What’s New and Important in Pediatric Ophthalmology and Strabismus for 2017
The All-Star Abridged Handout

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1. AMBLYOPIA

A pilot randomized clinical trial of intermittent occlusion therapy liquid crystal glasses versus traditional patching for treatment of moderate unilateral amblyopia


In this randomized controlled non-inferiority study, the effectiveness of intermittent occlusion therapy (IO therapy) using liquid crystal glasses was compared to continuous occlusion therapy using traditional adhesive patches for treating amblyopia. Children 3-8 years of age with previously untreated, moderate, unilateral amblyopia (visual acuity of 20/40 to 20/100 in the amblyopic eye) were enrolled. Amblyopia was associated with strabismus, anisometropia, or both. Prior to initiation of treatment all participants had worn any optimal refractive correction for at least 12 weeks without improvement. Subjects were randomized into two treatment groups: a 4-hour IO therapy group with liquid crystal glasses (Amblyz), set at 30-second opaque/transparent intervals (occluded 50% of wear time), and a 2-hour continuous patching group (occluded 100% of wear time). For each patient, visual acuity was measured using ATS-HOTV before and after 12 weeks of treatment. Data from 34 patients were available for analysis. Amblyopic eye visual acuity improvement from baseline was 0.15 +/- 0.12 logMAR (95% CI, 0.09-0.15) in the IO therapy group (n = 19) and 0.15 +/- 0.11 logMAR (95% CI, 0.1-0.15) in the patching group (n = 15). In both groups improvement was significant, but the difference between groups was not (P = 0.73). No adverse effects were reported. In this pilot study, IO therapy with liquid crystal glasses was not found to be inferior to adhesive patching. The authors concluded that it is a promising alternative treatment for children 3-8 years of age with moderate amblyopia. Even though there were some flaws with randomization the study was generally well designed. Some of the limitations were the short follow-up period and the large withdrawal from the study. Previous studies on Amblyz are discussed. It is approved as a medical device by the FDA and this pilot study can be a basis for evidence-based guidelines for prescribing these glasses.
Binocular treatment of amblyopia represents a paradigm shift in the treatment of this disease. Pilot studies demonstrated an improvement in visual acuity in those treated with a binocular iPad game. This study aims to address the need for a large randomized clinical trial. The authors designed a non-inferiority study comprised of 385 patients with anisometropic, strabismic or combined amblyopia age 5 to 12 years old. Participants were randomized to 2 hours a day of patching the dominant eye or to play a specially designed video game with dichoptic goggles 1 hour a day for 16 weeks. Mean amblyopic eye vision improved by 1.05 lines in the binocular group (2 sided CI 0.85-1.24) and 1.35 (2 sided CI 1.17-1.54) lines in the patching group. Visual acuity overall improved by 1 line. Younger children (age 5 to < 7) with no previous amblyopia treatment improved by about 2.5 lines in both groups. The adjusted treatment group difference was 0.31 lines favoring patching. This did not exceed the previously specified non-inferiority measure of 0.5 lines but the authors point out that the 1 sided upper limit of the confidence interval did, coming in at 0.53 lines.

Conclusion: A concern about the study is that only 22% of participants in the binocular group completed greater than 75% of the prescribed play. The authors conclude “VA improvement with this particular binocular iPad treatment was not as good as with 2 hours of prescribed daily patching”. Enthusiasm for binocular treatment of anisometropic, mixed and microstrabismic amblyopes may be blunted with this randomized controlled trial. The standard of care of patching, Atropinization or other monocular forms of penalization of the dominant eye should not yet be abandoned.

Previous pilot studies of binocular treatment of amblyopia used a falling block style of video game as the intervention in a comparison to part-time patching. Compliance with a Tetris or Pong-style video game was poor, up to 38% of participants. To address the possibility that the game was not interesting enough to engage children to play for the required amount of time, a new game, Digrush, developed with Dr. Robert Hess and Amblyotech and Ubisoft, was used in this randomized clinical trial. This was a crossover trial in which 14 amblyopes in the part time patching group at the end of 2 weeks, switched into the binocular group so all 28 amblyopes played Digrush for the last 2 weeks of the trial. The game was played one hour a day for 5 out of 7 days a week (10 hours per week). The
patching group patched 2 hours a day 7 out of 7 days a week (14 hours per week). 71% of children had prior amblyopia treatment. Compliance was excellent and similar between groups. Age range was 4.6 to 9.5 years and were comprised of anisometropic, mixed and strabismic amblyopes (with a tropia less than 4 prism diopters). Mean amblyopic vision was 20/63 at enrollment. The authors found a greater improvement in the binocular group compared with patching at the 2 week visit (mean increase of 1.5 lines in binocular group vs. 0.7 lines in the patching group). After crossover, patching group caught up and at 4 week study conclusion, there was no significant difference between the groups. Stereoacuity did not improve in either group. Limitations of the study include that there were 5/28 (18%) with severe amblyopia and yet they could be randomized to only 2 (not 6) hours of patching a day, so lack of improvement in patching group at 2 weeks could be because of inclusion of these undertreated severe amblyopes. Conclusion: Greater compliance was found in amblyopic children who played the binocular game, Digrush, compared with prior studies of random falling blocks. Visual acuity in the amblyopic eye 2 weeks into the study was significantly greater than the amblyopes who patched part time.

