001) and not affected by age (p = 0.98), type of IOL (p = 0.104), or site of IOL implantation (p = 0.603).

The authors concluded that different IOLs had comparable rates of visual axis obscuration. A strength of the study is the use of multiple regression to account for possible confounding factors when comparing outcomes after different IOLs.

**Postoperative outcomes of intraocular lens implantation in the bag versus posterior optic capture in pediatric cataract surgery.**


The purpose of this study was to determine whether using posterior optic capture in pediatric cataract surgery might obviate the need for anterior vitrectomy. In this prospective randomized single center study from India, pediatric cataract patients age 3 years and younger were randomized to 1) in-the-bag intraocular lens (IOL) with anterior vitrectomy or 2) creation of a manual posterior capsulorhexis, with optic capture of the IOL through the posterior capsulorhexis, and no anterior vitrectomy. All IOLs were MA60AC lenses. Postoperative visual axis obscuration (VAO), glaucoma, cell deposits on the IOL, and posterior synechiae were compared at 1, 3, 6, and 12 months. The study comprised 61 children (61 eyes). The mean ages were 14.8 months ±11.5 (SD) in Group 1 (n = 30) and 18.2 ± 11.5 months in Group 2 (n = 31). Only 1 eye in Group 1 developed a VAO
requiring membranectomy 4 months postoperatively, and 2 eyes in Group 1 developed glaucoma over 12 months (P = 0.49). Intraocular lens cell deposits and posterior synechiae were comparable between groups. The IOL could not be captured in 5 eyes (16.1%). In conclusion, optic capture of 3-piece MA60AC lens could be achieved in most eyes and did not increase visual axis opacification, even among young children. Posterior optic capture allows the anterior posterior capsulorhexis edges to fuse, trapping lens epithelial cells and preventing their migration across the anterior vitreous face. The technique has the same rationale as the bag-in-the-lens technique reported from Belgium and the Netherlands. Thus, optic capture of an IOL is an alternative surgical technique that can be used to avoid vitrectomy, even in children younger than 4 years. The main disadvantage of the technique is the difficulty in performing a manual posterior capsulorhexis of appropriate size, a challenge that may be overcome in the future with femtosecond laser.

Infantile cataract: comparison of two surgical approaches

Lens reproliferation after infantile cataract surgery can be a vision threatening complication. Some authors have advocated performing posterior optic capture of the implanted IOL without anterior vitrectomy to prevent lens reproliferation and maintain a clear visual axis. Others state that an anterior vitrectomy is mandatory to keep the visual axis clear. This study was a retrospective case series comparing two surgical approaches: either IOL implantation in the bag with posterior optic capture and no anterior vitrectomy (OC approach), or no optic capture of the IOL but with anterior vitrectomy (AV approach). 123 eyes were included in the analysis, 21 in the OC group, 102 in the AV group. Mean age at surgery was 57.3 months, and mean follow-up 63.1 months. Lens reproliferation occurred in 21.1% of eyes, with mean time for development 90 months. There was no statistical difference however between the two groups in reproliferation incidence or BCVA. There was a higher percentage of complications in the OC group, but this was not statistically significant. The smaller sample size of the OC group limited comparison. However the authors conclude that both approaches are safe.

Benchmarks for outcome indicators in pediatric cataract surgery.

Nihalani BR, VanderVeen DK. Eye (2017) 31, 417–421

Quality assurance programs have been instituted to identify the potential for improving outcomes. The most commonly used indicators in adult cataract surgery are best corrected visual acuity (BCVA) and refractive accuracy as reported in multiple benchmark studies. There are no publications focused on benchmark indicators in pediatric cataract surgery. The aim of
our study was to establish valid benchmark indicators in the pediatric population. Retrospective chart review of all patients older than 2 years of age undergoing cataract surgery with primary IOL implantation over an 11-year period (November 2005–February 2016). Exclusion criteria included ocular comorbidities known to potentially result in poor vision or inability to obtain accurate biometry (corneal opacity, glaucoma, uveitis, trauma, manifest nystagmus, retinal disease, or subluxated lenses). Data collected included pre- and post-operative VA measures, biometry data, and refractive outcomes. A total of eight different surgeons performed the procedures in this study. All children from 2 to 5 years of age received posterior capsulotomy and anterior vitrectomy, and children older than 5 years did not receive posterior capsulotomy or anterior vitrectomy. Two separate outcome measures were studied. Best corrected visual acuity. Only patients aged 2 years or older at the time of surgery, who were treated with bilateral cataract surgery, who were followed for at least 3 months after surgery, and who had a final VA measured with Snellen letters were included. This eliminated the possibility of dense amblyopia from congenital cataract with late presentation, or those with dense amblyopia due to unilaterality.

Prediction error absolute PE were calculated in the following manner: PE = predicted refraction − actual refraction
Absolute PE = |predicted refraction − actual refraction| Predicted refraction was calculated for the IOL power that was implanted in the eye using AL, K, and the manufacturer’s A-constant. One hundred and twenty-four eyes of 62 patients with bilateral cataract surgery were analyzed for VA outcomes. Mean age at surgery in this group was 8.3 ± 4.6 years (median age: 6.8 years). Mean follow-up duration was 3.7 ± 2.7 years. All but one patient had IOL implantation within the capsular bag. The IOL power was reduced by 1.0 D in the patient with sulcus implantation. BCVA at the last visit was 20/40 or better in 96% eyes. PE calculations were performed for 235 eyes of 179 patients (56 bilateral, 123 unilateral). The mean age at surgery was 6.3 ± 4.8 years. The mean AL was 22.3 ± 1.8 mm. The mean PE was 0.3 ± 1.1 D and the mean absolute PE was 0.9 ± 0.7 D. The PE was within 0.5 D in 43% eyes, 1.0 D of target in 66% eyes, and 2.0 D of target in 95% eyes. The mean absolute PE in the group of eyes with shorter AL was higher compared to eyes with long AL and the difference was significant statistically.

Quality management based on outcome indicators is increasingly finding its way into Ophthalmology practices. A reference for good quality or best practice is needed, the so-called benchmark. In the present study, children with bilateral cataract surgery achieved excellent VA outcomes, which is comparable to outcomes reported for surgery in adult eyes. For quality outcome measures, authors suggest that children older than 2 years at the time of bilateral cataract surgery with primary IOL implantation should achieve excellent visual outcomes in 96% of eyes. The PE in pediatric eyes is somewhat greater than benchmark reported in adult population studies, so that overall only 66% are within 1 D of the target refraction. Pe-
diatric patients often represent ‘complicated’ cases as the surgery can be technically challenging compared with the adult cataract surgery. VA measures can be compromised cooperation and co-existing conditions such as amblyopia, latent nystagmus, strabismus, or intentionally planned residual refractive error.

**Long-term Outcomes of Primary Intraocular Lens Implantation in Patients Aged 7 to 24 months.**
Allison G.Yeh, Linkgkun Kong, Kimberly G.Yen *Journal of Pediatric Ophthalmology & Strabismus* May/June 2017; 54(3): 149-155

This retrospective study reports the long-term outcomes of primary intraocular lens placement in 27 patients aged 7 to 24 months who underwent cataract surgery. The average follow-up was 62.7+/–41.7 months and the mean age of surgery was 14.4+/–5.6 months. Adverse events occurred in 25% of patients and included visual axis opacification and papillary block glaucoma in 1 patient one week after surgery. Strabismus was present in 70.4%. This study is limited by its retrospective nature and small size. Also the follow-up was not consistent with all patients and some data points were not available. Also, the young age of the patients limited the ability of the investigators to measure quantitative visual acuity. The authors concluded that IOL implantation in patients aged 7 to 24 months was associated with few surgical complications and that it can be a safe and effective intervention for treatment of cataracts in patients aged 7 to 24 months of age. Amblyopia likely limits vision improvement in many of the patients with unilateral cataracts and myopic shift should be considered when calculating postoperative target refraction for those patients.

**Primary and Secondary Intraocular lens Implantations in Children with Pediatric Cataract: Visual acuity and Strabismus at the age of 2 years and older.**

This study compares the visual outcomes of primary and secondary intraocular lens (IOL) implantations and identifies the risk factors for the development of strabismus in patients after pediatric cataract surgery. In this retrospective chart review, 220 eyes of 148 patients were included with an age range of 2 to 17 years. Strabismus developed in 23.73% of patients in the primary group and in 30% in the secondary group. There was a negative relationship between visual acuity and the development of strabismus, whereas there was a positive relationship between the follow-up period and the development of strabismus. The authors conclude that appropriate optical rehabilitation after pediatric cataract surgery is essential in order to prevent the development of strabismus. The study has a lot of limitations: it is retrospective, it includes a small number of patients with a wide range of age. Also because of the retrospective nature of the study, information about the age at which the cataract was diagnosed, the morphology
of the cataracts as well as the use of proper spectacles or contact lenses post-operatively was often missing.

**Myopic Shift 5 Years after Intraocular Lens Implantation in the Infant Aphakia Treatment Study.**

The Infant Aphakia treatment study is (IATS) is a randomized clinical trial comparing the visual outcome in infants 1 to 6 months of age who underwent primary implantation of an IOL vs. being left aphakic and receiving a contact lens correction after cataract surgery in infancy. These infants were targeted for 8 D undercorrection for infants aged < 48 days and a 6 D undercorrection for infants aged 48 to 210 days. Refractive error was measured at 1 month and 3 months and then at 3-month intervals until age 4.5 years and then at 5 years. The change in refraction over time was estimated by linear mixed model analysis. Intraocular lens implantation was completed in 56 eyes; 43 were analyzed (median age, 2.4 months; range, 1.0-6.8 months). Exclusions included 11 patients with glaucoma, 1 patient with Stickler syndrome, and 1 patient with an IOL exchange at 8 months postoperatively due 8 D of myopic shift between the visits 3 and 6 months. The mean rate of change in a myopic direction from 1 month after cataract surgery to age 1.5 years was 0.35 diopters (D)/month (95% CI, 0.29-0.40 D/month); after age 1.5 years, the mean rate of change in a myopic direction was 0.97 D/year (95% CI, 0.66-1.28 D/year). The mean refractive change was 8.97 D (95% CI, 7.25-10.68 D) at age 5 years for children 1 month of age at surgery and 7.22 D (95% CI, 5.54-8.91 D) for children 6 months of age at surgery. The mean refractive error at age 5 years was -2.53 D (95% CI, -4.05 to -1.02). After IOL implantation during infancy, the rate of myopic shift occurs most rapidly during the first 1.5 years of life. Myopic shift varies substantially among patients. If the goal is emmetropia at age 5 years, then the immediate postoperative hypermetropic targets should be +10.5 D at 4 to 6 weeks and +8.50 D from 7 weeks to 6 months. However, even using these targets, it is likely that many children will require additional refractive correction given the high variability of refractive outcomes.

**Cataract surgery in children with retinopathy of prematurity (ROP): surgical outcomes.**

Cataract development has been associated with ROP, development of which may be spontaneous or due to interventions to treat underlying ROP. The authors conducted a retrospective review of all cases of ROP at a single facility in India and identified children with cataracts that required surgery. Out of 2258 children with ROP, 22 (28 eyes) were included (0.97%). The most common
grade of ROP was stage 4, with most children undergoing some form of intervention (laser, injection, or most commonly pars plana vitrectomy). 5 eyes did not have any ROP intervention, suggesting that even with regression of ROP cataracts may still develop. The authors performed IOL implants in 19 eyes and reported complication rates no greater than that of children without ROP, although due to sample size a true statistical comparison was not done. The authors conclude that regardless of intervention for ROP, cataract formation is possible, and improved visual acuity can be achieved with surgical management.

**Pediatric cataract surgery complications**

**Endophthalmitis following Pediatric Cataract Surgery: An International Pediatric Ophthalmology and Strabismus Council Global Perspective.**

Almutez M. Gharaibeh, Luis H. Ospina, Eedy Mezer, Tamara Wygnaski-Jaffe


The purpose of this study is to compile international data on the risk factors, diagnosis, and treatment of endophthalmitis following pediatric cataract surgery. An e-mail containing a link to an online survey was sent to all members of the American Association for Pediatric Ophthalmology and Strabismus. The questionnaire examined the incidence, risk factors, treatment, outcomes, and prophylaxis of endophthalmitis following pediatric cataract surgery around the world. Two hundred thirty-seven ophthalmologists answered the questionnaire. Eight ophthalmologists (3.4%) encountered 22 cases of endophthalmitis following pediatric cataract surgery during their practice. Most patients with endophthalmitis following pediatric cataract surgery were 2 to 4 years of age (36.4%). An intraocular lens was implanted in 59.1% of cases, most of which were acrylic intraocular lenses (53.8%). The main presenting symptoms were photophobia (50%) and pain (40.9%). The most common signs were conjunctival injection (36.4%) and hypopyon (31.8%). The final visual acuity was counting fingers or worse in 86% of cases. The most common cultured organism was *Staphylococcus aureus* (31.8%). The most common management of endophthalmitis following pediatric cataract surgery was a combination of intravitreal, systemic, and topical antibiotics (36.4%). Most ophthalmologists (68.2%) administered prophylactic intracameral antibiotic treatment during surgery and 50% used vancomycin. The authors conclude that endophthalmitis following pediatric cataract surgery is an uncommon, multifactorial complication with poor visual prognosis. Efforts directed at minimizing its risk, such as treating potential predisposing systemic conditions, improving sterilization techniques, optimizing operative conditions to reduce complications and surgery duration, and using subconjunctival and intracameral antibiotics, decrease its incidence. Early postoperative evaluation, subsequent follow-up visits, and keeping a high index of suspicion should facilitate the recog-
tion of endophthalmitis following pediatric cataract surgery to avoid delaying treatment.

**Pediatric cataract surgery – other topics**

**Twenty-five-gauge sutureless lensectomy in infants with congenital cataract.**

The purpose of this retrospective study was to evaluate the incidence of intra- and postoperative complications of transconjunctival 25-gauge (25G) sutureless pars plicata lensectomy. The medical records of patients <12 months of age with congenital cataracts who underwent 25G sutureless lensectomy were reviewed retrospectively. Patients were evaluated at postoperative days 1, 7, 15, 30, 60, and 90 and every 3 months thereafter. Visual acuity outcomes and intra- and postoperative complications were described and analyzed. A total of 72 eyes of 44 infants were included; 28 patients (64%) had bilateral cataract. Median follow-up was 28 months (range, 12-93 months). In 47 eyes (81%) there was improved visual acuity after surgery. Median age at surgery was 2 months (range, 1-12 months). According to the age of the infants, 17 eyes (24%) had surgery at 1 month of age, 27 (38%) at 2 months of age, 13 (18%) at 3 months of age, and 20 at least 4 months of age. Intraoperative adverse events occurred in 9 eyes (13%). Postoperative complications occurred in 14 eyes (19%): 6 eyes (8%) had secondary visual axis opacification, 6 eyes (8%) had secondary glaucoma, 1 eye (1%) had posterior synechiae, and 1 eye (1.4%) had retinal detachment. The authors conclude that transconjunctival pars plicata 25G sutureless lensectomy is a minimally invasive technique for congenital cataract treatment. The current study is limited by its retrospective nature, and the relatively small number of cases. Nevertheless, good results were achieved in this cohort of patients with the transconjunctival pars plicata 25G sutureless lensectomy technique. Since the main concern was the safety and complication rate of this procedure, not much focus was put on visual function and best corrected VA at final follow-up.

**Factors influencing intraocular pressure, corneal thickness and corneal biomechanics after congenital cataract surgery**

Aphakic glaucoma is an important complication after congenital cataract surgery, with incidence rates within the first year of life of 6-41%. Several factors influence IOP readings, including corneal curvature, central corneal thickness (CCT), and biomechanics. The authors of the study evaluated IOP, CCT, and corneal biomechanics in patients with aphakia, pseudophakia, and matched controls. Included
were 36 aphakic eyes, 77 pseudophakic eyes (47 primary, 30 secondary), and 34 normal controls. IOP was significantly greater in aphakic eyes than in normal and primary pseudophakic eyes. Secondary pseudophakic eyes also had greater IOP than normal or primary pseudophakic eyes. Aphakic eyes had greater CCT than the other groups. Corneal hysteresis was greater in primary pseudophakic eyes compared to aphakic and secondary pseudophakic eyes. The results suggest that increases in CCT after congenital cataract surgery are attributable to aphakia rather than the surgery itself, and that IOL implantation at the time of surgery or later may prevent post-operative CCT increases. The authors hypothesize that after lens extraction forward flow of vitreous may be capable of changing the microstructure of the anterior eye and modifying corneal characteristics. IOP implantation may serve as a barrier to protect the cornea from these changes. Also, corneal hysteresis seemed to permanently decrease after lensectomy, likely due to corneal structure changes, and did not seem to be prevented or reversed by secondary IOL implantation.

Central corneal thickness and intraocular pressure changes after congenital cataract surgery with intraocular lens implantation in children younger than 2 years.

The purpose of this study was to evaluate changes in central corneal thickness (CCT) and intraocular pressure (IOP) in children younger than 2 years after congenital cataract surgery with primary intraocular lens implantation. Thirty-one patients (aged 3 to 24 months) were analyzed. There were 24 bilateral and 7 unilateral cases. The CCT increased significantly from a preoperative value of 529.8 μm ± 11.7 (SD) to a postoperative value at year one of 553 ± 15.5 μm (P = 0.02), or by 23.2 μm. Mean IOP also increased by 2.6 mm Hg at year one. The change in CCT correlated with the change in IOP at 1 year (P = 0.01). In the 7 unilateral cases, CCT increased in the operated eyes but not the fellow eyes, and both eyes had similar CCT at baseline. This study adds to the literature re: CCT and intraocular pediatric surgery but raises additional questions regarding what the increase in CCT means? CCT is higher in eyes having had cataract surgery due to the surgery itself, not just because of an underlying abnormality in the formation of the anterior segment. Whether increased postoperative CCT means that postoperative IOP rise is actually artifactual remains unanswered.

14.GLACUCOMA

Pediatric glaucoma - surgical management
Regular Versus Releasable Sutures in Surgery for Primary Congenital Glaucoma


The purpose of this prospective study was to compare releasable and regular sutures in combined angle and filtering surgery for primary congenital glaucoma. Thirty-nine eyes of thirty-nine patients who had primary congenital glaucoma treated with combined trabeculotomy-trabeculectomy with mitomycin C and scleral flap closure with regular or releasable sutures were included in the study. Follow-up was 24 months. Success of an initial glaucoma surgical procedure was defined as an IOP that was less than the presenting IOP for each eye and less than 16 mm Hg under general anesthesia without any IOP-lowering medications or hypotony-related complications, lack of IOP-related progression of the disease, or worsening of the ocular biometric characteristics (corneal diameter, axial length, or cup/disc ratio) beyond the usual for the age group studied. The need for further surgical intervention classified that eye as a failed initial glaucoma surgical procedure and complications were noted. An attempt was made to correlate the timing of releasable suture removal to the final success. The initial glaucoma surgery was successful in 13 (65%) and 13 (68.4%) eyes in the regular suture and releasable suture groups, respectively. The mean IOP was 17.4 ± 7.3 and 16.0 ± 5.4 mm Hg \( (P = .84) \) preoperatively and 8.0 ± 9.7 and 5.8 ± 3.6 mm Hg \( (P = .40) \) at the end of follow-up in the regular suture and releasable suture groups, respectively. There was no statistically significant difference in the clinical parameters between the two groups. Complications included rhegmatogenous retinal detachment, cataract, and superior lens subluxation, with each complication developing in one eye. The authors concluded that the use of releasable sutures was not more advantageous than the use of regular sutures in combined trabeculotomy-trabeculectomy with mitomycin C surgery for primary congenital glaucoma. The study has limitations: A relatively small number of eyes was included. The study used a combined angle and filtering surgery rather than a filtering surgery alone, thereby not clearly isolating the effect of the filtering surgery from the possible contribution of angle surgery. An additional limitation was the use of releasable sutures. The presence of a corneal limb and an exposed, although short, segment might pose the risk of exposure of the corneal limb and its extrusion from its corneal tunnel with eye rubbing, which could lead to possible infection, although no such events occurred in the study eyes. The set plan of postoperative follow-up is another limitation. Scheduling the first examination under anesthesia 1 month after surgery and relying solely on office examination and the parents’ report of any recurrence of preoperative symptoms during this period raises the possibility of an undetected rise in IOP that might have been managed by suture removal earlier than the next scheduled follow-up visit. Future studies are needed to evaluate releasable sutures for other types of childhood glaucomas.
Early Trabeculotomy Ab Externo in Treatment of Sturge-Weber Syndrome

Sturge-Weber Syndrome (SWS) is a sporadic and rare neurocutaneous disorder of capillary venous malformations causing glaucoma in up to 70% of patients. This is a retrospective cohort study evaluating the intermediate term efficacy and safety of trabeculotomy in congenital glaucoma in infants with SWS. The authors looked at 34 eyes of 32 patients with SWS induced glaucoma under 12 months who had trabeculotomy over a 6-year period. They evaluated baseline demographics as well as IOP and medication usage at last follow up. The patients had a median age of 3 months at the time of surgery and a median follow up time of 15 months. Surgical success was defined as complete if the IOP was less than 18 without deterioration of the nerve or the cornea without any medication or re-operation. Qualified success was defined as needing medical management to control IOP (<18) and stable nerve and cornea or IOP 18-20 without anti glaucoma medications. Overall success was either qualified or complete success. At time of last follow up, the overall success was 86.6% and complete success was 66.0% using the Kaplan-Meier method. Patients were on an average of 0.6 topical IOP lowering medications. Higher preoperative IOP and cornea edema were associated with surgical failure. Complications of surgery included transient shallow anterior chamber and hyphema. Compared to previous reports of glaucoma surgery for early onset glaucoma in patients with SWS this study had better results and the authors attribute this to earlier diagnosis due to improved surveillance in this patient population.

Circumferential Trabeculotomy Versus Conventional Angle Surgery: Comparing Long-term Surgical Success and Clinical Outcomes in Children With Primary Congenital Glaucoma

Circumferential trabeculotomy has been compared to conventional goniotomy and trabeculotomy for congenital glaucoma but only in short term studies; no long term outcomes have been evaluated. Thus the goal of this study was to look at the long term (more than 2 years follow up) success of circumferential trabeculotomy compared to conventional angle surgery. This was a retrospective observational case series of 58 eyes of 33 children followed for more than 2 years at a single academic tertiary care center. The authors defined surgical success as IOP less than 22 mmHg with or without glaucoma medications, without glaucoma progression, and without additional surgery. The authors found that circumferential trabeculotomy (illuminated microcatheter) had a success of 81% vs. 31% in those with conventional angle surgery (p<0.0001). Patients with circumferential trabeculotomy also had a better visual acuity, were on fewer IOP lower medications, and had comparable incidence of complications than the traditional angle surgery patients. One of the limitations of the study not highlighted by the authors was referral bias – more patients with the conventional surgery
were referred in and could have had a more severe, more difficult to treat glaucoma than those not referred to the academic medical center.

**Outcomes of Ahmed Glaucoma Valve Revision in Pediatric Glaucoma**

Glaucoma drainage devices for pediatric glaucoma are often used in pediatric glaucoma after failure of angle surgery. The success of Ahmed glaucoma valve implantation (AGVI) is lower in children than in their adult counterparts and this seems related to the development of a fibrotic encapsulation around the device. In adults, there are reports of revision of the AGVI but none in children. This was a retrospective cross-sectional study of 44 eyes with pediatric glaucoma who underwent AGV revision with a minimal follow up of 6 months. The main outcome was reduction of intraocular pressure from baseline and complete success was IOP 21 or less without medication. Qualified success was defined as IOP 21 or less with medications. During surgery the patients had excision of the fibrotic capsule that had formed around the plate. The authors found great short term success (100% at 1 month) but a rapidly decreasing rate of complete success - 38.6% at 6 months, 27.7% at one year, and 5.5% at 2 years after AGV revision. Qualified success was also low at 2 years (16%). There were few complications from the surgery. The authors concluded that while this procedure (AGVI) is relatively safe, that comparable studies in adults suggest that a second drainage device may have better success than AGVI.

**Safety and efficacy of a low-cost glaucoma drainage device for refractory childhood glaucoma**

Glaucoma drainage devices (GDD) have been shown to helpful in the treatment of refractory childhood glaucoma. In India, there is a high prevalence of childhood glaucoma cases that could benefit from a GDD, but the current options (Ahmed, Baerveldt) are too expensive for many patients. This study reports preliminary results of the Aurolab aqueous drainage implant (AADI), a low cost (US $50) non-valved implant with a similar plate area to the Baerveldt. This was a prospective, non-comparative interventional case series. 34 eyes (31 children) were included, at a mean age of 8.2 years. 19 eyes had primary congenital glaucoma and 15 had secondary glaucoma. Average follow-up was 18.3 months. Results showed a mean reduction of IOP from 27.4mm Hg to 12.8mm Hg at 1 year and 14.7mm Hg at 2 years. Mean number of topical medications decreased from 3.1 to 1.6 at 2 years. There were no reports of tube erosion or infection. In summary the AADI appeared to be effective with a similar safety profile to the other devices, and is a viable low-cost option.
Safety and efficacy of collagen matrix implantation in infantile glaucoma.

This preliminary retrospective case series evaluated the safety and efficacy of biodegradable collagen matrix implant (Ologen) designed to improve outcome in patients with infantile glaucoma undergoing combined trabeculotomy and trabeculectomy. A biodegradable collagen matrix (OculusGen) was placed in the subconjunctival space, partially over the scleral flap and the sclera in 20 eyes of 11 patients (mean age 5.7 +/- 5.69 months) with infantile glaucoma who underwent combined trabeculotomy and trabeculectomy. This theoretically, decreases scar formation and improves surgical success over trabeculectomy performed without the adjunctive antifibrotic agents. Excluded from the study were patients with previous glaucoma surgery. Patients were examined preoperatively and on the first postoperative day with multiple postoperative follow-up visits within 12 months after surgery. Mean duration of follow-up was 10.05 +/- 1.15 months (range 6-12 months). Examination included measurements of intraocular pressure (IOP), corneal diameter, and axial length, bleb evaluation, and funduscopy. Ultrasound biomicroscopy of bleb (bleb presence, wall reflectivity, and scleral route visibility) was done at 1, 3, and 6 months and the last follow-up visit. Any complication was recorded. Success was defined as IOP less than 21 mm Hg with stabilization of the ocular parameters including the corneal diameter and cup/disc ratio and without any vision-threatening complications. A statistically significant reduction in IOP and IOP-lowering medications was noted (mean preoperative IOP was 25.9 +/- 3.08 mm Hg compared to 17.7 +/- 3.51 mm Hg on last follow-up visit with 1.75 +/- 0.55 IOP-lowering medications pre-operatively verses 0.55 +/- 0.69 IOP-lowering medications). Overall success at last follow-up was 80%. None of the patients experienced systemic or ocular complication related to OculusGen. By the 6th month, complete Ologen degradation was evident in all cases. The authors conclude that the combined trabeculotomy and trabeculectomy with Ologen implantation could potentially provide a safe and effective procedure for infantile glaucoma patients, but emphasize that a longer duration of follow-up is required with a larger number of patients. This is an interesting approach that may prove to be safer than adjunctive antimetabolites. However there are some limitations to this series, including: small sample size, short follow-up, and the lack of a control group. It is not clear why angle surgery alone was not performed prior to combining trabeculotomy with trabeculectomy.

Combined vitrectomy and glaucoma drainage device implantation surgical approach for complex pediatric glaucomas.
Ozgonul, C., Besirli, C. G. and Bohnsack, B. L. JAAPOS Apr 2017; 21(2): 121-126.
The purpose of this retrospective case series was to evaluate efficacy of combined vitrectomy with posteriorly placed glaucoma drainage device (GDD) in lowering intraocular pressure (IOP) in children. The medical records of 20 children who underwent vitrectomy with posteriorly placed GDD were reviewed retrospectively. Patients with a minimum of 6 months’ follow-up were included. The first eye operated on for each patient was analyzed. Success was defined as IOP of 5-20 mm Hg and no additional IOP-lowering surgery or visually devastating complications. The following etiologies were included: primary infantile-onset glaucoma, 5 (25%); traumatic glaucoma, 3 (15%); Peters’ anomaly, 3 (15%); microphthalmia, 5 (25%); glaucoma following cataract surgery, 2 (10%); microspherophakia, 1 (5%); and retinopathy of prematurity, 1 (5%). Eyes with corneal opacification (8 [40%]) underwent endoscopic vitrectomy (5 [25%]), concurrent penetrating keratoplasty (3 [15%]) and/or keratoprosthesis surgery (1 [5%]). Mean follow-up was 1.9 ±1.1 years (range, 6.5-49.2 months). Vision remained stable or improved in 17 eyes (85%). Mean IOP decreased from 27.2 ± 10.1 mm Hg to 14.5 ± 6.8 mm Hg (P < 0.0001) at last follow-up or at failure. Kaplan-Meier curves showed 12- and 24-month rate of IOP control of 69% and 62%, respectively. The number of glaucoma medications decreased from a mean of 2.3 ± 1.4 to 1.3 ± 1.2 (P < 0.015) at last follow-up or at failure. Overall success rate was 65%. Complications included hypotony (3 [15%]), vitreous hemorrhage (1 [5%]), and retinal detachment (1 [5%]). Two eyes (10%) required surgery for hypotony; 4 eyes (20%) underwent additional glaucoma surgery. The authors conclude that combined surgical approach with vitrectomy and posteriorly placed GDD decreased IOP in complex pediatric glaucomas. Further, endoscope-assisted vitrectomy is useful in cases with corneal opacification. The authors state that the complication rates of this combined procedure appear to be comparable to traditional anterior chamber approach. Main limitation of this study is that it did not include a group of patients, who had GDD implanted in the usual anterior chamber approach.

**Randomized Trial on Illuminated-Microcatheter Circumferential Trabeculotomy Versus Conventional Trabeculotomy in Congenital Glaucoma.**

Traditionally primary congenital glaucoma has been treated by goniotomy or trabeculomtomy. In conventional partial trabeculotomy (CPT) approximately one third of the angle is opened. A newer, illuminated microcatheter has recently been introduced as a safer way to perform a 360-degree opening of the angle without the risk of catheter misdirection. Comparison between CPT and microcatheter-assisted circumferential trabeculotomy (IMCT) is limited to a few non randomized trials. The purpose of this study was to compared the 1 year outcomes in patients who had CPT and those who had IMCT. This was a randomized clinical trial of 40 eyes in 31 patients ages 2 and under with unilateral or bilateral primary congenital glaucoma. The primary outcome was the reduction in
intraocular pressure (IOP). Success was defined as IOP $\leq 12$ mmHg with or without IOP lowering medications. The mean age in the study population was 8.3 months and the mean preoperative IOP was slightly over 24 in each group. The authors compared the IOP, corneal clarity, corneal diameters, vertical cup to disc ratio and refractive errors in the two group. 80% of the patients in the IMCT group were able to have the 360degree cannulation. The overall success rates were 80% in the IMCT group and 60% in the CPT group and this was statistically significant. Both groups had a statistically significant reduction in IOP but the eyes in the IMCT group had a lower IOP at 12 months than those eyes that had CPT. Additionally, the IMCT group had lower eye pressures at 3 and 6 months post op and were less likely to need reoperation. The difference in success rates for IMCT vs. CPT was most pronounced in patients under 6 months old. The most significant complication in the IMCT group was hyphema which occurred in 90% of cases, this was much higher than the rate of hyphema in the CPT group, all patients had hyphema resolve without needing surgical intervention. The authors point out the small sample size and 1 year follow up as limitations of their study and suggest that a multi center trial would be well suited for studying this further. Additionally they point out that the technology for the IMCT technique is unlikely available in certain parts of the world due to the learning curve and the cost of the device. The authors concluded that in primary congenital glaucoma IMCT performed better than CPT at 1 year after follow up.


The purpose of this retrospective review was to evaluate longer term (6 months or longer) outcomes in patients who had an illuminated microcatheter-assisted 360-degree trabeculotomy for medically refractory juvenile open angle glaucoma (JOAG) or glaucoma following cataract surgery (GFCS). The authors studied 35 eyes, 10 with JOAG and 25 with GFCS who had surgery between 2008 and 2015. They defined success as IOP $\leq 22$mmHg or IOP reduction $< 20\%$ from baseline with or without glaucoma medications. The mean age at surgery was 5.6 years in the GFCS group and 16.7 years in the JOAG group. Success in the GFCS group was achieved in 18/25 eyes (72%) with a mean follow up of 32 ± 26 months. In the JOAG group, 6/10 eyes achieved success at a mean of 24 ± 20 months. The authors concluded that this technique was modestly successful for medically refractory JFCS and JOAG. This study was not designed to compare this technique to standard trabeculotomy or goniotomy and cannot determine the clock hours needed to treat these types of glaucoma. Additionally the authors point out another limitation of this study, which was small sample size. They concluded that illuminated microcatheter-assisted 360 degree trabeculotomy is a reasonable low-risk option for patients with GFCS or JOAG.

Pediatric glaucoma: review of recent literature
The authors discuss different diagnostic and management options through a review of recent literature. IOP measurements do not have a gold standard technique but the advent of the iCare has greater tolerability in children. A retrospective review comparing various techniques for obtaining IOP measurement in children found that the greatest success was with non-contact tonometry, followed by rebound and Goldmann applanation. IOP measured by iCare may trend higher than other techniques. IATS recently released their 5-year data regarding glaucoma related adverse events and found that the risk of developing glaucoma in unilateral cataract surgery with or without IOL placement was similar between the groups. Visual acuity was also not statistically different between the patients who developed glaucoma than those without. 360 degree vs. traditional trabeculotomy was compared in a study finding that the 360 degree group had better surgical success requiring fewer sequential surgeries in the first year, although the number of medications used in both groups was similar. Trabeculectomy with mitomycin-c was found to have a low complication rate and was well tolerated with 78% success rate at 1 year and 67% and 60% at 5 and 7 years respectively. A study looking at trabeculectomy with tenonectomy found that there may be a benefit with less medication use and failures but after multivariate analysis only the number of glaucoma surgeries was a risk factor associated with failure. A look at glaucoma drainage devices found that they enjoyed a high success rate of 87% at 1 year and 55% at 5 years. Patients with uveitis had a 5-year success of 75%. Multivariate analysis found that only the type of drainage device was a risk factor for failure with the S-2 Ahmed being more favorable than the FP-7 model.

In conclusion, the iCare has been and will continue to be an important tool for management of glaucoma. IATS shows that the risk of glaucoma at 5 years is similar in patients with IOLs vs aphakia in unilateral pediatric cataract. Glaucoma surgery continues to be a mainstay of therapy in the management of pediatric glaucoma.

Comparison of 360 degrees circumferential trabeculotomy and conventional trabeculotomy in Primary Pediatric Glaucoma surgery: Part 1
Christiana Celea, Serban Dragosloveanu, Mihai Pop, Christian Celea.

In this retrospective chart review, 79 eyes were operated and thirty-eight( n1=38) received traditional trabeculotomy (conventional group) whereas the other forty one(n2=41) received a 360 degrees circumferential trabeculotomy with a 40-gauge red-light-guided catheter( circumferential group). The post-operative exams were performed under sedation at 10 days, 1month, 6 months and 2 year
post-operatively and included intraocular pressures (IOP), corneal diameter, axial length and posterior and anterior segment exams. At 2 years postoperatively, the IOPs tended to slowly elevate in both groups with values in the circumferential group being statistically significantly lower than the conventional group. In terms of corneal diameters, there were statistically significant differences between the two groups and greater decrease in the circumferential group. Axial lengths were not influenced in either group. In the circumferential group, the surgery could not be completed in 7.1% of the case due to anatomic difficulties, and these cases were considered as procedure failures, which means that a conversion to traditional trabeculotomy can be indicated sometimes. The authors conclude that conventional trabeculotomy should be the first choice procedure in the surgical management of pediatric glaucoma.

**Pediatric glaucoma – corneal biometry, OCT and visual field**

**Comparison of Quality and Output of Different Optimal Perimetric Testing Approaches in Children with Glaucoma**

This study compared static and combined static/kinetic perimetry in visual field testing in children with glaucoma between 5/2013 through 6/2015 at two hospitals in London. The study included 65 children, ages 5 to 15 years with glaucoma (108 affected eyes). Results indicated a median age of 12 years, with 50.8% girls were tested. Of note, testing reliability improved with increasing age for both Humphrey and Octopus perimetry, with equivalence in children older than 10 years but better quality of testing with Humphrey perimetry achieved in younger children. Of the 7 severe cases of visual field loss, 5 had lower kinetic than static classification scores. In summary, a static perimetry test yields high-quality results in children younger than 10 years. The authors note that for children older than 10 years, the addition of kinetic perimetry allowed for the measurement of far peripheral sensitivity, which is important in children with severe visual field restriction associated with glaucoma.

**Pediatric glaucoma – other topics**

**Preliminary Study of Differences in Optic Nerve Head Hemoglobin Measures between patients with and without childhood glaucoma.**
The purpose of this study is to evaluate the effectiveness of quantifying color changes in the optic nerve head in fundus photographs of patients with childhood glaucoma. Three photographs of the optic nerve head were obtained in 28 patients with childhood glaucoma and 28 age- and sex-matched healthy participants (the childhood glaucoma and control groups, respectively). The Laguna Optic Nerve Head Hemoglobin (ONhE) software (Insoft SL, Tenerife, Spain) was used to determine hemoglobin levels in the optic nerve head. The following parameters were quantified: the hemoglobin levels in the optic nerve head across the whole disc, in 24 sectors (the optic nerve head divided by two concentric rings and eight 45-degree radial sectors), and in the vertical disc diameter (sectors 8 and 20), and the estimated cup–disc ratio and Glaucoma Discriminant Function, which combines the slope of the hemoglobin amount with the mean vertical disc diameter. Patient ages ranged from 9 to 14 years (median: 11 years) in the childhood glaucoma group, and 7 to 13 years (median: 9 years) in the control group ($P < .061$). Eyes in the childhood glaucoma group showed a significantly higher cup–disc ratio compared to eyes in the control group ($0.6 \pm 0.2$ vs $0.5 \pm 0.1$, respectively; $P < .0001$). In the childhood glaucoma group, the Glaucoma Discriminant Function was found to be significantly lower than in the control group ($-6.5 \pm 31.1$ vs $9.4 \pm 17.1$, respectively; $P < .0001$). There were no significant differences in the hemoglobin levels in the optic nerve head across the whole disc between eyes in the childhood glaucoma and control groups ($58.2\% \pm 10.9\%$ vs $58.5\% \pm 6.7\%$, respectively; $P = .847$). The Laguna ONhE software showed good reproducibility in measuring percentages of hemoglobin levels in both groups.

**Correlation of echographic and photographic assessment of optic nerve head cupping in children.**

Media opacities may preclude adequate optic nerve head (ONH) evaluation by direct visualization as well as by optical imaging modalities. The purpose of this retrospective study was to determine the diagnostic value of B-scan echography in ONH cupping estimation in children. The medical records of pediatric patients who had previously undergone examination under anesthesia and for whom both adequate B-scan echography images and optic nerve head (ONH) photographs and were available were reviewed retrospectively. The cup: disk ratio was estimated with a grading scale of 0-1.0 and rounded to the nearest tenth; degree of cupping was estimated from B-scan echography (small, medium, or large) by 5 masked graders (3 glaucoma specialists and 2 ophthalmic sonographers) on 2 separate occasions. Inter- and intraobserver agreement in echographic and photographic cupping assessment by the masked graders as well as correlation of echographic and photographic cup size estimation was evaluated. A total of 36 children were included. Glaucoma specialists reliably assessed cup: disk ratio with moderately good consistency across specialists (average intra-
class correlation coefficient [ICC] for intraobserver agreement, 0.86; average ICC for interobserver agreement, 0.71). Sonographers were extremely reliable in assessment of cup size when examining echographic images (ICC for both inter- and intraobserver variability, 1.0). However, the echographic estimate of cup size correlated poorly with cup: disk ratio (ICC, 0.34). The authors conclude that B-scan echography is a reliable and consistent diagnostic tool in estimating the degree of ONH cupping in children and can be very useful in patients in whom direct visualization is not feasible. Failure to account for disk size may have contributed to the poor correlation between echographic cup size and photographic cup: disk ratio. The authors advocate that glaucoma specialists should train on the analysis of B-scan ultrasonography with regards to ONH cup size estimation using representative images. Despite the author's conclusion, the discrepancy between the echographic cup size and photographic cup: disk ratio and the presented images were not entirely convincing that this modality is reliable.

A 3-month safety and efficacy study of travoprost 0.004% ophthalmic solution compared with timolol in pediatric patients with glaucoma or ocular hypertension.