Fine Motor Skills of Children with Amblyopia Improve Following Binocular Treatment

The purpose of this study was to determine whether reduced fine motor skills in children with amblyopia improve after binocular treatment provided by dichoptic iPod game play and whether improvements are sustained once treatment has ceased. Fine motor skills (FMS [Bruininks-Oseretsky Test of Motor Proficiency]), visual acuity (VA [Early Treatment of Diabetic Retinopathy Study chart]) and level of binocular function (BF [Randot preschool stereoacuity and Worth 4 Dot]) were measured in children with amblyopia (n = 20; age: 8.5 ± 1.3 years; 11 anisometropic; 5 strabismic; 4 mixed) and in a group of visually normal children (n = 10; age: 9.63 ± 1.6 years). Eighteen children with amblyopia subsequently completed 5 weeks of binocular treatment provided by home-based dichoptic iPod game play. FMS, VA, and BF were retested at the end of treatment and 12 weeks after treatment cessation. All visually normal children also completed FMS measurements at baseline and 5 weeks later to assess test-retest variability of the FMS scores. This study found that prior to treatment, FMS scores in children with amblyopia were poorer than those in children with normal vision (P < 0.05). In the children with amblyopia, binocular treatment significantly improved FMS scores (P < 0.05). Better baseline amblyopic eye VA and BF were associated with greater improvements in FMS score. Improvements were maintained at 12 weeks post treatment. In the visually normal children, FMS scores remained stable across the two test sessions. Binocular treatment provided by dichoptic iPod game play improved FMS performance in children with amblyopia, particularly in those with less severe amblyopia. This is the first demonstration of an improvement in standardized measure of fine motor skills involved in practical, everyday
tasks following amblyopia treatment. No amblyopia treatment studies to date (including ongoing clinical trials of binocular treatment) include an outcome measurement of visuomotor control. Whether the improvements found in this study are specific to binocular treatment or would also occur with conventional treatment is yet to be determined, but this study provides further evidence that the functional burden of amblyopia goes beyond visual acuity and binocular function.

**Randomised controlled trial of video clips and interactive games to improve vision in children with amblyopia using the I-BiT system**


In this study, the authors evaluate efficacy of a new treatment for amblyopia that uses virtual reality technology. This includes either DVD footage or computer games that present a common background to both eyes and the foreground, containing the imagery of interest, only to the amblyopic eye. This is a randomized controlled trial performed on patients with amblyopia aged 4–8 years with three treatment arms. All three arms had dichoptic stimulation using shutter glass technology. One arm had DVD footage shown to the amblyopic eye and common background to both, the second used a modified shooter game, Nux, with sprite and targets presented to the amblyopic eye (and background to both) while the third arm had both background and foreground presented to both eyes (non-interactive binocular treatment (non-I-BiT) games). Subjects could have strabismic, anisometropic or mixed amblyopia. Children who had prior treatment with either patching or atropine penalization were eligible. Visual acuity was assessed pretreatment (week 1), after three treatments (week 3), after six treatments (week 6) and 4 weeks after their final treatment (week 10). Treatment consisted of 30 min weekly for 6 weeks in the office. The study randomized 75 patients. Visual acuity improved in all three arms by modest measures, approximately 0.07 logMAR in the amblyopic eye at 6 weeks. There was no difference between I-BiT DVD and non-I-BiT games compared with I-BiT games (stated primary outcome) in terms of gain in vision. Treatment was well tolerated and safe. There was no difference between the three treatments in terms of primary stated outcomes but treatment duration was short and the high proportion of previously treated amblyopia and strabismic amblyopia disadvantaged dichoptic stimulation treatment. Because all three groups were wearing the shutter glasses, perhaps the stimulation did not make as much of a difference. But the study has a serious disadvantage of having extremely short therapy time (total of 3 hours over 6 weeks) and poor patient selection.

2. VISION SCREENING
Prospective Evaluation of photoscreeners in the pseudophakic eyes of children.
Rupal H.Trivedi, M.Edward Wilson, Mae Millicent W. Peterseim, Carrie Papa et al

This prospective study compared data of Plusoptix AO9 (Plusoptix, Inc., Atlanta, GA) and Spot (Welch Allen, Skaneateles Falls, NY) photoscreeners with retinoscopy, in pseudophakic eyes of children. A pediatric ophthalmologist was masked to the results of both photoscreeners. In bilateral pseudophakic eyes, one eye was randomly selected. Forty-four eyes were included, with a mean age of 7.4 ± 4.8 years. Refraction was estimated in all eyes using retinoscopy, but a refractive estimate was obtained in only 11.3% (5 of 44) of eyes using the Plusoptix binocularly and 63.6% (28 of 44) of eyes using the Spot. The authors concluded that Refraction was estimated in a higher number of pseudophakic eyes of children using the Spot as compared to the Plusoptix. Although a larger sample size is needed, this is the first study to evaluate and compare the refractive data of Plusoptix and Spot with retinoscopy in pseudophakic children.

3. REFRACTIVE ERROR

Prevalence and Risk Factors

Association Between Myopia, Ultraviolet B Radiation Exposure, Serum Vitamin D Concentrations, and Genetic

Association of Axial Length With Risk of Uncorrectable Visual Impairment for Europeans With Myopia

The prevalence of myopia is increasing worldwide, especially in urban areas in Asia. Increased risk of permanent visual impairment from glaucoma, cataract, retinal detachment, or myopic macular degeneration in myopes is increased, especially in high myopes, defined as a spherical equivalent of less than -6 diopters. The authors want to determine if there is an association between axial length and permanent visual impairment in myopes. This is a cross-sectional population based study derived from data from the Rotterdam Eye Study. There were 15 693 individuals in the study. Axial length ranged from 15.3 to 37.8 mm; 819 had an axial length of 26 mm or greater. Spherical equivalent ranged from −25 to +14 diopters; 796 had high myopia. Axial length and spherical equivalent were highly correlated. Average age was 61.3 years and 57% were female. Cu-
Cumulative incidence of visual impairment was 3.8% in those aged 75 years with an axial length of 24 to less than 26mm and greater than 90% with an axial length of 30mm or greater. The cumulative incidence of visual impairment in high myopes increased with increasing age as well. Visual impairment in high myopes (defined by spherical equivalent) was present in 5.7% in those aged 60 years and 39% in those aged 75 years. Permanent visual impairment increased with increasing axial length and myopic spherical equivalent.

Conclusion: Myopia begins in childhood. Identifying genetic and environmental factors in childhood may reduce the burden of visual impairment later, a burden which was elegantly demonstrated in this study. A drawback of this study is that the causes of visual impairment in the participants were not identified.

**Peripapillary Diffuse Chorioretinal Atrophy in Children as a Sign of Eventual Pathologic Myopia in Adults**


In this retrospective case series the authors studied 56 eyes of 29 patients with mean age of 10.2 years for ≥ 20 years of follow-up. Mean axial length was 27.0 mm at baseline and 29.7 mm at the last visit. At the last visit, 19 eyes (34%) had tessellated fundus alone, 31 eyes (55%) had diffuse chorioretinal atrophy, 3 eyes (5%) showed patchy chorioretinal atrophy, and 1 eye (2%) had macular atrophy. Thus, 35 eyes (63%) had pathologic myopia in adulthood. Among the 35 eyes, 29 (83%) already had diffuse chorioretinal atrophy at the initial visit in childhood and the remaining 6 eyes (17%) showed tessellated fundus in childhood. The diffuse chorioretinal atrophy seen in childhood was restricted to the area temporal to the peripapillary region. The presence of peripapillary diffuse chorioretinal atrophy in children with high axial myopia may be an indicator for the eventual development of advanced myopic chorioretinal atrophy in later life.

Comment: Figures 1 and 2 provide helpful images of childhood peripapillary chorioretinal atrophy which, by adulthood, had spread to affect the entire posterior fundus in 2 patients. These clues may be helpful to pediatric ophthalmologists in predicting future pathologic myopia.

**Reducing the Progression of Myopia**

**Efficacy Comparison of 16 Interventions for Myopia Control in Children a Network Meta-analysis**


In this meta-analysis of 30 randomized clinical trials of at least 1 year duration each (total 5422 eyes), the authors compared various myopia treatments to placebo using annual dioptic change in refraction (D/y) and change in mean in axial length (mm/y). The difference in refraction change
between high-dose atropine and control was 0.68 D/y and difference in axial length was -0.21 mm/y. For moderate-dose atropine the differences in refraction and axial length were, 0.53 D/y and -0.21 mm/y, respectively. For low-dose atropine, change was 0.53 D/y and -0.15 mm/y. Each dose of atropine markedly slowed myopia progression. Pirenzepine yielded refraction change of 0.29 D/y and axial length change -0.09 mm/y. Orthokeratology and peripheral defocus modifying contact lenses yielded moderate effect of -0.15 D/y and -0.11 D/y, respectively. Progressive addition spectacle lenses showed only slight effect.

Comment: Figure 3 is a good summary of interventions such as atropine and pirenzepine that had a positive effect on refraction and axial length and some interventions which had no significant positive effect such as rigid gas-permeable contact lenses, soft contact lenses, timolol, and undercorrected single vision spectacle lenses.