The objective of this prospective randomized, double-masked controlled study was to evaluate efficacy and safety of travoprost in pediatric patients with ocular hypertension or glaucoma and demonstrate its non-inferiority to timolol. Patients aged 2 months to <18 years with glaucoma or ocular hypertension were randomized to receive travoprost (0.004%) or timolol eye drops (0.25% for patients aged 2 months to <3 years and 0.5% for patients ≥3 years old) for 3 months. Intraocular pressure (IOP) was measured and patients were evaluated at 2 weeks, 6 weeks, and 3 months after treatment. Change in IOP from baseline to 3 months was the primary endpoint. Of 157 patients included (mean age, 9.6 years), 77 received travoprost and 75 timolol. All patients experienced a significant reduction in IOP in the study eye at 3 months: the mean IOP change from baseline was -5.4 mm Hg for travoprost; -5.3 mm Hg, for timolol. The mean difference between travoprost and timolol at month 3 was -0.1 mm Hg (95% CI, -1.5 to 1.4 mm Hg). The most common treatment-related adverse events for the travoprost group were ocular hyperemia and eyelash growth. No serious adverse events were reported. The authors conclude that travoprost is non-inferior to timolol in lowering IOP in patients with pediatric glaucoma or ocular hypertension. Trarvoprost was well-tolerated, and no treatment-related systemic adverse events were reported. The authors acknowledge some potential limitations of the current study including, the relatively short treatment duration (3 months), and the small number of patients under the age of 3 (16 patients). However, since there is limited data available on the use
of common IOP-lowering agents in pediatric patients. This well-designed study reinforces the safety and efficacy of travoprost in children.

**Long-term visual outcomes in children with primary congenital glaucoma**


The author did a retrospective study to determine the long-term visual outcomes and risk factors for visual loss in children with primary congenital glaucoma who underwent trabeculotomy, trabeculectomy, or combined trabeculotomy-trabeculectomy over a 21-year period. She found that the mean logMAR VA was 0.61 (about 20/80). VA of 20/50 or better was attained in 51% and less than 20/200 in 19%. Deprivation amblyopia was present in 64% of those with VA worse than 20/50, and was associated with corneal opacification and anisometropia. The mean spherical equivalent of refraction was -4.47 D. A high myopic shift was more frequent in those with VA less than 20/50. The author concludes that a favorable VA outcome was achieved in most patients. These findings are consistent with those of other studies.

**Ciliary body location in eyes with and without primary congenital glaucoma**


The position of the ciliary body (CB) may change in children as a result of primary congenital glaucoma and globe enlargement. The location of the CB is important in certain surgical procedures such as trans-scleral laser cyclophotoagulation. This cross-sectional study was designed to compare the location of the CB in children with and without congenital glaucoma. 15 glaucoma eyes and 15 control eyes were studied. The distance of the CB from the corneoscleral limbus was measured with calipers after identifying the anterior edge of the CB with a trans-illuminator. The mean difference between the 2 groups was 0.33mm. There was greater variability in the distance among different quadrants in the glaucoma eyes. The distance did show a significant correlation with axial length, corneal thickness, and corneal diameter in the glaucoma group. Overall the study showed that the anterior edge of the CB in glaucoma patients was farther from the limbus compared to control eyes, and this information could be helpful when planning cilio-destructive procedures in these patients.

**Epiblepharon in congenital glaucoma: case-control study**

Epiblepharon is a congenital anomaly where a fold of skin tilts the lashes causing them to rub against the eye. This may cause keratopathy and astigmatism, and surgery may be necessary. According to the authors, they have noticed children with congenital glaucoma also present with lower lid epiblepharon, often requiring surgery. Therefore, they performed a case-control observational study of congenital glaucoma cases and age-matched controls to find the prevalence and risk factors of epiblepharon among children with congenital glaucoma. The authors found a higher prevalence of lower lid epiblepharon in these children compared to the control group (40.7% vs 13.3%). Associated factors included high IOP at glaucoma diagnosis, presence of cornea erosion, and presence of buphthalmos. Also, unilateral epiblepharon was associated with unilateral glaucoma and buphthalmos. Severe corneal erosions in epiblepharon was more frequent in those with congenital glaucoma. Despite a possible selection bias, the authors conclude that patients with congenital glaucoma should be evaluated for epiblepharon, especially in unilateral cases.

Shantha Balekudaru, Nandhini Sankaranarayanan, Sumita Agarkar

In this retrospective analysis, 91 patients (180 eyes) with the diagnosis of aniridia were identified. The prevalence of glaucoma at presentation was 28.8%, which could be further categorized as ocular hypertension in 19 eyes (10.5%) and glaucoma in 33 eyes (18.3%). Thirty-one eyes (28.4%) developed elevated intraocular pressure (IOP) during the follow-up period: ocular hypertension in 23 eyes (17.9%) and glaucoma in 8 eyes (6.25%). The mean IOP at the time of diagnosis was 33.9 ± 8.6 mm Hg (range: 24 to 60 mm Hg). The mean duration of follow-up was 8.1 ± 5.7 years (range: 1 to 28 years). The cumulative probability of developing elevated IOP was 4% at the end of 8 years of follow-up; this increased to 88% at the end of 28 years of follow-up. Univariate logistic regression analysis identified higher baseline IOP (odds ratio [OR]: 1.2; 95% confidence interval [CI]: 1.2 to 1.4) and limbal stem cell deficiency (OR: 2.8; 95% CI: 1.4 to 5.6) as significant risk factors for the development of elevated IOP. Higher baseline IOP remained significant on multivariate analysis (OR: 1.2; 95% CI: 1.2 to 1.4). The authors conclude that glaucoma is a common complication in eyes with congenital aniridia. Higher baseline IOP appeared to be a significant risk factor for the development of glaucoma. Although increased CCT is common in this population and can confound the measurement of IOP, glaucoma was also seen to occur in eyes with increased corneal thickness. This study has several limitations: its retrospective design as well as the fact that serial gonioscopy was not performed therefore the role of progressive angle closure could not be ascertained. Also, optic disck evaluation was not possible to perform in 10% of the patients, and this could lead to underestimation of the incidence of glaucoma. However, this study has a mean follow-up period of at least 8 years.
Ultrasound biomicroscopy measurement of Schlemm's canal in pediatric patients with and without glaucoma.

The purpose of this observational study was to compare the diameter of Schlemm's canal in children with and without congenital glaucoma using ultrasound biomicroscopy. An 80 MHz iUltrasound probe (iScience Interventional Inc, Menlo Park, CA) placed near the limbus was used to identify and measure the canal's diameter with special attention to the anterior segment anatomy (especially in subjects with congenital glaucoma). A total of 20 subjects were included. Mean age of subjects without glaucoma was 6.6 ± 6.65 years; of those with glaucoma, 9.4 ± 11.80 months. The mean canal diameter in nonglaucomatous eyes was 142 ± 33.2 µm (range, 90-196 µm); in glaucomatous eyes, 64.9 ± 10.90 µm (P = 0.007). Schlemm's canal could not be identified in 50% of patients with congenital glaucoma. There was a trend toward smaller canal diameter in subjects with no glaucoma <2 years old. Mean canal diameter in nonglaucomatous eyes was 103 ± 8 µm (range, 90-115 µm) in subjects <2 years of age and 161 ± 20 µm (range, 110-196 µm) in subjects >2 years of age (P = 0.0012). The authors conclude that in their cohort of pediatric patients the diameter of Schlemm's canal varied by age and presence of glaucoma.

The current study has several limitations, including its small sample size and the fact that it was not masked. What makes it difficult to interpret is the fact that the glaucomatous patients were much younger than the healthy controls. In addition, refractive error, IOP, and axial length may affect the size of Schlemm's canal independent of age and these were not taken into account.

15. REFRACTIVE SURGERY

Phakic Intraocular Collamer Lens (Visian ICL) Implantation for Correction of Myopia in Spectacle-Averse Special Needs Children.

Many pediatric ophthalmologists and parents struggle with the challenge of correcting large magnitude ametropia in patients with neurodevelopmental disorders who are spectacle adverse. Some of these patients are also not able to wear contact lenses and they suffer due to uncorrected refractive error. Clear lens exchange and excimer laser are also options in these patients, but come with a loss accommodation, and refractive regression and corneal haze, respectively. The purpose of this study was to prospectively look at 40 eyes of 23 children who had the phakic intraocular collamer lens placed (Visian ICL) for moderate to high my-
opía. The mean age of the patients was 10.2 ± 5.3 years (range 1.8-17 years). All patients were placed under general anesthesia and the details of the surgical technique are described in the manuscript. The authors’ goal refraction was plano to +1 in all patients and they achieved this goal in 35 eyes (88%). Visual acuity was measured by a variety of methods and converted to Snellen acuity. The authors found an improvement in visual acuity of 2.2 fold in those who cooperated for visual acuity testing both before and after surgery. There were few complications with two patients having pupillary block before the authors changed their surgical technique and then no complications recorded after that, though the authors due note a short follow up time of 1 year or more. The visual acuity gains in these patients were comparable to those who received laser or lensectomy, but again with fewer untoward affects. The authors acknowledge that longer term complications may arise and they conclude that the Visian ICL is efficacious and reasonably safe method for treating myopia in special needs children who are spectacle non compliant.

**Visual outcomes of laser vision correction in eyes with preoperative amblyopia.**

This study evaluated the visual outcomes of photorefractive keratectomy (PRK) and laser in situ keratomileusis (LASIK) in adult amblyopic eyes. 327 amblyopic eyes of 327 patients with a preoperative corrected distance visual acuity (CDVA) of 20/33 or worse had PRK or LASIK. The corrected distance visual acuity (CDVA) improved more than 1, 2, and 3 Snellen lines in 147 eyes (45.0%), 75 eyes (22.9%), and 32 eyes (9.8%), respectively. The outcome in eyes with lower myopia was significantly better than in eyes with hyperopia (0.054 logMAR difference; *P* = .016) or high myopia (0.036 logMAR difference; *P* = 0.002). Moderately amblyopic eyes had significantly better visual outcomes than mildly amblyopic eyes (0.038 logMAR difference; *P* = 0.001). No significant difference was found between PRK and LASIK (*P* = 0.26). This study reports that laser vision correction might improve CDVA in a large portion of adult amblyopic patients. However, this study did not include a robust definition of amblyopia. Merely having BCVA of 20/33 or worse and a normal slit lamp exam (note no mention of normal fundus exam, and no mention of presence of amblyogenic risk factor) qualified as amblyopia.

**Pediatric Refractive Surgery**
Erin D. Stahl *Curr Opin Ophthalmol* July 2017;28:305-309

The author embarks on a review of pediatric refractive surgery Poor patient cooperation requiring sedation post-op eye rubbing and the use of relatively immobile equipment make hospital based procedures not readily available. Long term corneal changes due to increased inflammatory response in children leading to
haze and the continued growth of the eye leading to possible corneal thinning and refractive error shift are mentioned. Many patients to be considered for laser procedures have high refractive errors that exceed the abilities of the equipment. Patients younger than 18 must undergo special informed consent for both laser and phakic IOL (pIOL) placement with notification of off-label use. The indications for the procedure are most commonly anisometropic amblyopia, high ametropia, and refractive accommodative ET and in children with neurobehavioral issues that may not tolerate traditional therapy. LASEK and PRK have no flap and increased corneal stability but greater discomfort and healing time and LASIK has the converse. Lensectomy, pIOL, and refractive lens exchange have improved optics over spectacles, and correct very high refractive errors but the disadvantages of intraocular surgery and possible endothelial cell loss (ECL), UGH syndrome and cataract formation. The author reviews the published literature and highlights that in the studies done on laser procedures most had improved vision, stereo, and refractive correction. In those for ET, patients were ortho with low residual refractive errors. There are 7 published studies on pIOLs and endothelial cell loss was the most common complication as well as pupillary block and pigment dispersion. No lenses had to be removed.

For the future, a large study for long term safety and efficacy of refractive surgery vs traditional amblyopia therapy when used shortly after diagnosis is needed. Also, long term effects of pIOLs on ECL, cataract formation, IOP and change in lens position over time.

In summary, the author reviews refractive surgery considerations, indications for the procedure and the current literature which are all case series to highlight the need for a conscientious look at long and short term benefits of these procedures balanced with treating amblyopia for best results and avoiding potentially vision threatening complications for the patients.

V4B implantable collamer lens versus Intacs corneal rings to manage anisometropic myopic amblyopia in children

Anisometropic amblyopia is a common cause of monocular vision loss in children, and conventional treatment may fail in a significant portion of these patients. Refractive surgery is an option for children who fail conventional treatments, and includes refractive lens exchange and phakic intraocular lenses. Intacs are intra-stromal corneal rings that flatten the cornea and are used to correct myopia as well as ectasia. This study compared the efficacy and safety of phakic intraocular lens implantation (the V4B implantable collamer lens) to Intacs for correcting high myopia anisometropia in amblyopic children. The authors conducted a prospective, non-randomized study of 30 children in Saudia Arabia and Kuwait. The patients were grouped according to myopic error, with patients having >= -9.00 receiving the phakic intraocular lens (Group A) and those with less than -9.00 myopia receiving Intacs (group B). Post-operative patching of the fellow eye was recommended to patients. Mean spherical equivalent for group A
improved from -12.96D to -0.32D, and for group B from -8.60D to -5.12D. 77% of children in group A gained 4-6 lines of vision (with mean improvement of pre-op 1.08 to post-op 0.61 logMAR), and 70% of group B gained 4-6 lines (mean improvement pre-op 0.76 to post-op 0.60 logMAR. Stereoacuity improved in 93% in group A and 87% in group B. There was a significant decrease in endothelial cell count in the lens group at 9-months follow-up, but not in the Intacs group. However the loss was only 1.47% in endothelial cell count. There were no complications noted with the Intacs. With the lens group there were 2 cataracts, 1 case of glaucoma, and 1 case of uveitis. Overall, the study found that both methods were effective in correction of refractive error and improvement of vision. Intacs was found to have fewer complications without endothelial cell loss, but the correction of myopia error was smaller. The phakic intraocular lens corrects a larger range of myopia (up to -18D). Further studies with longer follow-up and randomized data are warranted.

16. GENETICS

Gene Therapy for Leber Hereditary Optic Neuropathy: Low- and Medium-Dose Visual Results.

Leber’s hereditary optic neuropathy (LHON) was first associated with a G-to-A transition at nt-11778 in the ND4 subunit gene of complex I of mitochondrial DNA. The authors recoded the ND4 subunit of complex I in the universal genetic code and imported it into mitochondrion from the cytoplasm by adding a targeting sequence (from P1 isoform of subunit c of ATP synthase). This combined sequence is referred as P1ND4v2. This was inserted into a self-complementary adeno-associated vector scAAV2(Y444, 500, 730F). This is a report on safety of their long-term follow-up of LHON patients who were treated with low and medium doses of this vector, AAV2(Y444,500,730F)-P1ND4v2. Fourteen patients with visual loss and mutated G11778A mitochondrial DNA were enrolled and received the injection of the vector to one eye. Six participants with chronic bilateral visual loss lasting more than 12 months (group 1), 6 participants with bilateral visual loss lasting less than 12 months (group 2), and 2 participants with unilateral visual loss (group 3) were treated. Nine patients had at least 12 months of follow-up. Clinical testing included visual acuity, visual fields, optical coherence tomography, pattern electroretinography, and neuro-ophthalmic examinations. Generalized estimating equation methods were used for longitudinal analyses. The main outcome was visual acuity. For groups 1 and 2, month 12 average acuity improvements with treatment relative to baseline were 0.24 logMAR. Fellow eyes had a 0.09 logMAR improvement. A post hoc comparison found that at month 12, the difference between study eye minus fellow eye improvement in group 2 patients of 0.53 logMAR was greater than that observed in our prior acute natural history patients of 0.21 logMAR (P = 0.053). At month 18, the difference between study eye minus fellow eye improvement in the acute group 2
gene therapy patients of 0.96 was more than that observed in the prior acute natural history patients (0.17 logMAR; P < 0.001). Two patients demonstrated asymptomatic uveitis that resolved without treatment. Optical coherence tomography of treated eyes showed an average temporal retinal nerve fiber layer thickness of 54 μm before injection and 55 μm at month 12. For fellow eyes before injection, it was 56 μm, decreasing to 50 μm at month 12 (P = 0.013). Generalized estimating equations suggested that PERG amplitudes worsened more in treated eyes than in fellow eyes by approximately 0.05 μV (P = 0.009 exchangeable). No difference between eyes in outcomes of other visual function measures was evident. The authors concluded that 12 month follow-up of this allotropic gene therapy for LHON seems safe and does not damage the temporal retinal nerve fiber layer, opening the door next for testing of the high dose.

Clinically Focused Molecular Investigation of 1000 Consecutive Families with Inherited Retinal Disease.


Genetic testing has changed dramatically in recent years. As genetic tests have become larger in scope and sensitivity, the need for exceptionally detailed and accurate clinical information also has increased. Very broad investigations will result in multiple plausible disease-causing findings that will need to be winnowed to one on clinical grounds. The authors have devised a comprehensive multi-platform genetic testing strategy for inherited retinal diseases. This testing strategy includes using detailed clinical exams, imaging studies and electroretinography. Based on the results each patient was assigned to 1 of 62 diagnostic categories, described in detail in the study, and this clinical diagnosis was used to define the scope and order of the molecular investigations that were performed. The authors conducted a review of one thousand consecutive families seen by a single clinician (E.M.S) between January 2010 and June 2016 to determine the current overall sensitivity of this testing strategy. The number of nucleotides evaluated in a given subject ranged from 2 to nearly 900,000. The authors found that disease-causing genotypes were identified in 760 families (76%). These genotypes were distributed across 104 different genes. More than 75% of these 104 genes have coding sequences small enough to be packaged efficiently into an adeno-associated virus. Mutations in ABCA4 were the most common cause of disease in this cohort (173 families), whereas mutations in 80 genes caused disease in 5 or fewer families (i.e., 0.5% or less). Disease-causing genotypes were identified in 576 of the families without next-generation sequencing (NGS). This included 23 families with mutations in the repetitive region of RPGR exon 15 that would have been missed by NGS. Whole-exome sequencing of the remaining 424 families revealed mutations in an additional 182 families, and whole-genome sequencing of 4 of the remaining 242 families revealed 2 additional genotypes that were invisible by the other methods. Performing the testing in a clinically focused tiered fashion would be 6.1% more sensitive and 17.7% less expensive and would have a significantly
lower average false genotype rate than using whole-exome sequencing to assess more than 300 genes in all patients (7.1% vs. 128%; P < 0.001). Genetic testing for inherited retinal disease is now more than 75% sensitive. A clinically directed tiered testing strategy can increase sensitivity and improve statistical significance without increasing cost.


This report investigates CHN1 (chimerin 1) gene mutations in patients with isolated nonsyndromic Duane syndrome and accompanying positive familial history, bilaterality, or various systemic disorders. Patients with Duane retraction syndrome (DRS) and a positive family history of congenital ocular motility disturbance or bilateral involvement or accompanying any congenital disorder(s) seen consecutively at a single center from 2013 to 2016 were enrolled. All subjects underwent full ophthalmologic examination, including refraction, best-corrected visual acuity, ocular alignment and motility, globe retraction, and biomicroscopic or fundus evaluation. DNA samples were investigated by direct sequencing of the coding regions of the CHN1 gene. A total of 30 patients (15 males) were included (mean age, 11.8 ± 10.4 years; range, 2-45 years): 8 cases presented with bilateral DRS; 22, with unilateral DRS. Family history of ocular motility abnormality was positive in 16 patients. Eleven cases had an additional congenital disorder. In 2 patients, 2 different mutations were detected in the CHN1 gene: p.E313K (c.937G>A) and p.N224S (c.671A>G).

CHN1 mutations were identified in 2 bilateral cases and in 1 parent of 1 affected case. One novel mutation occurred with additional vertical gaze abnormalities. Additional genetic studies evaluating chimerin 1 (CHN1) and its role in the development of the ocular motor axis are needed to provide new data about these mutations and phenotypic variations.


Temporal macular involvement in sickle cell disease can now easily be detected by optical coherence tomography (OCT). However, while recent studies have demonstrated its high prevalence, little is known about its potential consequences on visual function. This study aims to assess the visual function of patients with sickle cell disease with no visual symptoms despite temporal macular atrophy. The design is a retrospective case series which included data collection and explorations made in a single referral center for sickle cell disease in 2016. Three
patients with sickle cell disease exhibiting preserved visual acuity but showing temporal macular retinal atrophy were included. Patients underwent the following explorations: best-corrected distance and near visual acuity evaluation; dilated fundus examination; OCT with 12 × 6-mm thickness map; horizontal, vertical, and en face sections; OCT angiography of the 6 × 6-mm perifoveal retina; 30° and 12° central visual fields; Lanthony 15-hue color vision test; automated static contrast sensitivity test; and global electroretinography. The OCT thickness maps were checked for areas of retinal thinning, appearing as blue patches. When present, these areas were compared with the areas of superficial and deep capillary flow loss on OCT angiography and with the scotomas on visual fields. Contrast sensitivity and color vision loss were quantified.

All 3 patients included had homozygous sickle cell disease. They presented with a 20/20 distance visual acuity, and Parinaud 1,5 near visual acuity in both eyes. They were all followed up for a severe cerebral vasculopathy related to sickle cell disease. The areas of atrophy involved the inner retinal layers and were associated with an absence of signal in the deep capillary plexuses in OCT angiography. These patches of retinal thinning were also matching with scotomas in the automated visual fields. Color vision ability and contrast sensitivity were impaired in all patients. Global electroretinography findings were normal. The authors conclude that temporal macular atrophy in sickle cell disease may have direct consequences on visual function, including in children, even when visual acuity is preserved. Optical coherence tomographic imaging may be warranted when evaluating patients with sickle cell disease, even if asymptomatic with 20/20 visual acuity.


Infantile nystagmus syndrome (INS) is a group of disorders presenting with genetic and clinical heterogeneities that have challenged the genetic and clinical diagnoses of INS. Precise molecular diagnosis in early infancy may result in more accurate genetic counseling and improved patient management. This study aims to assess the accuracy of genomic data from next-generation sequencing (NGS) and phenotypic data to enhance the definitive diagnosis of INS. A single-center retrospective case series was conducted in 48 unrelated, consecutive patients with INS, with or without associated ocular or systemic conditions, who underwent genetic testing between June 1, 2015, and January 31, 2017. Next-generation sequencing analysis was performed using a target panel that included 113 genes associated with INS (n = 47) or a TruSight One sequencing panel that included 4813 genes associated with known human phenotypes (n = 1). Variants were filtered and prioritized by in-depth clinical review, and finally classified according to the American College of Medical Genetics and Genomics guidelines. Patients underwent a detailed ophthalmic examination, including electroretinography and optical coherence tomography, if feasible.
Among the 48 patients (21 female and 27 male; mean [SD] age at genetic testing, 9.2 [10.3] years), 8 had a family history of nystagmus and 40 were simplex. All patients were of a single ethnicity (Korean). Genetic variants that were highly likely to be causative were identified in 28 of the 48 patients, corresponding to a molecular diagnostic yield of 58.3% (95% CI, 44.4%-72.2%). FRMD7, GPR143, and PAX6 mutations appeared to be the major genetic causes of familial INS. A total of 10 patients (21%) were reclassified to a different diagnosis based on results of NGS testing, enabling accurate clinical management. These findings suggest that NGS is an accurate diagnostic tool to differentiate causes of INS because diagnostic tests, such as electroretinography and optical coherence tomography, are not easily applicable in young infants. Accurate application of NGS using a standardized, stepwise, team-based approach in early childhood not only facilitated early molecular diagnosis but also led to improved personalized management in patients with INS.

**Gene Therapy for Leber Hereditary Optic Neuropathy: Low- and Medium-Dose Visual Results.**


This prospective open-label study investigates the unilateral single-dose, intravitreal injection of AAV2(Y444,500,730F)-P1ND4v2 per participant. Fourteen patients with visual loss and mutated G11778A mitochondrial DNA were included. One eye received intravitreal injection with the gene therapy vector AAV2(Y444,500,730F)-P1ND4v2. Six participants with chronic bilateral visual loss lasting more than 12 months (group 1), 6 participants with bilateral visual loss lasting less than 12 months (group 2), and 2 participants with unilateral visual loss (group 3) were treated. Nine patients had at least 12 months of follow-up. Clinical testing included visual acuity, visual fields, optical coherence tomography, pattern electroretinography, and neuro-ophthalmic examinations. Generalized estimating equation methods were used for longitudinal analyses with the main outcome measure being loss of visual acuity. For groups 1 and 2, month 12 average acuity improvements with treatment relative to baseline were 0.24 logarithm of the minimum angle of resolution (logMAR). Fellow eyes had a 0.09-logMAR improvement. A post hoc comparison found that at month 12, the difference between study eye minus fellow eye improvement in group 2 patients of 0.53 logMAR was greater than that observed in the authors’ previously reported acute natural history patients of 0.21 logMAR (P = 0.053). At month 18, the difference between study eye minus fellow eye improvement in our acute group 2 gene therapy patients of 0.96 was more than that observed in the prior acute natural history patients (0.17 logMAR; P < 0.001). Two patients demonstrated asymptomatic uveitis that resolved without treatment. Optical coherence tomography of treated eyes showed an average temporal retinal nerve fiber layer thickness of 54 μm before injection and 55 μm at month 12.
For fellow eyes before injection, it was 56 μm, decreasing to 50 μm at month 12 (P = 0.013). Generalized estimating equations suggested that PERG amplitudes worsened more in treated eyes than in fellow eyes by approximately 0.05 μV (P = 0.009 exchangeable). No difference between eyes in outcomes of other visual function measures was evident. In conclusion, allotopic gene therapy for LHON at low and medium doses seems to be safe and does not damage the temporal retinal nerve fiber layer, opening the door next for testing of the high dose.

Early Patterns of Macular Degeneration in ABCA4-Associated Retinopathy.

The authors describe the earliest features of ABCA4-associated retinopathy. This is a case series of children with a clinical and molecular diagnosis of ABCA4-associated retinopathy without evidence of macular atrophy. The retinal phenotype was characterized by color fundus photography, OCT, fundus autofluorescence (FAF) imaging, electroretinography, and in 2 patients, adaptive optics scanning laser ophthalmoscopy (AOSLO). Sequencing of the ABCA4 gene was performed in all patients.

Eight children with ABCA4-associated retinopathy without macular atrophy were identified. Biallelic variants in ABCA4 were identified in all patients. Four children were asymptomatic, and 4 reported loss of VA. Patients were young (median age, 8.5 years; interquartile range, 6.8 years) with good visual acuity (median, 0.155 logarithm of the minimum angle of resolution [logMAR]; interquartile range, 0.29 logMAR). At presentation, the macula appeared normal (n = 3), had a subtly altered foveal reflex (n = 4), or demonstrated manifest fine yellow dots (n = 1). Fundus autofluorescence identified hyperautofluorescent dots in the central macula in 3 patients, 2 of whom showed a normal fundus appearance. Only 1 child had widespread hyperautofluorescent retinal flecks at presentation. OCT imaging identified hyperreflectivity at the base of the outer nuclear layer in all 8 patients. Where loss of outer nuclear volume was evident, this appeared to occur preferentially at a perifoveal locus. Longitudinal split-detector AOSLO imaging in 2 individuals confirmed that the greatest change in cone spacing occurred in the perifoveal, and not foveolar, photoreceptors. Electroretinography showed a reduced B-wave-to-A-wave ratio in 3 of 5 patients tested; in 2 children, recordings clearly showed electronegative results.

Authors conclude that in childhood-onset ABCA4-associated retinopathy, the earliest stages of macular atrophy involve the parafovea and spare the foveola. In some cases, these changes are predated by tiny, foveal, yellow, hyperautofluorescent dots. Hyperreflectivity at the base of the outer nuclear layer, previously described as thickening of the external limiting membrane, is likely to represent a
structural change at the level of the foveal cone nuclei. Electroretinography suggests that the initial site of retinal dysfunction may occur after phototransduction.

Rapid-Onset Chorioretinopathy Phenotype of ABCA4 Disease.

This article characterizes patients affected by a uniquely severe, rapid-onset chorioretinopathy (ROC) phenotype of ABCA4 disease. It is a comparative cohort study with sixteen patients selected from a large clinically diagnosed and genetically confirmed cohort (n = 300) of patients diagnosed with ABCA4 disease. Phenotypic characteristics were assessed on color fundus photographs, short-wavelength autofluorescence (488-nm), and near-infrared autofluorescence (NIR-AF, 787-nm) images. Subfoveal thickness measurements were obtained from enhanced-depth imaging OCT. Generalized retinal function was determined with full-field electroretinogram (ffERG) testing, and lipofuscin accumulation was assessed by quantitative autofluorescence (qAF). All patients exhibited advanced disease features, including pigment migration in the macula and retinal vessel attenuation at an early age, and reported a symptomatic onset, on average, at 7.4 years (average for ABCA4 disease is 21.9 years, P < 0.0001). Deterioration of the macula was observed to begin with an intense, homogeneous signal on short-wavelength autofluorescence, which corresponds to an attenuated NIR-AF signal and progresses to a patchy, coalescing pattern of chorioretinal atrophy within the subsequent decade. Measurement of choroidal thickness revealed a more rapid thinning of choriocapillaris with age of Sattler's layer compared with the rate in most other patients with ABCA4 disease (P < 0.001). Levels of qAF in the macula before atrophy were above both the 95% confidence intervals for healthy individuals and patients with Stargardt disease (STGD1) (>1000 qAF units). Severe attenuation of cone responses and notable decreases in rod responses were detected by ffERG. Sequencing of the ABCA4 gene revealed exclusively deleterious, null mutations, including stop codons; frameshift deletions; variants in canonical splice sites, which completely abolish splicing; and known deleterious missense alleles. The ROC phenotype is a unique classification of ABCA4 disease, which is caused by deleterious null biallelic ABCA4 mutations and is characterized by the rapid deterioration of retinal pigment epithelium and photoreceptor layers in the macula and significant choroidal thinning within the first 2 decades of life.

Correlation of novel PAX6 gene abnormalities in aniridia and clinical presentation

Aniridia is caused by heterozygous mutations in the PAX6 gene, although in 8-20% of cases no defects in the gene have been found. The phenotype of the dis-
ease is variable and does not appear to correlate well with genotype. This study evaluated the ocular presentation and genotype of people with aniridia in British Columbia, in particular the association of genotype to the grade of foveal hypoplasia. 33 patients were prospectively enrolled. Full ophthalmic exams and SD-OCT imaging was performed. Gene sequencing was performed. The average age was 25 years. 58% had nystagmus, and total absence of iris tissue was noted in 64%. Cataract or IOL was present in 72%, and a history of glaucoma was present in 48%. Foveal hypoplasia, as diagnosed with SD-OCT, was seen in 80% of eyes. Most of these cases were graded as severe hypoplasia. 91% of patients had PAX6 defects identified. Four novel mutations were found, and 4 novel 11p deletions that included PAX6 (or known PAX6 regulatory region) were found. In 3 patients, no PAX6 abnormality could be identified. BVCA had a broad range, from logMAR 0.0 to NLP, likely due to the many possible causes of reduced acuity in aniridia. The data in this study support molecular genetic testing in this disease, as future gene therapy could be targeted to a significant proportion of patients with aniridia.

Mutation spectrum of NDP, FZD4 and TSPAN12 genes in Indian patients with retinopathy of prematurity

ROP shares some resemblance of clinical findings with familial exudative vitreoretinopathy (FEVR). There are genes involved in FEVR, mainly the Norrin β-catenin signaling genes NDP, FZD4, and TSPAN12, that could be involved in ROP pathogenesis. The authors conducted a case-control study of ROP infants in India and performed molecular genetic analysis of their DNA. 246 ROP infants and 300 control infants without ROP were included. There were 3 cases of ROP where gene screening revealed a 14 base-pair deletion in the NDP gene. Screening of FZD4 revealed four heterozygous variants and one compound heterozygous variant. Two of the variants were found to be significantly associated with ROP. One heterozygous variant was found in the TSPAN12 gene of one patient, but phenotype correlation could not be established. The authors concluded that variants of these three genes were involved in the pathogenesis of ROP in this cohort, although due to study designs additional cases may have been missed and other genes in the Norrin pathway may be involved.

Three New PAX2 Gene Mutations in Patients with Papillorenal Syndrome.

Papillorenal syndrome (PAPRS; Mendelian Inheritance in Man [MIM] 120330) is an autosomal dominant disease characterized by the presence of congenital renal and optic nerve abnormalities. Until now, PAPRS has only been associated
with mutations of the PAX2 gene. However, it is estimated that approximately 50% of individuals with clinical findings characteristic of PAPRS do not present with an identified mutation of the PAX2 gene. Around 92% of patients with the presence of mutations for this syndrome are shown to have renal involvement and about 77% present with optic nerve involvement. The most frequent alteration is the presence of optic nerve dysplasia. A vacant optic nerve with a central excavation, absence of the central retinal artery, and presence of multiple cilioretinal arteries in radial formation has often been described in scientific literature. In this article, the authors present four patients with PAPRS who are carriers of three new PAX2 mutations, as well as another patient with a possible non-pathogenic variant of the PAX2 gene. All patients were given a full neurophthalmological examination, and all patients underwent a genetic test for PAX2. Patients 1 and 2 presented with the classic signs of PAPRS: renal disease associated with a congenitally abnormal optic disc, whereas patients 3 and 4 only presented with a congenital optic nerve abnormality and no renal involvement. In patients 1 and 2, the optic nerves were affected by the presence of a central excavation within the optic disc, absence of the central retinal artery, as well as multiple cilioretinal arteries radiating from the periphery of the optic disc. Bilateral optic nerve pits were seen in patient 3, and lastly, in patient 4 there was the presence of superficial gliotic tissue on the left optic disc. All patients presented with a missense mutation in the PAX2 gene, where in patient 4 possibly being only a non-pathogenic variant of the gene. In conclusion, the authors present two patients with classic clinical signs of PAPRS, having two new PAX2 mutations, which until now have not been described in the current literature; another patient with a new PAX2 mutation showing only ocular manifestations of the disease, and lastly, a patient who is a carrier of a variant of the PAX2 gene has a congenitally abnormal optic disc, which is probably not related to PAPRS. The authors have therefore amplified the spectrum of PAX2 mutations currently described in the literature and likewise have noted the possibility of the existence of other patients having PAX2 mutations with isolated ocular abnormalities.

Phenotypic Diversity in Autosomal-Dominant Cone-Rod Dystrophy Elucidated by Adaptive Optics Retinal Imaging.

Autosomal-dominant cone-rod dystrophy (AD-CRD) is a rare condition characterized by photoaversion, poor color discrimination and progressive loss of visual acuity leading to legal blindness in older adulthood. At least five genes associated with AD-CRD have been discovered, including guanylate cyclase activator A1A (GUCA1A), which encodes a guanylate cyclase activating protein, GCAP1. However, our understanding of how mutations in GUCA1A shape the retinal phenotype at a cellular level in human individuals with AD-CRD and ultimately lead to photoreceptor cell death has been limited by the rarity of the condition, the genetic and environmental heterogeneity in the human population, and our inability to assess single retinal cells over the time course of the disease. The au-
thors combine genotyping with high resolution adaptive optics retinal imaging to elucidate the retinal phenotype at a cellular level in patients with AD-CRD harboring a defect in the *GUCA1A* gene. Nine affected members of a four-generation AD-CRD pedigree and three unaffected first-degree relatives underwent clinical examinations including visual acuity, fundus examination, Goldmann perimetry, spectral domain optical coherence tomography and electroretinography. Genome-wide scan followed by bidirectional sequencing was performed on all affected participants. High-resolution imaging using a custom adaptive optics scanning light ophthalmoscope (AOSLO) was performed for selected participants. Clinical evaluations showed a range of disease severity from normal fundus appearance in teenaged patients to pronounced macular atrophy in older patients. Molecular genetic testing showed a mutation in *GUCA1A* segregating with disease. AOSLO imaging revealed that of the two teenage patients with mild disease, one had severe disruption of the photoreceptor mosaic while the other had a normal cone mosaic. AOSLO imaging demonstrated variability in the pattern of cone and rod cell loss between two teenage cousins with early AD-CRD, who had similar clinical features and had the identical disease-causing mutation in *GUCA1A*. This finding suggests that a mutation in *GUCA1A* does not lead to the same degree of AD-CRD in all patients. Modifying factors may mitigate or augment disease severity, leading to different retinal cellular phenotypes.

**Genotype-Phenotype Variability of Retinal Manifestation in Primary Hyperoxaluria Type 1.**

Primary hyperoxaluria type 1 (PH1) is a rare congenital metabolic disorder of the glyoxylate pathway, which manifests with nephrocalcinosis, urolithiasis, and end-stage renal failure (ESRD) as well as deposition of oxalate crystals within ocular tissues. Ocular involvement is a frequent cause of visual impairment in patients with PH1. The deposition of calcium-oxalate crystals involves all retinal layers including the choroid, as histopathologic reports and recent OCT imaging case series demonstrated. This report demonstrates classical ocular features of PH1 of the posterior pole and furthermore highlights the ocular genotype–phenotype variability among siblings with identical compound heterozygous alanine-glyoxylate aminotransferase (AGXT) mutations. Two siblings, an 8-year-old boy and an 18-year-old girl, with genetically confirmed AGXT mutation (c.364C>T (p.R122X) and c.33dupC), but different renal phenotype underwent an ophthalmic examination, including slit-lamp examination and funduscopy as well as optical coherence tomography (OCT), near-infrared autofluorescence (NIA), and microperimetry examination. The 8-year-old boy presented with a best-corrected visual acuity (BCVA) of 20/630. Fundus examination revealed bilateral, whitish oxalate deposits and prominent fibrotic macular scars. OCT imaging illustrated hyperdense deposits in all retinal layers and the choroid and the vitreous body along with a prominent dome-shaped macular fibrosis. NIA imaging outlined macular retinal pigment epithelium (RPE) atrophy with panretinal hyperreflective material. Bilateral symptomatic epiphora was putatively due to bilateral deposi-
tions of palpable nodular oxalate deposits at the level of the lacrimal sac. In con-
trary, the 18-year-old sister presented without any signs of ocular oxalate deposi-
tion and a BCVA of 20/20. In conclusion, PH1 is potentially accompanied with a
considerable decline in visual acuity due to macular scaring and fibrosis, where-
as a profound variability of ocular manifestations can be observed in PH1 pa-
tients with identical genotypes.

Repeatability and Longitudinal Assessment of Foveal Cone Structure in CNBG3-Associated Achromatopsia.

Achromatopsia is an autosomal recessive disease causing substantial reduction
or complete absence of cone function. Although believed to be a relatively sta-
tionary disorder, questions remain regarding the stability of cone structure over
time. Imaging studies using optical coherence tomography (OCT) demonstrate a
well-defined outer nuclear layer (ONL) at the fovea in the majority of cases of
achromatopsia. Moreover, the appearance of the ellipsoid zone (EZ) and the In-
terdigitation zone (IZ) can be nearly normal in appearance, although some level
of disruption is more typical. More recently, split-detection adaptive optics scan-
ning light ophthalmoscopy (AOSLO) has provided direct evidence for remnant
cone inner segments at the fovea of patients with CNGB3-associated achroma-
topsia, with peak density ranging from about 7,000 to about 53,000 cones/mm²,
well below normal peak cone density of around 85,000 to 324,000 cones/mm². In
this study, the authors sought to assess the repeatability of and examine longitu-
dinal changes in measurements of central cone structure in patients
with achromatopsia. This is the first longitudinal study of foveal cone density in
patients with CNGB3-associated achromatopsia. Forty-one subjects with
CNGB3- associated achromatopsia were imaged over a period of between 6 and
26 months using OCT and AOSLO. ONL thickness, EZ disruption, and
peak foveal cone density were assessed. ONL thickness increased slightly com-
pared with baseline (0.184 μm/month, P = 0.02). The EZ grade remained un-
changed for 34/41 subjects. Peak foveal cone density did not significantly change
over time (mean change 1% per 6 months, P = 0.126). In summary, foveal cone
structure showed little or no change in this group of subjects with CNGB3-
associated achromatopsia. Over the time scales investigated (6-26 months),
achromatopsia seems to be a structurally stable condition, although longer-term
follow-up is needed. These data will be useful in assessing foveal cone structure
after therapeutic intervention.

Copy-number variation is an important contributor to the genetic
causality of inherited retinal degenerations.
Despite substantial progress in sequencing, current strategies can genetically solve only approximately 55-60% of inherited retinal degeneration (IRD) cases. This can be partially attributed to elusive mutations in the known IRD genes, which are not easily identified by the targeted next-generation sequencing (NGS) or Sanger sequencing approaches. The authors hypothesized that copy-number variations (CNVs) are a major contributor to the elusive genetic causality of IRDs. Twenty-eight cases previously unsolved with a targeted NGS were investigated with whole-genome single-nucleotide polymorphism (SNP) and comparative genomic hybridization (CGH) arrays. Deletions in the IRD genes were detected in 5 of 28 families, including a de novo deletion. The authors suggest that the de novo deletion occurred through nonallelic homologous recombination (NAHR) and constructed a genomic map of NAHR-prone regions with overlapping IRD genes. CNV mapping substantially increased the genetic diagnostic rate of IRDs, detecting genetic causality in 18% of previously unsolved cases. Extending the search to other structural variations will probably demonstrate an even higher contribution to genetic causality of IRDs.