4. VISION IMPAIRMENT

Fitness Wearables and Youths with Visual Impairments: Implications for Practice and Application


Individuals with visual impairments are at risk for chronic health-related illnesses attributed to low physical activity and low fitness levels. This cross-sectional and descriptive study aimed to determine device preferences of 3 physical activity-monitoring wearables for children with visual impairments and to determine beneficial and impeding device components and suggested device changes. 25 individuals aged 9 – 22 years were recruited from a week-long sports camp for youths with visual impairments. Each day for 5 days, five of the participants wore the Nike+ FuelBand ES Activity Tracker, Garmin Vivofit, and Centrios all on the same day. Data was collected via demographic questionnaires and evening focus groups. Responses varied by level of visual impairment, such as with auditory and visual contrast components, and varied slightly by gender, such as with aesthetic components. All responses for beneficial and impeding components and suggested changes fell into nine coded themes: access to data, comfort, display, data measured, auditory, waterproof, aesthetics, goal-setting, and music. The study was limited by the small number of participants and short device usage time for each participant. Also, participants at a sports camp may be inherently more active than the average young population with visual impairments. Nevertheless, this study resulted in conclusions that should be considered in future physical activity promotion research and interventions for youths with visual impairments.

Binocular Vision in Chronic Fatigue Syndrome
Chronic Fatigue Syndrome (CFS) is characterized by found, disabling fatigue not caused by exertion and not relieved by rest. To diagnose the syndrome patient must also have 4 of the following symptoms within the past 6 months: sore throat, tender lymph nodes, muscle pain, multi-joint pain, post-exertional malaise, unrefreshing sleep, headaches, and impaired memory or concentration. Ocular complaints include pain, photophobia, blurred vision, intermittent diplopia, focusing difficulties, and dry eyes. The authors compared binocular vision measurements, accommodation, and convergence in patients with CFS vs. healthy controls and found that patients with CFS have highly significant smaller fusional amplitudes, reduced convergence capacity, and smaller accommodation range. Treatment for CFS patients with ocular manifestations should include progressive lenses =/- prism and convergence exercises.

Transient Smartphone "Blindness".

The authors present two patients who reported transient monocular “blindness” lasting up to fifteen minutes. After a careful history, the authors determined that the “blindness” occurred in after the patient was lying in bed on her side, with one eye obscured by a pillow and one eye viewing a bright smartphone screen. Thus, one eye became dark adapted and the other light adapted, and subsequent binocular viewing in dim light made the light adapted eye seem “blind.” The authors then subjected themselves to smartphone viewing and electroretinography, showing that the b wave amplitude decreased in the smartphone adapted eye. The effect lasted minutes.

As pediatric ophthalmologists, we get questions about smartphone use; this brief report provides an interesting story about transient “blindness” from staring at the bright screen, which we can share with our patients’ families.

5. NEURO-OPHTHALMOLOGY

Avoiding Clinical Misinterpretation and Artifacts of Optical Coherence Tomography Analysis of the Optic Nerve, Retinal Nerve Fiber Layer, and Ganglion Cell Layer
John J. Chen, MD, PhD, Randy H. Kardon, MD, PhD.

*This excellent review article is a must read for anyone using OCT. It provides important information that will help the practitioner avoid error in interpretation of*
this rapidly expanding technology. Data resulting in misinterpretation- unless carefully scrutinized- may be as high as 40%.

RNFL is age dependent. There is a natural decrease in mean RNFL of 0.365 mm per year increase in age so make sure date of birth entered correctly. Signal strength needs to be adequate (this is device dependent) or the results inaccurate and likely non-reproducible. Any media opacity (e.g. dry eye, cataract or vitreous hemorrhage) decreases measurable RNFL and produces regions of dropout which reduce mean RNFL and alter segmentation analysis. Decrease in signal strength can have similar impact. Local areas with a thickness less than 40 mm are typically due to errors in segmentation unless the patient has longstanding extremely severe optic neuropathy. Improper alignment of scan can increase or decrease apparent RNFL and distort segmentation analysis. Papilledema can make it difficult to determine the neural canal opening and can result in measurement of a seemingly large optic disc which is not present, and distorts segmentation of RNFL and may gives areas of non-physiological RNFL drop-out. Increased axial length and myopia above 5 D are associated with reduce measured RNFL which often is most often non-pathologic in nature. These changes may go unrecognized or improperly interpreted in patients post refractive or cataract surgery. Due to the more temporal shift of the RNFL peaks in myopia, the temporal RNFL thickness may appear to be elevated, while the superior and inferior RNFL thickness may be reported as decreased when they are actually “normal” for myopes. Exceptionally hyperopic eyes tend to show a more acute vertical angle of entry of the arcuate bundle also altering the segmentation distribution plot. Cyclo-rotation of the eyes, for example from superior oblique palsy, will cause a change in RNFL profile making it difficult to compare to the normative database. This error has been largely corrected in the Spectralis software. Gliosis of the optic nerve, common after chronic papilledema, can result in an increase in apparent RNFL thickness in the clinical setting of significant optic atrophy. In this case, and in the case of papilledema in general, the macular ganglion cell layer-inner plexiform layer (GCL-IPL ) complex available on the macula cube will show atrophy while the peripapillary RNFL appears thickened due to the elevation created by gliosis or edema. Myelinated nerve fiber layer can also lead to an measured increase in RNFL thickness. Acute edema of the inner retina due to artery occlusions, and epiretinal membrane can also cause an increase in measured RNFL thickness that can obscure pathologic loss of axons. Patients with megalopapilla or, conversely those with small neural canals (including optic nerve hypoplasia) may show abnormal cup to disc ratio as software is not designed for these anomalies. The GCL-IPL complex is thickest in the macula, has a larger dynamic range than the RNFL in the papillomacular bundle, and provides a more sensitive measure of neuronal loss than the papillomacular bundle-- and been found to correlate with field loss and optic nerve diseases such as glaucoma, optic neuritis, ischemic optic neuropathy, hereditary optic neuropathy, toxic optic neuropathy, optic nerve glioma, and idiopathic intracranial hypertension. Errors in GCL-IPL segmentation may appear as spoke-like blue regions of thinning called the “propeller sign”. The perifoveal re-
Idiopathic Intracranial Hypertension

**Anatomic and visual function outcomes in pediatric idiopathic intracranial hypertension**


There is a paucity of literature describing risk factors for vision loss in pediatric idiopathic intracranial hypertension (IIH). The authors investigated the final visual function, spectral domain optical coherence tomography (SD-OCT) and enhanced depth imaging (EDI)-OCT findings in children with papilledema caused by IIH. This is a retrospective review of 31 patients with pediatric IIH (age ≤ 17 years) from January 2010 to August 2013. Patients were required to meet the revised diagnostic criteria for IIH proposed by Friedman, Liu and Digre, which includes lumbar puncture opening pressure exceeding 28 cm H\(_2\)O (or 25 cm H\(_2\)O if not sedated). Optic disc photographs on presentation and automated perimetry, SD-OCT and EDI-OCT imaging on final follow-up visit were statistically analyzed to identify patient characteristics and anatomic findings associated with irreversible vision loss. Permanent visual acuity or visual field loss developed in 19% of study eyes. Papilledema of modified Frisén grade ≥ 3 on presentation was highly predictive of permanent vision loss (p<0.001), while associations between pubertal status and visual function outcome failed to reach statistical significance. SD-OCT revealed optic atrophy in 13% and photoreceptor loss in 19% of eyes, with both findings highly associated with vision loss (p<0.0001). Optic disc drusen was noted in 48% of study eyes by EDI-OCT but was not found to be predictive of visual outcome. The authors concluded that clinical observation of high papilledema grade on presentation is predictive of poor visual outcomes. Vision loss is associated not only with optic atrophy but also with photoreceptor damage. Interestingly, a high proportion of study eyes had optic disc drusen, which was not associated with vision loss, but can be a diagnostic challenge in distinguishing true papilledema from pseudopapilledema.

Although the authors gathered information on body habitus, they did not comment on this risk factor in the study. It will be interesting to see whether other studies with pediatric IIH have a similarly high percentage of children with optic disc drusen.

**Factors Affecting Visual Field Outcomes in the Idiopathic Intracranial Hypertension Treatment Trial**


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

Perimetry

Optic Nerve Imaging

Optic pathway glioma volume predicts retinal axon degeneration in neurofibromatosis type 1

This cross-sectional analysis of patients with NF1 associated optic pathway gliomas (OPG) evaluated optic pathway glioma size and its relationship to axonal damage of the anterior visual pathways. NF1 Children with OPG included in this analysis had to have a high-resolution MRI and an OCT of the RNFL within 2 weeks of each other. The authors found 38 patients, 55 eyes to include, with 20% of the OCTs performed using a hand-held device. For patients with isolated optic nerve gliomas, there was no correlation of RNFL thickness with optic nerve diameter or volume. However, a correlation with increasing anterior visual pathway volume and decreasing RNFL thickness was found. Each 1mL increase in anterior visual pathway volume led to an approximately 5-micron decrease in RNFL thickness. When anterior visual pathway volume was greater than 3mL it had a positive predictive value (PPV) of 87% for abnormal RNFL (<80 microns). When anterior visual pathway volume was less than 3mL it had a negative predictive value (NPV) (with normal RNFL >80 microns) of 94%. All patients with visual acuity or visual field loss had RNFL thicknesses less than 80 microns. Chiasmal volumes of >1.3mL had a 100% PPV for abnormal RNFL, while volumes <1.3mL had a 95% NPV. This study demonstrates that tumor size is a risk factor for vision loss and axonal damage. Validation of this study may mean that
children with smaller OPGs may need to be monitored less frequently, with the converse true for those with larger OPGs. A multi-center prospective study would be ideal to confirm this.