**Efficacy and safety of voretigene neparvovec (AAV2-hRPE65v2) in patients with RPE65-mediated inherited retinal dystrophy: a randomised, controlled, open-label, phase 3 trial.**

Phase 1 studies have shown potential benefit of gene replacement in RPE65-mediated inherited retinal dystrophy. This phase 3 study assessed the efficacy and safety of voretigene neparvovec in participants whose inherited retinal dystrophy would otherwise progress to complete blindness. The article reports the results of an open-label, randomized, controlled phase 3 trial done at two sites in the USA. Individuals aged 3 years or older with, in each eye, best corrected visual acuity of 20/60 or worse, or visual field less than 20 degrees in any meridian, or both, with confirmed genetic diagnosis of biallelic RPE65 mutations, sufficient viable retina, and ability to perform standardized multi-luminance mobility testing (MLMT) within the luminance range evaluated, were eligible. Participants were randomly assigned (2:1) to intervention or control using a permuted block design, stratified by age (<10 years and ≥10 years) and baseline mobility testing passing level (pass at ≥125 lux vs <125 lux). Graders assessing primary outcome were masked to treatment group. Intervention was bilateral, subretinal injection of $1.5 \times 10^{11}$ vector genomes of voretigene neparvovec in 0.3 mL total volume. The primary efficacy endpoint was 1-year change in MLMT performance, measuring functional vision at specified light levels. The intention-to-treat (ITT) and modified ITT populations were included in primary and safety analyses. Between Nov 15, 2012, and Nov 21, 2013, 31 individuals were enrolled and randomly assigned to intervention (n=21) or control (n=10). One participant from each group withdrew after consent, before intervention, leaving an mITT population of 20 intervention and nine control participants. At 1 year, mean bilateral MLMT change score was 1.8 (SD 1.1) light levels in the intervention group versus 0.2 (1.0) in the control group (difference of 1.6, 95% CI
Specific Alleles of CLN7/MFSD8, a Protein That Localizes to Photoreceptor Synaptic Terminals, Cause a Spectrum of Nonsyndromic Retinal Dystrophy.

Recessive mutations in CLN7/MFSD8 usually cause variant late-infantile onset neuronal ceroid lipofuscinosis (vLINCL), a poorly understood neurodegenerative condition, though mutations may also cause nonsyndromic maculopathy. A series of 12 patients with nonsyndromic retinopathy due to novel CLN7/MFSD8 mutation combinations were investigated in this study. Affected patients and their family members were recruited in ophthalmic clinics at each center where they were examined by retinal imaging and detailed electrophysiology. Whole exome or genome next generation sequencing was performed on genomic DNA from at least one affected family member. Immunofluorescence confocal microscopy of murine retina cross-sections were used to localize the protein.

Compound heterozygous alleles were identified in six cases, one of which was always p.Glu336Gln. Such combinations resulted in isolated macular disease. Six further cases were homozygous for the variant p.Met454Thr, identified as a founder mutation of South Asian origin. Those patients had widespread generalized retinal disease, characterized by electroretinography as a rod-cone dystrophy with severe macular involvement. In addition, the photopic single flash electroretinograms demonstrated a reduced b- to a-wave amplitude ratio, suggesting dysfunction occurring after phototransduction. Immunohistology identified MFSD8 in the outer plexiform layer of the retina, a site rich in photoreceptor synapses.

This study highlights a hierarchy of MFSD8 variant severity, predicting three consequences of mutation: (1) nonsyndromic localized maculopathy, (2) nonsyndromic widespread retinopathy, or (3) syndromic neurological disease. The data also shed light on the underlying pathogenesis by implicating the photoreceptor synaptic terminals as the major site of retinal disease.
Paper evaluates the role of a promoter region polymorphism rs1800629 (-308G>A) in the inflammatory pathway component TNF-α and its effects on the expression of TNF-α and downstream molecules tumor necrosis factor receptor 1 and 2 (TNFR1 and TNFR2), v-rel avian reticuloendotheliosis viral oncogene homolog A (RELA), and interleukin 6 (IL-6) in KC development. TNF-α promoter polymorphism rs1800629 (-308G>A), was genotyped in 257 sporadic KC patients and 253 healthy controls. Enzyme-linked immunosorbent assay (ELISA) was performed to assess for the -308G>A genotypes. Quantitative polymerase chain reaction (qPCR) was carried out to compare the mRNA expression of TNF-α, TNFR1, TNFR2, RELA, and IL6 in the corneal tissues of 20 KC patients and 20 donor controls.

The -308G>A genotype GA was found to be significantly associated with KC development (dominant model [odds ratio (OR) = 6.67 (95% confidence interval [CI] = 4.28-10.42), P < 0.001]) and allele-A (OR = 4.30, 95%CI = 2.93-6.34, P <0.001). TNF-α serum levels were significantly raised in patients with GA genotype (196.5 ± 69.5 pg/mL) compared to reference genotype GG (21.7 ± 8.2 pg/mL) (P <0.0001). There was a significant overexpression of TNF-α (P = 0.002), TNFR2 (P = 0.0001), RELA (P = 0.0117), and IL6 (P = 0.0007) in the KC corneal tissues as compared to the control.

The authors conclude that GA genotype of the TNF-α -308G>A polymorphism is a significant genetic risk factor for the pathogenesis of KC. Moreover, this single nucleotide polymorphism (SNP) was observed to be associated with deregulated expression of downstream molecules, thus further reinforcing the role of the inflammatory pathway components in the development of KC.

Iris Malformation and Anterior Segment Dysgenesis in Mice and Humans With a Mutation in PI 3-Kinase.


The authors determine the ocular consequences of a dominant-negative mutation in the p85α subunit of phosphatidylinositol 3-kinase (PIK3R1) using a knock-in mouse model of SHORT syndrome, a syndrome associated with short stature, lipodystrophy, diabetes, and Rieger anomaly in humans. A knock-in mice heterozygous for the SHORT syndrome mutation changing arginine 649 to tryptophan in p85α (PIK3R1) is investigated using physical examination, optical coherence tomography (OCT), tonometry, and histopathologic sections from paraffin-embedded eyes, and compared the findings to similar investigations in two human subjects with SHORT syndrome heterozygous for the same mutation. While overall eye development was normal with clear cornea and lens, normal anterior chamber volume, normal intraocular pressure, and no changes in the retinal structure, OCT images of the knock-in mouse eyes revealed a significant decrease in thickness and width of the iris resulting in increased pupil area and irregularity of shape. Both human subjects had Rieger anomaly with similar defects including thin irides and irregular pupils, as well as a
prominent ring of Schwalbe, goniosynechiae, early cataract formation, and glaucoma. Although the two subjects had had diabetes for more than 30 years, there were no signs of diabetic retinopathy.

The authors conclude that a dominant-negative mutation in the p85α regulatory subunit of PI3K affects development of the iris, and contributes to changes consistent with anterior segment dysgenesis in both humans and mice.

**Association of Steroid 5α-Reductase Type 3 Congenital Disorder of Glycosylation With Early-Onset Retinal Dystrophy.**


The authors investigate a series of patients with the same mutation in the SRD5A3 gene and thereby characterize its retinal manifestations and other associated features. Seven affected individuals from 4 unrelated families with early-onset retinal dystrophy as a primary manifestation underwent comprehensive ophthalmic assessment, including retinal imaging and electrodiagnostic testing. Developmental and systemic findings were also recorded. Molecular genetic approaches, including targeted next-generation sequencing, autozygosity mapping, and apex microarray, were tried to reach a diagnosis; all participants were mutation negative. Whole-exome sequencing or whole-genome sequencing was used to identify the causative variant. Biochemical profiling was conducted to confirm a CDG type I defect. Patient phenotype data were collected over the course of ophthalmic follow-up, spanning a period of 20 years, beginning March 20, 1997, through September 15, 2016.

The cohort consisted of 7 participants (5 females and 2 males) whose mean (SD) age at the most recent examination was 17.1 (3.9) years and who were all of South Asian ethnicity. Whole-exome sequencing and whole-genome sequencing identified the same homozygous SRD5A3 c.57G>A, p.(Trp19Ter) variant as the underlying cause of early-onset retinal dystrophy in each family. Detailed ocular phenotyping identified early-onset (aged ≤3 years) visual loss (mean [SD] best-corrected visual acuity, +0.95 [0.34] logMAR [20/180 Snellen]), childhood-onset nyctalopia, myopia (mean [SD] refractive error, -6.71 [-4.22]), and nystagmus. Six of the 7 patients had learning difficulties and psychomotor delay. Fundus autofluorescence imaging and optical coherence tomographic scans were abnormal in all patients, and electrodiagnostic testing revealed rod and cone dysfunction in the 5 patients tested.

Mutations in the SRD5A3 gene may cause early-onset retinal dystrophy, a previously underdescribed feature of the SRD5A3-CDG disorder that is progressive and may lead to serious visual impairment. SRD5A3 and other glycosylation disorder genes should be considered as a cause of retinal dystrophy even when systemic features are mild.
Novel Insights Into the Phenotypical Spectrum of KIF11-Associated Retinopathy, Including a New Form of Retinal Ciliopathy.

This study sought to characterize the ophthalmic and extraocular phenotype in patients with known and novel KIF11 mutations. Four patients (3, 5, 36, and 38 years of age, one father-daughter constellation) from three unrelated families were characterized by retinal examination including multimodal retinal imaging, investigation for syndromic disease manifestations, and targeted next-generation sequencing. The subcellular localization of Kif11 in the retina was analyzed by light and electron microscopy.

Results: There was considerable interindividual and intrafamilial phenotypic heterogeneity of KIF11-related retinopathy. Two patients presented with a progressive retinal dystrophy, one with chorioretinal dysplasia and one with familial exudative vitreoretinopathy (FEVR) in one eye and thinning of the photoreceptor layer in the fellow eye. Obvious syndromic disease manifestations were present only in the youngest patient, but minor signs (e.g. reduced head circumference) were present in the three other individuals. Immunohistochemistry results demonstrated Kif11 localization in the inner segment and ciliary compartments of photoreceptor cells and in the retinal pigment epithelium.

Progressive retinal degeneration in KIF11-related retinopathy indicates a role for KIF11 not only in ocular development but also in maintaining retinal morphology and function. The remarkable variability of the ocular phenotype suggests four different types of retinopathy which may overlap. KIF11 should be considered in the screening of patients with retinal dystrophies because other syndromic manifestations may be subtle. Evaluation of head circumference may be considered as a potential clue to the genetic diagnosis. The localization of Kif11 in photoreceptor cells indicates a retinal ciliopathy.

Whole-Exome Sequencing Identifies Biallelic IDH3A Variants as a Cause of Retinitis Pigmentosa Accompanied by Pseudocoloboma.

In this case series of seven patients from four unrelated families with autosomal recessive retinitis pigmentosa and macular pseudocoloboma, the authors performed homozygosity mapping and whole-exome sequencing and identified IDH3A variants. Subsequently, Sanger sequencing and segregation analysis were performed and the medical history of patients carrying the variants was reviewed. The authors note 7 different variants in IDH3A in 4 unrelated families, that is, 5 missense, 1 nonsense, and 1 frameshift variant. All participants showed symptoms early in life, ranging from night blindness to decreased visual acuity, and were diagnosed between the ages of 1 and 11 years. Four participants with
biallelic IDH3A variants displayed a typical arRP phenotype and 3 participants were diagnosed with arRP and pseudocoloboma of the macula. IDH3A variants were identified as a novel cause of typical arRP in some individuals associated with macular pseudocoloboma. The authors observed both phenotypes in 2 siblings carrying the same compound heterozygous variants, which could be explained by variable disease expression and warrants caution when making assertions about genotype-phenotype correlations.

Benign Yellow Dot Maculopathy: A New Macular Phenotype.

This Retrospective, observational case series describes thirty-six affected individuals (from 23 unrelated families) with a characteristic macular phenotype. Twenty-six of 36 subjects were female. The median age of subjects at presentation was 15 years (range, 5-59 years). The majority of subjects were asymptomatic and presented after a routine eye examination (22/36 subjects) or after screening because of a positive family history (13/36 subjects) or by another ophthalmologist (1/36 subjects). Of the 3 symptomatic subjects, 2 had reduced visual acuity secondary to nonorganic visual loss and bilateral ametropic amblyopia with strabismus. Visual acuity was 0.18 logarithm of the minimum angle of resolution (logMAR) or better in 30 of 33 subjects. Color vision was normal in all subjects tested, except for the subject with nonorganic visual loss. All subjects had bilateral symmetric multiple yellow dots at the macula. In the majority of subjects, these were evenly distributed throughout the fovea, but in 9 subjects they were concentrated in the nasal parafoveal area. The dots were hyperautofluorescent on fundus autofluorescence imaging. The OCT imaging was generally normal, but in 6 subjects subtle irregularities at the inner segment ellipsoid band were seen. Electrophysiologic studies identified normal macular function in 17 of 19 subjects and normal full-field retinal function in all subjects. Whole-exome analysis across 3 unrelated families found no pathogenic variants in known macular dystrophy genes. Haplotype sharing analysis in 1 family excluded linkage with the North Carolina macular dystrophy (MCDR1) locus.

A new retinal phenotype is described, which is characterized by bilateral multiple early-onset yellow dots at the macula. Visual function is normal, and the condition is nonprogressive. In familial cases, the phenotype seems to be inherited in an autosomal dominant manner, but a causative gene is yet to be ascertained.

Panel-Based Clinical Genetic Testing in 85 Children with Inherited Retinal Disease.

The aim of this study was to assess the clinical usefulness of genetic testing in a pediatric population with inherited retinal disease (IRD). These conditions are
Clinically and genetically diverse and are linked to more than 250 genes. Identifying genetic subtypes to help in management of these children is important as visual symptoms can be presenting features of syndromic conditions such as a ciliopathy or neurometabolic disorder. Also, distinguishing progressive from non-progressive disorders can help in management. In this study, multigene panel testing was selected as a first-tier test because it is relatively inexpensive and rapid, and it is associated with a low rate of nonspecific or incidental findings. In a single-center retrospective case series, 85 unrelated children with a diagnosis of isolated or syndromic IRD who were referred for clinical genetic testing between January 2014 and July 2016 were included in the study. Participants underwent a detailed ophthalmic examination, accompanied by electrodiagnostic testing (EDT) and dysmorphologic assessment where appropriate. Ocular and extraocular features were recorded using Human Phenotype Ontology terms. Subsequently, multigene panel testing (105 or 177 IRD-associated genes) was performed in an accredited diagnostic laboratory, followed by clinical variant interpretation. Overall, 78.8% of patients (n = 67) received a probable molecular diagnosis; 7.5% (n = 5) of these had autosomal dominant disease, 25.4% (n = 17) had X-linked disease, and 67.2% (n = 45) had autosomal recessive disease. In a further 5.9% of patients (n = 5), a single heterozygous ABCA4 variant was identified; all these participants had a spectrum of clinical features consistent with ABCA4 retinopathy. Most participants (84.7%; n = 72) had undergone EDT and 81.9% (n = 59) of these patients received a probable molecular diagnosis. The genes that most frequently mutated in the present cohort were CACNA1F and ABCA4, accounting for 14.9% (n = 10) and 11.9% (n = 8) of diagnoses respectively. Notably, in many cases, genetic testing helped to distinguish stationary from progressive IRD subtypes and to establish a precise diagnosis in a timely fashion. The multigene panel testing pointed to a molecular diagnosis in 84.7% of children with IRD. The diagnostic yield in the study population was significantly higher compared with that in previously reported unselected IRD cohorts. Approaches similar to the one described herein are expected to become a standard component of care in pediatric ophthalmology. The authors propose the introduction of genetic testing early in the diagnostic pathway in children with clinical and/or electrophysiologic findings, suggestive of IRD.

**Defining Outcomes for Clinical Trials of Leber Congenital Amaurosis Caused by GUCY2D Mutations.**

In order to design a clinical trial of gene therapy for patients with GUCY2D mutations causing Leber Congenital Amaurosis (LCA), validated outcome measures must be determined. This is especially important in photoreceptor diseases like this one since structure and function do not always correlate. This was a retrospective observational case series of 28 patients with GUCY2D- LCA between the ages of 2 and 59. The patients had chromatic full field sensitivity testing
(FST), optical coherence tomography (OCT), pupillometry, and NEI Visual Function Questionnaires (VFQ). FST results were used to divide the patients into cohorts by severity of rod and cone dysfunction. OCT studies demonstrated a lack of foveal budge in 2/3 of patients and reduction in the inner segment/outer segment reflectivity at the fovea and also in the rod-dense superior retina. Pupillometry sensitivity for most patients also demonstrated ability to be an objective outcome and NEI VFQ scores were similar to patients with other types of severe retinal diseases. The authors concluded that in addition to standard outcomes such as visual acuity and VFQ, that outcomes more specific to patients with GUCY2D-LCA such as FST and OCT of the fovea and superior retina need to be included when studying these patients in clinical trials.

Prevalence of Macular Abnormalities Assessed by Optical Coherence Tomography in Patients with Usher Syndrome.

Usher syndrome (USH) comprises a group of autosomal recessive disorders presenting with hearing and vision loss. The estimated prevalence is 3-6 in 100,000. About 50% of cases of inherited combined deafness and blindness are due to USH which also accounts for about 18% of all cases (isolated and syndromic) of retinitis pigmentosa (RP). USH is classified into three clinical subtypes: Usher 1 (USH1), Usher 2 (USH2), and Usher 3 (USH 3), based on the severity and progression of hearing loss, presence of vestibular dysfunction, and age of onset of RP. The authors investigate the prevalence of macular abnormalities in a cohort of Italian patients affected by Usher syndrome (USH), by comparing the clinical findings between two types (i.e., USH1 and USH2). A retrospective study was performed by reviewing optical coherence tomography (OCT) in 134 USH patients to determine the presence of macular abnormalities, including cystoid macular edema (CME), epiretinal membrane (ERM), vitreomacular traction syndrome (VMT), and macular hole (MH). Macular abnormalities were observed in 126/268 (47.0%) examined eyes. The most frequent abnormality was ERM observed in 51 eyes (19%), followed by CME observed in 42 eyes (15.7%). Moreover, CME was significantly (p < 0.05) associated with younger age (CME: 30.1 ± 11.1 years; without CME: 36.9 ± 14.9 years), whereas VMT and full thickness MH were associated with older age (p < 0.05). Moreover, a significantly (p < 0.05) decreased best-corrected visual acuity was associated with MH compared to eyes without MH. Finally, CME was more frequent in USH1 compared to USH2. In conclusion, this study, for the first time in the literature, showed the distribution of all macular abnormalities assessed by SD-OCT in a large USH cohort, comparing USH1 and USH2 patients. The authors observed that ocular abnormalities are highly prevalent in USH patients compared to general population, with ERM and CME being the most common alterations. Based on these findings, OCT screening in USH patients is recommended for early detection of macular changes and early treatment.
Quantitative Analysis of Retinal Structure Using Spectral-Domain Optical Coherence Tomography in RPGR-Associated Retinopathy.


RPGR mutations account for 70%–80% of XLRP with RP2 variants accounting for a further 6%–20%. RPGR-associated RP is particularly severe, with an early onset of disease in childhood. There is marked phenotypic heterogeneity in the condition, and rate of disease progression varies between affected individuals. RPGR mutations have also been associated with other clinical phenotypes, including cone-rod dystrophy, macular atrophy, and, rarely, syndromic XLRP. RPGR is an important focus for gene therapy research, with recent successes demonstrated in animal models and human clinical trials in preparation. The current lack of natural history data in individuals harboring pathogenic mutations in RPGR, however, poses a limiting factor. The authors sought to quantify retinal structure and progression using spectral-domain optical coherence tomography (SDOCT) in patients with retinitis pigmentosa (RP) associated with retinitis pigmentosa GTPase regulator gene (RPGR) mutations. At Moorfields Eye Hospital, London, United Kingdom, both eyes of 32 patients were studied with a SDOCT follow-up period of > 1 year (3.1 ± 1.4 years). Ellipsoid zone (EZ) width (EZW) and outer nuclear layer (ONL) and inner retinal layer (IRL) thickness measurements were taken. Progression rates, interocular symmetry, and association with age and genotype were investigated. Significant differences were observed between baseline and final measurements of EZW and ONL thickness, but not for IRL thickness. Baseline and final EZWs were 2438 ± 1646 mm and 1901 ± 1423 mm for right eyes (P<.0001); 2420 ± 1758 mm and 1922 ± 1482 mm for left eyes (P<.0001). EZW constriction rates were 176.6 ± 130.1 m/year and 173.1 ± 146.8 mm/year for right and left eyes. ONL thinning rates were 2.58 ± 2.85 m/m/year and 2.52 ± 3.54 m/m/year for right and left eyes. Interocular differences in EZW and ONL progression were not significant. Strong correlations were found between EZW constriction rates of right and left eyes and between EZW constriction and baseline EZW. There was moderate negative correlation between EZW constriction and age. Correlation between ONL thinning and age was not significant, as were differences between EZW and ONL progression rates with respect to genotype. In conclusion, this study provides SDOCT progression rates for RPGR-associated RP. There is overall interocular symmetry with implications for future treatment trials where 1 eye could serve as a control.

Mutations in INPP5K, Encoding a Phosphoinositide 5-Phosphatase, Cause Congenital Muscular Dystrophy with Cataracts and Mild Cognitive Impairment.

Phosphoinositides are small phospholipids that control diverse cellular downstream signaling events. Their spatial and temporal availability is tightly regulated by a set of specific lipid kinases and phosphatases. Congenital muscular dystrophies are hereditary disorders characterized by hypotonia and weakness from birth with variable eye and central nervous system involvement. In individuals exhibiting congenital muscular dystrophy, early-onset cataracts, and mild intellectual disability but normal cranial magnetic resonance imaging, the authors identified bi-allelic mutations in \textit{INPP5K}, encoding inositol polyphosphate-5-phosphatase K. Mutations impaired phosphatase activity toward the phosphoinositide phosphatidylinositol (4,5)-bisphosphate or altered the subcellular localization of \textit{INPP5K}. Downregulation of \textit{INPP5K} orthologs in zebrafish embryos disrupted muscle fiber morphology and resulted in abnormal eye development. These data link congenital muscular dystrophies to defective phosphoinositide 5-phosphatase activity that is becoming increasingly recognized for its role in mediating pivotal cellular mechanisms contributing to disease. In summary, the clinical presentation of individuals with bi-allelic \textit{INPP5K} mutations was relatively homogeneous. The most salient features were bilateral cataracts that required surgery in the first years of life, predominantly proximal muscle weakness from birth, delayed motor or global development, first followed by rather stationary course of the disease but later progression to loss of ambulation, mild intellectual disability, and elevated serum CK levels.

\textbf{Retinal miRNAs Variations in a Large Cohort of Inherited Retinal Disease.}


Inherited retinal disease (IRD) is a group of hereditary ocular disorders characterized by progressive retinal degenerations, leading to severe visual impairment. Although great efforts have been paid on identification of genetic predisposition in the IRD, genetic causes of a large proportion of patients remain a mystery. This dilemma makes us attempt to speculate that genetic components other than coding genes might be an additional pool predisposing IRD. MicroRNAs (miRs), a class of small non-coding, short (19–25 nucleotides) RNAs, have emerged as crucial post-transcriptional regulators involved in controlling various developmental and physiological processes in the retina. Targeted ablation of retinal miRs in mice leads to significant retinal degeneration. In this study, the authors aim to perform a mutational screening in a large cohort of IRD patients with a particular focus on retina-specific or abundant miRs. A total of 324 unrelated patients with IRD were recruited. Targeted next-generation sequencing (tNGS) was performed to survey genetic mutations in 32 known miRs highly expressed in the retina, followed by validation with Sanger sequencing, co-segregation analysis in each family, and computational assessments. Novel genotype-phenotype associations were uncovered. In total, six different variants in the miRs were identified, including four rare ones, miR-216a (n.56C>A), miR-216b (n.43_44insG), miR-7–2 (n.107C>T), and miR-7–3 (n.95G>A). The other two variants, miR-182 (n.106G>A) and miR-216a (n.105T>A), were considered as polymorphic. In
summary, the authors for the first time screened potential retinal miRs in a large Chinese cohort with IRD. Although there is no convincing evidence that these variants are responsible for the IRD, and further functional experiments are needed, the results not only enhance the current knowledge of the associations between IRD and miRNAs variants, but also provide a new clue for genetic etiology of IRD.

Choroidal and Retinal Atrophy of Bietti Crystalline Dystrophy Patients with CYP4V2 Mutations Compared to Retinitis Pigmentosa Patients with EYS Mutations.

Bietti crystalline dystrophy (BCD) is a rare retinal dystrophy characterized by the presence of yellow and shiny deposits on the cornea and posterior pole of the retina, along with progressive atrophy of the retina, choriocapillaris, and choroid. BCD is caused by mutations of the CYP4V2. The symptoms of BCD, including night blindness and progressive constriction of the visual field, are similar to those of retinitis pigmentosa (RP). However, gene expression patterns of CYP4V2 and the causative genes for RP are reportedly different. Although the RPE is generally thought the site of the primary pathological abnormality in to be BCD patients with CYP4V2 mutations, it has been suggested that CYP4V2 expression occurs in the choroid. In contrast, the human gene EYS, which is the most frequently mutated gene in Japanese RP patients, encodes a protein that is localized in the outer segments of photoreceptors. Thus, the difference in expression patterns of the causative genes is responsible for the degree and the timing of the damage to each neuroretinal and choroidal layer. The authors compared atrophy of the choroid and retina between BCD patients and EYS-RP patients with a similar degree of central visual field defects, age, and axial length (AL). Nine eyes of nine BCD patients with CYP4V2 mutations (BCD group) were examined. Moreover, the authors selected 10 eyes of 10 RP patients with EYS mutations matched for age, axial length, and mean deviation (measured with the 10-2 SITA standard program; EYS-RP group), and 10 eyes of 10 normal volunteers matched for age and axial length (control group). Macular thicknesses of the choroid and retina were measured via swept-source optical coherence tomography. The macular choroid was significantly thinner in the BCD group than in the EYS-RP and control groups, although the thickness did not significantly differ between the EYS-RP and control groups. The macular retina was significantly thinner in the BCD and EYS-RP groups than in the control group, although the thickness did not significantly differ between the BCD and EYS-RP groups at most sites. In conclusion, BCD patients with CYP4V2 mutations showed more severe macular choroid atrophy as compared to EYS-related RP patients. These different damage patterns suggest differences in choroidal expression between CYP4V2 and EYS.
Genetic Factors Influencing the Reduction of Central Corneal Thickness in Disorders Affecting the Eye.

Central corneal thickness (CCT) is one of the most heritable human traits with heritability estimated from 0.6 to 0.95. The normal mean value of CCT in white adults is expected to be 535 μm with a range of 503–565 μm. CCT measurements are essential in eye care procedures for refractive surgery and in medical examinations for glaucoma due to the fact that IOP measurements by applanation tonometry can be significantly influenced by CCT. The authors aimed to summarize and discuss the current knowledge about genetic factors influencing the reduction of CCT in disorders affecting the eye, such as primary open-angle glaucoma (POAG), brittle cornea syndrome (BCS), keratoconus (KTCN), Ehlers–Danlos syndrome (EDS; types I, II, and VI), osteogenesis imperfecta (OI), and myopia. A review of the published literature by use of key databases such as PubMed was undertaken in accordance with PRISMA guidelines and experience based on own research findings was applied. The differences in CCT measurements among those affected with diverse disorders and healthy individuals were evaluated. Then the authors considered the influence of genetic factors on CCT reduction. Disorders were compared based on phenotypes and sequence variants found in patients. In conclusion, specific sequence variants in COL8A2, PRDM5 and ZNF469, COL5A1 and ZNF469, and COL5A1 and COL5A2 could probably contribute to a CCT reduction in POAG, BCS, KTCN, and EDS, respectively. Similar sequence variants and phenotypes were identified and assessed in more than one disease. There are still areas of research lacking information, which are essential for full understanding of correlations between CCT, eye diseases, and genetics.

Variant Lattice Corneal Dystrophy Associated With Compound Heterozygous Mutations in the TGFBI Gene.

Mutations in the transforming growth factor-B-induced gene (*TGFBI*; MIM 601692), located on chromosome 5q31, have been associated with a variety of corneal dystrophies, including: lattice corneal dystrophy (LCD) associated with stromal amyloid deposition; granular corneal dystrophy (GCD) type I and II, characterized by amorphous stromal aggregates and the Bowman layer dystrophies, also known as Thiel-Behnke and Reis Buckler (RBCD) corneal dystrophies. To date, more than 50 different autosomal dominant coding region mutations have been identified in *TGFBI*, with the vast majority of the affected individuals demonstrating a single pathogenic coding region mutation. However, in populations in which *TGFBI* mutations are relatively common, such as Korea where 1 in every 875 individuals carries the mutation associated with GCD type II, individuals who are homozygous for the mutant allele demonstrate an earlier onset and more severe manifestation of the affected phenotype.
The authors report the clinical, histopathological and genetic features of a variant of LCD associated with two pathogenic mutations in the TGFBI gene. These findings were described in a 42-year-old woman who presented with progressive photophobia and decreased visual acuity in both eyes. Slit lamp examination demonstrated punctate and linear branching opacities in the mid and posterior corneal stroma, corresponding to hyper-reflective opacities noted on IVCM and amyloid deposition noted on histopathological examination of an excised corneal button. TGFBI screening revealed two previously reported heterozygous missense mutations: c.337G>A (p.(Val113Ile)) in exon 4 and c.1673T>C (p.(Leu558Pro)) in exon 12. Screening of an affected sibling with a similar phenotype revealed that she was also heterozygous for both mutations, while screening of another sibling with punctate but not linear stromal opacities revealed that she was heterozygous for only the p.(Leu558Pro) mutation. In summary, the p.(Val113Ile) mutation results in an alteration of the atypical LCD phenotype associated with the p.(Leu558Pro) mutation. This represents only the second report of the alteration of the phenotype of a TGFBI dystrophy by a second, non-homozygous pathogenic mutation, and thus provides insight into the phenotype-genotype correlation of the TGFBI dystrophies.

A unique case series of autosomal recessive bestrophinopathy exhibiting multigenerational inheritance.

Best vitelliform macular dystrophy (VMD2, #153700) is a progressive, degenerative macular disease first described by Best in 1905. Autosomal recessive bestrophinopathy (ARB) is a retinal disease caused by biallelic mutations of the BEST1 gene. It has a variable phenotype with white flecks in the retina, multifocal yellow subretinal deposits, macular edema, choroidal neovascularization, hyperopia, and electrophysiological abnormalities. The authors describe a family with ARB and multigenerational inheritance. Three generations of a Middle Eastern family (a woman, one son, and two grandchildren) were evaluated by an interdisciplinary ocular genetics team at the University of Arkansas for Medical Sciences. Eye examinations, fundus photography, and optical coherence tomography (OCT) were performed. Genetic testing was obtained on examined patients and available relatives. The proband demonstrated counting fingers vision and white flecks in the retinal periphery, with macular subretinal fluid (SRF), loss of outer photoreceptor segments, and epiretinal membrane (ERM) on OCT. Two grandchildren demonstrated decreased vision, multifocal yellow subretinal deposits, and SRF on OCT. Two grandchildren examined elsewhere were reported to be similarly affected. A son’s examination was normal except for extra-macular scars (from prior toxoplasmosis) and ERM. Genetic history revealed consanguinity and testing showed homozygosity for BEST1 mutations in the proband and two grandchildren c.473G>A/c.473G>A (R218H/R218H) and heterozygosity in two unaffected sons and two unaffected daughters-in-law c.473G>A/WT (p.R218H/WT). The authors present a consanguineous family of five affected individuals with ARB and four confirmed carriers. Their pedigree was consistent...
with dominant inheritance and incomplete penetrance. Genetic testing clarified the diagnosis and mode of inheritance. There are several important features that this report highlights in our understanding of the bestrophinopathies. First, the highly variable range of reported phenotypes is notable. More than 20 different homozygous and compound heterozygous (missense/non-sense) mutations have been reported for ARB with highly suggestive correlation between genotype and phenotype, particularly within families. Second, it is also interesting that the specific mutation noted in this family has been documented in several reports of autosomal dominant VMD2. Finally, based on the pedigree of the proband, autosomal dominant inheritance with incomplete penetrance was initially assumed, given the presence of the disorder in the proband, possibly in her siblings, and in four grandchildren. However, the phenotype was not consistent with this diagnosis. Further history revealing consanguinity and genetic testing showing homozygosity in affected individuals allowed for the correct diagnosis of ARB with multigenerational inheritance secondary to consanguinity. In summary, the authors describe a unique case series of ARB exhibiting multigenerational inheritance, presenting with a highly variable range of phenotypes.

Ophthalmic findings in patients with arterial tortuosity syndrome and carriers: A case series.

Arterial tortuosity syndrome (ATS) is a rare autosomal recessive disease hallmark marked by tortuosity, stenosis, and aneurism development of large- and medium-sized arteries. Mutations in SLC2A10, a gene that encodes the facilitative glucose transporter GLUT10, cause ATS. Several case reports have noted associated ophthalmic findings such as keratoconus, keratoglobus, and myopia without detailed descriptions or standardized examinations. Additional connective tissue features may be identified in the skeleton, skin, and other elastic soft tissues. The authors report a series of detailed ophthalmologic findings for one adult and four pediatric patients diagnosed with ATS, as well as one adult and two children carrying monoallelic defects in SLC2A10. These five ATS patients and three carriers were identified through an ATS specialty clinic at the Arkansas Children’s Hospital in Little Rock, Arkansas. Patients underwent complete eye examinations, including corneal pachymetry, topography, and optical coherence tomography when indicated. All five patients with ATS had myopia and thin corneas with an average central corneal thickness of 426 μm, and three had corneal ectasia, two with early keratoconus and one with keratoglobus and deep stromal corneal opacities. One patient had bilateral high irregular astigmatism, and one had unilateral high regular astigmatism. All carriers had myopia, one had corneal thinning, and one developed keratectasia in one eye many years after laser-assisted in situ keratomileusis (LASIK) surgery. The authors document a spectrum of ophthalmologic manifestations of ATS with universal findings of myopia, corneal thinning, and a propensity for corneal ectasia leading to keratoconus or keratoglobus. Heterozygous carriers may develop keratectasia after corneal refractive surgery. The authors recommend annual eye examinations including vision testing, refrac-
tion, corneal topography, pachymetry, and detailed slit-lamp examination for all ATS patients and carriers. Care plans should be individualized given the clinical findings, and caution is warranted for refractive surgery in patients and carriers. Consideration should be given to corneal cross-linking in cases of progressive corneal ectasia.

Clinical Presentation and Disease Course of Usher Syndrome Because of Mutations in MYO7A or USH2A


This group evaluated the differences in the visual phenotype and natural history of Usher syndrome caused by mutations in MYO7A or USH2A, the most commonly affected genes of Usher syndrome Type I (USH1) and Type II (USH2), respectively. 88 patients with a clinical diagnosis of USH1 (26 patients) or USH2 (62 patients) were retrospectively evaluated. Of these, 48 patients had 2 disease-causing mutations in MYO7A (10 USH1 patients), USH2A (33 USH2 patients), and other USH genes (5 patients). Clinical studies included BCVA, Goldmann visual field, fundus photography, ERG, and audiologic and vestibular assessments. Median follow-up time was 3.5 years. Results revealed that patients carrying mutations in MYO7A had a younger age of onset of hearing and visual impairments than those carrying mutations in USH2A, leading to earlier disease diagnosis. Longitudinal analysis showed that visual acuity and visual field decreased more rapidly in subjects carrying MYO7A mutations than in those carrying USH2A mutations, and the patients with MYO7A mutations reached legal blindness on average 15 years earlier than patients with USH2A mutations. This longitudinal investigation confirms a more severe disease progression in USH1 patients than in USH2 patients. In addition, most visual symptoms occurred at an earlier age in USH1 patients carrying mutations in MYO7A. Considering the successful results of preclinical trails for MYO7A gene replacement in USH1B, disease progression data can be useful for the design of gene therapy clinical trials in the future.

A Unique Case of Bilateral Microphthalmia That May Be Related to 14q32.33


2-day-old Hispanic boy was transferred to us with concerns of a small left eye. The pregnancy was uncomplicated, and both parents are healthy. Examination showed a left orbit that appeared to be empty with conjunctival tissue. The right eye had a 7 mm clear cornea, and retinal exam showed areas of thin or absent tissue and no visible optic nerve. MRI revealed a hypoplastic left orbit with an orbital cyst. The anterior-posterior diameter of the right globe was 14 mm and the left globe was 4 mm. Genetic microanalysis showed genetic abnormalities (845
kb gain) on chromosome 14 at q32.33. A diagnosis of bilateral microphthalmia with an orbital cyst was made. This is an isolated case of bilateral microphthalmia possibly associated with 14q32-33. This is a first published case of bilateral microphthalmia without family history.

**Exotopic Duane syndrome with synergistic divergence and no mutations in COL25A1.**

Typical Duane retraction syndrome, a common form of congenital cranial dysinnervation disorder (CCDD), is rarely due to a monogenic mutation. However, the unusual form of exotropic Duane syndrome with synergistic divergence was recently associated with bi-allelic mutations in the gene COL25A1, raising the possibility that this particular Duane syndrome phenotype could be a monogenic recessive CCDD. To explore this possibility, the authors tested 4 consecutive unrelated subjects with the diagnosis for COL25A1 mutations. None harbored pathogenic variants, evidence that exotropic Duane syndrome with synergistic divergence is not specifically caused by mutations in the gene.

**17. TRAUMA**

**Pediatric Orbital Blowout Fractures** Stella Y. Chung, Paul D. Langer


The authors provide a comprehensive review of the evaluation and management of blowout fractures. There are a number of key points that they make which provide an excellent framework in which to approach these patients. Firstly, all patients with orbital fractures require ophthalmic evaluation to rule out serious injury to the eye. Forced duction testing is usually unnecessary in awake patients. If a child has sudden loss of upgaze without other signs of CNIII, and an orbital floor fracture on imaging, there is no need to perform forced ductions. Nausea and vomiting have a PP factor of 75% in trapdoor fractures and 83.3% for IR entrapment. CT scan is gold standard for imaging adult and pediatric orbital fractures with dedicated thin cut orbital scan with coronal and sagittal reconstruction preferred to limit radiation. Trapdoor fractures are found almost exclusively in children and require urgent repair usually within 24 hours if there is severe motility restriction or oculocardiac reflex. The authors rely exclusively on clinical findings to determine whether non-trapdoor fractures require surgical intervention. If diplopia is improving one may wait and the presence of enophthalmos is not an indication for surgery unless determined to be cosmetically unacceptable by patient and parent. There is no indication that early repair in these cases leads to better outcome. Surgical approach may be done in a transconjunctival manner having the advantage of no cutaneous scar, generally does not require canthotomy and cantholysis, and has excellent exposure. Goal of surgery is to reposition herniated tissue and placement of an implant to cover defect.
taking care that it is on the posterior bony ledge of the fracture. The authors prefer the use of alloplastic implants. Most children with blowout fractures will not require surgery and those that do have excellent outcomes if the above recommendations are followed. This article is an excellent review with clear guidelines to manage these patients and avoid unnecessary surgery without sacrificing good outcomes.

**Orbital and Orbitocranial Trauma From Pencil Fragments: Role of Timely Diagnosis and Management.**

Wooden pencils are a common cause of organic retained foreign bodies in the orbit since they are commonly found in homes and classrooms. The purpose of this study was to highlight the importance of detection of organic foreign body and to better understand the radiologic findings in these cases caused by orbital or orbitocranial penetrating pencil injuries by presenting a modern cohort of 4 patients. This was a retrospective chart review of penetrating orbital or orbitocranial trauma whose mechanism of trauma was from a pencil. The authors found that all four patients were male and 3 of the 4 were under the age of 2 years. The initial detection of the foreign body was delayed in 3 cases. Penetration of the orbital wall was seen in 3 cases. One case resulted in infection that spread to the brain and caused seizures. Three dimensional CT scans were used to differentiate the pencil fragments from the orbital wall. The authors concluded that penetrating injuries to the periorbital structure by pencils and delayed detection of retained pencil pieces can result in a threat to both life and vision. Radiologic exams are key to detecting retained foreign bodies.

**Detergent Pod-Related Eye Injuries Among Preschool-Aged Children**

This research letter emphasizes that the readily available laundry detergent pods has led to an increase in injuries in children, including but not limited to: choking, poisoning, burns, cornea and conjunctival injuries. The authors report 5 years of data (2010-2015) in 120 children to the Emergency Room, showing an increase from 12 instances in 2012 to 480 instances in 2015. The authors also suggest because the laundry pod is packaged in bright colors—it appears like candy to preschool-age children. The key public health message is that it is important for us to educate parents and caregivers to not allow 3-4 year-old children to hold/handle the laundry detergent pods.