Optic Nerve Head Development in Healthy Infants and Children Using Handheld Spectral-Domain Optical Coherence Tomography

In this prospective cross-sectional study the authors aim to characterize optic nerve head development in full-term infants using handheld spectral-domain optical coherence tomography (SDOCT) without sedation. 352 children aged 1 day to 13 years were imaged with a single scan. Authors collected disc and cup diameter (expressed as distance in micrometers and visual angle in degrees), cup depth, retinal thickness, Bruch’s membrane opening minimum rim width (BMO-MRW) and retinal nerve fiber layer (RNFL; 1700mm and 6 degrees from the disc center). 70% of participants were imaged successfully. Interexaminer reliability was excellent with intraclass correlation coefficients (ICCs) >0.89 for diametric and retinal thickness parameters. Right and left eyes were similar for diametric measurements (ICC,>0.79), but more variable for nasal, RNFL, and retinal thickness. The mean disc and cup diameter increase by 30% and 40%, respectively, between birth and 13 years of age when expressed as a distance measure, but remained constant (at 5-5.5 degrees and 2 degrees, respectively) when expressed as a visual angle with reference to the eye nodal point. The peripapillary temporal RNFL demonstrated a marked initial decrease of nearly 35% between birth and approximately 18 months of age. This was followed by a slow increase up to 12 years of age when measured at 1700mm from the disc center, although there was little change when measured at 6 degrees from the disc center.

Comment: This study provides a normative database of the developing optic nerve head. In addition to the data in the paper, the authors provided a helpful animated video cartoon depicting the progression of optic nerve head development from birth to age 13 years. The video is found at aao.org.

6. NYSTAGMUS

7. PREMATURITY

8. ROP
ROP and imaging

ROP and Anti-Vascular Endothelial Growth Factor Treatment

A lower dose of intravitreal bevacizumab effectively treats retinopathy of prematurity
Khodabande, A., Niyousha, M. R. and Roohipoor, R.

This prospective, non-comparative, interventional case series addresses the question of optimal dose for the treatment of type 1 retinopathy of prematurity (ROP). It included a total of 49 eyes of 25 consecutive infants (24 bilateral and 1 unilateral), who underwent intravitreal injection of a reduced dose (0.25 mg/0.01 mL) of intravitreal bevacizumab. Infants were followed for ROP persistence or recurrence until 90 weeks' postmenstrual age. In this case series ROP regressed in all eyes. No recurrences of plus disease or neovascularization were noted.

In this cohort of patients the lower dose of 0.25mg/0.01ml intravitreal bevacizumab seemed to be effective, with no recurrence of plus disease or neovascularization.

Retinal Vascular Development with 0.312 mg Intravitreal Bevacizumab to Treat Severe Posterior Retinopathy of Prematurity: A Longitudinal Fluorescein Angiographic Study

This study investigated the efficacy of intravitreal bevacizumab (IVB) 0.312 mg per eye in infants with treatment-requiring ROP in Zone 1 and posterior Zone II including APROP, and described the effects of the treatment on the developing retinal vasculature using FA. 0.312 mg is a lower dose than is typically administered to adults, and lower than the dose reported in most previous studies of anti-VEGF therapy for ROP (0.625 mg). 17 premature infants were treated with 0.312 mg IVB because of acute ROP in posterior Zone II or Zone I, including APROP. Infants were examined by FA using RetCam II or III before IVB, within 6 weeks, 8 – 13 weeks, and up to 45 months after treatment. Acute ROP regressed in 19/27
(70%) analyzed eyes, including 100% of posterior Zone II eyes and 80% Zone I eyes, but in only 25% of APROP eyes. Early recurrences (11%, all APROP) and late reactivations (18%) were observed within 1 week and at 9–12 weeks, respectively. All eyes demonstrated leakage at the junction of the vascularized zone and capillary malformations on FA prior to treatment. Vessel branching abnormalities and circumferential vessel formation were common features on FA after treatment.

This study was limited by small sample size. In addition, IVB monotherapy was not compared to laser monotherapy, and no control group of imaging data from healthy infants was included. Although FA data from every patient at every time point could not be obtained, a total of 75 FA imaging data sets were examined and reveal interesting new clinical data. That the lower dose of IVB showed similar results in posterior Zone II and Zone I disease compared to higher doses in other studies is important given the unknown consequences of anti-VEGF medication on developing babies. 0.312 mg IVB was not effective for treating APROP in this study. The authors emphasize that FA may be helpful in defining and diagnosing APROP and other short and long term vessel alterations related to ROP.


This study analyzed the medical records of 101 eyes of 51 consecutive infants with Type 1 ROP in Zone 1. Infants treated between November 2004 – June 2011 received conventional laser photocoagulation (Group I), those treated between July 2011 – October 2012 received combined intravitreal bevacizumab injection and Zone 1 sparing laser (Group II), and those treated between November 2012 – December 2013 received intravitreal bevacizumab with deferred laser treatment (Group III). In Group I, 10 of 44 eyes (22.7%) demonstrated an unfavorable anatomical outcome. However, in Groups II and III, all eyes had favorable anatomical outcomes without reactivation or retreatment. The refractive error was less myopic in Group III (spherical equivalent -1.40 +/- 2.19 D) than in Groups I (-4.62 +/- 4.00D) and II (-5.53 +/-2.21 D).

This study’s major limitation is that it is a historical rather than a simultaneous comparison which may be a source of confounding and bias. Temporal trends such as oxygen treatment protocols and management of sepsis and nutrition might influence the development and behavior of ROP, which would affect treatment outcomes. In addition, the study did not include a group treated with intravitreal bevacizumab alone. Although a prospective study is necessary, the authors conclude that intravitreal bevacizumab with deferred laser may afford a favorable anatomic outcome, lower possibility of reactivation, less frequent examinations after treatment, and
preservation of larger unlasered retinal areas with less myopia than other
treatment strategies.

Clinical Management of Recurrent Retinopathy of Prematurity after Intravitreal Bevacizumab Monotherapy

In this retrospective case series, the authors aimed to determine incidence, risk factors, risk period, and characteristics of recurrent retinopathy of prematurity (ROP) following intravitreal bevacizumab (IVB) monotherapy. IVB monotherapy performed in 241 infants (471 eyes) was studied. Risk factors for recurrence were appearance of neovascularization as acute posterior ROP (P=0.006), extended duration of hospitalization (P=0.01), and lower birth weight (P=0.024). Recurrence risk period was between approximately 45 and 55 weeks adjusted age (mean recurrence of 51.2 weeks adjusted age) and mean interval of 16.2 weeks between treatments. Recurrence characteristics included plus disease (20/20 infants [100%]) and neovascularization, which appeared at the following sites: stage 3+ ROP with confluent neovascularization recurred both at the advancing edge and at the initial ridge and extraretinal fibrovascular proliferative complex (12/14 infants [85.7%]). However, APROP (6/6 infants [100%]) and stage 3+ ROP with nonconfluent neovascularization (2/14 infants [14.3%]) recurred only at the advancing edge. Also, the anterior extent of retinal vascularization was decreased (mean, 1.76 disc diameters [DD] vs. 4.48 DD), and the rate of retinal vascularization was delayed (mean, 0.11 DD/week vs. 0.23 DD/week) in those with versus without recurrence, respectively. After retreatment with IVB, retinal vascularization proceeded minimally and slowly. The authors concluded that premature children with severe ROP are being treated successfully with IVB monotherapy, but recurrence is not uncommon. They recommended vigilant follow-up to ensure timely re-treatment. Knowledge of recurrence incidence, risk factors, risk period, and characteristics allows for tailored clinical management.

Comment: With more treatment options comes more complexity in ROP management decision-making. The study results and fundus photos and angiograms included in the paper are helpful in gaining a better feel for the expected clinical course following injection of Avastin.

Neurodevelopmental Outcomes Following Bevacizumab Injections for Retinopathy of Prematurity
Julie Morin, Thuy Mai Luu, Rosanne Superstein, Luis H. Ospina, et al. Pediatrics April 2016; 137 (4); e20153218

Bevacizumab, a vascular endothelial growth factor, is used to treat retinopathy of prematurity. There is limited information regarding the long-term effects of a sys-
temically absorbed medication on the development of these children. To evaluate the developmental effects, a retrospective study was conducted by the Canadian Neonatal Network and the Canadian Neonatal Follow-Up Network. The study identified patients born at less than 29 weeks gestation between 2010-2011 and who were treated with either bevacizumab or laser. Neurodevelopmental outcomes at 18 months were obtained from a database that provided the Bayley Scores of Infant and Toddler Development Third Edition. These developmental tests were administered by pediatricians across Canada. The study showed that infants treated with bevacizumab scored lower on a motor composite score but not on language or cognitive scores. Odds of severe neurodevelopmental disabilities (low Bayley score, cerebral palsy, hearing aids, or bilateral blindness) was 3.1 times higher in infants treated with bevacizumab than laser. The rates were adjusted for variables such as gender, maternal education, and severity of systemic illness. Weaknesses of the study include the observational nature of the research, the lack of information about why an infant received bevacizumab versus laser, and that the bevacizumab group had more severe retinopathy of prematurity. It is impossible to know whether the increased severity of the bevacizumab group’s retinopathy of prematurity or the medication itself led to the differences in developmental outcome. But, this study raises some concerns about the long-term safety of bevacizumab and demonstrates the importance of further study evaluating the developmental effects of systemic medications given in infancy.