**Orbital Compartment Syndrome Following Post-Traumatic Subgaleal Hematoma**
Orbital extension of subgaleal hematoma is rare. This report describes the case of an otherwise healthy 10-year-old girl who developed delayed contralateral proptosis and external ophthalmoplegia after relatively minor right-sided forehead trauma. She was found to have bilateral subgaleal hematomas communicating with a left superior subperiosteal orbital hematoma. Over the course of 2 days, she developed an orbital compartment syndrome requiring emergent canthotomy and cantholysis, followed by surgical incision and drainage of her scalp hematoma without orbitotomy. Hematologic work-up revealed heterozygous factor VII deficiency. The authors point out the importance of following children with subgaleal hematomas carefully until resolution as orbital extension usually presents after a delay.

**NON-ACCIDENTAL HEAD TRAUMA**

**Characteristics of non-vitreoretinal ocular injury in child maltreatment: a systematic review**


The National Society for the Prevention of Cruelty to Children survey data reported that 6.9% young people aged 11–17 had experienced abuse or neglect at the hands of their parents or guardians. This systematic review was undertaken to identify the spectrum of non-retinal ocular abusive injury. Studies of children aged 0–18 years experiencing non-vitreoretinal ocular injury due to physical abuse or fabricated or induced illness, with adequate confirmation of the cause of injury and details of the injuries sustained. Any study that included cases of ‘suspected’ abuse or that relied solely on physical findings without a multidisciplinary assessment or publications where the children had not been examined by an ophthalmologist, or a healthcare worker that performed regular ocular examinations were excluded. Five of 49 articles reviewed met the inclusion criteria. Total data includes 26 children, 14 males, and 12 females. Mean age across the included articles was 36.0 months, range 1.0–168.0 months. Authors reported 3 data sets: data set 1 ocular injury as a consequence of physical abuse; data set 2: ocular injury as a result of fabricated or induced illness (FII) and data set 3: ocular injury as a result of corporal punishment. Data set 1 included 18 patients. The most common finding (100%) was subconjunctival hemorrhage. Four of those patients (22%) were seen before with ocular complaints and discharge without maltreatment being recognized. Data set 2 included one 5-month girl who underwent repeated examination, and on the fifth presentation a diagnosis of maltreatment was made following the identification of uncharacteristic ocular findings. Data set 3 included 7 patients with an age range of 4 to 14 years who sustained trauma with a belt. These children are significantly older than those in Da-
ta sets 1 and 2. All had hyphema frequently associated ocular and extra-ocular clinical findings and significantly impaired vision.

It is estimated that in 33% of patients the diagnosis of physical abuse is initially missed. All the children that had suffered physical abuse with ocular injury had subconjunctival hemorrhages. Unexplained subconjunctival hemorrhages may be a potential sentinel injury of maltreatment and warrant careful evaluation. This study confirms the wide spectrum of non-vitreoretinal ocular injuries seen in child abuse or fabricated or induced illness.

**Non-contact ultra-wide field retinal imaging of infants with suspected abusive head trauma**


Abusive head trauma (AHT) is associated with a 30% mortality. AHT classically presentation includes encephalopathy, intracranial hemorrhage and retinal hemorrhages. The diagnosis of AHT is imperative. Detection of retinal hemorrhages appearance, distribution, laterality, and severity is critical in distinguishing between accidental and non-accidental causes of head injury in infancy. RetCam, a portable device that requires coupling fluid and ocular contact to acquire retinal images on a supine infant is the current ‘gold standard’ method of documentation, able to image a 130° field. Sedation may be required for RetCam imaging in some cases, especially if retinal angiography is required. Optos P200MA Scanning Laser Ophthalmoscope (Optos, Dunfermline, UK) has demonstrated to attain high-quality retinal images in infants with pediatric retinal disorders without the need for ocular contact. Optos captures a 200° retinal field enabling documentation of the retinal periphery in a single image, typically without the need for sedation. Authors report 4 infants with suspected AHT who were imaged using Optos. Infants did not required sedation. All infants were positioned “in the flying baby” position. Pseudo-color fundal images were acquired from both eyes. Ultra-wide field fluorescein angiography was performed in one infant after 10% sodium fluorescein was injected at a dose of 0.1 mg/kg, with images acquired from both eyes. Optos fundus images are presented in pseudo color, balanced from green and red laser images. Authors reported 5 patients who underwent non-contact ultra-wide field retinal imaging. Optos P200MA scanning laser ophthalmoscope effectively documented acute and chronic AHT-related retinal hemorrhages and location. Compared to RetCam, authors found several advantages when obtaining Optos P200MA scanning laser ophthalmoscope images including non-contact imaging, no sedation, confocal optics allowing uniform focusing of multiple retina areas and ultra-wide field result in shorter acquisition time, and ultra wide field simultaneous angiogram of several retinal areas. Disadvantages of Optos P200MA scanning laser ophthalmoscope compared to RetCam include portability and accessibility.
The clinical presentation of bradyopsia in children.

Diagnosing bradyopsia can be challenging in young children because structural ophthalmic examination is typically normal and visual acuity can improve with pinhole despite no significant refractive error. This case series highlights the clinical presentation of bradyopsia of 5 affected children (3 Arab families) who harbored the same homozygous RGS9 frameshift mutation, which seems to represent a founder effect for the Arabian Peninsula. The authors make the point that in these cases extended ERG testing is needed to reveal one of the key features of bradyopsia. Standard ERG is insufficient to make the diagnosis. It shows abnormal cone responses under photopic conditions, whereas rod response under scotopic conditions and bright flash are often normal or near normal with non-specific evidence for cone dysfunction. Extended ERG testing (scotopic red flash) shows a normal B1 cone response and is diagnostic for bradyopsia in this setting.

Inflammatory and Neuronal Biomarkers Associated With Retinal Thinning in Pediatric HIV

This study aimed to assess whether neuroretinal thinning in clinically stable perinatally HIV-infected children was associated with biomarkers of immune activation, inflammation, and neuronal damage. Inflammation-associated and neuronal damage markers were measured in blood and cerebrospinal fluid (CSF) of HIV-infected children aged 8 to 18 years. Using mixed-effects regression analyses, associations between these biomarkers and neuroretinal layer thickness were assessed, as measured with spectral-domain optical coherence tomography. Thirty-two HIV-infected children (median age 13.6 years, 50% male) were included. Blood plasma levels of interleukin-6, monocyte chemoattractant protein-1, and soluble intercellular adhesion molecule-1 were inversely correlated with foveal inner plexiform layer thickness (coef = -4.40, P < 0.001; coef = -9.67, P = 0.047; coef = -10.48, P = 0.042, respectively). Plasma interleukin-6 was inversely correlated with foveal ganglion cell layer thickness (coef = -2.49, P = 0.010). Total Tau levels in CSF were inversely correlated with outer nuclear layer and inner segments thickness (foveal: coef = -19.3, P = 0.029; pericentral: coef = -18.09, P = 0.006) and pericentral total retinal thickness (coef = -28.2, P = 0.017). Neuroretinal thinning was associated with inflammation-associated and neuronal
injury biomarkers in a cohort of antiretroviral therapy-treated perinatally HIV-infected children. These findings suggest that ongoing immune activation, inflammation, and neuronal injury occur in parallel with retinal thinning in pediatric HIV. The sample size was small, and since the majority of patients were cART treated, the effects of HIV and retroviral drugs cannot be differentiated. Also, since this is a cross-sectional study, causality cannot be determined.

Optical Coherence Tomography Angiography and Ultra-widefield Fluorescein Angiography for Early Detection of Adolescent Sickle Retinopathy
Prevalence of sickle cell retinopathy varies widely in the literature (0-40%) due to the different ways in which is diagnosed. Most of the pervious studies use biomicroscopy to diagnose sickle cell retinopathy, but with newer and more sensitive techniques such as ultra-widefield fluorescein angiography (UWFA) and optical coherence tomography angiography (OCT-A) the authors speculated that the prevalence of sickle cell retinopathy in adolescence with sickle cell disease (SSD) as actually higher. This was a prospective, cross sectional study of 16 adolescent patients with sickle cell disease and 5 age matched controls. The patients had visual acuity, slit lamp photos, UWDA, spectral domain OCT, and OCT-A performed as part of the study. The authors found that 22 of the 32 eyes in patients with SCD had retinopathy on biomicroscopy, but that 100% of the eyes that had adequate UWFA demonstrated sickle retinopathy. The authors concluded that pediatric sickle retinopathy is likely more prevalent than previously suspected and that newer techniques could improve screening for these patients. The authors highlight the main limitations of the study being the small sample size and that not all patients had adequate UWFA to analyze.

Diplopia following retinal detachment repair: prisms or surgery long term?
Geraldine McBride Br Ir Orthopt J 2016; 13: 52-55
Diplopia following retinal detachment repair surgery is a known but rare complication. Reported incidence in the literature between 1.5% and 25%. The diplopia is thought to be secondary to mechanical restriction of the muscles from the buckle. It can be managed with prisms, botox, and strabismus surgery. Controversy exists as to whether or not the scleral buckle ought be removed to alleviate the diplopia. The author states the conservative approach of incorporated prisms in generally sufficient. The author presents a patient who presented with diplopia following scleral buckle placement who responded favorably with prism lenses.

Practical approach to syndromic pediatric retinal dystrophies
Inherited retinal dystrophies are the main cause of incurable blindness in the Western world and can occur in isolation or as part of a systemic syndrome. Syndromic retinal dystrophy accounts for 20-30% of cases and is more frequently diagnosed in children. The author undertakes a comprehensive review to discuss the approach in syndromic diagnosis. Early diagnosis may be challenging but it is important to approach it in a systematic way. History and pedigree are two important factors and comprehensive eye exam is imperative. Recognition of the ophthalmic findings suggestive of retinal dystrophy along with other ocular abnormalities should prompt a careful evaluation for systemic findings. The physician needs to evaluate by organ systems including facies, growth and nutrition, intellectual disability, hearing impairment, smell and taste as well as dental issues. Integument, musculoskeletal, cardiac, GI, neurologic, and respiratory symptoms and signs must be observed. Finally, examination for endocrine, GU and metabolic issues must be completed. In addition, diagnostic testing with color vision, visual fields, electrodiagnostic testing and OCT may be employed. Genetic testing can provide an accurate and definitive diagnosis to be able to assess risk and counsel patients and their families. With the advent of gene-based therapies, genetic testing may be even more important. Whole exome sequencing may be useful to diagnose new retinal dystrophies that are rare, with their associated complex systemic findings. The author undertakes a comprehensive review with excellent tables highlighting some of the pathognomic and systemic findings in different retinal dystrophies related to syndromic patients as well as discussing diagnostic techniques that may be useful to assist in early identification of these disorders.


This retrospective review evaluated the electrooculogram (EOG) in a series of patients with Best disease and autosomal recessive bestrophinopathy. Patients with Best disease or AR bestrophinopathy who had a normal or atypical EOG light rise were identified. Main outcome measures included EOG amplitude, clinical phenotype, and genotype. 113 patients were identified with likely disease-causing sequence variants in BEST1 (99 Best disease and 14 AR bestrophinopathy); electrooculograms had been performed in 75 of the patients. 20 patients (27%) had no detectable light rise (Arden ratio 100%) and 49 (65%) had Arden ratios between 100 – 165%. 6 patients (8%) had an EOG light rise > 165% No cases demonstrated interocular asymmetry in EOG amplitude. This study demonstrates that the EOG phenotype in Best disease and AR bestrophinopathy is more variable than is currently generally appreciated. As a normal EOG has been shown to occur in the presence of a classic fundus appearance, the authors
argue that consequences of a BEST1 mutation may be independently expressed and may be mediated through differential effects on intracellular calcium homeostasis.

**Ultrawidefield Autofluorescence in ABCA4 Stargardt Disease**


This retrospective cohort study reported ultrawidefield fundus autofluorescence (UWF-FAF) patterns in ABCA4 Stargardt disease. 58 eyes of 29 patients with a clinical diagnosis of Stargardt disease, confirmed ABCA4 genotype, and ultrawidefield fundus autofluoresence imaging were included. 4 independent graders evaluated the images. UWF-FAF images were evaluated for the presence of posterior pole and peripheral findings, and were classified into 1 of 3 types: Type I: lesions confined to the macula with no peripheral findings; Type II: macular atrophy with flecks only in the periphery; Type III: macular atrophy and varying degrees of peripheral atrophy. Peripheral (outside the 55 degree view of standard nonwidefield FAF imaging) alterations on UWF-FAF were present in 76% of eyes. The UWF-FAF pattern was classified as Type I in 24% eyes (14/58), Type II in 24% (14/58), and Type III in 52% (30/58). The most common genetic mutations identified were present in 20.7% and 17.5 % of patients.

Limitations of this study include its retrospective nature with clinical data and imaging collected at only one point in time. Age of onset of disease was often unavailable, and without longitudinal follow-up it is not certain whether the noted patterns represent progressive stages of STGD or rather a spectrum of disease severity. The authors note that most of the genetic testing methods used in this study were unable to detect all variants, and future sequencing of the entire 140 kb ABCA4 locus could detect additional genetic aberrations. Despite these shortcomings, the authors demonstrate via UWF-FAF that abnormalities in the peripheral retina are present in the majority of patients with STGD and would otherwise be missed on conventional nonwidefield FAF. The correlation of UWF-FAF phenotypes with ABCA4 genotypes remains a challenge, though as UWF-FAF is increasingly incorporated into patient care, the ability to stage and offer prognosis to patients with STGD will continue to evolve.

**Novel Classification System for Combined Hamartoma of the Retina and Retinal Pigment Epithelium**


This study presented an anatomical classification scheme for combined hamartoma of the retina and RPE and suggested recommendations for follow-up interval based on the lesion classification. The retrospective review included 11 patients (13 eyes) with combined hamartoma of the retina and RPE examined during a 7-year period. The clinical presentation, fundus examination, and OCT were analyzed. Lesions were classified based on location: macular/peripapillary – Zone 1, mid-periphery – Zone 2, far periphery – Zone 3; associated fundus find-
ings: no retinal traction – Stage 1, retinal traction and/or retinoschisis – Stage 2, retinal detachment – Stage 3; and OCT findings: epiretinal component only – A, partial retinal involvement – B, complete retinal and RPE involvement – C. The authors suggest complete ophthalmologic evaluation at least every 6 months for patients younger than 12 years, with more frequent follow-up for patients with lesions in Zone 1 or Stage 2 and 3. Surgical intervention is recommended in patients with vision loss secondary to macular traction or retinal detachment.

Study limitations include the retrospective design and small subject number, though the rarity of combined hamartoma of the retina and RPE makes substantially larger studies unlikely. This classification scheme provides a comprehensive evaluation of these variable lesions, and may allow for greater standardization in clinical practice and collaborative research studies.

### Repeatability and Longitudinal Assessment of Foveal Cone Structure in CNGB3-Associated Achromatopsia


Although congenital achromatopsia is believed to be a relatively stationary autosomal recessive disorder, questions remain regarding the stability of cone structure over time. This study sought to assess the repeatability of and examine longitudinal changes in measurements of central cone structure in patients with achromatopsia. 41 subjects with CNGB3-associated achromatopsia were imaged over a period of between 6 – 26 months using OCT and adaptive optics scanning light ophthalmoscopy (AOSLO). Outer nuclear layer (ONL) thickness, ellipsoid zone (EZ) disruption, and peak foveal cone density were assessed. ONL thickness increased slightly compared to baseline (0.184 um/month). The EZ grade remained unchanged for 34/41 subjects. Peak foveal cone density did not change significantly over time (mean change 1% per 6 months).

One significant shortfall of this study is that it spanned a relatively short time frame – less than 2 years for most subjects. The stability observed may be due to a very slowly progressing nature of this condition, and additional follow-up might reveal decreasing cone populations over a longer time course. However, these results are promising for the development of gene therapy since a cellular target remains present in retinas for a long period, as demonstrated by the presence of foveal cones in retinas over a wide age range. The authors suggest that OCT and AOSLO may be useful in monitoring structural changes after treatment.

### Stargardt Disease: Beyond Flecks and Atrophy


This retrospective study used OCT to identify changes in the outer retina in areas without atrophy or flecks of Stargardt disease (STGD). 23 STGD patients and 26 control subjects were assessed for outer retina (from outer border of Bruch
membrane [BrM] to the inner border of the inner segment ellipsoid zone [EZ]), BrM—RPE apex, EZ thickness, and apical process interdigitation zone. Patients with STGD had increased BrM—EZ thickness in areas without apparent disease versus control subjects at 1000, 1500, 2000, and 2500 um superior and 1500, 2000, and 2500 um inferior to the fovea. The greatest difference (3.4 um) was at 2500 um superiorly. The BrM—RPE segment showed larger fractional contribution of 0.48 – 0.51 to the overall BrM—EZ thickness compared to 0.35 – 0.42 in control subjects. The thickness of EZ and the interspace between the RPE apex and the EZ were smaller in the STGD patients. Patients with STGD displayed an interrupted interdigitation zone in 16 of 19 eyes (84.2%) versus 6 of 26 eyes (23.1%) of the control subjects. The BrM—EZ segment of the outer retina of STGD patients lacked the typical normal trilaminar pattern.

Although numbers were somewhat small, this study demonstrated that subtle changes are present within the BrM—EZ segment of the outer retina in STGD patients in areas that are devoid of atrophy and flecks, suggesting that pathologic changes in STGD are more widespread than that seen by clinical examination. Future studies may determine the extent that these changes precede flecks and atrophy and whether they can be used as an indicator for disease extent and progression, and thus whether they may serve as markers in prospective studies or in early clinical disease detection.

Comparison of Visual Outcomes in Coats' Disease: A 20-Year Experience.

This is a single-center retrospective cohort study of patients with Coats’ disease. All consecutive patients aged 18 years or younger at presentation have Coats disease identified clinically, angiographically, or both from 1995 through 2015. Patients were divided into 2 groups based on date of presentation: decade 1 (1995-2005) and decade 2 (2006-2015). Management methods included observation (defined as no treatment for posterior manifestations of Coats’ disease; some patients in this group still underwent cataract or strabismus surgery); ablative therapies including cryotherapy, 532-nm laser, or both; vitreoretinal surgery, which included any combination of subretinal fluid drainage, scleral buckle, pars plana vitrectomy, epiretinal membrane removal, and intraocular gas or silicone oil tamponade; IVT injection; or enucleation. After 2008, off-label intravitreal bevacizumab was given to selected eyes based on treating physician preference. Of the total 55 patients identified 39 patient met the inclusion criteria. Eyes were classed into the following stages: Stage 1 has retinal telangiectasia (RT) only; stage 2A refers to eyes with RT and extrafoveal exudation; stage 2B denotes eyes with RT and foveal exudation; stage 3A represents eyes with RT, exudation, and subtotal retinal detachment (RD); stage 3B describes eyes with RT, exudation, and total RD; stage 4 eyes demonstrate RT, exudation, total RD, and secondary glaucoma; and stage 5 eyes are defined as blind eyes with RT, exudation, total RD, and anterior chamber involvement or phthisis (advanced end-stage disease). Forty-seven percent of eyes in decade 1 demonstrated ad-
vanced stages of disease (stage 3B or worse) compared with 20% of eyes in decade 2. There was a trend for the mean initial presenting VA (±SD) for decade 1 eyes to be worse (2.05±1.29 logMAR) than for decade 2 eyes (1.45±0.99 logMAR; P = 0.1). From initial to final follow-up visit, mean VA also worsened for decade 1 eyes (P = 0.03), but remained stable for decade 2 eyes (P = 1.0). At the end of follow-up, there was a trend for mean VA for decade 1 eyes (2.28±1.17 logMAR) to be worse than for decade 2 eyes (1.60±1.15 logMAR; P = 0.07). The authors concluded that the earlier presentation of disease in decade 2 suggests improvements in disease detection over time. Furthermore, there was a trend for eyes to have better final VA in this decade. This is due to a combination of factors, including earlier presentation of disease, fewer eyes being observed without treatment, and eyes, when treated, receiving a higher number of procedures.

Long-Term Anatomical and Functional Outcomes Following Vitrectomy for Advanced Coats Disease


This retrospective study assessed the long-term anatomical and functional results of vitreoretinal surgery in patients with advanced Coats disease. 23 patients that underwent 23-gauge pars plana vitrectomy combined with transsceral cryotherapy, laser photocoagulation, and intraocular tamponade from 2005 – 2014 and had follow-up of at least 1 year were included. The primary outcomes were mean visual acuity and anatomical success. The average age at the time of surgery was 8.7 +/- 1.3 years and the mean follow-up period was 55.2 +/- 31 months. In 16 eyes (70%), further treatment was not necessary. In 7 patients (30%), revision surgery with silicone oil tamponade was required. In 20 eyes (87%), the retina was reattached. At the final visit, 8 eyes (35%) had improved mean Snellen visual acuity from 20/1,000 to 20/160, 3 eyes (13%) showed stabilization, and 6 eyes (26%) had decline in visual acuity. No enucleation was necessary, and there was no progression to neovascular glaucoma.

The authors conclude that 23-gauge PPV combined with cryotherapy, laser and intraocular tamponade could be an effective treatment option for advanced Coats disease, achieving high anatomical success and stable or improved visual acuity with minimal need for retreatment. The study was limited by its single-center retrospective design with a single surgeon performing both preoperative and postoperative evaluation. A large prospective randomized trial would be helpful to investigate the optimal treatment modality for each stage of Coats disease, but due to the rarity of this condition such a study seems unfeasible.

Surgical Outcomes and Complications of Rhegmatogenous Retinal Detachment in Eyes with Chorioretinal Coloboma Abouammoh

This retrospective review reported the outcomes of management of rhegmatogenous retinal detachment in eyes with chorioretinal colobomas. Data were collected on the site of the retinal break, type of surgery, anatomical success, and complications for 119 patients with chorioretinal colobomas who underwent surgical repair. The primary retinal break was at the intercalary membrane in 58.8% of eyes. Vitrectomy with endolaser and silicone oil tamponade was the most common surgical intervention (77.3% of eyes). Final anatomical success was achieved in 87.4% of eyes, and was significantly higher in eyes that received long-acting tamponade. Cryotherapy was associated with failure of primary vitrectomy, and placement of an encircling band did not affect anatomical outcomes. 60% of eyes with recurrent retinal detachment after primary vitrectomy had a primary break within the normal retina.

This study was limited by its retrospective nature, relatively small number of patients, and multi-surgeon participation. However, it is the largest reported series of patients with retinal detachment in eyes with chorioretinal colobomas, and suggests that PPV with long-acting tamponade and retinopexy at the edge of the coloboma in addition to the primary identified breaks likely provides the best outcome for these eyes.

**Peripheral Visual Fields in ABCA4 Stargardt Disease and Correlation With Disease Extent on Ultra-widefield Fundus Autofluorescence.**


Stargardt disease (STGD) is the most common inherited macular dystrophy in both children and adults. However, the disease is not limited to the macula. Over time, the disease progresses centrifugally from the macula to the far periphery along the nasal, temporal, superior, and inferior meridians, with variable rates of progression. Recently ultra-widefield FAF (UWF-FAF) has been used to describe peripheral changes that would not have been detected using 30- or 50-degree FAF and a new classification based on this method has been proposed: type I, consisting of lesions confined to the macula without peripheral changes; type II, consisting of central atrophy with peripheral flecks only; and type III, consisting of central atrophy, with varying degrees of flecks and atrophy in the periphery. The impact of the peripheral changes observed in patients with STGD remains unclear. The authors chose to evaluate disease extent on UWF-FAF in patients with *ABCA4* STGD and correlate these data with functional outcome measures. Sixty-five patients with clinical diagnosis and proven pathogenic variants in the *ABCA4* gene were studied. The UWF-FAF images were obtained using Optos (200 degrees) and classified into 3 types. Functional testing included kinetic widefield perimetry, full-field electroretinogram (ffERG), and visual acuity (VA). All results were evaluated with respect to UWF-FAF classification. The main out-
come measures were: classification of UWF-FAF; area comprising the I4e, II4e, and IV4e isopters; ffERG patterns; and VA. For UWF-FAF, 27 subjects (41.5%) were classified as type I, 17 (26.2%) as type II, and 21 (32.4%) as type III. The area of each isopter correlated inversely with the extent of the disease and all isopters were able to detect differences among UWF-FAF types (IV4e, P = .0013; III4e, P = .0003; I4e, P < .0001 = 3.93e⁻⁸). ffERG patterns and VA were also different among the 3 UWF-FAF types (P < .001 = 6.61e⁻⁵ and P < .001 = 7.3e⁻⁵, respectively). Patients with widespread disease presented with more constriction of peripheral visual fields and had more dysfunction on ffERG and worse VA compared to patients with disease confined to the macula. In conclusion, UWF-FAF images may provide information for estimating peripheral and central visual function in STGD. In addition, the loss of peripheral visual field in a subset of patients in this study contradicts the conventional wisdom that STGD is a maculopathy with preservation of peripheral vision, which may affect patient counseling.

Peripheral Fundus Findings in X-linked Retinoschisis.

X-linked retinoschisis (XLRS) is an inherited retinal degeneration presenting in the first decade of life and characterized by a splitting of the inner retina in the macula with cystic cavities. Approximately 50% of individuals have schisis cavities in the peripheral retina as well. Vitreous hemorrhage (VH) and retinal detachment (RD) cause a precipitous decline in vision in a subset of patients with XLRS, an otherwise a slowly progressive condition. This study aims to report the frequency of macular and peripheral retinal findings in a large cohort of patients with XLRS and to determine whether peripheral retinal findings are associated with VH and RD. A retrospective observational case series was performed in 65 patients with XLRS with a pathogenic variant in retinoschisin 1. Chart review included examination notes, fundus photographs and optical coherence tomography (OCT). Fisher exact tests and univariable logistic regression analysis were used to determine the association between peripheral retinal findings (including retinoschisis, metallic sheen, vascular sheathing, pigmentary changes, white spiculations and vitreous veils) and complications (including VH and RD). Seven eyes (8%) showed normal macular structure on OCT. Peripheral retinoschisis was significantly associated with both VH and RD. Out of 10 eyes with complications, 9 (90%) had peripheral retinoschisis, compared with 33 out of 116 eyes (28%) without complications (p=0.0014). In addition, each additional peripheral finding increased the odds of RD by a factor of 4.06 (95% CI 1.58 to 10.39, p=0.028). There were no complications in the 28 eyes with a normal periphery (p=0.84) or in the 35 eyes with metallic sheen (p=0.42). Importantly, the data suggest that patients with peripheral are at increased risk for VH and RD. Furthermore, patients with additional peripheral retinal findings together with peripheral schisis may carry additional risk for RD. A normal retinal periph-
ery and a retinal metallic sheen may both portend a good prognosis with respect to risk for complications.

**Everolimus to treat aggressive retinal astrocytic hamartoma in tuberous sclerosis complex.**

Retinal astrocytic hamartomas (RAH) are the most frequent ocular manifestation of tuberous sclerosis complex and are usually indolent, requiring only observation. The authors report an aggressive RAH subtype in a child unresponsive to anti-VEGF and laser therapy. Treatment with systemic everolimus was well-tolerated and significantly reduced ocular (and nonocular) tumor size and fluid exudation.

**Vancomycin-Associated Hemorrhagic Occlusive Retinal Vasculitis: Clinical Characteristics of 36 Eyes.**

This is a non-pediatric disorder but nonetheless an important disease entity to be aware of for all ophthalmologists and those performing pediatric cataract surgery. Hemorrhagic occlusive retinal vasculitis is a rare but potentially devastating condition that can develop after cataract surgery or intraocular injection. The authors report 36 eyes of 23 patients that developed HORV after receiving intraocular vancomycin via intracameral bolus (33/36) and via intravitreal injection (1/36) or through the irrigation bottle (2/36). Characteristic findings of HORV included unremarkable postoperative day 1 undilated examination, delayed-onset painless vision loss, mild anterior chamber and vitreous inflammation, sectoral retinal hemorrhages in areas of ischemia, and predilection for venules and peripheral involvement. Patients sought treatment with HORV 1 to 21 days after surgery or intravitreal injection. Visual results usually were poor: 22 of 36 eyes (61%) had 20/200 or worse visual acuity and 8 of 36 eyes (22%) had no light perception (NLP). Neovascular glaucoma developed in 20 of 36 eyes (56%). Seven eyes received additional intravitreal vancomycin after surgery; 5 of these 7 eyes had NLP visual acuity at the most recent examination. Three eyes received intravitreal corticosteroids and had final visual acuities of 20/40, 20/70, and hand movements. Disease course and findings suggest that HORV is caused by a delayed hypersensitivity reaction to vancomycin. Early treatment with corticosteroids likely is beneficial. Subsequently, anti-vascular endothelial growth factor injections and panretinal photocoagulation are important to prevent neovascular glaucoma, a common complication. Avoidance of additional intravitreal vancomycin is recommended if HORV is suspected.

**Macular Sensitivity Measured With Microperimetry in Stargardt Disease in the Progression if Atrophy Secondary to Stargardt Disease (ProgStar) Study: Report No. 7**
This was a retrospective multicenter cohort study of 199 patients and 326 eyes with confirmed mutation of ABCA4 STGD1 to study the natural history of atrophy progression in Stargardt Disease. Patients had testing with Nidek MP-1 microperimeter to determine normal, relative or deep scotomas. Patients had a mean age of 34.2 years and findings indicated that microperimetry provides a comprehensive assessment of retinal function, as mean sensitivities (MS) from the fovea were lower as compared to the inner and outer rings. In addition, MS per eye were lower per additional year of life. In summary, future clinical trials for children with Stargardt disease will benefit from this study of the level of macular sensitivities in patients with ABDA4 STGD1.

Incidence of Atrophic Lesions in Stargardt Disease in the Progression of Atrophy Secondary to Stargardt Disease (ProgStar) Study: Report No. 5

This was a retrospective multicenter cohort study of 217 patients to determine outcome measures to improve treatment options and ultimately, prognosis for children suffering from Stargardt Disease. The incidence of atrophic lesions was determined by fundus autofluorescence. The amount of autofluorescence was defined at a central reading center in two categories: definitely decreased autofluorescence (DDAF) and questionably decreased autofluorescence (QDAF). The patients had a mean age of 21.8 years with a mean follow-up of 3.9 years. Results indicated that 50% of the eyes without an initial DDAF will develop an atrophic lesion within 5 years. This study suggests that for future clinical trials, DDAF incidence could be an outcome measure for children with Stargardt Disease.

Association of Maternal Smoking During Pregnancy and Birth Weight with Retinal Nerve Fiber Layer Thickness in Children Aged 11 or 12 Years: The Copenhagen Child Cohort 2000 Eye Study

This is a prospective, population-based cohort eye study of 1406 children born in 2000 in Copenhagen, Denmark. From this cohort, an eye exam, including evaluation of peripapillary retinal nerve fiber layer (RNFL) thickness was performed on 1323 children at 11 or 12 years old. Exposure to maternal smoking and low birth weight were independently associated with having a thinner RNFL at age 11
or 12 years. As previous research also suggests, this large cohort study found it is better to avoid smoking during pregnancy to avoid retina and optic nerve abnormalities in children to prevent amblyopia.

**Impact of Retinitis Pigmentosa on Quality of Life, Mental Health, and Employment Among Young Adults.**

Previous studies in retinitis pigmentosa (RP) have shown that visual acuity (VA) and visual field (VF) abnormalities are strong predictors of self-reported visual quality of life, anxiety, and depression. Severe visual impairment is associated with lower employment rates, decreased productivity, and wellness at work. In the United States, the employment rate was estimated at 42% in subjects with severe visual impairment vs 69.5% in subjects with normal vision; only 22% of the 4 million Americans with vision loss are employed. In France, 29% with low vision or blindness were employed vs 65% with mild impairment. Studies focused on RP also show lower education levels, lower income levels, and a higher rate of unemployment by the age of 40 vs age-paired controls. These results suggest that an insufficient number of visually disabled workers benefit from disability aids, despite structured state-funded disability policies in developed countries. However, there is limited research taking into account the impact of mental health and work conditions on employment sustainability in visually disabled individuals. The authors sought to determine the relationship between visual function and quality of life, education, mental health, and employment among young adults with RP. The authors included 148 patients (mean age 38.2 ± 7.1 years) diagnosed with RP, living in France. Quality of life was assessed using the National Eye Institute Visual Function Questionnaire (VFQ-25), mental state with the Hospital and Anxiety and Depression Scale (HADS), and employment with a specifically designed questionnaire. Limited visual impairment was noted in 22.3%, low vision in 29.7%, and legal blindness in 48.0%. There was a correlation between quality-of-life scores and residual visual field. Mental health scores were suggestive of anxiety in 36.5% and depression in 15.5%. The rates did not increase with disability level. The percentage of subjects with higher education did not significantly decrease with disability level. The employment rate did not significantly decrease with disability level. It was lower in subjects reporting depression. Self-rated impact of RP on employment increased with disability level. The results differ from previous results showing lower education rates and employment rates in young adults with RP. Further research is warranted focusing on the impact of mental health, education, workplace conditions, and employment aids on employment rate vs age- and education-matched normally sighted controls to guide visual disability strategies in RP.

**Vessel Density analysis in Patients with Retinitis Pigmentosa by Means of Optical Coherence Tomography Angiography.**
The authors describe the vascular abnormalities in patients affected by retinitis pigmentosa (RP) by means of optical coherence tomography angiography (OCT-A). Patients with RP presenting at the Medical Retina Service of the Department of Ophthalmology, University Vita-Salute San Raffaele in Milan were recruited. Inclusion criteria were: diagnosis of RP, clear ocular media, adequate pupillary dilation, and stable fixation. Patients underwent best-corrected visual acuity (BCVA), biomicroscopy, shortwavelength fundus autofluorescence (SW-FAF), and 3Å~3 Swept Source OCT-A. 30 healthy subjects were chosen as controls. The main outcome was identification of abnormalities in density of the superficial capillary plexus (SCP) and deep capillary plexus (DCP), along with abnormalities of the choriocapillaris (CC). Sixteen patients (32 eyes) were recruited (6 females, 37.4%). Mean age was 53±18 years; mean BCVA was 0.5±0.3 LogMAR. Vessel density analysis disclosed a statistical significant difference in the SCP (29.5±6.8 vs 34.1±4.3; p=0.009) and in the DCP (28.7 ±7.5 vs 35.5±5.7; p=0.001) between the patients and the controls. No difference was found at the level of the CC (51±4.4 vs 51.3±2.2; p=0.716). RP patients showed a bigger foveal avascular zone at the DCP level compared to controls (p<0.001). This study showed that most of the vascular impairment in patients affected by RP localized in the DCP, with relative sparing of the SCP and CC. DCP alterations were more pronounced outside the hyper-autofluorescent ring on SW-FAF. Vascular impairment may preclude good treatment outcomes in RP patients.

Prevalence, Age at Diagnosis, Mortality, and Cause of Death in Retinitis Pigmentosa in Korea—A Nationwide Population-based Study.

Retinitis pigmentosa (RP) is one of the most common hereditary retinal degenerations. It is characterized by progressive dysfunction of photoreceptors, leading to hallmark symptoms such as nyctalopia and contraction of the visual field. To the best of our knowledge, mortality of RP patients has never been investigated as yet. Given that RP is not associated with fatal conditions, one can assume that RP alone does not increase mortality. Nonetheless, RP causes visual impairment, which could impact patient mortality, as supported by recent studies suggesting that the visual impairment had a significant influence on the mortality. The authors sought to determine the prevalence and mortality of RP patients in Korea. The authors used data covering the 2011-2014 period from the Rare Intractable Disease (RID) registry and Health Insurance Review and Assessment (HIRA) service, which include information on all patients diagnosed with RP based on predefined diagnostic criteria. Using the HIRA-RID database, the authors evaluated the prevalence and age at diagnosis of RP patients across the entire Korean population. We further linked the data from Statistics Korea to the
HIRA-RID database to confirm mortality and causes of death. The prevalence in the total population across all ages was 11.09 per 105 people, and the prevalence in those over the age of 40 was 16.16 per 105 people. The age at diagnosis ranged from 0 to 95 and, on average, was 44.8. The standardized mortality ratio (SMR) was 1.56 for all ages, peaking at 2.61 in men aged 40–59, which was attributed to 6.6-fold higher suicide rates than the same age group in the general male population. This the first nationwide epidemiologic study of RP patients covering the entire population of all ages. The results suggest that the prevalence of RP in Korea is about 1 in 9000 for all ages and 1 in 6000 for those over 40 years of age. The higher mortality of RP patients than that of the general population is attributable to a high suicide rate in male RP patients of working ages, which necessitates a careful attention to their mental health.

Dynamic and Static Vessel Analysis in Patients with Retinitis Pigmentosa.

Retinitis pigmentosa (RP) is a heterogeneous group of diseases characterized by progressive degeneration of rod and cone cells. The clinical features of typical RP include “bone-spicule” retinal pigment, thinning and atrophy of the retinal pigment epithelium, “waxy pallor” of the optic nerve head, and attenuation of retinal arteries. Attenuation of the retinal blood vessels is a funduscopic hallmark of RP and was thought historically to result from diminished ganglion cell metabolism after photoreceptor degeneration. The Dynamic Vessel Analyzer (DVA; Imedos, Jena, Germany) is a new clinical tool that allows the noninvasive investigation of static and dynamic features of retinal vessels. The aim of the present study is to use DVA to make an in vivo evaluation of the vascular anatomy and functionality in a population of patients with early manifestation of RP and compare the results with those of a group of normal subjects. Fourteen patients with early RP and 14 normal subjects were consecutively enrolled in this observational, prospective study. Each patient underwent a complete ophthalmologic examination, including dynamic and static retinal vessel analysis using the Dynamic Vessel Analyzer. The patients with RP and the control group were well matched in age and sex. Patients with RP had a mean best-corrected visual acuity of 20/25 (range: 20/40–20/20). Dynamic vessel analysis performed in patients with RP showed an arterial and venous dilation during flicker stimulation of 5.28 ± 1.7% and 4.07 ± 1.78%, respectively. Only arterial dilation was statistically different compared with control subjects (3.33 ± 0.99%, P = 0.0062). Static retinal vessel analysis in patients with RP showed a decreased mean central retinal artery equivalent and central retinal vein equivalent compared with control subjects. By contrast, the arterial-to-venous ratio was similar in both groups (RP: 0.79 ± 0.11, control group 0.86 ± 0.04, P = 0.072). In conclusion, the data confirm that retinal arterial and venous narrowing is present at an early stage in patients affected by RP. However, dynamic vessel analysis shows how the retina of patients with RP with no best-corrected visual acuity loss presents an augmented
artery dilation response compared with normal subjects and retained neurovascular coupling.

**Measurement and Reproducibility of Preserved Ellipsoid Zone Area and Preserved Retinal Pigment Epithelium Area in Eyes With Choroideremia.**

Choroideremia (CHM) is an X-linked recessive, progressive retinal degenerative caused by null mutations in the *CHM* gene (Xq21), which leads to the absence of an intracellular protein called Rab escort protein-1 (REP1). As a result, progressive but slow degenerative changes in the neurosensory retina, retinal pigment epithelium (RPE), and choroid start from the periphery and expand centripetally. There is still uncertainty whether the neuroretina, RPE, and choroid are all primarily affected, or whether one or more of these layers is secondarily affected. Of note, visual acuity does not decrease until very late in the disease course. Thus, by relying on visual acuity as the only outcome measure, just very advanced CHM cases would be enrolled in interventional clinical trials. Therefore, other outcome measures, either anatomic or physiological or both, should be applied in clinical trials of CHM. The authors identify valid and reproducible methods for quantifying anatomic outcome measures for eyes with choroideremia (CHM) in clinical trials. In this multicenter study, patients with confirmed genetic diagnosis of CHM were enrolled. All cases underwent spectral-domain optical coherence tomography (SDOCT) and fundus autofluorescence (FAF) imaging. Two graders independently delineated boundaries of preserved autofluorescence (PAF) and preserved ellipsoid zone (EZ) on FAF and OCT images, respectively. The results of the 2 independent gradings of both FAF and OCT images were compared to assess the reproducibility of the grading methods. A total of 148 eyes from 75 cases were included. In 21% of eyes PAF and in 43% of eyes preserved EZ had extended beyond the image capture area. After exclusion of these eyes and low-quality images, 114 FAF and 77 OCT images were graded. The mean PAF areas from 2 independent gradings were 3.720 ± 3.340 mm² and 3.692 ± 3.253 mm², respectively. Intraclass correlation coefficient (ICC) for these gradings was 0.996. The mean preserved EZ areas from 2 independent gradings were 2.746 ± 2.319 mm² and 2.858 ± 2.446 mm², respectively. ICC for these gradings was 0.991. In conclusion, in the largest-ever natural history study of the choroideremia, the authors have identified reproducible methods for grading of FAF and OCT to quantify the area of preserved RPE and preserved EZ, respectively. These variables would be potential anatomic outcome measures for CHM clinical trials and could be studied and tracked longitudinally in choroideremia.

**Functional and Anatomical Outcomes of Choroidal Neovascularization Complicating BEST1-Related Retinopathy.**
The bestrophinopathies are a spectrum of inherited retinal dystrophies that result from mutation of the \textit{BEST1} gene. The commonest presentation within this group is Best disease (BD; Vitelliform Macular Dystrophy; OMIM 153700), a macular dystrophy characterized by bilateral accumulation of subretinal yellow material with later eruption into the photoreceptor layer and symptomatic reduction in vision. This form of the disease is most commonly associated with heterozygous missense mutations usually within the first half of the \textit{BEST1} gene. In Best disease, central visual acuity (VA) may be affected at any stage, although this usually is associated with either intraretinal fluid (IRF) accumulation, disruption of the photoreceptor layer during the vitelliruptive stage of dominant disease, or later atrophy. Rarely, visual decline may be the result of choroidal neovascular membrane (CNVM) formation. Although there are a few case reports and small series suggesting that CNVM can be successfully treated with intravitreal injections of recombinant antibodies directed against vascular endothelial growth factor (VEGF) (Ranibizumab, Bevacizumab), there is no evidence to suggest that outcomes are better than conservative management (observation alone). The authors describe the presenting features and functional outcomes the largest case series of patients with choroidal neovascular membrane complicating \textit{BEST1}-related retinopathy (Best disease and autosomal recessive bestrophinopathy). Patients were identified retrospectively over an 11-year period. Records were reviewed to extract demographic as well as functional and anatomical outcome data. Fourteen eyes of 12 patients were identified (11 Best disease and 1 autosomal recessive bestrophinopathy). Median follow-up was 2.8 years (range 0.8–6). The median age at choroidal neovascular membrane discovery was 15.5 years (range 6–72). Choroidal neovascular membranes were active early in the disease course before vitelliruptive. Seven eyes were treated with intravitreal bevacizumab, 7 eyes were monitored by observation alone. On average, patients required a single treatment (median = 1, range 1–10). The median gain in visual acuity was greater in the treated versus the observed group - 0.46 versus 0.17 decimalized units of Snellen acuity, respectively. Although a significant reduction in central macular thickness was evident in both groups, 150 mm (treated) and 104 mm (observed), active treatment was not associated with greater thinning than observation. In conclusion, there is a high rate of spontaneous recovery of \textit{BEST1}-related choroidal neovascular membrane, and overall the authors observed a gain in visual acuity associated with a reduction in central macular thickness. Active treatment, here with intravitreal bevacizumab, is associated with better functional outcomes than observation alone.

\textbf{Assessment of the Retinal Structure in Children with Incontinentia Pigmenti}


These investigators used hand-held SDOCT to evaluate the retinal microanatomy in 7 children (4 weeks – 13 years) examined in the clinic or during an examination under anesthesia. The scans were analyzed for anatomical changes in the outer and inner retina by certified graders, and the medical records were as-
sessed for systemic findings. Despite normal foveal structure and normal visual acuity in all but one eye, abnormal retinal findings were observed unilaterally in three children. Inner and outer retinal thinning was present temporally in two children; the thinning was present prior to and persisted after treatment. One child demonstrated a distorted foveal contour and significant retinal thickening secondary to dense epiretinal membrane and vitreomacular traction. All other children had normal retinae. The authors emphasize that hand-held SDOCT imaging of the retina has revealed retinal structural defects that were previously unreported and not visualized via routine clinical examination including retinal photography. Despite a normal foveal structure and visual acuity, functional assessment such as visual field testing and multifocal ERG could provide information on the location of specific functional defects and the dysfunctional components of the retina in children with IP, particularly in the corresponding areas of OCT-identified inner and outer retinal thinning.

**Unusual Father-to-Daughter Transmission of Incontinentia Pigmenti Due To Mosaicism in IP Males**

Francesca Fusco, Matilde Immacolata Conte, Andrea Diociaiuti, Stefania Bigoni, Maria Francesca Branda, Alessandra Ferlini, Maya El Hacehem, and Matilde Valeria Ursini *Pediatrics*. September 2017; 140(3)

Incontinentia Pigmenti is an X-linked dominant ectodermal disorder that affects the skin and eyes. The disorder is caused by mutations that have thought to be lethal in males and therefore always transmitted from an IP-affected mother to her daughter. The article presents two families with father-to-daughter transmission of IP and show first time evidence that the combination of somatic and germ-line mosaicism for IKBKG/NEMO loss of function mutations in IP males resulted in the transmission of the disease from a male father to female child. The researchers searched for the mutant allele for IKBKG/NEMO in blood, urine, skin, and sperm DNA. They found that the two fathers had somatic and germ-line mosaics for the mutation or the exon deletion of IKBKG/NEMO genes. The highest level of mutant cells were detected in the sperm which may explain the recurrence of the disease. The authors recommend that careful clinical evaluation for skin lesions in IP males/fathers as well as investigate the sperm, blood, urine, and skin for gene mutations. This investigation of the fathers can help ensure correct genetic counseling and prevent risk of paternal transmission of IP.

**Use of a Carbonic Anhydrase Inhibitor in X-Linked Retinoschisis: Effect on Cystic-Appearing Macular Lesions and Visual Acuity**


This retrospective analysis sought to evaluate changes in cystic-appearing macular lesions and visual acuity in patients with X-linked retinoschisis being treated with a carbonic anhydrase inhibitor. 68 eyes from 36 patients between the ages 5
61 years were monitored. The most commonly used CAI was dorzolamide in 86%. Macular cystic-appearing lesions were monitored with OCT, and analyses for changes in visual acuity and macular cysts included comparisons between treatment and pretreatment segments. 45 eyes (66%) had a reduction of their cysts while on a carbonic anhydrase inhibitor. 20 eyes (29%) showed no discernable change in cystic appearance on OCT while on a CAI, and 3 eyes (4%) demonstrated worsening of their cysts with treatment. The estimated average ETDRS equivalent improvement in acuity was 0.09 logMAR, or slightly less than one line on the ETDRS chart. Although the acuity improvement is small and of uncertain clinical significance, the authors argue that better preservation of retinal structure by reducing retinal thickness associated with reduction in the size of cystic lesions could result in long-term preservation of visual acuity by limiting the development of atrophic macular lesions.

Electroretinographic and Visual-Evoked Potential Changes in Relation to Chelation Modality in Children with Thalassemia


This study evaluated the possible benefits of using electrophysiologic investigations to detect preclinical retinal and visual pathway changes and to correlate them with chelation modality in children with thalassemia. 60 patients on a single oral iron chelator (deferrioxamine) (Group 1), 60 on deferoxamine chelator (Group 2), and 60 controls (Group 3) were enrolled and underwent full ophthalmologic examination, pattern VEP, pattern ERG, and multifocal ERG. In all patients the fundus showed no abnormalities. Multifocal ERG mean P1 amplitude showed significant differences in all 5 rings, with amplitudes lower in Groups 1 and 2 than Group 3; amplitudes were also lower in Group 2 than Group 1. There was a significant difference between groups regarding P50 wave latency and N35-P50 of pattern ERG amplitude, but no significant differences between groups regarding N95 wave of pattern ERG and pattern VEP waves' amplitude and latency. Notably, the electrophysiologic tests that showed significant differences between patients and controls were multifocal ERG and P50 wave of pattern ERG, which are tests that evaluate macular function. Pattern VEP and N95 wave of pattern ERG assess visual pathway and optic nerve function and were statistically insignificant among the groups. Multiple regression analysis demonstrated that chelator was the most important determinant for multifocal ERG and P50 parameters, with defereroxamine found to be more toxic on the macula than oral chelator. Because these findings of electrophysiologic changes detected prior to any visual deterioration or fundus changes, the authors recommend regular electrophysiologic evaluation for children with thalassemia for possible early preclinical detection of macular changes and potential chelator regimen adjustment or shift from defereroxamine to oral chelator.

Vigabatrin Toxicity in Infancy is Associated with Retinal Defect in Adolescence: A Prospective Observational Study
This prospective cross-sectional study evaluated whether vigabatrin (VGB)-attributed retinal toxicity defined by ERG in early childhood is associated with visual system defect in adolescents after discontinuation of VGB. 24 children aged 7 years or older who were previously treated with VGB and monitored in early childhood by ERG were included; 10 had been diagnosed with VGB-attributed retinal defect (Group I) and 14 had no VGB-attributed retinal defect (Group II). The investigators assessed the extent of monocular visual fields using Goldmann kinetic perimetry, and RNFL thickness at the optic nerve head using OCT. Of those children able to complete testing (6 eyes in Group I and 16 eyes in Group II), Goldmann results revealed visual field loss in Group I and not in Group II. OCT demonstrated attenuation of the RNFL in all 6 eyes of Group I subjects and in 1/10 eyes of Group II subjects. The reduction in nerve fiber layer was associated with the severity of the functional reduction in amplitude of the 30-Hz flicker from baseline, and the most prominent difference between individuals in Groups I and II occurred at the inferior and superior quadrants of the optic nerve head with relative sparing of the temporal quadrant. It is not known whether seizure type, developmental delay, or the presence of other comorbidities have an effect on the risk of developing visual field defects, which is a possible confounder in this cohort. Some of the tested subjects also took other antiseizure medications that may have contributed to the observed visual field defects. In addition, the 30-Hz flicker can be abnormal unrelated to VGB, though this short-fall was mitigated by defining toxicity based on each child’s own baseline ERG response. Another study limitation is the lack of control for the number of ERG assessments: individuals with more assessments are more likely to be categorized as having toxicity. Group I participants were treated with VGB for a longer period of time than Group II participants. Despite these limitations, this study associates visual field reductions and RNFL attenuation with previously determined VGB toxicity as measured by ERG. Incorporating ERG and OCT could be advantageous in monitoring VGB use in a patient population that is unable to undergo standard visual field testing.

OCT imaging in disease

Optical coherence tomography in Best vitelliform macular dystrophy.

The purpose of this observational cross-sectional study was to analyze spectral-domain optical coherence tomography (SD-OCT)-specific findings in the different stages of vitelliform macular dystrophy (VMD). Thirty-seven patients (mean age 36.6 ± 21.3 years; range 3-74) were recruited. All the patients underwent a com-
plete ophthalmologic examination, including best-corrected visual acuity (BCVA), biomicroscopy, and SD-OCT. The examined findings were vitelliform material, neurosensory detachment, intraretinal hyper-reflective foci, and the status of external limiting membrane, ellipsoid zone, and retinal pigment epithelium. The primary outcome was the stratification of SD-OCT findings in each VMD stage. Secondary outcomes included the description of different characteristics related to intraretinal hyper-reflective foci. Outer retinal layers were preserved almost exclusively in stage 1 (range 70%-100%), whereas their disruption and absence were typical of stages 2 to 4 (83%-100%) and stage 5 (67%-83%), respectively. Vitelliform material was always found in stages 2 and 3, 89% of stage 4, and rarely in stage 5 (33%). Neurosensory detachment was to some extent representative of stages 3 and 4 (80% and 72%, respectively), when compared with the other stages (p<0.001). Hyper-reflective foci (16% of all eyes) demonstrated a progressive increase across stages 2 to 4, with slightly reduced figure in stage 5. These foci were located in the outer nuclear and plexiform layers, they were of different sizes, and were not associated with a visual acuity reduction (p = 0.64). The authors conclude that a progressive deterioration of the outer retinal layers was noticeable in more advanced stages of VMD. The reduction of vitelliform material from stage 3 to 4 was paralleled by an increased evidence of neurosensory detachment. Although showing different size and location, hyper-reflective foci did not correlate with worse BCVA.

The main limitation of this study is that it is not longitudinal; the authors recruited patients at different stages of the disease to demonstrate the changes that occur in these patients over time.

Spectral domain optical coherence tomography findings of patients under treatment for pediatric acute lymphoblastic leukemia


The purpose of this cross-sectional study was to investigate the use of spectral domain optical coherence tomography (SD-OCT) findings in pediatric acute lymphoblastic leukemia (ALL) patients. Children that were diagnosed with precursor B-cell ALL and classified as belonging to the medium-risk group for relapse were selected for this study. Individuals who were in continuous remission and on maintenance therapy were included in the study group. Cases that had central nervous system involvement were excluded. Age-matched, otherwise healthy children were selected for the control group. Each study participant underwent a comprehensive eye examination and SD-OCT evaluation. A total of 112 eyes of 56 children were included; 54 eyes in the study group and 58 in the control group. Study group mean age was 9.22 ± 4.0 years (range, 5-18 years). Subfoveal and temporal choroidal thicknesses of the posterior pole were significantly thinner in the study group compared to controls (P < 0.005). Similarly, peripapillary choroidal thicknesses were significantly thinner in most sectors of the study group compared to controls (P < 0.005). There were no major differences be-
tween groups in terms of central macular thicknesses and overall RNFL thicknesses. The authors conclude that in their cohort of pediatric ALL patients, choroidal attenuation was demonstrated. They state that further studies are warranted to clarify the utility of SD-OCT in detecting subclinical ocular involvement and monitoring treatment response and risk of relapse in patients with pediatric leukemia.

Despite the small sample size, the study is well designed. The authors went to great lengths to make sure that refractive problems did not influence their results. However, there was not information regarding other characteristics and demographic data of both groups. It seems that patients were recruited a few years post initial diagnosis and a longitudinal study might have given more information regarding the choroidal changes that were recorded.

**OCT IMAGING – DATA ON NORMAL EYES**

**Functional analysis and associated factors of the peripapillary retinal nerve fibre layer in former preterm and full-term infants**

It is uncertain whether retinal nerve fiber layer (RNFL) thickness is a marker of visual function in preterm infants. The purpose of this study was to use SD-OCT to measure RNFL thickness in former preterm and full-term infants and assess factors related to visual function. 432 patients were analyzed in this prospective study. 193 were former preterm infants (≤32 weeks) and 239 were former full-term infants (≥37 weeks). Global RNFL thickness was found to be thinner in infants ≤28 weeks compared to infants with GA 29 to 32 weeks and to full-term infants. This was independent of the occurrence of ROP. In fact, the data indicates that the more premature the infant, the more the RNFL was affected regardless of ROP development. RNFL was positively associated with higher birth weight and gestational age. Reduced RNFL was related to decreased visual function, and this correlation was found in all peripapillary sectors. However, the authors do state the reduced/altered RNFL does not mean it is the cause of decreased visual function. In conclusion preterm infants are at risk of peripapillary RNFL changes that are associated with reduced visual function.

**Retinal structure assessed by OCT as a biomarker of brain development in children born small for gestational age**

Previous research has shown thinning in the retinal nerve fiber layer (RNFL) in school-age children born small for gestational age (SGA). Also, thinner RNFL may relate to brain structure and neurodevelopment in early preterm infants. This
study evaluated the relationship between retinal structure and brain changes in children age 6-16 who were born SGA. The children in the cohort underwent full ophthalmological exam and retinal imaging with SD-OCT. 25 children born SGA were paired with 25 children born at appropriate weight for gestational age. On MRI, SGA children showed lower total white matter, parietal lobe, and thalamus volumes. No direct correlation was found between retinal thickness and brain volumes. Children with abnormal OCT (GCL-IPL thickness) did show lower total intracranial volumes, decreased total gray and white matter volumes, and other decreased volumes in certain brain regions. Therefore, retinal ganglion cell layer is a potential biomarker of neuronal damage in the brain of children born SGA. The GCL-IPL seems to be the most affected structure, with its thinning corresponding to the most profound brain anomalies.

COAT’S DISEASE

Subfoveal Nodule in Coats’ Disease: Toward an Updated Classification Predicting Visual Prognosis


This study examined the prevalence, clinical characteristics, and nature of subfoveal nodules in Coats’ disease and the associated impact on long-term visual outcome. Consecutive cases of Coats’ disease with foveal exudation were retrospectively reviewed, and the presence of a subfoveal nodule or macular fibrosis was recorded. Among 40 patients presenting with unilateral Stage 2B or 3A1 Coats’ disease, a subfoveal nodule was detected in 21 patients (52.5%). Three patients (15.8%) without subfoveal nodule and 21 patients (100%) with subfoveal nodule progressed to a macular fibrotic scar; the mean time of macular fibrosis onset was 11.0 months. Final visual acuity was worse in patients who presented with a subfoveal nodule at diagnosis. Of 18 cases with subfoveal nodule that underwent FA, retinal-retinal anastomosis and neovascularization were detected in 13 (72.2%) and 2 eyes (11.1%), respectively. Histopathologic analysis of an enucleated eye with a subfoveal nodule revealed an aggregate of proteinaceous material including fibrin, spindle cells, macrophages, and pigmented cells.

The study was limited by its retrospective nature and small number of patients due to the low prevalence of Coats disease, and also by limited imaging in some cases due to availability or patient cooperation. However, strong statistical association supports the conclusion that the presence of a subfoveal nodule at presentation is a predictive factor for macular fibrosis development and worse visual outcome in patients with Coats’ disease. The authors suggest an updated classification with two subcategories within Stage 2B: without subfoveal nodule (Stage 2B1) and with subfoveal nodule (Stage 2B2).
Progressive Retinal Vasodilation in Patients With Type 1 Diabetes: A Longitudinal Study of Retinal Vascular Geometry

This study evaluated longitudinal retinal vascular geometry (RVG) changes in adolescents with type 1 diabetes to determine whether chronic diabetes complications could be predicted. The authors followed 102 adolescents (baseline: 47.1% male, mean [SD] age 14.4 [1.6] years, diabetes duration 7.2 [3.1] years, HbA1c 8.1% [1.3%] over three visits, with a mean follow-up of 2.6 years. Retinal vascular geometry was measured using a standardized computer-assisted protocol from retinal photographs at each visit. Multivariable linear mixed-models and logistic regression were used to examine predictors of RVG and diabetic retinopathy. During follow-up, mean arteriolar caliber, venular caliber, and venular tortuosity increased, from 156.0 (SD, 14.5) to 164.9 (14.0) µm, 215.9 (22.5) to 230.3 (20.6) µm, and 1.096 (0.014) to 1.099 (0.016), respectively (all P < 0.005). Other RVG measurements (fractal dimension, branching angle, length to diameter ratio) remained stable. Higher than baseline HbA1c and longer diabetes duration were associated with greater venular vasodilation. Retinopathy developed at any time-point in 24% of subjects, and the highest tertile arteriolar fractal dimension was associated with cumulative incidence of retinopathy (multivariable odds ratio 3.2, 95% confidence interval 1.0–9.6; P = 0.04), suggesting value as a potential biomarker for diabetic complications. Limitations of this study include small sample size (limiting number of variables able to be tested), and less-motivated participants (who did not show up for 3 visits) may have had poorer systemic metabolic control and may not have been included in the study, so results may not be generalizable to this group.

Risk Factors for Posterior Subcapsular Cataract in Retinitis Pigmentosa

This study investigated the risk factors for posterior subcapsular cataract (PSC) development in retinitis pigmentosa (RP). A total of 322 eyes of 173 patients who were diagnosed with typical RP were retrospectively studied. The authors considered the following possible risk factors for PSC: age, sex, hypertension, diabetes mellitus, high myopia, asthma, history of steroid intake, and aqueous flare. Aqueous flare values were measured consecutively in 2012 and 2013 using a laser flare cell meter. The lens including PSC was examined with a slit lamp after dilation with tropicamide 1% and phenylephrine 2.5%. The geometric mean values of aqueous flare and mean values of visual acuity were significantly higher for the RP patients with PSC compared to those without PSC (P = 0.0003, P = 0.0004, respectively). When the aqueous flare values were assessed continuous-
ly, each 1-log-transformed increase in flare levels was associated with an elevation of the likelihood of having PSC after multivariable adjustment (odds ratio: 1.71; 95% confidence interval: 1.05–2.77). There were no significant associations of the other possible risk factors with PSC. This study demonstrated that elevated aqueous flare (suggesting an association of inflammation) is a significant risk factor for PSC formation in RP. The main strength of this study lies in the large sample size, however limitations include the possibility of unknown confounding factors, findings were based on a single flare measurement, and due to the cross-sectional nature, causal relationships between inflammation and PSC cannot be determined.

Clinical correlation between retinal sensitivity and foveal thickness in retinitis pigmentosa patients.


The purpose of this observational cross-sectional study was to investigate the relationship between retinal structure and retinal sensitivity using spectral-domain optical coherence tomography (SD-OCT) and microperimetry in retinitis pigmentosa (RP) and healthy patients. A total of 49 patients (98 eyes) with RP (mean age ± SD of 46.3 ± 13.9 years) were included and divided into 4 groups according to the OCT findings: group A, patients with no macular changes; group B, patients with cystoid macular edema (CME); group C, patients with vitreomacular traction (VMT); group D, patients with retinal thinning. As a control group, 27 healthy subjects (mean age ± SD of 52.8 ± 13.3 years) were enrolled. All subjects underwent a complete ophthalmologic examination, including SD-OCT and microperimetry. There was no significant difference in best-corrected visual acuity (BCVA), foveal thickness, or retinal sensitivity between group A and the healthy subjects (p>0.05). In group B, linear regression of logMAR versus foveal thickness and retinal sensitivity versus foveal thickness gave r values of 0.931 and 0.786, respectively. In group C, r values were 0.786 and 0.842, respectively, while in group D they were 0.816 and 0.795. The authors conclude that the new microperimeter MP3 has proven to be very sensitive in detecting functional abnormalities in patients with RP. They recommend that future studies investigate further the relationships among photoreceptor cell loss, retinal sensitivity, and fixation in patients with RP. The study shows the applicability of the new microperimeter MP3 in patients with RP. The lack of proper statistical representation of the results makes it difficult for the reader to interpret the presented results.
Intravitreal chemotherapy has emerged as an important modality for treating vitreous seeding in retinoblastoma. Intravitreal melphalan (IVM) has virtually eliminated the use of external beam radiation therapy for the treatment of vitreous seeding. IVM, however, has dose dependent toxic effect on RPE cells as well as anterior ocular toxicity. A classification system based on morphology of seeds (dust, spheres, cloud) has been described as predictive of response to IVM. Previously, a similar study was already published in patients who have received intra-arterial chemotherapy. The objective of this study was to evaluate the outcomes of retinoblastoma treated with intravenous chemotherapy and IVM as salvage for vitreous seeding, and further to determine whether vitreous seed classification is predictive of the total number and dose of IVM injections required for treatment in this cohort. The authors conducted a retrospective review of patients with vitreous seeding from retinoblastoma treated with intravenous chemotherapy and IVM from 2012 to 2016. This study excludes patients treated with intra-arterial chemotherapy. After completion of chemotherapy, patients were referred for IVM injections if persistently active or recurrent vitreous seeds were found during an EUA. From 2012 to 2014, the dose used was 20 to 40 μg based on clinical features. Once it became known that there is toxicity at doses greater than 30 μg, a dose of 25 μg was routinely used. Children were examined weekly under anesthesia during treatment. Primary outcome measure was eradication of seeds and globe salvage. Secondary measures included IVM-associated toxicity and complications. Overall, 28 eyes of 25 patients were included, with a total of 110 IVM injections. The median cumulative dose of IVM across all groups was 85 μg. By seed classification, eyes with dust (n = 15) required a median of 3 injections, spheres (n = 8) required 4 injections, and clouds (n = 5) required 6 injections. Spherical seeds were only seen in recurrent vitreous seeding. Of the 28 treated eyes, 9 were enucleated, 6 for recurrent retinal disease, and 3 due to persistent retinal detachment and neovascular glaucoma with very poor visual prognosis. The resulting overall globe salvage rate was 68%. The salvage rate secondary to active retinoblastoma was 79%. Dust classification was the most prevalent seeding type of the 9 enucleated eyes. There was 100% regression of vitreous seeds after intravitreal injection and no eye was treated with radiation or enucleated for seeding. Twelve eyes demonstrated grade 3 or greater IVM-associated retinal or anterior segment toxicity post injection. Mean follow-up was 33 months (range, 9-51 months). This study shows that seed classification is predictive of the total number and dose of IVM injection in eyes treated with intravenous chemotherapy. More importantly, IVM is effective in controlling vitreous seeds in patients who received intravenous chemotherapy.
A recent classification system for the vitreous seeds of retinoblastoma (RB) distinguishes 3 classes based on the morphologic features of the seeds. Class 3, or clouds, typically occur in unilateral disease in relatively older children at a median age of 32 months. The clouds take longer to regress and, as a result, the patients receive the greatest amount of intravitreous melphalan and the highest number of injections. It has been shown that clouds can be effectively treated with ophthalmic artery chemosurgery (OAC). In this study the authors compared whether OAC alone or combination treatment with intravitreous and periocular chemotherapy is superior. This retrospective study included 40 eyes with clouds of 40 retinoblastoma patients (19 treated with OAC alone and 21 treated with OAC plus intravitreous and periocular chemotherapy). Ocular survival, disease-free survival and time to regression of seeds were estimated with Kaplan-Meier estimates. Ocular toxicity was evaluated by clinical findings and electroretinography: 30-Hz flicker responses were compared at baseline and last follow-up visit. The results show that there were no disease- or treatment-related deaths and no patient demonstrated externalization of tumor or metastatic disease. There was no significant difference in the age, laterality, disease, or disease status (treatment naïve vs. previously treated) between the 2 groups. The time to regression of seeds was significantly shorter for eyes treated with OAC plus intravitreous chemotherapy (5.7 months) compared with eyes treated with OAC alone (14.6 months; P < 0.001). The 18-month Kaplan-Meier estimates of disease-free survival were significantly worse for the OAC alone group: 67.1% (95% confidence interval, 40.9%-83.6%) versus 94.1% (95% confidence interval, 65%-99.1%) for the OAC plus intravitreous chemotherapy group (P = 0.05). The 36-month Kaplan-Meier estimates of ocular survival were 83.3% (95% confidence interval, 56.7%-94.3%) for the OAC alone group and 100% for the OAC plus intravitreous chemotherapy group (P = 0.16). The mean change in electroretinography responses was not significantly different between groups, decreasing by 11 μV for the OAC alone group and 22 μV for the OAC plus intravitreous chemotherapy group (P = 0.4). Based on the findings, the authors recommend treating vitreous seed clouds with OAC and intravitreous and periocular chemotherapy, compared with OAC alone, as this results in in a shorter time to regression and was associated with fewer recurrences requiring additional treatment and fewer enucleations. The toxicity to the retina does not seem to be significantly worse in the OAC plus intravitreous chemotherapy group.
Vitreous Seeds in Retinoblastoma: Clinicopathologic Classification and Correlation

Vitreous seeding in retinoblastoma has been recognized as one of the strongest predictors of treatment failure. However, intravitreal chemotherapy injection treatments recently have demonstrated efficacy in improving outcomes in these patients. Munier delineated 3 distinct vitreous seeding patterns as dust, spheres and clouds. Dust is thought to result from displacement of individual tumor cells, and spheres are believed to result from similar cellular displacement followed by spherical clonal expansion. Clouds are assumed to result from massive transfer of tumor cells into the vitreous. The authors in this study correlated this clinical classification scheme with its histopathologic features. They conducted retrospective review of enucleated eyes received at the pathology department of the Retinoblastoma Center of Houston from 2010 to 2015. Macroscopic photographs of the enucleated eyes of patients with retinoblastoma were analyzed to select those with vitreous seeds. Cases with adequate material for clinicopathologic correlation were selected for further analysis, and clinical photographs were reviewed. Routine histopathologic slides were reviewed and compared with the clinical and macroscopic photographs. Seeds were classified as type 1 ("dust"), type 2 ("sphere"), or type 3 ("cloud"). To confirm the presence of macrophages, CD68 immunohistochemical staining was used. Synaptophysin was used to stain retinoblastoma cells. A total of 14 eyes with adequate amounts of tumor seeds along with clinical and macroscopic photographic correlation were selected from a total of 138 eyes reviewed. Type 1 seeds consisted of individual viable tumor cells and scattered macrophages. Type 2 seeds consisted of 2 submorphologies: spheres with viable cells throughout and spheres with an outer rim of viable cells but necrotic cells centrally. Type 3 seeds were composed of more than 90% necrotic material admixed with few macrophages and viable cells at their outer rim. Untreated (8/14) and previously treated (6/14) eyes showed similar histopathologic features for each type of seeds. Treated eyes had more type 1 and 3 seeds. This is the first histopathologic correlation of the clinical classification scheme for vitreous seeds in retinoblastoma. "Dust" is formed by scattered single cells alternating with macrophages. "Spheres" with translucent centers contain multiple layers of viable tumor cells that shed single cells and may be more clinically aggressive. "Cloud" seeds are mostly composed of necrotic material, explaining their lack of therapeutic response. Pretreated eyes showed tumor seeds morphologically similar to untreated eyes. Knowledge of the underlying histopathology of vitreous seed types is a fundamental component of classification and may aid in understanding clinical response to treatment.

Epidemiological trends in 1452 cases of retinoblastoma from the Surveillance, Epidemiology, and End Results (SEER) registry
Reports indicate that the incidence of retinoblastoma in the US were stable from 1975 to 2004, although there has been a steady improvement in survival. This study aimed to evaluate epidemiological trends in retinoblastoma over 37 years in the US, using the Surveillance, Epidemiology and End Results (SEER) tumor registry. This is a population-based cancer registry in the US, and contains information on over 7 million cancer cases diagnosed since 1973. All cases of retinoblastoma in the database were identified from 1973-2009. There were 1452 cases found and analyzed. Mean age at diagnosis was 1.44 years. 70.1% of cases were unilateral. Mean follow-up was 129.1 months. Survival over the time period did increase. Bilateral disease 10-year survival was 90.3%, compared to 96.1% for unilateral disease. There were also more nonocular malignancies associated with bilateral retinoblastoma. Grade 3 and 4 tumors were associated with decreased overall survival. There did not appear to be an affect on survival according to age at diagnosis. The data of this study adds to the prognostic information available to clinicians and families.

Reduction of severe visual loss and complications following intra-arterial chemotherapy (IAC) for refractory retinoblastoma
There is limited safety profile data for intra-arterial chemotherapy (IAC) in the management of retinoblastoma. Risk factors for visual loss include high doses of melphalan, catheterization complications, and previous radiotherapy. In this paper the authors conducted a retrospective cohort study to evaluate how modification of these factors could lessen complications. They identified 9 eyes (9 patients) treated with IAC from January 2013 to December 2015 that met inclusion criteria (tumors involving the fovea were excluded). Median age at first treatment was 14 months. There was difficulty in 7 of 27 catheterizations. Six patients suffered severe autonomic episodes. One patient developed a temporary sixth nerve palsy and choroidal ischemia, but the ischemia was nasal and did not affect visual acuity. Tumor control was achieved in 6 eyes, and 3 went on to eventually have enucleation. No child had deterioration of vision (prior to the enucleation in the 3 cases for progressive disease). There were two cases of slight ptosis and one patient had a sluggish pupil at last follow-up. 8/9 patients had normal post-treatment ERG’s, with one showing subtle reduction of cone and rod function. The authors conclude that visual and ocular motility complications may be reduced by giving age-adjusted doses of melphalan.

Retrobulbar ocular blood flow changes measured by colour Doppler imaging after intra-arterial chemotherapy in retinoblastoma
Intra-arterial chemotherapy (IAC) is now a popular treatment option for retinoblastoma. However, vaso-occlusive disease is a potential complication following IAC. Therefore, techniques have been developed to detect vascular complications/alterations in orbital vessels. This includes color Doppler imaging (CDI). This study aimed to evaluate the blood flow characteristics using CDI in retinoblastoma patients treated with intra-arterial melphalan. 20 eyes (10 patients) with unilateral retinoblastoma were evaluated in the study. Peak systolic and end diastolic velocities of the ophthalmic, central retinal, and posterior ciliary arteries were measured. Treated eyes were compared to the untreated eyes and with itself prior to the IAC. The authors found higher peak systolic and end-diastolic velocities of the central retinal artery in the retinoblastoma eyes before treatment, while velocities in the posterior ciliary and central retinal arteries significantly decreased after IAC. While sample size was small, the authors discuss that the findings could have significant clinical implications. The blood flow velocities measured could be good indicators of the capillary flow of the optic nerve head, retina, and choroid. Further study is warranted based on their conclusions.

_Intraocular pressure changes following intravitreal Melphalan and Topotecan for the treatment of retinoblastoma with Vitreous seeding._
Matthew D. Karl, Jasmine H. Francis, Saipriya Iyer, Brian Marr et al
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The purpose of this study is to investigate the impact of intravitreal chemotherapy on intraocular pressure (IOP) in children with retinoblastoma. In this retrospective chart review, 10 eyes of 10 patients with retinoblastoma and vitreous seeding were injected intravitreally with melphalan and topotecan. IOP was measured with a Tonopen at baseline prior to injecting and then repeatedly following each intravitreal injection. The mean pre-injection IOP 1 to 30 seconds after intravitreal melphalan was 45.4+/-14.3 mmHg. The IOP of 89.5% of patients declined to 29mmHg or less in a mean 153+/-97.5 seconds. Mean IOP 1 to 30 seconds after intravitreal injection of topotecan was 44.5+/-11.0 mmHg, which decreased to 31.0+/-5.0 mmHg by 150 seconds after injection. No significant relationship was found between age and post- injection IOP elevation. IOP exceeded the mean arterial perfusion pressure in four cases. The authors conclude that intravitreal injections of melphalan and topotecan for the treatment of retinoblastoma with vitreous seeding can cause transient and significant elevation in the IOP which can exceed the mean arterial perfusion pressure and thus risk occlusion of the central retinal artery. This is a great study especially in the era of intravitreal injections for the treatment of retinoblastoma, but it is limited by its small number of subjects involved, its retrospective design and the use of Tonopen instead of the Gold-standard Goldmann applanation tonometry.

_Clinical presentation and Outcomes of Stage III or Stage IV Retinoblastoma in 80 Asian Indian Patients._
The purpose of this study is to describe the clinical features and outcomes of patients with stage III or IV retinoblastoma. 80 patients were included in the study based on the International Retinoblastoma Staging System (IRSS). The demographic data, presenting complaints and duration of symptoms were reviewed. Examination under sedation, bone marrow aspiration, cerebrospinal fluid analysis, computerized tomography (CT) of the orbits and brain were also reviewed in all cases as well as the treatment details, histopathology details of the enucleated/exenterated specimen, and outcome (alive or dead). Out of the 80 patients, 42 (53%) were compliant to treatment and 38 (47%) were non-compliant. All 38 patients who were not compliant to treatment died within 13 months from diagnosis. Of the 42 patients complaint with treatment, 22 (52%) died before completion of treatment. Twenty patients with Stage III diseases could complete the multimodal treatment and seventeen were alive at a median follow-up duration of 77 months. The authors conclude that the multimodal treatment regimen of high-dose chemotherapy with vincristine, etoposide, and carboplatin followed by enucleation or orbital exenteration, external beam radiation, and extended high-dose chemotherapy was beneficial in patients with IRSS stage III disease, achieving an event-free survival rate of 71% at a median follow-up of 77 months. However, the treatment was not beneficial in patients with IRSS stage IV disease.

Intravitreal chemotherapy in the management of vitreous disease in retinoblastoma.

The purpose of this retrospective non-comparative case series was to evaluate the therapeutic outcome of intravitreal melphalan injection in the management of vitreous disease in patients with retinoblastoma. The authors aim was to assess whether higher melphalan dose with lower number of injections was more effective and associated with fewer side effects. A total of 39 eyes of 37 patients were included. Vitreous seeds were classified as dust, sphere, and cloud types. Intravitreal injections were performed through pars plana free of any visible tumor using 30-G needle. Response of the seeds (disappearance, conversion into inactive debris, or progression) and enucleation rate were determined as outcome measures. All patients previously received systemic or intra-arterial chemotherapy. Vitreous seeding was primary in 54% of eyes and secondary in 46% of eyes. Vitreous seeds were classified as dust in 9 (23.1%) eyes, sphere in 24 (61.5%) eyes, and cloud in 6 (15.4%) eyes. Melphalan dose varied between 20 and 40 micrograms, and 20 (51.3%) eyes received >30 micrograms. The total number of injections was 70 (range 1-5, mean 1.8 per eye). Regression was obtained in 27 (69.2%) eyes. Sphere-type seeds were the most responsive to melphalan. Non-response and disease progression were noted in 12 (30.8%) eyes. After a mean
follow-up of 11.8 months, 17 (44%) eyes were enucleated. Vitreous hemorrhage (18%) and retinal pigment epithelial alterations (8%) were the most common side effects. The authors conclude that intravitreal melphalan at 30-40 micrograms in 1 or 2 injections proved effective in 69.2% of eyes with vitreous disease. Since this study is non-comparable, it is difficult to assess the advantages of a higher dose of Melphalan over a lower dose. Also no data was available regarding possible toxic effects of higher doses of Melphalan. A prospective study that compares different doses and includes full field ERG may give more information regarding the advantages and disadvantages of higher versus lower dose of intravitreal Melphalan.

Efficacy and Toxicity of Intravitreous Chemotherapy for Retinoblastoma: Four-Year Experience.

Intravitreous chemotherapy (IVC) for retinoblastoma has shown that it effectively treats vitreous seeds and saves eyes that once would have been enucleated. The authors previously reported a 5.8-μV decrease in ERG recording for every injection. Toxic effects can also be seen in the anterior segment of the eye including iris recession, cataract, iris depigmentation and iris thinning along with scleromalacia. Alternative to IVC is intra-arterial chemotherapy (IAC), which requires a team of experts and resources not readily available in all retinoblastoma centers. The authors conducted a retrospective investigation of the efficacy and toxicity of intravitreous melphalan for treatment of retinoblastoma, as a single agent or with concomitant topotecan. The study also evaluated patient and treatment characteristics to see how these factors affect retinal toxicity. A total of 130 eyes of 120 patients with retinoblastoma received 630 intravitreous (melphalan, topotecan) or topotecan periocular injections. Periocular or intravitreal topotecan was used to supplement when intravitreal melphalan did not produce a desired response. Between September 2012 and September 2016, a total of 83 (64%) of these eyes were treated with concomitant ophthalmic artery chemosurgery (OAC) using melphalan, topotecan, and carboplatin. Indirect ophthalmoscopy and clinical imaging were used to evaluate clinical response. Ocular survival and disease-free survival were estimated using Kaplan-Meier methods in 130 eyes. Ocular toxicity was evaluated by clinical findings and electroretinography (ERG) on 244 evaluable injections in 63 patients using 30-Hz flicker responses. Data were analyzed for ocular survival, disease-free survival, and ERG: peak-to-peak ERG amplitudes in response to 30-Hz photopic flicker stimulation. There were no disease- or treatment-related deaths, and no patient developed externalization of tumor or metastatic disease. Two-year Kaplan-Meier estimates of ocular survival and disease-free survival were 94.2% (95% CI, 89.2-99.4) and 86.2% (95% CI, 78.7-94.5), respectively. There was a significant association between the number of injections and diminished ERG responses, such that on average each intravitreous melphalan injection was associated with a 5.3-μV decrease in ERG amplitude \( P < 0.001 \). Concomitant intra-
arterial chemotherapy \((P = 0.01)\) and greater inherent ocular pigment also were significantly associated with a reduction in ERG \((P = 0.045)\). Patient age and weight, new injection site location, addition of topotecan, concomitant focal treatment, and time interval between injections were not significantly associated with toxicity. Intravitreous melphalan is an effective treatment for vitreous seeding in retinoblastoma, resulting in high rates of ocular survival and disease-free survival. However, in this study, each injection of melphalan was associated, on average, with a decrement in ERG response. The findings suggest increased toxicity (1) when OAC is given within 1 week of the intravitreous injection and (2) in more deeply pigmented eyes.

Optical Coherence Tomography-Guided Decisions in Retinoblastoma Management.

In this study, the authors compare clinical evaluation against OCT findings in guiding management decision in children with retinoblastoma. This was a retrospective review of all children newly diagnosed with retinoblastoma from January 2011 to December 2015 who had an OCT session during their active treatment at The Hospital for Sick Children in Toronto, Canada. The OCT sessions for fellow eyes of unilateral retinoblastoma without any suspicious lesion and those performed more than 6 months after the last treatment were excluded. Biophtigen hand-held OCT systems were used to obtain volumetric scans composed of nonaveraged OCT scans. The data collected included age at presentation, sex, family history, RB1 mutation status, 8th edition TNMH cancer staging and International Intraocular Retinoblastoma Classification (IIRC), and number of OCT sessions per eye. An OCT session was assessed as informative if it provided sufficient data about the main indication and as directive if the information obtained guided management decisions affecting diagnosis, treatment or follow-up. Directive guidance that confirmed the pre-OCT clinical decision was considered confirmatory and influential if it changed a pre-OCT clinical decision. Details of each session were scored for indication-related details (informative or not) and assessed for guidance (directive or not), diagnosis (staging changed, new tumors found or excluded), treatment (modified, stopped, or modality shifted), or follow-up modified. Results show that sixty-three eyes of 44 children had 339 OCT sessions over the course of clinical management (median number of OCT scans per eye, 5; range, 1-15). The age at presentation and presence of a heritable RB1 mutation significantly correlated with an increased number of OCT sessions. Indications included evaluation of post-treatment scar (55%) or fovea (16%), and posterior pole scanning for new tumors (11%). Of all sessions, 92% (312/339) were informative; 19 of 27 noninformative sessions had large, elevated lesions; of these, 14 of 19 were T2a or T2b (IIRC group C or D) eyes. In 94% (293/312) of the informative sessions, OCT directed treatment decisions (58%), diagnosis (16%), and follow-up (26%). Optical coherence tomography influenced and
changed management rom pre-OCT clinical plans in 15% of all OCT sessions and 17% of directive sessions. The authors concluded that optical coherence tomography is an important tool in improving the accuracy of clinical evaluation in retinoblastoma management.

**High-Risk Histopathology Features in Primary and Secondary Enucleated International Intraocular Retinoblastoma Classification Group D Eyes.**


The International Intraocular Retinoblastoma Classification (IIRC) predicts chemotherapy salvage rate of ≥90% for groups A, B, and C eyes and a 47% salvage rate for group D eyes. Group E eyes are usually enucleated because of irreversible ocular damage and a higher chance of adverse histology. This poses some dilemma in management of group D eyes. This study is aimed at understanding the clinical factors that might favor use of intra-arterial chemotherapy (IAC) as a first-line conservative treatment. This is a retrospective analysis of 64 enucleated group D eyes (62 patients), of which 40 (40 patients) were primary and 24 (22 patients) were secondary to other treatments. High-risk histopathologic features were defined as the presence of anterior chamber seeds, iris infiltration, ciliary body/muscle infiltration, massive (≥3 mm) choroidal invasion, retrolaminar optic nerve invasion, or combined non-massive choroidal and prelaminar/laminar optic nerve invasion. Of the 64 group D eyes, 37 (58%) were classified as cT2bN0M0H0, 24 (38%) were classified as cT2bN0M0H1, and 3 (5%) were classified as cT2aN0M0H1, according to the 8th edition cTNMH Retinoblastoma Staging. High-risk histopathologic features were detected in 10 eyes (16%) in the entire cohort, 5 eyes (13%) of the primary enucleated group (pT3aNxM0, n = 2 and pT3bNxM0, n = 3, 8th edition pTNM), and 5 eyes (21%) of the secondary enucleated group (pT2bNxM0, n = 2, pT3aNxM0, n = 2 and pT3cNxM0, n = 1). Absence of vitreous seeds at presentation was the only predictive factor found for high-risk histopathologic features in the primary enucleation group (P = 0.042), whereas none were found in the secondary group (P ≥ 0.179). Invasion of the anterior structures (anterior chamber, iris, ciliary body/muscle) was detected significantly more frequently after secondary enucleation (P = 0.048). All patients with high-risk histopathologic features were treated with adjuvant chemotherapy, and no metastases were recorded in a median follow-up time of 73.2 months (mean, 71.5; range, 13.7-153.0). The choice of primary treatment for group D retinoblastoma should be carefully weighed, because according to this study, 13% of eyes harbor high-risk histopathologic features at presentation, with the absence of vitreous seeds being a potential risk factor. It is of special importance in group D eyes being considered for nonsystemic treatment, such as primary intraophthalmic artery chemotherapy, that vitreous seeds at presentation were found significantly more often in patients with no high-risk histopatho-
logic features. Secondary enucleated group D eyes with high-risk histopathologic features more commonly involved anterior structures, warranting meticulous clinical and histologic examinations for this subset of patients.

Long-term Visual Acuity, Strabismus, and Nystagmus outcomes Following Multimodality Treatment in Group D Retinoblastoma Eyes.

Due to intraophthalmic artery chemotherapy many eyes with Group D Retinoblastoma (Rb) are now salvaged. There is little data about the long term visual outcomes in these eyes since many of the studies are based around globe salvage as the primary outcome. The was a retrospective interventional case series over 13 years looking at eyes with Group D Rb with the purpose of analyzing the long-term visual acuity, nystagmus and strabismus. The patients had follow up for at least 1 after last treatment. 32 eyes of 27 patients met the inclusion criteria. The final mean visual acuity was 20/283 with an average of 64 months from presentation. The authors concluded that half of the patients had vision 20/200 or worse and that transpupillary thermotherapy was a risk factor for worse vision. Additionally 60% of patients had strabismus and 22% had nystagmus. The authors point out that the study was limited by the retrospective design and the lack of full sensory motor exam on all the patients due to age and various levels of cooperation.


There is increasing interest in the possibility of occupational or environmental exposures in the development of retinoblastoma (Rb). Previous reports have associated Rb with air pollution, parental exposure to oil mists, employment in radio or television repair, shoe or leather work, electrical work and the metal try. Previous association with herbicides and insecticides has been shown in other childhood cancers but not in Rb. The purpose of this study was to determine if parental pesticide exposure contributes to the development of sporadic Rb. This was a case control study of parents of 99 unilateral and 56 bilateral age matched and case controlled pairs. The authors interviewed the families and found that unilateral Rb was associated with parental insecticide use (OR 2.8) and the use of professional lawn or landscape services ((OR 2.8). The authors point out that recall bias is a limitation in this study since case patients are more likely to over report exposures and controls are more likely to under report. Additionally since Rb is rare, the number of patients in this study is limited. This study
Rhegmatogenous Retinal Detachment After Intraarterial Chemotherapy for Retinoblastoma: The 2016 Founders Award Lecture

This retrospective case series sought to evaluate rhegmatogenous retinal detachment (RRD) in eyes with retinoblastoma after intraarterial chemotherapy (IAC). 167 eyes of 157 consecutive patients treated with IAC in a single center were studied. IAC was primary in 75/167 (45%) eyes and secondary in 92/167 (55%) eyes. In total, 10 eyes (6%) developed RRD after IAC; 6/75 (8%) eyes after primary IAC and 4/92 (4%) after secondary IAC. A comparison of eyes with RRD versus without RRD revealed greater mean age at presentation (38 vs. 18 months), greater 4-quadrant vitreous seeding (50% vs. 17%), and absence of subretinal fluid (30% vs. 65%). Eyes at greatest risk for post-IAC RRD included those with advanced Group E retinoblastoma, endophytic configuration, suggestion of full-thickness retinal tumor at risk for atrophic hole, and extensive vitreous seeding. The cause of RRD was tumor regression-related atrophic retinal hole(s) in 7, cryotherapy-induced single atrophic hole in 2, and single flap-tear from posterior vitreous detachment in one. The RRD was not related to intravitreal injection any case. Primary RRD repair involved pars plana vitrectomy in three, scleral buckle without drainage in one, laser barricade in one, and observation in 5 eyes. After 24 months mean follow-up, the retina showed complete reattachment in 3 eyes, partial reattachment in 2 eyes, and persistent detachment in all eyes (5) that were observed. Enucleation was necessary for tumor recurrence in 4/10 eyes and neovascular glaucoma in 1 eye. There were no tumor-related metastases or death. The authors conclude that although IAC provides outstanding retinoblastoma control, with tumor regression there is a 6% risk for RRD, particularly in advanced eyes and usually related to rapid full-thickness tumor regression leaving atrophic retinal hole.

Prenatal versus Postnatal Screening for Familial Retinoblastoma.

In this retrospective, observational study, the authors compare overall outcomes of conventional postnatal screening of familial retinoblastoma and prenatal RB1 mutation identification followed by planned early-term delivery. The study participants are Twenty children with familial retinoblastoma born between 1996 and 2014 and examined within 1 week of birth. Cohort 1 included spontaneously delivered neonates examined within 1 week of birth and confirmed postnatal to carry their family's RB1 mutant allele. Cohort 2 included infants identified by amniocentesis to carry their family's RB1 mutant allele, and therefore scheduled for early-term delivery (36-38 weeks' gestation). Main outcome measures are Age at first tumor in each eye, eye stage, treatments given, ocular salvage, treatment
success (defined as avoidance of enucleation, external-beam irradiation, or both), visual outcome, number of anesthetics, pregnancy or delivery complications, and estimated treatment burden. Vision-threatening tumors were present at birth in 4 of 8 infants in cohort 1 and in 3 of 12 infants in cohort 2. Eventually, all infants demonstrated tumors in both eyes. At the first treatment, 1 of 8 infants in cohort 1 had eyes in stage cT1a/cT1a or cT1a/cT0 (smallest and least vision-threatening tumors), compared with 8 of 12 infants in cohort 2 (P = 0.02). Null RB1 germline alleles induced earlier tumors than low-penetrance alleles (P = 0.03). Treatment success was achieved in 3 of 8 children in cohort 1 compared with 11 of 12 children in cohort 2 (P = 0.002). Acceptable vision (better than 0.2 decimal) was achieved for 8 of 16 eyes in cohort 1 compared with 21 of 24 eyes in cohort 2 (P = 0.014). Useful vision (better than 0.1, legal blindness) was achieved for 8 of 9 children in cohort 1 compared with 12 of 12 children in cohort 2. There were no complications related to early-term delivery. Median follow-up was 5.6 years, cohort 1 and 5.8 years, cohort 2. The authors conclude that when a parent had retinoblastoma, prenatal molecular diagnosis with early-term delivery increased the likelihood of infants born with no detectable tumors, better vision outcomes, and less invasive therapy. Prenatal molecular diagnosis facilitates anticipatory planning for both the child and family.

**NON-RETINOBLASTOMA**

**Clinical Features Differentiating Benign From Malignant Conjunctival Tumors in Children**

This retrospective case series (1975 to 2015) points out the importance of features that distinguish benign from malignant pediatric conjunctival tumors in 806 patients. Analysis indicated that 97% of the conjunctival lesions were benign (nevi, benign reactive lymphoid hyperplasia, nodular conjunctivitis, dermoid, primary acquired melanosis) as compared to 3% of the conjunctival lesions were malignant (melanoma, lymphoma). Features such as mean tumor thickness, tumor base measurement, location, age at presentation, lack of intrinsic cysts, and hemorrhage were the main differences between the tumors. Of these 806 patients, melanoma was associated with older children (>10 years-15 years) with a larger tumor, hemorrhage and lack of cysts as compared to nevus. Lymphoma was associated with larger tumor size and diffuse involvement as compared to benign reactive lymphoid hyperplasia. In summary, this 40-year retrospective study of 806 children found that conjunctival tumors are nearly always benign.
Ocular Coherence Tomography and Infrared Images of Astrocytic Hamartomas Not Revealed by Fundoscopy in Tuberous Sclerosis Complex


This study sought to detect, describe, and classify the morphologic characteristics of astrocytic hamartomas in tuberous sclerosis complex (TSC) using SD-OCT and infrared imaging. 10 subjects (20 eyes) with TSC underwent a complete ophthalmologic examination and SD-OCT and infrared imaging. Using multimodal imaging, 44 hamartomas were detected in 8 patients. Lesions were bilateral in 5 cases. 30 of the hamartomas had not been revealed by previous ophthalmoscopy. Each of the 44 hamartomas was measured and morphologically characterized as to type of tumor, retinal and/or vitreous involvement, calcifications, and posterior optical shadowing. Due to difficulty in categorizing approximately 20% of the detected astrocytic hamartomas, the authors proposed a new subtype of hamartoma to complete a previous classification based on OCT images alone. This study is limited by its cross-sectional design, which does not allow reasonable conclusions about the ability of SD-OCT and IR imaging to detect changes in hamartomas over time. SD-OCT also requires sufficient patient cooperation which eliminates participation of very young or developmentally challenged individuals. Nevertheless, these results advocate the combined use of SD-OCT and IR imaging to better evaluate the presence/absence and the characteristics of astrocytic hamartomas in people with TSC.

20. ORBIT

Combined Oral and Topical Beta Blockers for the Treatment of Early Proliferative Superficial Periocular Infantile Capillary Hemangioma.

Hatem M. Marey, Hesham F. Elmazar, Sameh S. Mandour, Hany A. Khairy

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The purpose of this randomized, controlled comparison trial is to evaluate the safety and efficacy of combined oral and topical beta blockers for the treatment of superficial periocular infantile hemangioma at the early proliferative stage. Patients were randomly enrolled into two groups: the topical and systemic treatment and systemic treatment only groups. The topical and systemic treatment group was treated with oral propranolol (1 mg/kg per day initially, increased to 2 mg/kg per day gradually in 2 weeks) and timolol maleate 0.5% gel. The systemic treatment only group received oral propranolol (1 mg/kg per day initially, increased to 2 mg/kg per day gradually in 2 weeks) and simple eye ointment to be applied to the lesion. The Hemangioma Activity Score was used to record the proliferative activity of the hemangioma. The main outcomes of the study were the change in the hemangioma size, the proliferative activity, and the treatment side effects. At the end of the treatment period, the Hemangioma Activity Score was significantly
improved in both groups from their values before treatment. However, the score obtained after treatment was significantly better in the topical and systemic treatment group ($P < .05$). Regarding the response to treatment, 10 and 3 cases in the topical and systemic treatment and systemic treatment only groups, respectively, showed a good response, with a significant difference between the two groups ($P < .50$). There were no recorded serious local or systemic complications during treatment in either group. The results from combining topical with oral beta blockers showed that topical beta blockers are of additive value in treating superficial periorbital infantile hemangioma in the early proliferative stage. The limitations of this study included the small number of patients and the short follow-up period.

The effect of enucleation on orbital growth in patients with retinoblastoma.

The purpose of this retrospective study was to measure orbital volume using serial magnetic resonance imaging (MRI) scans to determine the effect of enucleation on orbital growth over time. The medical records of patients who underwent unilateral enucleation for retinoblastoma with a minimum of 2 MRIs were reviewed. Orbital asymmetry was calculated using MRI measurements. Nonlinear and linear mixed effect regression models were used to predict the effect of age at time of enucleation on degree of orbital asymmetry. A total of 27 patients were included (mean age at enucleation, 2 years; range, 2.5 months to 5 years). Age at scan ($P = 0.046$) and age at enucleation ($P = 0.0006$) were found to have a significant effect on orbital asymmetry. Change in orbital asymmetry over time was more pronounced after enucleation in children enucleated at <1 ($P < 0.0001$) or <2 years of age ($P = 0.0109$). Younger age at enucleation was associated with a greater degree of asymmetry over time, although this effect was extinguished for patients enucleated after the age of 3 years. The authors concluded that enucleation with orbital implant before 3 years of age in patients with retinoblastoma, has a significant effect on orbital volume asymmetry. After the age of 3, this effect appears to be less detrimental to the degree of orbital asymmetry. It is well known that in children orbital growth is affected by enucleation, but this small retrospective case series clarifies the effect that age at time of enucleation has on limiting orbital growth.

Periorbital lesions misdiagnosed as dermoid cysts.

Several periorbital lesions can be clinically misdiagnosed as dermoid cyst. In this short retrospective report 97 consecutive biopsied periorbital le-
Sions diagnosed as dermoid cysts were compared to their histopathological assessment. Misdiagnosis occurred in 5 cases. Of these 4 cases were eventually diagnosed with vascular malformations (hemangiomas and cavernous venous malformation) and one patient. In all cases the lesions were not located laterally near the zygomatico-frontal suture but either medially or under the central brow. Despite its small sample size and retrospective nature, this study highlights the possibility of misdiagnosing early childhood periorbital lesions, when they are located the medial part or the center of the brow. The correct diagnosis may alter the treatment and therefore the authors suggested that lesions in these locations may justify imaging.

Biphasic growth of orbital volume in Chinese children

The orbital volume in children is important when surgeons are implanting an ocular implant after orbital content removal. Proper size of implants can help stimulate orbital bone growth and reduce risk of craniofacial deformities. This study aimed to measure the orbital volume in Chinese children up to age 15 using spiral CT. CT scans were performed on 109 children to measure orbital volume, exophthalmos, and other measurements. They found that orbital volume and age does not have a linear relationship. Growth followed a biphasic pattern with a growth phase before 3 years of age, and a second growth phase between 7 and 12 years of age. The first growth phase was three times faster than the second phase. There was no difference between males and females before age 12, but after age 12 boys developed a significantly larger orbital volume. This clinical data can help surgeons time interventions for surgery involving the craniofacial/orbital structures, such as placing an implant early during the fast phase or orbital growth.

Postoperative Changes in Strabismus, Ductions, Exophthalmometry, and Eyelid Retraction After Orbital Decompression for Thyroid Orbitopathy

Surgical rehabilitation of thyroid orbitopathy involves reducing proptosis, treating strabismus, lengthening the eyelids, and managing aesthetic changes. Not all are necessary in each patient; however, they often are. The current investigation intends to describe postdecompression changes that may influence the staging of these procedures. In this retrospective cohort study, records of 169 patients who underwent orbital decompression between 1983 and 2001 were reviewed. A single orbital specialist confirmed all measurements. Time to follow up was defined as the most recent follow up after decompression and prior to any secondary procedures. No strabismus or eyelid surgery was performed at the time of decompression. Strabismus was measured with alternating prism cover test. Duc-
tions were estimated utilizing Hirschberg’s method. Exophthalmometry was measured with Hertel. Eyelid positions were defined relative to the pupillary light reflex. Strabismus data were analyzed within eye pairs. Ductions, exophthalmometry and eyelid position were analyzed for each eye. T-test for paired data was utilized to compare means pre- and postoperatively. The study population was on average 45 years old and 73.4% women. Average length of follow up was 1.2 years. Esotropia was significantly increased after decompression by an average of 8.1 prism diopters (p < 0.01). Exotropia and vertical deviations were not significantly altered. Ductions decreased by >5 degrees in at least one meridian for 68.1% of the population. Upper eyelid retraction remained unchanged; however, lower eyelid retraction improved by 50% from 1.4 mm to 0.7 mm (p < 0.01). Exophthalmometry improved from 23.5 mm to 19.7 mm (p < 0.01), and this result was correlated with the number of walls removed (Pearson r = −0.302, p < 0.01). On average, esotropia and ductions tend to worsen with decompression surgery. This result supports the clinical dictum to avoid strabismus surgery until after decompression. The improvement in lower eyelid retraction suggests that at least lower eyelid-lengthening surgery should be reserved for after decompression, as there may be significant spontaneous improvement, while the same may not be true for upper eyelid retraction, which does not tend to change with decompression.

Clinical and Radiological Evaluation of Periocular Infantile Hemangioma Treated With Oral Propranolol: A Case Series

This is a prospective interventional case series in which the authors evaluated the clinical and radiological response and clinical efficacy of propranolol (3 mg/kg/day) in the treatment of of 9 infants with orbital and/or palpebral infantile hemangioma (IH) and at risk for amblyopia (n = 8) and aesthetic deformity (n = 1) treated with propranolol. The patients were underwent complete ophthalmologic examination, gray-scale and Doppler ultrasonography, and nuclear magnetic resonance imaging. Lesion regression was evaluated clinically and radiologically during follow-up. The dose was increased at weekly intervals, from 0.5 mg to 3 mg/kg/day. The age at onset of treatment was 2–28 months and treatment lasted 2-12 months (mean 7.1 months). Follow-up lasted up to 48 months. Clinical regression (attenuation of color and reduction in size) was observed in 88% during the first days of treatment. Partial recurrence was observed during follow-up in a patient treated for 6 months. On Doppler ultrasonography, during the first 6 months of treatment lesion volume and vascular density decreased while the arterial resistivity index (RI index, which is an indicator of vascular activity) increased, followed by a decline. The authors concluded that propranolol at 3 mg/kg/day was clinically and radiologically efficacious against deep IH in the proliferative stage in the first 6 months of treatment, with no recurrence in patients treated for 12 months. Despite the small sample, the results suggest that, in cases of deep orbitopalpebral lesions, the decision to withdraw the medication
should be based on criteria of clinical improvement and on Doppler US parameters, including the arterial RI and that RI might help determine when treatment can be safely ended.

**The association of maternal factors with epibulbar dermoid of newborn: a retrospective, matched case–control study.**


Epibulbar dermoids are the most common form of epibulbar choristomas and the most common ocular congenital tumors. Most cases are sporadic although some chromosomal abnormalities are associated to the presence of corneal dermoids. PAX6 is an important factor in limbal stem cells and corneal epithelium. Some evidence that PAX^ is absent from corneal dermoid tissue. Nicotine is a potential environmental factor associated with this PAX6 absence. The current study attempted to investigate the potential association of maternal and paternal factors and exposure during pregnancy with ED in a large and well-defined group of patients who were diagnosed and followed at a national medical center. A paired case–control design performed between 2014-2015, compared 121 consecutive Chinese children with epibulbar dermoids with 121 Chinese children without epibulbar dermoids. The mothers of patients were interviewed after a diagnostic work-up was obtained without knowing of any possible risk factors associated with epibulbar dermoids. The questionnaire was divided in 4 sections. Section 1 related to personal history. Section 2 corresponded to prenatal maternal problems and treatments. Section 3 focused on maternal environmental exposures. And section 4 was based on parental socioeconmomic status.

Patients were not age matched to controls but matched for sex, gestational age (±1 week apart), birth weight (±100 g difference), and parental socioeconomic status level. There was a significantly higher prevalence of history of maternal inevitable miscarriage, use of progesterone in the 1st trimester, exposure to common cold in the first trimester in cases compared to controls. The factor with the greatest statistical significance and the greatest odds ratio was paternal smoking of more than 10 cigarettes per day. Previous miscarriage, maternal common cold and smoke exposure during pregnancy are possibly linked with fetal inflammation and abnormal vascular development. These factors might potentially affect the differentiation of surface ectoderm and mesoderm during embryogenesis. Nicotine could induce CpG methylation of a PAX6-binding motif, inhibiting downstream steroid hormone production essential to anti-inflammatory effect and fetal development potentially correlating with PAX6 loss. Paternal smoking might also genetically affect sperm.

**A prospective study of the role of intralesional bleomycin in orbital lymphangioma.**
The purpose of this prospective non-comparative interventional case study was to evaluate the efficacy of intralesional bleomycin injection in the management of lymphangiomas of the orbit. A total of 13 patients with orbital lymphangiomas were recruited. Reconstituted bleomycin 1-5 ml (0.5 IU/kg body weight; maximum, 15 IU/ml) was injected with 2% lignocaine in the lesion as seen on imaging or, in deeper lesions, under ultrasound guidance. Repeat injections were administered when required every 4 weeks. The decision to retreat was based on clinical and radiological evidence of response. Patients were treated with 1-6 injections of bleomycin 0.5 IU/kg body weight. Dramatic response was achieved in all cases. During the mean follow-up period of 19.69 months (range, 7-26 months) none of the patients experienced recurrence or significant complication. The authors conclude that in this patient cohort, lymphangiomas of the orbit showed favorable and promising results with intralesional injections of bleomycin. They state that this treatment should be considered as a first-line therapy for lymphangiomas of the orbit.

**Teprotumumab for Thyroid-Associated Ophthalmopathy**


Thyroid-associated ophthalmopathy, a condition commonly associated with Graves’ disease, remains difficult to treat medically. Glucocorticoids are the most commonly used medication but have limited efficacy and present safety concerns. Inhibition of the insulin-like growth factor I receptor (IGF-IR) is a new therapeutic strategy to attenuate the underlying autoimmune pathogenesis of ophthalmopathy. This study was a multicenter, double-masked, randomized, placebo-controlled trial to determine the efficacy and safety of teprotumumab, a human monoclonal antibody inhibitor of IGF-IR, in patients with active, moderate-to-severe ophthalmopathy. 88 patients were randomly assigned to receive placebo or active drug administered intravenously. The primary end point was the response in the study eye. This response was defined as a reduction of 2 points or more in the Clinical Activity Score (scores range from 0 to 7, with a score of ≥3 indicating active thyroid-associated ophthalmopathy) and a reduction of 2 mm or more in proptosis at week 24. Secondary end points, measured as continuous variables, included proptosis, the Clinical Activity Score, and results on the Graves’ ophthalmopathy–specific quality-of-life questionnaire. In the intention-to-treat population, 29 of 42 patients who received teprotumumab (69%), as compared with 9 of 45 patients who received placebo (20%), had a response at week 24 (P<0.001). Therapeutic effects were rapid; at week 6, a total of 18 of 42 patients in the teprotumumab group (43%) and 2 of 45 patients in the placebo group (4%) had a response (P<0.001). Differences between the groups increased at subsequent time points. Patients receiving teprotumumab also had a reduction in subjective diplopia symptoms that was statistically significant.
The only drug-related adverse event was hyperglycemia in patients with diabetes, which was controlled by adjusting diabetic medications. In conclusion, teprotumumab was more effective than placebo in reducing proptosis and the Clinical Activity Score in patients with Graves ophthalmopathy. This study is of high relevance to strabismologists because we do not currently have any medical treatments to treat diplopia due to Graves ophthalmopathy. Of note, the study was funded by the drug manufacturer.

**Optic Pathway Glioma of Childhood**

OPG is the most common tumor of anterior visual pathway and is found both in NF-1 associated with inactivation of the NF-1 tumor suppressor gene, and in sporadic cases with a rearrangement of the B-Raf gene. In NF-1 OPGs are usually indolent, asymptomatic and do not require intervention, however sporadic gliomas are usually more aggressive and present with visual impairment. Risk factors for poor visual outcome include younger age at presentation, extension postchiasmally, and optic nerve pallor. Screening guidelines recommend clinical examination as the gold standard for diagnosis and follow-up. Exams should occur every 3 months for the first year after diagnosis and based on the stability the subsequent intervals may be determined. Visual acuity is the most accurate and reliable way to measure clinical progression. Worsening of 2 Snellen lines is considered significant, though no universally accepted guidelines exist. Visual field testing should also be attempted in all children. Neuroimaging with MRI of the brain and orbits is the best modality for identifying the extent of involvement. Thin cuts through the optic nerves should be performed however there is poor correlation between radiographic findings and associated visual acuity impairment. Even if there appears to be improvement on imaging with treatment this does not correlate with improved visual function. Management is based on clinical progression and may include chemotherapy, most commonly with carboplatin regimens which shows reasonably good progression free survival (PFS)- 68% at 3 years. However the use of chemotherapy did not improve visual outcomes. Radiation is an effective treatment with PFS of up to 90% at 10 years. External beam radiation has good efficacy but there is risk of endocrine dysfunction, developmental delay and cognitive effects. It also has the risk of secondary visual loss due to radiation damage, moyamoya syndrome, and cerebro-occlusive disease. Stereotactic radiotherapy and proton beam therapy have smaller studies with good results but it is unclear what are the long term side effects. Surgery is used in cases of severe visual compromise or evidence of chiasmal extension.

In conclusion, current screening guidelines focus on following patients with serial clinical exams and observation as the primary management. Where treatment is indicated, chemotherapy is first line although which regimen is best is still debated. Radiation is second line treatment because of its side effect profile. Surgery is used only in specific cases.
Surgical rehabilitation of thyroid orbitopathy involves reducing proptosis, treating strabismus, lengthening the eyelids, and managing aesthetic changes. Not all are necessary in each patient; however, they often are. The current investigation intends to describe post-decompression changes that may influence the staging of these procedures. In this retrospective cohort study, records of 169 patients who underwent orbital decompression between 1983 and 2001 were reviewed. A single orbital specialist confirmed all measurements. Time to follow up was defined as the most recent follow up after decompression and prior to any secondary procedures. No strabismus or eyelid surgery was performed at the time of decompression. Strabismus was measured with alternating prism cover test. Ductions were estimated utilizing Hirschberg’s method. Exophthalmometry was measured with Hertel. Eyelid positions were defined relative to the pupillary light reflex. Strabismus data were analyzed within eye pairs. Ductions, exophthalmometry and eyelid position were analyzed for each eye. T-test for paired data was utilized to compare means pre- and postoperatively.

The study population was on average 45 years old and 73.4% women. Average length of follow up was 1.2 years. Esotropia was significantly increased after decompression by an average of 8.1 prism diopters (p < 0.01). Exotropia and vertical deviations were not significantly altered. Ductions decreased by >5 degrees in at least one meridian for 68.1% of the population. Upper eyelid retraction remained unchanged; however, lower eyelid retraction improved by 50% from 1.4 mm to 0.7 mm (p < 0.01). Exophthalmometry improved from 23.5 mm to 19.7 mm (p < 0.01), and this result was correlated with the number of walls removed (Pearson r = −0.302, p < 0.01).

The authors conclude that since on average, esotropia and ductions tend to worsen with decompression the authors conclude that their results support the clinical dictum to avoid strabismus surgery until after decompression. However the findings suggest that upper eyelid surgery may be combined with decompression.

Clinical Outcomes of Ruptured Periorbital and Orbital Dermoid Cysts

This multicenter, retrospective study of all cases of periorbital and orbital dermoid cysts with histopathological evidence of rupture, including those with clinical rupture, was performed over a 10-year period to evaluate the clinical outcomes of
ruptured dermoid cysts. Demographics and clinical outcomes of ruptured dermoid cysts were recorded. Persistent inflammation was defined as the presence of edema, erythema, and discomfort for at least 28 days. Eighty-six cases of dermoid cysts were identified. Median age was 5.5 (range, 1–63) years. Location of cyst was either periorbital (n = 60, 70%) or orbital (n = 26, 30%). There were 29 cases with clinically apparent rupture: 27 surgically ruptured (93%) and 2 spontaneous rupture (7%). Persistent inflammation was found in 1 spontaneous cyst rupture case (50%) and 1 surgically ruptured cyst (3.7%). Older age (p = 0.01) and bony attachment (p = 0.001) were significant factors for cyst rupture, while there was no influence from cyst location (p = 0.14). The authors present the largest series of intraoperative dermoid cyst ruptures and conclude that rupture dealt with meticulous in a controlled surgical setting results in far less frequent inflammation compared to spontaneous rupture, pointing out the benefit of earlier surgery on orbital dermoids. The also point out that older age and bony attachment are risk factors for cyst rupture.

Severe Pediatric Thyroid Eye Disease: Surgical Case Series

Thyroid eye disease (TED) usually has mild manifestations in pediatric patients, and orbital decompression is rarely necessary. The authors present the clinical course of 3 pediatric patients age 16 or younger at the time of decompression surgery with severe orbitopathy. Case 1 is a 9-year-old prepubertal Asian-American female with Graves’ disease and TED who underwent balanced decompression for compressive optic neuropathy. Case 2 is a 14-year-old white female with Graves’ disease and TED who underwent balanced decompression for compressive optic neuropathy, stretch optic neuropathy, and globe subluxation. Case 3 is a 14-year-old African-American male with unilateral euthyroid TED who underwent staged right-sided lateral, medial, and floor decompressions for asymmetric proptosis. All cases also had disfiguring proptosis and exposure keratitis, and in all cases, surgery successfully ameliorated the indications. Children, both pre- and post-pubertal, can rarely manifest visually threatening severe orbitopathy due to TED. This represents the first reports of thyroid-related optic neuropathy and globe subluxation in pediatric patients. This report illustrates some practical approaches to dealing with pediatric TED but highlights the importance of further studies to elucidate differences between adult and pediatric TED management.

Orbital Myositis as Both a Presenting and Associated Extraintestinal Sign of Crohn’s Disease

Orbital myositis is a rare extraintestinal manifestation of inflammatory bowel dis-
ease and has been reported to occur at variable times relative to gastrointestinal symptoms, including years before, concurrently to, and years after the gastrointestinal diagnosis. Here, the authors report 3 cases of Crohn’s disease associated orbital myositis, adding to the 18 previously reported cases. The authors describe 2 cases of middle-aged females presenting with orbital myositis during clinical remission of Crohn’s disease. The authors also describe the first reported case of orbital myositis-associated Crohn’s disease diagnosed prior to any gastrointestinal symptoms in a teenage male presenting with corticosteroid responsive intermittent eyelid swelling. These cases demonstrate the importance of consideration of systemic conditions in children with recurrent orbital myositis.

**Metastatic Embryonal Conjunctival Rhabdomyosarcoma in 4-Year-Old Boy**


The authors report the case of a 4-year-old boy who presented with unilateral ptosis and a mass lesion of palpebral conjunctiva of the left upper eyelid, that had been present for 2 weeks, and had rapidly enlarged. The lesion was salmon colored and was easily distinguished from the conjunctiva. There was no obvious orbital extension in the MRI studies. Excisional biopsy was performed through a conjunctival approach. The histopathology was consistent with embryonal rhabdomyosarcoma. Thoraco-abdominal CT scans revealed nodules in both lungs, indicating stage 4 disease. The patient received chemotherapy and intensity-modulated radiation therapy. Rhabdomyosarcoma confined to the conjunctiva and distant metastasis without orbital involvement is rare. It should be included in the differential diagnosis of any atypical conjunctival mass lesions in children, and histopathology is necessary to establish proper treatment. As the case indicates, detailed systemic evaluation and careful systemic follow up of these patients are mandatory. This case shows the importance of early diagnosis and treatment of conjunctival lesions.

**Childhood Optic Nerve Glioma: Vision Loss Due to Biopsy**


Two children without neurofibromatosis type 1 presented with unilateral decreased vision and MRI revealing optic nerve tumors. In the first case, chemotherapy was initiated empirically for presumed optic pathway glioma, but the lesion increased in size with associated clinical worsening, raising concern for a possible alternate diagnosis. Biopsy of the involved optic nerve resulted in worsening of vision due to a branch retinal artery occlusion and showed a grade I pilocytic astrocytoma. In the second case, sudden symptom onset and rapid tumor growth prompted an optic nerve biopsy, resulting in vision loss due to a central retinal artery occlusion and revealing grade I pilocytic astrocytoma.
In both cases, tissue diagnosis did not alter the course of management. Instead, biopsy was associated with additional vision loss, highlighting the risk of biopsy in children with isolated optic nerve tumors and imaging that is most consistent with an optic pathway glioma. The cases demonstrate the potential morbidity of biopsy of optic nerve lesions.

**Pediatric Orbital Osteoradionecrosis**  

Orbital osteoradionecrosis is a rare complication of orbital radiotherapy. It can occur in children, associated with orbital radiotherapy treatment, mimicking recurrence of malignancy and infection. In children, it is most likely to be associated with orbital malignancies treated with higher doses of radiotherapy, such as recurrent orbital rhabdomyosarcoma. This is the first report of osteoradionecrosis in a child and only two other reports are noted in the literature.

**Trends over time in the incidence of congenital anophthalmia, microphthalmia and orbital malformation in England: database study.**  

Anophthalmia and microphthalmia are congenital conditions which present a significant challenge to ophthalmologists and families. Genetic and environmental factors could play a role in their development. In England, there are concerns of increasing hospital admission rates for anophthalmia, microphthalmia and other congenital orbital malformations. The authors conducted an analysis of hospital admission rates for these conditions using English National Hospital Episode Statistics (HES), which links successive records for the same person together in English National Health Service hospitals. Their results showed a mean annual incidence of 1.5/100,000 infants for anophthalmia and 8.6/100,000 for microphthalmia. Congenital orbital/lacrimal malformation incidence was 0.5/100,000. Overall the incidence of these conditions has remained stable, although admission rates for microphthalmia has increased, possibly due to better understanding of the need for growth of the orbit and the custom care that this entails.

**21. OCULOPLASTICS**

The purpose of this retrospective chart review was to compare the success and extrusion rates of the monocanalicular and bicanalicular Crawford Intubation systems in patients who were diagnosed with congenital nasolacrimal duct obstruction and were treated with lacrimal intubation. One hundred sixty-eight eyes were included in the study. Bicanalicular intubation was used in 80 eyes (bicanalicular group) and monocanalicular intubation was used in 88 eyes (monocanalicular group). Success occurred in 63 (78.75%) and 82 (93.18%) eyes in the bicanalicular and monocanalicular groups, respectively (P = 0.00653). Extrusion occurred in 24 (30%) and 11 (12.5%) eyes, respectively (P = 0.00528).

The current study supports the benefits and superiority of the monocanalicular system. Success and reoperation rates were significantly better with the monocanalicular tube. Similarly, extrusion with the monocanalicular system was less than with the bicanalicular system (12.5% vs 30%). Further, extrusion observed in the monocanalicular system was less problematic compared to the bicanalicular system. When the monocanalicular tube was extruded, it simply fell out. Alternatively when the bicanalicular tube was extruded, a loop of silicone tubing remained that ran from the upper to lower punctum and required removal. An emergent clinic visit usually ensued to deal with the externalized tube. The authors conclude that monocanalicular intubation for congenital nasolacrimal duct obstruction is superior to bicanalicular intubation. Extrusion and reoperation rates are significantly lower. If a bicanalicular intubation system must be used due to availability, an attempt to secure the tube is necessary so that early extrusion does not occur, which might reduce the success rate.

The value of the Frontalis suspension procedure as a repeat intervention in Congenital Blepharoptosis.


The purpose of this retrospective study is to evaluate the therapeutic benefits of frontalis suspension as a repeat intervention in congenital blepharoptosis. Eighty-four eyes of 77 patients with simple congenital ptosis (44 males and 33 females) were evaluated. The mean ages at diagnosis and first surgery were 6.4 ± 0.6 years (range: 0 to 15 years) and 8.1 ± 0.5 years (range: 1 to 16 years), respectively. The mean follow-up period was 8.4 ± 0.7 years (range: 2 to 29 years). Levator function, margin-reflex distance, and ocular motility data were included for each visit. Ptosis was categorized as mild (≤ 2 mm), moderate (> 2 mm and < 4 mm), and severe (≥ 4 mm). According to the clinical algorithm followed by the operating surgeon, either modified Fox-Pentagon frontalis suspension or anterior approach levator resection was used for primary interventions depending on the baseline levator function. Patients who required repeat surgical interventions underwent frontalis suspension. A successful outcome was defined as a postoperative margin-reflex distance of 3 mm or greater at the time of the last postoperative examination. Surgical success was achieved in 61.9% of pa-
tients with single surgery (75.9% for levator resection vs 54.5% for frontalis sus-
pension; $P = .06$) and in 77.4% of patients following repeated surgeries (93.1% vs 69.1% for patients who initially underwent levator resection vs frontalis sus-
pension, respectively; $P = .012$). A higher success rate was associated with bet-
ter preoperative levator function ($P = .01$) and a higher margin-reflex distance
($P = .004$), and was inversely proportional to ptosis severity ($P = .04$). The au-
thors suggested that both levator resection and frontalis suspension as initial in-
terventions for congenital ptosis provide satisfactory functional outcomes, but re-
currences are to be expected with longer follow-up periods. In cases with recur-
rence, additional interventions such as frontalis sling offer the opportunity for fur-
ther improvement and are recommended for optimum outcomes.

**Manifestation and grading of ocular involvement in patients with Tessier number 10 clefts.**


Tessier classification of craniofacial clefts uses the orbit as a central hallmark. The clefts are numbered from 0 to 14 and extend along constant axes through the eyebrows or eyelids, the maxilla, the nostrils, and the lip. Number 10 cleft is a rare condition consisting of congenital coloboma of middle third of the upper eye-
 lids, eyebrow deformities, and a wedge-shaped anterior hairline extension. It may also be accompanied by other ocular anomalies, including symblepharon, cuta-
neous pterygium (skin growing onto the globe), and corneal complications. De-
spite its potentially devastating nature and the increasing indications for ocular reconstructive surgery, there is currently no standardized method for evaluating the spectrum of ocular manifestations and the severity of ocular involvement in this congenital disease. Fifty-nine patients (85 eyes) diagnosed with Tessier number 10 clefts were recruited. Authors analyzed four components of ocular involvement: upper eyelid defect, symblepharon with cutaneous pterygium, cor-
eal complications (opacification, neovascularization, keratinization, and limbal stem cell deficiency), and lower eyelid ectropion; each component was graded on a scale from 0 to 3, depending on the severity of involvement. Upper eyelid de-
fect Grade 0 no defect; grade 1 less than one-third of the eyelid was affected;
grade 2 greater than one-third but less than one half of the eyelid was affected;
grade 3 more than one half the eyelid was affected. Symblepharon with cutaneous pterygium 0 = no symblepharon, 1 = symblepharon and cutaneous pterygium confined to the corneal limbus, 2 = symblepharon and cutaneous pterygium extending up to the pupil margin, and 3 = symblepharon and cutaneous pterygium extending beyond the pupil into the central cornea. Cornea grade 0 = clear cornea, grade 1 = corneal opacity and keratinization localized at the periphery less than two continuous hours; grade 2 = corneal opacity and cutaneous pterygium less than four continuous hours; grade 3 = extensive opacity, cutaneous pterygium, keratinization, or neovascular-
ization with more than four continuous hours. Lower eyelid ectropion grade 0= no
ectropion; grade 1 less than one-third of the lower eyelid affected; grade 2 greater than one-third but less than two-thirds of the eyelid affected; grade 3 when more than two-thirds of the lower eyelid affected.

85 eyes of 36 male and 23 female patients. Median age at the time of presentation was 3 years and 42/59 patients were children under 6 years old. Twenty-six of 59 presented bilaterally. 100% of the patients presented with upper eyelid coloboma, eyebrow deformities, and a wedge-shaped anterior hairline extension. More than 50% of the patients with upper eyelid coloboma were classified as grade 3. Symblepharon was seen in 95% of the patients with more than 47% having grade 3 disease. Corneal involvement was only seen in 5% of the cases, however 50% of those had severe disease. Lower eyelid ectropion was seen in almost 50% of the patients but most cases were classified as grade 0. Upper eyelid defect is seen in all patients with Tessier 10. A strong correlation was found between the upper eyelid defect and the severity of all other ocular findings.

**Etiology of pediatric acquired blepharoptosis.**

The purpose of this retrospective study was to describe the etiology of acquired pediatric blepharoptosis and to elucidate the causes of the disease. The medical records of all patients presenting with acquired blepharoptosis at two specialist ocular plastics practices and a pediatric ophthalmology practice during a period of up to 25 years were reviewed retrospectively and classified according to their diagnosis. Patients were grouped into children (<18 years), younger adults (18-40 years), and older adults (>40 years). A total of 268 patients <18 years of age were identified. The most common identifiable causes of acquired blepharoptosis in children were infantile hemangioma (n = 92 [34.3%]) and trauma (n = 41 [15.3%]). In 42 cases (15.7%) a definite diagnosis could not be made. The authors concluded that the etiology of pediatric acquired blepharoptosis can frequently be determined by history and examination; additional diagnostic tests are sometimes required. In this pediatric cohort there was a high percentage of patients with blepharoptosis of unknown cause. Despite many years of follow-up the cause has remained elusive in all of these children.

One of the main strengths of this study compared to previous reports on this subject is its very large sample size. However, during the 25-year period of patient recruitment, new diagnostic tools have been developed and new pathological processes have been identified, reassessment and repeated imaging may have reduced the number of idiopathic cases.
Congenital ptosis repair with a frontalis silicon sling: comparison between Fox’s single pentagon technique and a modified Crawford double triangle technique.

The purpose of this randomized clinical trial study was to compare the results of two different frontalis sling surgery techniques with silicon rod for ptosis: Fox’s single pentagon technique and a modification of Crawford’s double triangle technique. A total of 52 eyes of 50 patients with severe ptosis and poor levator function (≤ 4 mm) were randomly assigned to the Fox group or the modified Crawford group. Cosmetic outcome, functional success, and lagophthalmos were compared. The patients achieved a fair to good cosmetic outcome by subjective grading and a fair outcome by objective grading (masked observer) in both groups. The intergroup difference was not statistically significant (P > 0.05). However, patients with preoperative lateral droop had better cosmetic outcome in the modified Crawford group. Mean increase in marginal reflex distance 1 (MRD-1) was 4.0 ± 1.7 mm in the Fox group and 3.7 ± 1.1 mm in the modified Crawford group. Change in MRD-1 within groups was significant (P < 0.0001); however, the difference in the groups was not (P = 0.44). The mean lagophthalmos in the Fox group was 1.3 ± 0.7 mm versus 0.6 ± 0.7 mm in the modified Crawford group at final follow-up. This intergroup difference in lagophthalmos was statistically significant (P = 0.001). The authors conclude that both techniques were effective in reducing the amount of blepharoptosis and achieving a natural appearing cosmetic outcome. In cases with predominant lateral droop, the modified Crawford’s technique seems to produce better results, although the small number of cases does not permit statistical comparison. Despite small sample size, the study was well designed.

Use of the Masterka for complex nasolacrimal duct obstruction in children.

The Masterka stent has been recommended solely for treatment of simple distal membranous nasolacrimal duct obstruction (NLDO). The purpose of this retrospective study was to evaluate the Masterka stent as a primary treatment in complex forms of NLDO, including bony ductal stenosis and proximal and serial membranous obstruction. The medical records of patients who underwent treatment for congenital nasolacrimal duct obstruction with the mono-canalicular Masterka stent were reviewed retrospectively. Both simple and complex forms of NLDO were primarily treated with probing and irrigation, followed by placement of the Masterka stent. A total of 72 eyes (53 patients) were included: 17 cases were simple forms of NLDO; and 55 were complex. Success was achieved in 15 of 17 simple cas-
es (88%) and 39 of 55 complex cases (71%); the overall success rate was 75%. In patients <24 months of age, success rates were 100% for simple and 78% for complex forms. The authors conclude the Masterka stent can be useful in a younger subset of patients with more complex forms of congenital NLDO. A lower success rate is noted in children >2 years of age and complex forms of NLDO, especially those with bony stenosis. Apart from being limited by its retrospective nature and its relatively small sample size, the study failed to demonstrate a comparable success rate to other types of silicone tube intubation in NLDO.

**A Novel One-Stage Obstruction-Based Endoscopic Approach to Congenital Nasolacrimal Duct Obstruction**

This paper reported 10-year results of a 1-stage, obstruction based, endoscopic approach to treating children with congenital nasolacrimal duct obstruction (CNLDO) with and without prior failed probing/intubation. This was a retrospective study, which included children >6 months old with primary CNLDO who previously failed probing/intubation, or who had acute dacryocystitis or dacryocele at any age, and at least 6 months follow up. Diagnosis was based on history of tearing and dye disappearance test. The study excluded patients with complete puncto-canalicual obstruction and craniofacial anomaly. Type of CNLDO was confirmed using endonasal endoscopic guided probing. An endoscopic probing was performed for membranous, intubation for incomplete complex, and dacryocystorhinostomy for complete complex CNLDO. The patients were followed at 1 week, 1, 3, and 6 months, and then after. Success was defined as no or occasional tearing related to noxious stimulus at least 6 months after the procedure. The study looked at 226 eyes (200 patients) with a mean age of 26.72 months. Previous failed probing/intubation was present in 34.1%. Inferior turbinate impaction in 73.5% and septal deviation in 2.7% were noted. Membranous CNLDO was found in 38.9%, incomplete complex in 57.9%, and complete complex in 3.1%. Mean time of tube removal was 11.9 weeks and last follow-up time was 24.3 months. There was no significant effect of any variables on the final success rates (probing: 96.5%, intubation: 95.4%, dacryocystorhinostomy: 100%). The study found that the one-stage, obstruction-based endoscopic approach to CNLDO resulted in a high success rate for different types of CNLDO (membranous, incomplete complex, and complete complex).

**Anatomical characterization of Nasolacrimal Canal Based on Computed Tomography in children with Complex Congenital Nasolacrimal Duct Obstruction.**
Chengyue Zhang, Gang Yu, Yanhui Cui, Qian Wu, Wenbin Wei
The purpose of this study was to identify anatomical variations of the nasolacrimal canal in patients with complex congenital nasolacrimal duct obstruction. The authors retrospectively reviewed the computed tomography radiographs of 25 children (17 boys and 8 girls, mean age 60 months, range of 4 to 137 months), with congenital nasolacrimal canal dysplasia who had failed probings. Anomalous development of the nasolacrimal canal was confirmed on computed tomography. Two main types of malformations were observed: fundamental (20 patients) and special (5 patients). In the fundamental type, the upper portion of the nasolacrimal canal was relatively normal and became significantly stenotic, or even atretic, at the middle and terminal segments. In the special type, the upper portion of the nasolacrimal duct was malformed. Only the special type showed an association with systemic abnormalities. In patients with unilateral fundamental type malformation (11 patients), the transverse and anteroposterior diameters of the upper segment of the nasolacrimal canal on the affected side were significantly larger than that of the normal side ($P = .000$). The height of the nasolacrimal canal on the normal side was significantly larger than that of the affected side ($P = .000$). The authors conclude that computed tomography is useful for delineation of anatomical characteristics of the nasolacrimal canal and to diagnose nasolacrimal canal malformation.

**Factors Predictive of Success in Probing for Congenital Nasolacrimal Duct Obstruction**

Joao Beato, Agata Mota, Nuno Goncalves, Renati Santos-Silva et

This retrospective case series reports the success rate of probing for congenital nasolacrimal duct obstruction (CNLDO) and the factors relating to the failure of the procedure. 88 eyes of 62 patients were included in the study. Success was defined as resolution of epiphora at the one month postoperative visit. The overall success rate of the first probing was 77.3% and decreased in children older than 4 years, although not statistically significant. The success rate after the second probing was 85.7%, and the median interval between the two procedures was 3 months. 30% of children with persistent obstruction had an otolaryngology evaluation that revealed adenoid hypertrophy requiring surgical correction. Although otolaryngology evaluations were not performed in all patients, the authors suggest that children with a failed second probing should be evaluated.

**A survey of management of congenital nasolacrimal duct obstruction by pediatric primary health care providers in Spain.**

The purpose of this descriptive study was to survey the management of congenital nasolacrimal duct obstruction (CNLDO) by pediatric primary health care providers in Spain. A web-based questionnaire was used to evaluate the experience of the members of the Pediatric Primary Care Society in Castilla-Leon, Spain (APAPCYL), regarding management of CNLDO. The questionnaire contained 14 direct questions and was sent by e-mail to all the pediatricians. All the responses were analyzed by the frequency of occurrence and percentages. Ninety physicians responded to the questionnaire, which accounts for 42.45% of all of general pediatricians in the region. Massage 2 or 3 times a day was the initial treatment advised by 60.47% of pediatricians. Nearly half of the pediatricians recommended continuing massage until symptoms resolved. Fewer than 50% of children required referral to an ophthalmologist. Reasons for an ophthalmic consult included persistence of symptoms among 87.21% of pediatricians and parental/guardian request among 10.5% of pediatricians. According to 45.6% of pediatricians, their knowledge about CNLDO is limited, and 92.2% would like to receive further training on CNLDO. The authors conclude that massage was the main initial treatment for managing CNLDO among pediatricians. The outcomes of this survey indicated that massage fails in approximately 50% of patients and an ophthalmic referral is required for these cases. The outcomes of the current survey indicate that pediatricians manage CNLDO appropriately and refer to an ophthalmologist if the patient requires further assessment and management, but one of the main limitations of this study is that only around 40% of APAPCYL members responded to its survey and this introduces a selection bias and may not reflect the actual practice that is applied in CNLDO.

**Lacrimal Gland Involvement in Blepharophimosis-Ptosis-Epicanthus Inversus Syndrome.**


In this study, the authors describe the involvement of the lacrimal gland (LG) in blepharophimosis-ptosis-epicanthus inversus syndrome (BPES). In an observational, cross-sectional study, the authors examined 21 patients with BPES from 3 Brazilian medical centers and 1 Portuguese medical center. Patients had their ocular surface evaluated with slit-lamp biomicroscopy, and tear production quantified with the Schirmer test I. The LG volumes were measured on computed tomography (CT) scans in the BPES sample and in a group of age-matched subjects imaged for nonorbital diseases. Sixteen patients were screened for mutations in the FOXL2 gene. Absence of LG was detected bilaterally in 9 patients (42.8%) and unilaterally in 2 patients (9.5%). When considering only patients with measurable LG, the median volume was 0.22 cm³ in the right eye (range, 0.06-0.36 cm³) and 0.24 cm³ in the left eye (range, 0.08-0.34 cm³). These values were significantly lower than those for the age-matched controls (median = 0.54 right eye and 0.53 left eye; P < 0.05). There was a significant association between deficiency of tear production and LG volume reduction and agenesis.
Molecular analysis of the FOXL2 gene revealed the presence of 8 distinct mutations, 4 of them novel ones. A significant reduction of LG size or agenesis was associated with mutations affecting protein size (due to underlying changes in the stop codon location) or the DNA-binding forkhead domain (Fisher exact test, P = 0.021). In 3 probands, the underlying genetic defect was not found. This is the first study reporting LG volumes in BPES, describing a significant number of patients with LG agenesis. The association between alacrima and BPES is not incidental, and a thorough evaluation of tear production is recommended. The authors emphasized the importance of this clinical finding, especially when ptosis correction is considered, since most of ptosis surgeries in BPES will lead to nocturnal lagophthalmos and reduced spontaneous blink amplitude.

**Factors Associated with Surgical Outcomes in Congenital Ptosis: A 10 – Year Study of 319 Cases.** 

This was a retrospective review of 319 patients over 10 years who had surgical correction for congenital ptosis. The authors sought to better describe success rates for ptosis surgery and factors associated with a good postoperative outcome. They defined excellent lid height as a marginal reflex distance of >3mm and a recurrence as a lid height of less than 50% of the initial post op result. 97.2% of patients had a surgical success. They found that levator resection procedure (as opposed to frontalis sling), absence of Marcus Gunn jaw-winking syndrome, and better pre op MRD were all predictive of better post op result. Additionally, the recurrence rates were higher in patients who had a frontalis sling than those with a levator resection. The author's point out the limitations in the study, which were the retrospective nature of the study and the variation in surgical procedure due to surgeon technique. It is interesting that the authors did not measure levator function in these children. They point out the difficulties in getting accurate measurements in this population and question its clinical utility in obtaining a good postoperative result.

**Congenital Paradoxical Lower Eyelid Retraction With Upgaze due to an Anomalous Extraocular Muscle**

Congenital anomalous orbital structures are rare and associated with strabismus, globe retraction, and dystopia. The authors present a case of congenital paradoxical right lower eyelid retraction with upgaze due to an anomalous extraocular muscle in a 17-year-old, healthy, female patient. Orbital computed tomography showed an intraconal, inferolateral soft-tissue band extending from the orbital apex to the inferior oblique muscle and lower eyelid. There was resolution of lower eyelid retraction and exposure symptoms after resection of the anterior
portion of the fibromuscular band from the lower eyelid retractors and eyelid elevation with ear cartilage. To the authors’ knowledge, this case is the first to report anomalous orbital structure as a rare cause of congenital paradoxical lower eyelid retraction, which can be improved with resection. This report showcases another clinical entity to consider in atypical strabismus evaluation.

Subepidermal Calcified Nodules of the Eyelid Differ in Children and Adults
Saeed AlWadani, Maria J. Suarez, Jonathan J. Kass, Emily MacQuaid, et al.

Subepidermal calcified nodule of the eyelid is considered as one of the types of calcinosis cutis. It generally occurs in children, and is not known to be associated with systemic disease. The authors report histopathological and clinical findings in 14 cases of subepidermal calcified nodule of the eyelid, including 3 older patients with unique microscopic features. Clinical records and pathological materials were critically reviewed in each case, including von kossa, CD3, CD20, and CD68 stains. The 14 cases presented clinically as nodular eyelid lesions. All were treated with surgical excision. The authors found 2 distinct histopathological patterns which correlated with the patients’ age. In young patients, the authors observed multiple, small calcified bodies within the dermis surrounded by chronic inflammation and granulomatous foreign body reaction. On the other hand, in elderly patients, lesions were characterized by a single, large, well-demarcated amorphous calcified deposit surrounded by fibrous tissue, without chronic inflammation or foreign body reaction. One of these patients, a 70-year-old man, also suffered from gout. The presence of subepidermal calcified nodule was not documented as a pre-operative diagnostic possibility in any of the cases. Subepidermal calcified nodule of the eyelid is a rare condition, but should be considered in any patient presenting with a painless white to yellowish colored nodule of the ocular adnexa, particularly during the teenage years. Clinicians and pathologists should be aware that this entity has a distinct appearance and could be associated with systemic conditions in elderly patients. This is the first report of the histopathological differences in the nodules based on age.

Maximal levator resection in unilateral congenital ptosis with poor levator function.
Ju-Hyang Lee, Orapan Aryasit, Yoon-Duck Kim, Kyung In Woo, et al.

Options for correction of congenital ptosis are varied, but include frontalis suspension and levator resection. Treatment for unilateral or asymmetric cases can be challenging. The authors of this study performed a retrospective case series of children with severe unilateral or asymmetric ptosis with poor levator function, who underwent unilateral maximal levator resection. 243 cases were included,
210 of which (86.4%) were unilateral. Surgical outcomes were reported as poor, good, or excellent depending on post-operative MRD1. Excellent outcomes were obtained in 76.5% of patients, good in 16.5% and poor in 7.0%. The reoperation rate was 11.1%, and the most common complications included exposure keratopathy, lid crease asymmetry, and entropion. Preoperative levator function did not affect surgical results. Despite its retrospective nature, the large group of patients suggests that large levator resection is an effective strategy to treat severe ptosis cases with poor pre-operative levator function.

### 22. INFECTIONS

**Surveillance Surveys for Reemergent Trachoma in Formerly Endemic Districts in Nepal from 2 to 10 Years After Mass Drug Administration Cessation**


This study sought to determine the prevalence of trachoma from surveys in four districts in Nepal that had surveillance intervals of 2, 4, 8, and 10 years, respectively, after cessation of MDA. The cross-sectional surveys were carried out in 2015 and 2016, with data analyses performed from 3/2016 through 9/2016. Results indicated that of the 3024 children surveyed, 48.0% were female and the mean age of the children was 5.4 years. Eleven cases of TF were found, with a TF prevalence less than 1% in all four districts. Three cases of infection were found and seropositivity for pgp3 antibody varied from 1.4% with a 10-year surveillance interval to 2.5%. In summary, the TT prevalence was less than 1 case per 1000 among the total population in all four districts. In summary, the authors found that their study found no evidence of re-emergence of trachoma up to 10 years after cessation of MDA in four districts in children in Nepal.

**Quantitative Assessment of Microstructural Changes of the Retina in Infants With Congenital Zika Syndrome**


This case series of 8 infants with CZS, 5 girls and 3 boys in the age range of 3-5 months. All eight infants with CZS had foveal abnormalities in the 8 analyzed eyes, including thinning of the central retina with discontinuities of the ellipsoid zone and severe structural disorganization with 3 eyes showing pseudocolobomas. Of note, the SD-OCT cross sections were segmented and each retinal layer thickness was measured at critical eccentricities using the position of the signal peaks and troughs on longitudinal reflectivity profiles. In summary, CZS showed central retinal degeneration with severe GCL loss, borderline inner nuclear layer thinning, and less prominent photoreceptor loss. The findings provide the first, to
date, in vivo evidence in humans for possible retinal maldevelopment, especially with retinal GCL loss in CZS, consistent with a murine model of the disease. In summary, the authors note that their findings are suggest of in utero depletion of this neuronal population as a consequence of the Zika virus infection.


Congenital Zika syndrome (CZS) is associated with the following five main features: severe microcephaly, brain anomalies, neurological impairment, congenital muscle contractures, and ocular findings. Previous reports had shown that 36% of babies with CZS had hypo-accommodation, and 59% had significant refractive errors. The goal of this cross-sectional study was to describe the immediate response to correction of refractive errors and hypoaccommodation in children with CZS. Children born between May and December 2015 with a confirmed diagnosis of CZS and enrolled in a multidisciplinary early intervention program were included in this study. All children received a comprehensive ophthalmic examination, including dynamic retinoscopy and cycloplegic refraction. Children were prescribed their full correction if they met the criteria for refractive error, and additional plus 3.00 overcorrection was prescribed for accommodative dysfunction, and/or low vision. Monocular and binocular visual responses to Lea Grating Test at 30 cm, with and without eyeglasses, were measured on day 1 of glasses wear. A total of 60 children were evaluated (mean age at evaluation, 11.5 ±1.1 months; range, 9.0-16.0 months). Lea Grating Test responses were abnormal in all children prior to spectacle correction. Hypoaccommodation was present in 17 of 21 children (81%) that had fixation and were able to perform the dynamic retinoscopy test. Overcorrection was prescribed for all children. Visual responses were subnormal even with glasses use; however, immediate improvement in binocular vision was found in 37 children (62%) and in 74 of 119 eyes (62.2%). There was a statistical difference between the cycloplegic refraction of the children on initial assessment and the refraction 3 months later, including emmetropia (P = 0.001), hyperopia (P = 0.000), myopia (P = 0.007), and astigmatism (P = 0.004). Although funduscopic change was detected in 42% of children, visual impairment was found in all (100%). The authors conclude that eyeglasses can improve visual acuity in children with CZS. Significant changes in their refractive status over time requires periodic updates. The study highlights that similar to other infants with neurological visual impairment, patients with CZS have limited power of accommodation, poor visual acuity, high refractive errors, and strabismus.

The goal of this cross-sectional study was to describe the visual impairment associated with ocular and neurological abnormalities in a cohort of children with congenital Zika syndrome (CZS). It included infants with microcephaly born in Pernambuco, Brazil, from May to December 2015. Immunoglobulin M antibody capture enzyme-linked immunosorbent assay for the Zika virus on the cerebrospinal fluid samples was positive for all infants. Clinical evaluation consisted of comprehensive ophthalmologic examination including visual acuity (Teller Acuity Cards II), visual function assessment, visual developmental milestone, neurologic examination, and neuroimaging. A total of 32 infants (18 males [56%]) were included. Mean age at examination was 5.7 +/- 0.9 months (range, 4-7 months) were included in the study. Visual impairment was detected in all 32 participants. Retinal and/or optic nerve findings were observed in 14 patients (44%). There was no statistical difference between the patients with ocular findings and those without (P = 0.180). Nystagmus was identified in 28% of infants; strabismus, in 75%. All patients (100%) demonstrated neurological and neuroimaging abnormalities; 3 (9%) presented with late-onset of microcephaly. Despite the relatively small sample size, and the presence of motor impairment in certain cases, which may have limited the child’s response for visual function testing, this is a well-designed study. The authors conclude that children with CZS demonstrated visual impairment regardless of retina and/or optic nerve abnormalities. This finding suggests that cortical/cerebral visual impairment may be the most common cause of blindness identified in children with CZS.

The visual system in infants with microcephaly related to presumed congenital Zika syndrome.


The purpose of this cross-sectional study was to describe and analyze ocular features in infants with microcephaly due to presumed congenital Zika syndrome. Ophthalmologic evaluation, including indirect ophthalmoscopy and eye fundus imaging, visual acuity testing with Teller Acuity Cards, and strabismus assessment were performed in infants with microcephaly at a nongovernmental organization clinic for visually disabled children. RESULTS: A total of 70 infants with microcephaly were referred to the clinic. Of these, 25 (mean age, 3 months; 14 males) had ophthalmologic changes: 18 (26%) had intraocular abnormalities, including macular chorio-retinal atrophy, mottled retinal pigment epithelium and optic nerve pallor; 7 patients (10%) had strabismus or nystagmus without intraocular abnormalities. Visual acuity was below normal range in all 11 infants tested. The authors conclude that ophthalmologic abnormalities are frequent in presumed congenital Zika syndrome. Macular circumscribed chorio-retinal atrophy, focal
mottled retinal pigment epithelium, optic nerve pallor, early-onset strabismus, nystagmus and low visual acuity were common ophthalmological features in infants with microcephaly due to presumed congenital Zika syndrome. The main limitation of this study is the lack of laboratory evidence with specific serological testing to confirm Zika virus. Longer ophthalmologic follow-up with retinal imaging and visual development assessment are needed for further understanding of the CZS the consequences for visual performance.

Epidemiology of Pediatric Zika Virus Infections

In July 2016, transmission of Zika virus was announced in Miami-Dade County, Florida. This report characterizes the signs and symptoms of pediatric patients who were confirmed cases of ZIKV. The patients were identified through active surveillance methods of (1) provider reports of suspected ZIKV in symptomatic patients, (2) routine screening of asymptomatic pregnant women, and (3) epidemiologic investigations of ZIKV clusters by urosurveys. Of the 478 cases, 6.9% of the patients were children between the ages of 1 and 17. Of the 31 symptomatic patients, 100% had a rash, 80.6% reported fever, 29.0% reported conjunctivitis, and 22.6% reported arthralgia. About 50% of the confirmed ZIKV cases presented with 2 of the 4 primary symptoms. 81.8% of patients had travel associated infections and 18.2% of the cases locally acquired their infection in Miami-Dade County. There were clusters of infections within families that seek care which may be attributed to one mosquito infecting multiple members of a family. This finding supports family education to prevent mosquito bites while traveling to infected areas.

Zika virus and the eye

Congenital Zika Syndrome (CZS) is described in this review with special attention to the ocular findings. CZS consists of microcephaly, ocular findings, and arthrogryposis. Infants with CZS and microcephaly had 34-55% possibility of severe ocular abnormalities with posterior findings most frequently focal pigment mottling and CR atrophy predisposed to affect the macular area. Optic disc anomalies also occur and rarely congenital glaucoma. OCT findings in patient with macular impairment show severe neurosensory involvement. Fundus abnormalities in infants with presumed Zika infection were associated with smaller cephalic diameters and mothers who reported symptoms during the first trimester. For disease prevention the control of the carrier mosquito population as well as vaccine development are imperative. Women should avoid endemic areas and use
repellants. All microcephalic infants should be monitored for fundus changes.

Pediatric blepharokeratoconjunctivitis: is there a ‘right’ treatment?


The author reviews the diagnosis and treatment options for blepharoconjunctivitis (BKC) in children. BKC should be suspected in patients with frequent, multiple chalazia, recurrent photophobia, redness and foreign body sensation. Clinically, patients may have eyelash flaking, collarettes, along with posterior blepharitis with inspissated Meibomian glands, telangiectasia, and irregular lid margins. The cornea may have pannus formation, SEI and punctate keratopathy which may be bilateral and asymmetrical. Pediatric ocular rosacea and Demodex should be suspected in cases of chronic BKC. Treatment regimens vary but usually include hot compresses to assist in melting glandular secretions followed by vigorous massage to express gland material and eyelid scrubs with baby shampoo. Tea tree oil may be helpful in cases although there are no pediatric studies about this. Use of topical lubrication to improve tear film disruption as well as bacitracin and erythromycin ointment applied to lid margins at bedtime may help limit colonization of bacterial lid flora. In severe cases topical steroids may be required and in some cases Restasis may be used as a steroid sparing agent. In adults, oral antibiotics can be effective. Due to issues with dentition in children erythromycin may be used for severe BKC at doses between 12.5-40 mg/kg/day divided bid and continued up to 12 months. Oral azithryomycin at 5mg/kg/day divided bid has also been used although one must be aware of the GI side-effects and reversible hearing damage. The authors comment on the lack of RCTs for BKC in children with most studies cited either being adult studies or small case series.

Ultrasound biomicroscopic imaging in paediatric ocular toxocariasis


Ocular toxocariasis can present with a peripheral or posterior granuloma and moderate to severe vitreous inflammation. Vitreous/retinal traction can be present. The purpose of this paper was to determine the usefulness of using ultrasound biomicroscopy (UBM) as a diagnostic technique in children with ocular toxocariasis. In this retrospective study, 41 eyes (41 patients) who underwent vitrectomy in Beijing were examined with UBM. Mean age was 7.32 years, and median time from onset to surgery was 6 months. UBM was possible in all pa-
tients without complications. The lesions appeared as vitreous condensations or membranes of varying character. 15/41 eyes had peripheral granulomas and pseudocystic changes in the peripheral vitreous. The UBM was able to demonstrate dense vitreous adhesions to peripheral granulomas. The infero-temporal and nasal quadrants were most frequently involved. There was a significant difference in the number of clock-hours of peripheral pathology detected by UBM compared with indirect ophthalmoscopy. Overall the UBM appears to be a reliable diagnostic tool for these patients, and also allowed for the placement of safe scleral incisions during vitrectomy.

**Medical management of blepharoconjunctivitis in Children: A Delphi Consensus.**


The purpose of this study is to describe a pragmatic approach to the medical management of blepharoconjunctivitis in children, based on published evidence and clinical experience. The authors used the Delphi consensus method to explore the preferred management patterns of four senior clinicians at one institution to reach agreement on indications and dosage schedules for commonly used treatments. Four iterations were created, with electronic questionnaires distributed via an online survey platform. Initial questions were based on recent systematic reviews and clinical experience. After each round, a facilitator summarized the responses and fed these back to the expert participants, together with an invitation to complete the next round of questions. Typical and specific eyelid, corneal, and conjunctival disease features influenced management decisions, and treatments were targeted toward specific findings in these tissues rather than to overall disease severity. Active keratitis was considered the main indication for high potency steroids, systemic antibiotics and possibly systemic immunomodulators. Other indications for systemic antibiotics were chronic active blepharitis and recurrent troublesome chalazia. Oral antibiotics were used for their anti-inflammatory and antimicrobial properties. There was little agreement on the role of dietary modifications, topical lubricants, and preference for oral or topical antibiotics. The authors presented a pragmatic treatment algorithm to assist in the management of blepharoconjunctivitis in children based on evidence and clinical experience. Nevertheless, further work needs to be done in order to evaluate the efficacy of this approach in the management of blepharoconjunctivitis.

**Cytomegalovirus Retinitis in Pediatric Stem Cell Transplants: Report of a Recent Cluster and the Development of a Screening Protocol.**

The incidence of Cytomegalovirus (CMV) retinitis in pediatric allogeneic hematopoietic stem cell transplant (HSCT) patients is unknown. The authors noted a cluster of five patients over a 1 year period at a tertiary medical center, Children’s Hospital Colorado. The authors reviewed the incidence of CMV viremia from the previous 3 years to the most recent year and found that there was not a statistically significant increase in the viremia but that there was a statistically significant increase in CMV retinitis in that same timeframe. In this paper the authors reviewed these five cases and describe a new monitoring protocol for the pediatric HSCT population. They postulate that there might be a rise in incidence of CMV retinitis. The screening protocol described includes the baseline dilated exam prior to HSCT with the addition of fundus photos for these patients. In patients without CMV, the dilated exam is repeated at 3 and 12 months post transplant. For patients who develop CMV viremia or disease, the authors suggest a new baseline exam within a few weeks of diagnosis with fundus photos followed by a repeat exam every 6-8 weeks until deepened immune competent by the BMT physician. For all patients in whom CMV retinitis is suspected, they recommended photos, as well as fluorescein angiogram, fundus autofluorescence and a visual field. The authors hope that the initiation of this protocol will help detect asymptomatic and vulnerable patients from this potentially blinding disease.

**Zika virus infection and myasthenia gravis: report of 2 cases**

This is a brief report of two patients from New Caledonia who suffered from Zika virus infection (confirmed by RT-PCR) and developed acetylcholine receptor antibody positive myasthenia gravis. Both cases were associated with thymomas. Zika virus infection can provoke other autoimmune diseases such as Guillain-Barre syndrome, and the authors discuss that Zika virus infection prior to the development of myasthenia gravis could be coincidental, could initiate disease, or could provoke symptoms in a previously asymptomatic patient.

**Ophthalmic Manifestations of Congenital Zika Syndrome in Colombia and Venezuela**

The authors report a prospective case series of 43 patients with microcephaly associated with clinically diagnosed Zika virus, from October 2015 to June 2016. In Colombia and Venezuela, all 43 children had bilateral disease, with a mean age of 2.1 months at examination. Ocular abnormalities included optic nerve hypoplasia (11.6%), mild to severe pigment mottling (63%), lacunar maculopathy (7%), chorioretinal scarring (7%), congenital glaucoma (12%). In summary, of the affected children, 12% had anterior segment disease and 88% had macular and optic nerve disease. While we don’t know how amblyopic these children will become in the years ahead, this case series shows severe ophthalmic manifesta-
tions in congenital Zika syndrome. Therefore, from these findings, it is important that all children with congenital Zika syndrome have a full ophthalmic examination.

**Neonatal Orbital Abscess Secondary to Pseudomonas Aeruginosa Conjunctivitis**


Pseudomonas aeruginosa conjunctivitis, although rare in healthy infants, may cause serious ocular and systemic complications. A 30-day-old, otherwise healthy male infant was referred with the diagnosis of right orbital abscess. The patient had been diagnosed as having Pseudomonas conjunctivitis 9 days previously at the referring center. Despite antibiotic treatment, his ocular findings had worsened and marked proptosis had developed. Other examination findings were ptosis, restriction of eye movements, periorbital erythema, and chemosis. Radiologic studies showed a large, homogenous mass with a thick capsule in the lateral retrobulbar orbit. The abscess was drained through a lateral orbitotomy. A culture of the abscess yielded *P. aeruginosa*. After surgery, the ocular findings improved rapidly without any complication. No other focus of infection or immune system abnormality was found. The patient did not experience any other significant disease during a follow up of 23 months. This case report describes a unique case and highlights the importance of timely diagnosis and treatment of bacterial conjunctivitis.

**Video Game Vision Syndrome: A New Clinical Picture in Children?**

Caterina Rechichi, Gilda De Moja, Pasquale Aragona


The purpose of this observational, cross-sectional study is to explore the possible relationship between exposure to video games/electronic screens and visual issues in children between 3 and 10 years of age. Three hundred twenty children (n1=159 boys, n2=161 girls) with a mean age of 6.9 years +/- 2 years were recruited at an outpatient unit accredited by the Italian Regional Health Service. Two groups of children were examined according to the average amount of time spent playing video games daily: children who played video games for less than 30 minutes per day and not every day (control group) and children who played video games for 30 minutes or more every day (video game group). Both groups were then divided into two subgroups: children using other types of electronic screens (eg, televisions, computers, tablets, and smartphones) for less than 3 hours daily (low electronic use subgroup) and children using other types of elec-
tronic screens for 3 hours or more per day (high electronic use subgroup). All pa-
tients underwent both ophthalmological and orthoptic examinations including
ocular motility, identification of the dominant eye using the Dolman method, cover
test for distance and near vision using the Lang Fixation Cube (LANG-
STEROTEST AG, Kusnacht, Switzerland) as a target for near fixation, and the
4 prism diopter base-out test. Stereopsis was tested with Lang-Stereotests I and
II( LANG STEREOTEST AG). Refraction was assessed using the KR8100P au-
torefractometer (Topcon Corporation, Tokyo, Japan) by taking at least 5 meas-
urements for each eye before the evaluation of subjective monocular visual acuity
with optotypes at a distance of 3 m in both non-cycloplegic and cycloplegic
conditions. A questionnaire was also used at the end of the ophthalmologic ex-
amination in order to collect the following information from the parents: estimated
average time spent playing video games, estimated average daily time spent us-
ing other types of electronic screens and any asthenopic symptoms (such as
burning, blurred vision, ocular dryness, tearing, eye strain, eye ache, transient
diplopia, dizziness, headache, and eyelid tic). The authors concluded that asthe-
nopia (especially headaches, eyelid tic, transient diplopia, and dizziness), ab-
sence of fine stereopsis, and refractive errors were statistically more frequent in
children in the video group. This study is limited by its methodology: no baseline
data prior to the use of video games were obtained. Also data considering esti-
mated playing time and parent-reported symptoms could have been biased by
the perceptions of parents. Although the authors conclude that the constant use
of video games in children may have an adverse effect on their visual system,
large prospective studies will be needed in the future in order to investigate in
depth these interesting hypotheses.

Sensorimotor outcomes in children with prenatal exposure to
methadone.
Yoo, S. H., Jansson, L. M. and Park, H. J. J AAPOS. 2017 Aug; 21(4):316-
321.
The aim of this retrospective study was to report the presentation and
characteristics of strabismus in children with prenatal methadone expo-
sure. The medical records of children with prenatal methadone exposure
were retrospectively reviewed. Those who were evaluated by pediatric oph-
thalmology were included. Information on the timing and types of prenatal
exposure by trimester of pregnancy was then collected from the patients’
mothers’ charts. The children’s perinatal histories and ophthalmologic find-
ings were collected from their pediatric clinic charts and ophthalmology
clinic charts, respectively. A total of 210 children with prenatal methadone
exposure were identified, of whom 32 (15.2%) underwent eye examinations
and 21 (10%) had strabismus. Five patients had esodeviations, with a mean
age of onset of 11.6 months; 16 had exodeviations, with a mean age of on-
set of 6.8 months. Three patients with strabismus were born prematurely,
and 2 had intracranial disease. Two patients underwent strabismus sur-
gery. The authors concluded that the incidence of strabismus in patients
with prenatal methadone exposure was higher than in the general popula-
tion (10% vs 3%-4%). Intermittent exotropia was the most common type of strabismus and presented earlier than in the general population, with no association with other systemic disease. Prenatal exposure to methadone was likely confounded by exposure to other substances, environmental factors, and genetics. The study essentially validated previous data. Poor compliance with follow-up reduced the power of the study and limited its sample size.

**Melanopsin System Dysfunction in Smith-Magenis Syndrome Patients.**

Smith-Magenis syndrome (SMS) causes sleep disturbance that is related to an abnormal melatonin profile. It is not clear how the genomic disorder leads to a disturbed synchronization of the sleep/wake rhythm in SMS patients. The authors recorded pupillary light responses (PLR) in SMS patients to evaluate the integrity of the intrinsically photosensitive retinal ganglion cell (ipRGC)/melanopsin system, the transducers of the light-inhibitory effect on pineal melatonin synthesis. Subjects were SMS patients (n = 5), with molecular diagnosis and melatonin levels measured for 24 hours and healthy controls (n = 4). Visual stimuli were 1-second red light flashes (640 nm; insignificant direct ipRGC activation), followed by a 470-nm blue light, near the melanopsin peak absorption region (direct ipRGC activation). Blue flashes produce a sustained pupillary constriction (ipRGC driven) followed by baseline return, while red flashes produce faster recovery.

Pupillary light responses to 640-nm red flash were normal in SMS patients. In response to 470-nm blue flash, SMS patients had altered sustained responses shown by faster recovery to baseline. SMS patients showed impairment in the expected melatonin production suppression during the day, confirming previous reports.

SMS patients show dysfunction in the sustained component of the PLR to blue light. The authors conclude that this could explain their well-known abnormal melatonin profile and elevated circulating melatonin levels during the day. Synchronization of daily melatonin profile and its photoinhibition are dependent on the activation of melanopsin. This retinal dysfunction might be related to a deficit in melanopsin-based photoreception, but a deficit in rod function is also possible.

**Presentation and Diagnosis of Tuberous Sclerosis Complex in Infants**

Tuberous sclerosis complex (TSC) is a neurocutaneous genetic disorder with an incidence of approximately 1 in 6000 live births. In the 1990’s, the biochemical
pathway at the root of the disorder was mapped leading to effective treatments aimed at the underlying disease mechanism. With these treatments available, it is optimal to diagnose patients with TSC as early as possible. The study was a longitudinal observational study conducted in five geographically distributed sites across the United States with 130 participants. The most common initial presenting feature was cardiac rhabdomyomas (59%) and hypomelanotic macules (39%), with 85% of patients presented with either or both. 35% of infants presented prenatally, 41% at birth or the first month of life, and 74% met criteria for diagnosis at or within 30 days of presentation. 73% of patients developed epilepsy within the first year of life. Of the patients with epilepsy, 57% have infantile spasms, 55% have focal seizures, and 12% had another type of seizure. Earlier seizure onset and higher seizure frequency were associated with worse developmental outcomes. Analysis of the patients demonstrated 3 distinctive subtypes of TSC. The largest group had multisystem organ involvement and the 2nd largest group had a neuro-predominant presentation and no TSC1 variants. The least common was a subgroup with milder presentation and fewer organ systems affected. Studies are underway to treat infants with TSC with the intention of preventing epilepsy. Early detection and support for families may improve the treatment and outcomes for the patients.

Adapting the orthoptic investigation for children with autism spectrum disorders: how can research from other healthcare areas be applied to orthoptic practice? A literature review
Alia Harrison BSc, Ann O’Connor PhD Br Ir Orthopt J 2016; 13: 9-13

Autism spectrum disorder (ASD) is a developmental disorder affecting social communication, interaction, and imagination. ASD affects 1% of the United Kingdom population, and affects males 4 times more often than females. ASD has a high association strabismus, saccadic abnormalities, and smooth pursuit initiation and maintenance. Strategies need to be developed within the orthoptic clinic to evaluate ASD patients, which can be extrapolated from research in other medical fields when assessing ASD patients. To assist the orthoptist, patient, and family with a medical examination many tools can be implemented. Desensitization can help alleviate anxiety, pre-teaching, utilizing caregivers as therapists to reduce fear, and altering the investigative procedure such as using Teller acuity cards to assess vision as opposed to optotypes.

Hematopoietic Stem-Cell Gene Therapy for Cerebral Adrenoleukodystrophy.

X-linked adrenoleukodystrophy is a demyelinating disease characterized by adrenal dysfunction, relentlessly progressive visual loss due to demyelination of the optic pathways, and neurodegeneration. It is often diag-
nosed in boys ages 3-15 years presenting with learning and behavioral problems or with poor vision. Disease progression can be halted only with allogeneic hematopoietic stem-cell transplantation. However, stem-cell transplantation carries a mortality of approximately 20%, and there is concern that the delay involved in finding a good match costs the recipient further irreversible brain damage. This study enrolled boys with cerebral adrenoleukodystrophy to investigate whether gene therapy might be an alternative to allogeneic hematopoietic stem-cell transplantation. This was a single-group, open-label, phase 2−3 safety and efficacy study. The investigational therapy involved infusion of autologous CD34+ cells transduced with a lentiviral vector. This vector contains cDNA for the ABCD1 gene, the gene that is mutated in X-linked adrenoleukodystrophy. The primary end point was being alive and having no major functional disability at 24 months after infusion. Cortical blindness was one of the prespecified major functional disabilities. A total of 17 boys received the gene therapy. The median follow-up was 29.4 months (range, 21.6 to 42.0). No treatment-related death or graft-versus-host disease had been reported; 15 of the 17 patients (88%) were alive and free of major functional disability, with minimal clinical symptoms.

Early results of this study suggest that gene therapy may be a safe and effective alternative to allogeneic stem-cell transplantation in boys with early-stage cerebral adrenoleukodystrophy. Additional follow-up is needed to assess the duration of response and long-term safety. This study is of relevance to pediatric ophthalmologist who may be among the first to suspect this diagnosis (a boy presenting with learning difficulties and poor vision), and early diagnosis is key. Also, gene therapy for X-linked adrenoleukodystrophy and for retinitis pigmentosa caused by RPE65 mutations are among the few FDA approved gene therapies.

Incidental Findings on Brain Imaging in the General Pediatric Population.

This study of 3966 children (mean age, 10.1 years; range, 8.6 to 11.9) reports the prevalence of incidental findings on brain magnetic resonance imaging (MRI) in a large, single-center study involving a general pediatric population. At least one incidental finding was present in 25.6% of the children (95% confidence interval [CI], 24.2 to 27.0), although the prevalence of findings requiring clinical follow-up was only 0.43% (95% CI, 0.26 to 0.70). The most common findings were cysts of the pineal gland (in 665 children; 16.8%; 95% CI, 15.6 to 18.0), arachnoid cysts (in 86; 2.17%; 95% CI, 1.75 to 2.68), and developmental venous anomalies (in 63; 1.59%; 95% CI, 0.12 to 2.04). Common normal variants were mega cisterna magna (in 104 children; 2.62%, 95% CI, 2.16-3.18) and cavum
Among less frequent findings were Chiari I malformations (in 25 children; 0.63%; 95% CI, 0.42 to 0.94) and subependymal heterotopia (in 19; 0.48%; 95% CI, 0.30 to 0.76). This study will aid in counseling the families of patients who are found to have incidental findings on brain MRI.


Hutchinson-Gilford Progeria syndrome (HGPS or Progeria) (MIM176670) is a rare, fatal genetic disorder characterized by premature aging. Children can appear normal at birth, but by the first year of life they start displaying features of the disease. Clinical features include short stature, delayed growth, micrognathia, craniofacial disproportion, alopecia, prominent eyes and scalp veins, and lack of subcutaneous fat, giving the skin an aged appearance. The purpose of this study is to describe in detail the ophthalmologic manifestations of a diverse (in age and ethnic origin) Progeria population. This was a retrospective case series of patients with Progeria who were seen between 2007 and 2016. Fourteen patients (28 eyes) with HGPS were included for statistical analysis from a total of 84 patients who were enrolled in clinical trials for Progeria at Boston Children's Hospital. Clinical treatment trial patients who were not seen at the Department of Ophthalmology, but for whom we had detailed clinical ophthalmologic records, were also included. This essentially represents an estimated 20% of the world's known patients with Progeria. Ophthalmic manifestations noted were hyperopia and signs of ocular surface disease owing to nocturnal lagophthalmos and exposure keratopathy. Additional ophthalmic manifestations included reduced brow hair, madarosis, and reduced accommodation. Most patients had relatively good acuity; however, advanced ophthalmic disease was associated with reduced acuity In summary, patients with Progeria can experience significant ocular morbidity and vision loss owing to ocular surface disease. Exposure keratopathy and nocturnal lagophthalmos are significant contributing factors to the ocular surface disease, with corneal limbal stem cell deficiency and induction of inflammatory mediators possibly contributing factors. Children with Progeria should have an ophthalmic evaluation at the time of diagnosis and at least yearly after that. Aggressive ocular surface lubrication is recommended, including the use of tape tarsorrhaphy at night.


Leber hereditary optic neuropathy (LHON) (OMIM 535000) is a mitochondrial disorder that classically presents with acute or subacute bilateral loss of central vision in young adult men. Childhood-onset disease is relatively rare and less than 10% of patients were 12 years old or younger at the time of diagnosis in previously published case series. Although there are limited data on this im-
important patient subgroup, the phenotype seems distinct from classical adult-onset LHON with atypical patterns of vision loss and a better visual prognosis as reported previously. This study describes the clinical and molecular genetic features observed in this specific LHON subgroup. The retrospective study consisted of a UK pediatric LHON cohort of 27 patients and 69 additional cases identified from a systematic review of the literature. Patients were included if visual loss occurred at the age of 12 years or younger with a confirmed pathogenic mitochondrial DNA mutation: m.3460G>A, m.11778G>A or m.14484T>C. In the UK pediatric LHON cohort, three patterns of visual loss and progression were observed: (1) classical acute (17/27, 63%); (2) slowly progressive (4/27, 15%); and (3) insidious or subclinical (6/27, 22%). Diagnostic delays of 3-15 years occurred in children with an insidious mode of onset. Spontaneous visual recovery was more common in patients carrying the m.3460G>A and m.14484T>C mutations compared with the m.11778G>A mutation. Based on a meta-analysis of 67 patients with available visual acuity data, 26 (39%) patients achieved a final best-corrected visual acuity (BCVA) ≥0.5 Snellen decimal in at least one eye, whereas 13 (19%) patients had a final BCVA <0.05 in their better seeing eye. Although childhood-onset LHON carries a relatively better visual prognosis, approximately 1 in 5 patients will remain within the visual acuity criteria for legal blindness in the UK. In conclusion, childhood-onset LHON represents a distinct phenotypical subgroup characterized by a more varied clinical evolution and a more favorable visual prognosis compared with classical adult LHON. Importantly, children do not always develop acute or subacute visual symptoms and a high index of suspicion is required in children presenting with unexplained subnormal vision and optic disc pallor to avoid potentially long diagnostic delays.

Pupillary Manifestations of Marfan syndrome: From the Marfan Eye Consortium of Chicago.

Marfan syndrome (MFS) is a genetic disorder that affects multiple organ systems, including the eye. The most common ocular manifestations include ectopia lentis and retinal detachment. The current literature qualitatively cites that MFS patients have miotic or "poorly dilating" pupils. This study was the first to quantitatively assess pupillary function in MFS patients. 57 eyes from 29 MFS patients, 36 eyes from 18 pediatric age- and gender-matched controls, and 44 eyes from 22 adult age-matched controls were measured in a clinic-based cross sectional study. Pupillometry data were measured in scotopic conditions using the handheld NeurOptics PLR-200™ Pupillometer (NeurOptics, Irvine, CA, USA). Data obtained with the pupillometer were maximum and minimum diameter, constriction percentage, latency, average and maximum constriction velocities, average dilation velocity, and 75% recovery time (T75). Pediatric patients with MFS had significantly slower average constriction velocity measurements (β = 0.65, p = 0.0003), maximum constriction velocity measurements (β = 0.51, p = 0.0150) and average dilation velocity measurements (β = -0.19, p = 0.0029) compared to control patients. In the adult cohort, results indicated significantly slower average
dilation velocity measurements ($\beta = -0.13, p = 0.0077$) compared to controls. Our data highlight pupillary parameters within a population of MFS patients under scotopic conditions. Constriction and dilation velocities were slower in the pediatric MFS patients compared to age- and gender-matched controls, and dilation velocities were slower in the adult MFS patients compared to age-matched controls. These findings, for the first time, quantitatively demonstrated differences in pupillary function in patients with MFS. The authors hypothesize that myopathy in pupil constrictors and dilators may explain the statistically significant decreases in constriction and dilation velocity seen in this population.

**Ocular Manifestations of Familial Transthyretin Amyloidosis.**

Among patients with familial amyloidosis, mutation in the transthyretin (TTR) protein is the most common type. TTR is synthesized in the choroid plexuses of the brain as well as the retinal pigment epithelial cells. Patients with TTR amyloidosis have been noted to have ocular, especially vitreous, involvement. Thirty-two of 130 (25%) reported TTR mutations have been noted to have ophthalmic involvement. Few studies have looked at ocular manifestations in large cohorts of familial amyloidosis. In this report, an analysis of the types and frequency of ocular manifestations in TTR amyloidosis is presented. Two hundred and sixty-three patients who presented to Mayo Clinic with TTR amyloidosis between January 1, 1970, and November 1, 2014, were studied. Fifty-four patients had ocular examinations at a mean of 4.25 ± 3.93 months after systemic symptoms. Of 108 examined eyes in 54 patients with TTR amyloidosis, there were 26 eyes (24%) in 13 patients with ocular involvement. Patients with ocular involvement were more likely to be women than those without ocular involvement (46% vs 15%, respectively) and have significantly worse visual acuity (VA) at presentation (logMAR 0.24 [Snellen equivalent 20/30] vs logMAR 0.00 [Snellen equivalent 20/20]). The ophthalmic findings included vitreous amyloid (26/26, 100%), neurotrophic keratitis (2/26, 8%), glaucoma (5/26, 19%), and tortuous retinal vessels (4/26, 15%). The glaucoma was classified as open-angle (2/26), exfoliative (2/26), and neovascular following central retinal vein occlusion from amyloidosis (1/26). Ten patients underwent vitrectomy for visually significant vitreous amyloidosis, which significantly improved VA from a baseline of logMAR 0.70 (Snellen equivalent 20/100) to logMAR 0.05 (Snellen equivalent w 20/20). Three TTR mutations, Glu89Lys, Gly47Arg, and homozygous Gly6Ser, not previously described, were associated with vitreous amyloid. In conclusion, this large cohort of patients with TTR amyloidosis, female sex and decreased VA were associated with ocular amyloid. This study is unique because it described the incidence of ocular involvement among 22 different TTR mutations and is the largest of such report in the United States to date. Other studies have been conducted on the incidence of ocular involvement in TTR amyloidosis, but have focused on large populations with Val30Met mutations. In addition, three mutations that have not been previously reported to have vitreous involvement were described: Glu89Lys, Gly47Arg, and homozygous Gly6Ser.
Temporal Retinal Thinning and the Diagnosis of Alport Syndrome and Thin Basement Membrane Nephropathy.

Alport syndrome is an inherited disease characterized by renal failure, hearing loss, and ocular abnormalities, including fleck retinopathy and temporal retinal thinning. Inheritance is X-linked (85%) or autosomal recessive (15%) and caused by pathogenic variants in the COL4A5, or COL4A3 and COL4A4 genes, respectively. The authors investigated whether temporal retinal thinning was useful in the diagnosis of Alport syndrome, and whether retinal thinning distinguished Alport syndrome from other renal diseases. Alport syndrome was diagnosed on renal biopsy and genetic testing. Subjects underwent optical coherence tomography. Retinal thinning was determined from horizontal macular OCT scans through the foveal center using the formula: Temporal thickness index (TTI) = (nasal – temporal thickness) ÷ nasal thickness x 100%, and compared with the normal range for each age group. The mean temporal retinal thickness index was 12.4 ± 5.2% in men (n = 19) and 7.4 ± 1.4% in women (n = 28) with X-linked Alport syndrome; 13.1 ± 4.5% (n = 4) in recessive disease; 6.4 ± 2.2% (n = 5) in Thin basement membrane nephropathy; and 6.3 ± 3.3% (n = 14) in other renal diseases. Thinning was worse in men than women with X-linked disease (p < 0.01), and worse in men who developed early onset renal failure (R² = 0.75). Temporal retinal thinning was 84% sensitive for men with X-linked Alport syndrome and 67% specific (AUC = 0.83) compared with other renal diseases. In summary, retinal temporal thinning is diagnostic for X-linked Alport syndrome in men and distinguishes them this condition from Thin basement membrane nephropathy, but only in men (p = 0.002). Temporal retinal thinning may also identify men and women with the rarer autosomal recessive disease.

Are there any changes in posterior ocular structure parameters in pediatric migraine patients?

The purpose of this observational cross-sectional study was to evaluate the thickness of the peripapillary retinal nerve fiber layer (RNFL), total macula, macular ganglion cell layer (GCL), inner plexiform layer (IPL), and choroid in pediatric migraine patients and compare the values with healthy controls. The study included 40 consecutive patients in the migraine group (median age 14 years, range 6-17 years, 75% females) and 40 age-matched healthy controls (median age 13 years, range 7-18 years, 75% females). The thickness of the peripapillary RNFL, total macula, GCL, and IPL were analyzed with spectral-domain optic coherence tomography, while choroidal thickness was analyzed with the enhanced depth imaging protocol. All measurements of the migraine patients were taken in the attack-free period. Only the right eye per subject was included in the study.
There was no significant difference between the 2 groups in age or gender or refraction error (p>0.05). The peripapillary RNFL thickness was not significantly different between the 2 groups in any quadrant. The total macula, GCL, and IPL thickness were also not significantly different in the 9 separate macular areas defined on the basis of the Early Treatment Diabetic Retinopathy Study (p>0.05). The choroidal thickness at 5 different measurement points was not statistically significantly different between migraine patients during the attack-free period and the healthy subjects (p>0.05). The authors conclude that childhood migraine does not cause changes in posterior ocular structure parameters.

Objective Evaluation of Corneal and Lens Clarity in Children With Type 1 Diabetes Mellitus.

Previous studies of the effects of diabetes on lens and corneal clarity have focused on older patients whose studies can be confounded by age related changes. The purpose of this study was to evaluate the effects of abnormal glucose metabolism and the duration of diabetes on the corneal and lens clarity in pediatric patients by comparing the corneal and lens clarity in patients with well controlled type 1 Diabetes Mellitus (DM) to their healthy counterparts. The authors performed a cross-sectional prospective study of 56 patients with DM and 51 controls. They recorded the duration of the DM and levels of glycosylated hemoglobin (HbA1c) and used the Pentacam imaging system to determine the density of the cornea. The lens thickness and clarity were determined by the same Pentacam HR device. The authors found that the corneal densitometry values were similar in both the patients with and without DM, but the lens densitometry values and lens thickness measurements were statistically significantly different in the two groups. Additionally the duration of DM was found to be a significant factor but the HbA1c levels did not have any correlation. The authors speculated that the thicker lenses in patients with DM1 are due to the elevated polyol pathway activity in the lens. The lack of corneal changes that have been seen in previous studies of adults with diabetes was thought to possibly be due to the shorter duration of disease in this pediatric patient group. The authors point out that this study was limited by a small number of patients and that they excluded patients with diabetic retinopathy. Additionally the exclusion of patients with lens opacities could have skewed their data. The authors concluded that the patients with type 1 DM had thicker lenses and decreased lens clarity even when the DM was well controlled.

Standardizing the Evaluation of Nonaccidental Trauma in a Large Pediatric Emergency Department
Lauren C. Riney, Theresa M Frey, Emily T. Fain, Elena M. Duma, Berkeley L. Bennett, Eileen Murtagh Kurowski Pediatrics. January 2018; 141(1)
In Pediatric Emergency Departments, there is variable evaluation of non-accidental trauma (NAT) due to inconsistent physician practices, misconceptions, and bias. Because a missed diagnosis can lead to further abuse and even death, early detection and intervention is crucial. Implementation of guidelines for NAT evaluation can improve differences in care that occur because of the race and ethnicity of the patient and family. At the Cincinnati Children’s Hospital ED, the authors sought to reduce this variability through a quality improvement project with a Specific, Measurable, Achievable, Realistic, and Timely aim to improve the adherence of the guidelines from 47% to 80%. The authors educated the care providers and created an order set with educational prompts for the ordering providers. The adherence to the age-specific guidelines were monitored for the patients in this ED. A total of 640 encounters were evaluated with concern for NAT and the monitored whether or not the providers follow the guidelines. The adherence improved from 47% to 69%. Key factors for the improvement were education and electronic support. The authors demonstrate how a monitored quality improvement project can lead to greater evidence-based medicine and ideal patient care.

**Physical Abuse of Children**

Approximately 700,000 cases of child abuse and neglect are reported annually in the United States. Neglect is by far the most common, with over 500,000 cases annually. The review article on physical manifestations of child abuse summarizes abusive head trauma, fractures, abdominal trauma, and cutaneous and oral cavity findings.

Key clinical points are:
- Physically abused children, particularly infants, may present with nonspecific symptoms and signs, such as vomiting or apnea; the possibility of abusive head trauma requires consideration in such cases.
- Physical findings, such as bruising of the face, neck, or torso, or intraoral lesions, such as torn frenula, in nonambulatory infants should arouse suspicion of inflicted trauma.
- The evaluation of infants and young children for suspected inflicted trauma should include a complete physical examination of the child, with particular attention to the skin, oral cavity, and abdomen; imaging of the brain; a funduscopic examination; a skeletal survey; and measurement of hepatic and pancreatic enzymes.
- Physicians are mandated to report to child protective services cases in which they have a reasonable suspicion of child abuse.

**Imaging Strategies for Suspected Acute Cranial Shunt Failure: A Cost-Effectiveness Analysis**
Ventricular shunts account for approximately $1 billion dollar per year in health care costs for hydrocephalus. Given that the frequency of shunt failure is high (one study demonstrated 33% over the first year) and the symptoms of shunt failure are non-specific, clinicians frequently rely on neuro-imaging for diagnosis. The current modalities that are utilized include CT scans, fast sequence magnetic resonance imaging (fsMRI), and optic nerve sheath diameter (ONSD) measured by point of care ultrasound (POCUS). Two different studies have suggested variable sensitivity of ONSD for detecting shunt failure with one study demonstrating high sensitivity and another showing a much lower sensitivity (61%). The researchers want to determine an optimal cost-effective imaging approach while reducing the malignancy risks of CT scans. They examined four strategies for evaluating for shunt failure: 1) CT scan, 2) fsMRI, 3) screening POCUS combined with CT scan, and 4) screening POCUS combined with MRI. The researchers performed a cost-effectiveness analysis using a computer model that incorporated data from a literature review rather than primary acquired patient data. The four imaging strategies were compared in terms of QALYs, total lifetime costs, incremental cost-effectiveness ratios, and net monetary benefit. The modeling demonstrated that a screening POCUS followed by a fsMRI was the most cost effective model for both direct costs and quality of life measures.

There are many limitations to the study including: 1) variable radiation risk from CT scans, 2) the model’s analysis is limited only to factors that directly contribute to patient outcomes rather than societal outcomes, and 3) the literature used to generate probabilities has heterogeneous statistics. The study shows that CT for VP shunt malfunction may cause more long-term harm than benefit because of the excess lifetime risk of radiation induced malignancy. If the probability of shunt malfunction is low, then the model suggests that a screening bedside ONSD followed by fsMRI to be most cost effective.

Upper Respiratory Infections and Airway Adverse Events
Michael D. Mallory, Curtis Travers, Courtney McCracken, James Hertzog, Joseph P. Cravero Pediatrics. July 2017; 140(1)

This study aims to determine the relationship between upper respiratory infections (URIs) and airway adverse events during pediatric procedural sedation. Given the high frequency of URIs in children as well as procedural sedations, it is important to understand the effect of URIs on sedation safety. The researchers prospectively collected data from 105,728 sedations through a large Pediatric Sedation Research Consortium database. The participating practitioners record data about the sedation event as well as the characteristics of any URIs. Adverse airway events (AAEs) were defined as airway obstruction, apnea oxygen desaturation, cough, secretions requiring suction, laryngospasm, stridor, wheezing, emergent airway intervention, and snoring. Of the 105,728 sedations, the researchers utilized information from 83,491 sedations. The two most common
types of procedures that were performed during sedation were radiology procedures followed by hematology/oncology procedures. The two most common types of medications used were propofol and ketamine. There was a significant relationship between URIs and AAEs with the percentage of patients who had AAEs increasing from 6.3% with no URIs to 9.1% with recent but not current URIs to 22.2% with current URIs with thick/green secretions. Despite the statistically significant relationship between URIs and AAEs, the rates of major AAEs such as laryngospasm, aspiration, and emergent call for anesthesia were <1% regardless of URI status. This research provides information that helps predict the risk of AAEs in children with URIs but supports the general safety of procedural sedation in children with URIs.

24. UVEITIS/ SYSTEMIC

Safety and efficacy of chloral hydrate for procedural sedation in paediatric ophthalmology: a systematic review and meta-analysis.

Chloral hydrate (CH) has been used for procedural sedation in children, although due to concerns about severe adverse events it is not used in some countries. Some recent studies have shown that pediatric ophthalmologists have used CH in an outpatient setting without severe side effects, and propose that it is a cost-effective drug. Others continue to avoid the drug. This study aimed to review the literature on CH’s safety and efficacy. The authors reviewed 104 articles, of which 13 were randomized controlled trials included in the meta-analysis. They found that CH was shown to be a successful sedative without altering IOP, but there were significant limitations. Common adverse events included transient nausea, vomiting, prolonged sedation, and paradoxical reaction. However there were more serious reactions including two deaths that were likely related to comorbidity. Overall the analysis showed CH to be more efficient to midazolam and similar to other drugs without difference in safety, but caution that it should be used in a hospital setting.

Uveitis and Juvenile Psoriatic Arthritis or Psoriasis

Pediatric psoriatic arthritis is known to be associated with uveitis however there are limited papers that characterize this association. This paper is an observational case series of 6 patients from two university-based referral clinics (one in England and the other in the US) that describes the phenotype of the uveitis that
accompanies juvenile psoriatic arthritis or psoriasis. The authors found that five of the 6 children in this series had onset of disease at or before age 6 (P < .0008), suggesting that there may be 2 distinct subsets of the disease (one with onset under age 6 and one with onset closer to age 11). All children in this series had an inadequate response to topical corticosteroids. Most of the children were treated with systemic corticosteroids for many months, yet all of them went on to require methotrexate. Therapy with systemic methotrexate did not suffice, as all the patients also required some form of biologic therapy. Five of 6 had surgeries such as vitrectomy, cataract extraction, or a procedure for glaucoma control. The authors conclude the uveitis that accompanies juvenile psoriatic arthritis might be a distinct disease/entity that is particularly severe when its onset affects children aged 6 years or younger.

**Biometry Characteristics in Adults and Children with Marfan Syndrome: From the Marfan Eye Consortium of Chicago.**


Previous biometry information in patients with Marfan syndrome (MFS) has been described in a Scandinavian population, but no studies on complete refractive and biometry data on contemporary American has been reported nor has a study on patients with MFS who meet diagnosis criteria by the newer Ghent 2 criteria. The authors performed a cross-sectional study on 117 subjects. Patients older than 16 were defined as adults for this study. The authors looked at refractive error, axial lengths (AL), keratometry, anterior chamber depth, lens thickness, and central corneal thickness with the goal of better describing the eye characteristics in MFS. 74 of the 117 subjects definitely met criteria for the diagnosis of MFS and were included in the study. Of those, 35 were adults, 32 were children between 5-15 years old, and 7 children were less than or equal to 5 years. The adult patients had longer eyes and thicker lenses than the children but both groups had flat corneas. The patients who had ectopia lentis also had a flatter cornea and higher amount of corneal astigmatism. The limitations of this study include the lack of control groups with which to compare, multiple examiners at different locations, and some missing data on the younger patients due to cooperation. The authors note that although corneal curvatures and axial lengths are not part of the diagnostic criteria for MFS that this data might be helpful in young children who are suspicious of having MFS.

**Risk Factors for the Development of Cataract in Children with Uveitis.**


Cataract formation is the most common complication of pediatric uveitis and occurs in approximately 35% of patients with juvenile idiopathic arthritis (JIA)-associated uveitis. Cataracts can form in these patients due to inflammation or can be due to treatment of the uveitis (steroids). While the risk factors for the devel-
Development of cataracts in JIA-associated uveitis have been described, there is no previous study looking at risk factors in children with uveitis of any etiology. This study is a cohort study of 247 eyes of 140 children with uveitis. The authors evaluated the demographic, clinical, and treatment data of these patients. The main outcome of the study was cataract formation. The authors found a prevalence of cataract of 44.2% in their cohort. The highest prevalence was found in the patients with panuveitis (77.1%), chronic anterior uveitis (48.3%), and intermediate uveitis (48.0%). The authors estimate that 69% of patients develop uveitis-related cataract with time. The main risk factors included the number of uveitis flares per years, cystoid macular edema, posterior synechiae at presentation, and the use of injected steroids. Topical and systemic steroids were not found to be significant risk factors. The rate of cataract formation in this study was higher than those looking just at patients with JIA-associated uveitis and the authors hypothesize that this is due to the screening programs for children with JIA and earlier diagnosis. The data also suggest that inflammation is a stronger risk factor than steroid use and thus inflammation may contribute more to the cataract formation than the treatment of the uveitis. While the retrospective design is a limitation, this is a large cohort of patients with a long duration of follow up. The authors conclude that disease control should continue to be the primary goal when treating uveitis.

Ophthalmic Screening Patterns Among Youths With Diabetes Enrolled in a Large US Managed Care Network
Sophia Y. Wang, Chris A. Andrews, Thomas W. Gardner, Michael Wood et al.

This is a longitudinal, retrospective study to evaluate youths < 21 years old with a new diagnosis of diabetes from 2001-2014. This study was performed at a large managed care network and evaluated demographics of the patient population and the time from initial diabetes diagnosis (type one and type two) to the time of the initial eye examination. The majority of the youths (64.9%) had an initial eye exam by 6 years after the initial diagnosis of type 1 diabetes (5453 youths) and type 2 diabetes (7233 youths). Of note, the median age was 11 years and 19 years for type 1 and type 2, respectively. In addition, the authors looked at race, ethnicity, and household net worth as statistically significant variables regarding adherence to clinical practice guidelines to monitor for diabetic retinopathy. In summary, looking at ‘big data’ over 13-year-period at one managed care network may not be the most effective way to study barriers to best clinical eye practices for racial minorities and youth from less affluent families.

Adalimumab plus Methotrexate for Uveitis in Juvenile Idiopathic Arthritis.
Adalimumab, a fully human anti–tumor necrosis factor α monoclonal antibody, is effective in the treatment of juvenile idiopathic arthritis (JIA). This study tested the efficacy of adalimumab in the treatment of JIA-associated uveitis. The study was a multicenter, double-blind, randomized, placebo-controlled trial of adalimumab in children and adolescents 2 years of age or older who had active JIA-associated uveitis. Patients who were taking a stable dose of methotrexate were randomly assigned in a 2:1 ratio to receive either adalimumab (at a dose of 20 mg or 40 mg, according to body weight) or placebo, administered subcutaneously every 2 weeks. Patients continued the trial regimen until treatment failure or until 18 months had elapsed. They were followed for up to 2 years after randomization. The primary end point was the time to treatment failure, defined according to a multicomponent intraocular inflammation score.

The trial was stopped early owing to a strong beneficial effect in the adalimumab group. There were 16 treatment failures in 60 patients (27%) in the adalimumab group versus 18 treatment failures in 30 patients (60%) in the placebo group (hazard ratio, 0.25; 95% confidence interval [CI], 0.12 to 0.49; P<0.0001). Patients who received adalimumab had a much higher incidence of adverse events and serious adverse events than those who received placebo. The most common adverse events in the adalimumab group were minor infections, respiratory disorders, and gastrointestinal disorders. In conclusion, adalimumab therapy controlled inflammation and was associated with a lower rate of treatment failure than placebo among children and adolescents with active JIA-associated uveitis who were taking a stable dose of methotrexate.

This study is important to pediatric ophthalmologists in offering high quality evidence that adalimumab is effective in treating JIA-associated uveitis that is refractory to methotrexate, as use of adalimumab in this setting has already become “standard clinical practice.” We do not have high quality evidence regarding how adalimumab compares to other TNF alpha inhibitors like infliximab, however.

**Editorial: Adalimumab in the Treatment of Uveitis in Juvenile Idiopathic Arthritis**


The editorial’s author emphasizes the strengths of the “Adalimumab plus Methotrexate for Uveitis in Juvenile Idiopathic Arthritis” trial. Many other uveitis trials were done in adults and included multiple types of uveitis. This trial focused on children and enrolled only uveitis due to JIA. The author praised the study design in using a standardized uveitis grading scale. The editorial author cautions, as do the original study authors, that the duration of the adalimumab trial was not long enough to detect serious adverse events like cancer and demyelinating disease. Because adalimumab was given in combination with methotrexate, no conclusions may be made about the effectiveness of adalimumab alone in the
Clinical features of uveitis in children and adolescents at a tertiary referral centre in Tokyo
Hiroshi Keino, Takayo Watanabe, Wakako Taki, Makiko Nakayama, et al.

Childhood uveitis can be a difficult disease with vision-threatening complications. Causes of uveitis in children vary, and the epidemiology of the disease also varies with location. There are few reports on the manifestations of childhood uveitis in Asia, and none in Japan per the authors. Therefore they performed a retrospective review of consecutive children with uveitis that presented to a single eye center in Tokyo. Patients with less than 3 months of follow-up were excluded. 64 patients were identified, with a mean age of 12.9 years and mean follow-up of 46 months. 70.3% were girls, 81.2% had bilateral disease, and 56.3% were classified as anterior uveitis. There were no reports of intermediate uveitis. The most common diagnoses was “unclassified uveitis” in 57.8%, followed by juvenile chronic iridocyclitis without JIA and neuroretinitis. Systemic association was found in 10.9% of cases: most common was 2 cases of Behcet’s and 2 cases of tubulointerstitial nephritis and uveitis. Again there were no cases of JIA. 18.7% (12 patients) required systemic therapy, most commonly methotrexate. Ocular complications were found in 71.9%, including optic disc edema (40.6%), followed by vitreous opacities, posterior synechiae, elevated IOP, cataract, and chorioretinal atrophy. The authors conclude that most children in this study had bilateral disease and no systemic association, and most had a good visual outcome. Part of the reason why no cases of intermediate uveitis were found could be that HLA-DR15 and MS has a lower prevalence in Japan. JIA also has a low prevalence in Japan, with cases of oligoarthritis less common compared to North America and Europe; together these could explain the lack of JIA associated uveitis seen in this study.

Impact of healthcare strategies on patterns of pediatric sight impairment in a developed population.

In 1999, WHO published its initiative for eliminating avoidable blindness, VISION 2020—The Right to Sight. Childhood blindness is one of the priority eye diseases highlighted in this document. An estimated worldwide prevalence of 1.4 million
blind children confers significant social, economic, and emotional impact on society. Preventable or treatable causes that are felt to account for 40% of childhood blindness. The main avoidable causes of visual impairment worldwide are corneal scarring, cataract, glaucoma, retinopathy of prematurity (ROP), and refractive errors. The United Nations Children’s Fund (UNICEF) estimates significant reduction in Vitamin A deficiency-related visual impairment due to the implementation of the Vitamin A Global Initiative. The Measles initiative has reduced measles-related deaths by 28% from 1999 to 2004 and an associated reduction in the incidence of corneal scarring is expected. The aim of the study was to analyze pediatric sight-impairment trends in Northern Ireland (NI) over a 28-year period to give us a better understanding of the impact which changes in health-care provision may have had on childhood sight loss and to enable us to assess our progress towards achieving the WHO aims for VISION 2020. The Department of Health, Certificate of Visual Impairment defines severe sight impairment as Snellen visual acuity 03/60, or visual acuity between 3/60 and 6/60 with a very contracted field of vision, or visual acuity 46/60 but contracted field of vision especially inferiorly. In the pediatric population, equivalent visual acuity measurements using other optotypes were valid, or if visual acuity could not be measured formally, clinical features of visual defects for example not fixing or following to light were included but classified as SI. Sight impairment is defined as Snellen visual acuity between 3/60 and 6/60 with full field, visual acuity up to 6/24 with moderate field contraction, opacities in the media or aphakia, or visual acuity of 6/18 or better with marked field contraction. The causes were classified in two ways: by individual disorders, grouped by the anatomical site affected, and by timing of specific causal factors leading to vision loss and further. Further classified the individual disorders causing sight loss into preventable or non-preventable and treatable or non-treatable based on current understanding with a view to identifying the proportion of avoidable vision loss. For every 4-year period between 1984 and 2011, we identified the number of registrations for each condition and estimated the annual incident rates per million population aged <16 years. Five hundred and ninety-eight children were registered as having impaired vision over the 28-year period. Two hundred and thirty-four (39%) were registered as SI and 364 (61%) were registered as SSI. In all, 53% were males and 26% had associated systemic conditions. The mean age at registration was 7.4 years (SD ± 4.6 years, Range 2 months to 16 years). The timing of the insult was prenatal in 69% (of which 77% were hereditary/congenital), perinatal/neonatal in 22%, and childhood in 9%. Three hundred and fifty-seven cases (60%) were neither preventable nor treatable. Of the remaining 238 cases, 132 (22%) were considered either preventable or treatable and 104 (18%) were considered to be possibly preventable or treatable. The majority (37%) of registrations for impaired vision were due to retinal disorders. Only 31% of these 218 patients with retinal pathology had potentially preventable/treatable causes, such as ROP or autosomal-dominant retinal dystrophy. The most common cause of vision loss was optic atrophy (16%); of these 39% were primary optic atrophy and 61% had secondary optic atrophy. The subsequent five main causes in order after optic atrophy were, albinism (12%), cerebral visual impairment (CVI; 11%), congenital cataract (8%),
ROP (8%), and congenital motor nystagmus (CMN; 7%). For optic atrophy and albinism there was no significant change. Visual loss due to either optic atrophy or albinism can neither be prevented nor treated. CVI shows a general upward trend. The incident rate significantly increased from 1.77 per million (CI 0.36–5.16) in 1984–1987 to 12.51 per million (CI 7.53–19.54) in 2008–2011. CMN also shows an initial significant upward trend with an incident rate of 0.59 per million (CI 0.01–3.28) in 1984–1987 increasing to 8.87 per million (CI 4.85–14.88) in 2000–2003 (P for difference = 0.0003); at which point, it dramatically reduces to 0.66 per million (CI 0.02–3.67) in 2008–2011 (P for difference = 0.0006). The incident rate for congenital cataract decreased from 5.89 per million (CI 2.82–10.83) in 1984–1987 to 2.63 per million (CI 0.72–6.74) in 2008–2011. The incident rate for ROP reduced from 5.30 per million (CI 2.42–10.06) in 1984–1987 to 0.80 per million (CI 0.02–4.45) in 1988–1991 (P for difference = 0.03) but peaked again during 2000–2003 with an incident rate of 8.87 per million (CI 4.85–14.88). Thereafter, there was a statistically significant reduction in incident rate to 1.98 per million (CI 0.41–5.77) in 2008–2011 (P for difference = 0.008). Two important preventable causes of blindness are ROP and congenital cataracts. The ETROP study was pivotal in highlighting the importance of early ablative therapy in improving visual outcomes for patients with high-risk ROP. The incidence of congenital cataract is relatively low in developed countries; it remains the leading cause of surgically correctable blindness worldwide. Early detection of cataract is vital in providing timely treatment for what is an extremely amblyogenic condition.

**Measuring the differences in work ratios between pediatric and adult ophthalmologic examinations.**


The American Academy of Pediatrics pointed out that the health reimbursement system may not accurately reflect the work required to provide care to children, and that their services are undervalued. The purpose of this observational study was to assess the differences in work needed for pediatric and adult ophthalmologic examinations. Seven ophthalmology residents conducted slit-lamp and refraction examinations on children 3-7 years of age and adults 20-69 years of age. The examiners reported the magnitude estimate (ME) of their work in relation to two references (cross-reference ME): average adult examination and average pediatric examination. The magnitude estimate (ME) is adopted from the field of psychophysics to obtain subjective assessments of the all dimension of work, including: time, mental effort and judgment, technical skill and physical effort, and psychological stress. The examination time was also measured. For the slit-lamp examination, 50 children and 58 adults were recruited. The ME was 1.45 (95% CI, 1.30-1.62) times higher for the pediatric examinations than for the adult examinations when the reference was an average adult case. With respect to time, the pediatric examinations took 1.22 (95% CI, 1.06-1.41) times longer than the adult examinations. For the refraction examinations, 58 children and 96
adults were recruited. The ME was 1.35 (95% CI, 1.21-1.52) times higher for the pediatric examinations. The pediatric examination took 1.32 (95% CI, 1.16-1.50) times longer than the adult examination. The cross-reference ME ratios measuring the pediatric over adult examinations against both the pediatric and adult reference cases were equivalent in both the slit-lamp and the refraction examinations. The authors conclude that cross-reference ME showed that pediatric ophthalmologic examinations require more work than the adult examination with validity and reliability. The time estimate was insufficient as a single indicator for work estimation.

It is a well-designed study, but the tool that the author’s chose to quantify the work load of the examiner is a subjective assessment. In the discussion the authors discuss the controversy surrounding the ME as an objective method and measurable evaluation. However, it is a customary tool of assessing work load, which the reader may not be familiar with. This made interpreting the results slightly challenging.

**Pediatric ophthalmology and strabismus fellowship Match outcomes, 2000-2015.**
Dotan, G., Karr, D. J. and Levin, A. V. JAAPoS June 2017; 21(3): 181.e181-181.e188.

The purpose of this retrospective study was to analyze trends in US pediatric ophthalmology and strabismus (PO&S) Match over the last 16 years. The authors reviewed the PO&S Match outcomes from 2000 to 2015, evaluating the number of participating programs, positions offered, and match rate, comparing it with other subspecialties, and analyzing results of US graduates versus international medical graduates (IMGs). A survey of PO&S program directors explored exposure to PO&S, policies on acceptance of IMGs, fellowship gross salary, job opportunities, and fellow placement after training. The PO&S matching rate varied yearly but was consistently lower compared to other subspecialties. The supply of fellowship positions was always higher than the demand, with an annual average of 32% unmatched positions, ranging from a low of 12% in the year 2010 to a high of 52% unmatched positions in 2004. In 2013 to 2015, 31% (from 24% to 38%) of PO&S matched fellows were IMGs, which is significantly more compared to all other ophthalmic subspecialties combined during the same time period (mean, 15%; from 15% to 16%; P < 0.001) and a significant increase from the 3 years before (mean, 20%; from 12% to 26%; P = 0.041). The survey revealed that academic and clinical exposure of residents to PO&S usually begins during the first year of residency (PGY2). Residents spend on average 16 weeks of their training in PO&S, often with more than one faculty member. The authors conclude that the interest in PO&S remains lower than other ophthalmology subspecialties despite an apparent national need for trained pediatric ophthalmologists.

The study could only reflect the information that was available through the Match, even though the actual number of fellows is higher. Another limitation of the study is that the survey response rate was only 73% and does not reflect all pro-
The effectiveness of a mobile clinic in improving follow-up eye care for at risk children.

Wei Diano, Jinali Patel, Melanie Snitzer, Michael Pond et al

This article investigates the potential of a mobile ophthalmic unit in the school yard in order to improve compliance of children who have failed the optometric in-school screening program. In this study, out of a total of 132 students that were referred by the optometric program, sixty-two percent had a full ophthalmologic examination by the mobile unit. Compared to the historical rate of 53% for completion of ophthalmologic consultation, a statistically significant improvement in follow-up was noted. The authors stressed the potential benefit of a mobile eye unit in schools for children with poor access to ophthalmic care.

Preferred Practice Pattern

Pediatric Eye Evaluations Preferred Practice Pattern: I. Vision Screening in the Primary Care and Community Setting; II Comprehensive Ophthalmic Examination

- Pediatric providers should provide vision screening of older and infant toddlers.
- After 6 months of age, children should have normal binocular alignment.
- Instrument based screening can be valuable starting at age 1, since the testing is rapid, non-invasive and minimal cooperation is required.
- Many 3 year-olds can participate in monocular visual acuity testing but this is more successful with a 4 year old.
- After age of 4, visual acuity testing becomes the focus of vision screening.
- Recommended optotypes are LEA symbols of HOTV letters for young children, and Sloan letters for older children.
- Elements of comprehensive eye exam in children are described in the PPP and readers can refer to the document.

Esotropia and Exotropia Preferred Practice Pattern

Highlighted findings and recommendations include the following
• Strabismus in children under 4 months of age sometimes resolves, particularly if the deviation is intermittent, variable, or measures less than 40 prism diopters.
• Repeat cycloplegic refraction is indicated when esotropia does not respond to the initial prescription of hyperopic refraction or when the esotropia recurs after surgery.
• Bilateral lateral rectus recession and unilateral recess-resect are both reasonable strategies for initial surgery of intermittent exotropia.
• Young children with intermittent exotropia and good fusional control can be followed without surgery because there is a low rate of deterioration to constant exotropia or reduced stereopsis.
• Children with untreated strabismus can have reduced binocular potential and impaired social interactions, which may affect their interactions and quality of life.
• Simultaneous prism and cover testing, which measures the manifest angle of strabismus, and prism and alternate cover testing, which measures the total angle of misalignment, are important elements of binocular testing. Both inform the ophthalmologist’s decisions regarding management and surgical indications.
• Convergence insufficiency occurs in children and adults, and symptoms with near viewing (typically reading) can often be improved using vergence exercises.

Amblyopia preferred practice pattern

• Treatment of refractive error alone can improve visual acuity in children who have untreated anisometropic and strabismic amblyopia. Visual acuity of children who have bilateral refractive amblyopia also can substantially improve with refractive correction alone.
• Most children who have moderate amblyopia (20/40 to 20/80) respond to initial treatment consistent of 2 hours of daily patching or weekend atropine.
• Following treatment of amblyopia caused by strabismus, anisometropia or both combined, continued monitoring and treatment, if needed, is associated with long-term stability of the visual acuity improvement.
• Suitable treatment options for amblyopia may include optical correction, patching, pharmacological treatment, optical treatment, Bangerter (translucent) filters, and/or surgery to treat the cause of amblyopia.
• Patching may be effective in older children and teenagers, particularly if they have not previously been treated.