ROP - Other Topics

Use of a Supplemental Oxygen Protocol to Suppress Progression of Retinopathy of Prematurity

This study compared the progression of retinopathy of prematurity (ROP) before and after institution of an oxygen therapy protocol at the University of Iowa Neonatal Intensive Care Unit to inhibit active proliferation and progression of ROP in premature infants. This was a retrospective cohort study was performed of premature infants undergoing ROP screening before (cohort A) and after (cohort B) implementation of an oxygen therapy protocol to inhibit further progression for those with stage 2 ROP or worse. In cohort B, oxygen saturation target was increased to ≥97% after diagnosis of prethreshold or worse ROP, based on the STOP-ROP trial, which showed a significant reduction in progression of stage 2 to stage 3 ROP. Oxygen saturations were kept at this level until ROP regression began. In cohort A, without oxygen therapy protocol (2002–2007), 44% (54/122) of infants progressed beyond stage 2, compared to 23% (24/103) of infants after protocol implementation (cohort B, 2008–2012) (P = 0.001). No significant differences between cohort A and B were found for gestational age, birth weight, survival, sepsis, bronchopulmonary dysplasia, oxygen at discharge, or need for diuretics. Infants with stage 2 ROP in cohort B, with oxygen therapy protocol, had
significantly decreased risk of ROP beyond stage 2 (odds ratio 0.37, 95% confidence interval 0.20–0.67; P = 0.0013), compared to cohort A, correcting for differences in birth weight and necrotizing enterocolitis. Progression from stage 2 to stage 3 ROP in premature infants was significantly decreased after implementation of an oxygen therapy protocol, without a corresponding increase in pulmonary morbidity (unlike in the STOP-ROP trial). The lack of increase in pulmonary morbidity may be a result of the protocol used. In this study, to minimize hyperoxic exposure, effective oxygen exposure was limited to FiO2 ≤ 0.50–0.60 even if this meant that some infants did not consistently achieve the desired oxygen saturation of ≥97%. This study suggests that appropriate oxygen therapy may play a role in inhibiting progression of stage 2 ROP, potentially decreasing the risk of lifelong visual loss in this vulnerable population. Although this study is limited in that it is a retrospective cohort study, limiting the ability to control for nonsystematic changes in clinical practice, the results are compelling and support the implementation of a standardized targeted supplemental oxygen therapy approach to inhibit the progression of ROP.

9. STRABISMUS

Extraocular muscle anatomy

Rectus Extraocular Muscle Size and Pulley Location in Concomitant and Pattern Exotropia

In this prospective case-control study, the authors aim to use MRI to determine whether rectus extraocular muscle (EOM) sizes and pulley locations contribute to exotropia. Nine patients with concomitant exotropia, 6 patients with pattern exotropia, and 21 orthotropic normal control participants underwent. High-resolution surface-coil MRI scans were obtained in contiguous, quasicoronal planes. Rectus pulleys were located differently in patients with A-pattern, versus V- and Y-pattern, exotropia. The lateral rectus (LR) pulleys were displaced significantly superiorly, the medial rectus (MR) pulleys were displaced inferiorly, and the inferior rectus pulleys were displaced laterally in A-pattern exotropia. However, the array of all rectus pulleys was excyclorotated in V- and Y-pattern exotropia. The volume of the medial rectus muscle was statistically subnormal by approximately 29% in concomitant, but not pattern, exotropia (P < 0.05). The LR volume to MR volume ratio in concomitant exotropia was significantly greater than in control participants and those with pattern exotropia (P < 0.05). The authors conclude that abnormalities of EOMs and pulleys contribute differently in pattern versus concomitant exotropia. Abnormal rectus pulley locations derange EOM pulling directions that contribute to pattern exotropia, but in concomitant exotropia, pul-
ley locations are normal, and relatively small medial rectus size reduces relative adducting force.

Comment: This paper contains images and biomechanical analyses that are very convincingly support the authors’ conclusions stated above. This interesting paper sheds a good deal of light on the pathophysiology of a very common clinical entity in the practice of pediatric ophthalmology.

A Randomized Trial Evaluating Short-term Effectiveness of Overminus Lenses in Children 3 to 6 Years of Age with Intermittent Exotropia


In this randomized, clinical pilot trial, the authors aim to evaluate the short-term effectiveness of overminus spectacles in improving control of childhood intermittent exotropia (IXT). 58 children aged 3 to <7 years with IXT were randomly assigned to overminus spectacles (-2.50 D over cycloplegic refraction) or observation (non-overminus spectacles if needed or no spectacles) for 8 weeks. Outcome testing was conducted with children wearing their study spectacles or plano spectacles for the children in the observation group who did not need spectacles. At 8 weeks, mean distance control was better in the 27 children treated with overminus spectacles than in the 31 children who were observed without treatment (2.0 vs. 2.8 points, adjusted difference = -0.75 points favoring the overminus group; 2-sided 95% confidence interval, -1.42 to -0.07 points). Side effects of headaches, eyestrain, avoidance of near activities, and blur appeared similar between treatment groups. The authors concluded that for a pilot study, overminus spectacles improved distance control at 8 weeks in children aged 3 to <7 years with IXT.

Comment: Whether the improvement in IXT control is lasting or not, overminus glasses may at least be considered to temporize and defer surgery until an older age. PEDIG is currently enrolling IXT patients in a larger study of overminus glasses.

Relationship Between Binocular Summation and Stereoacuity After Strabismus Surgery.


This study is a prospective case series of 130 post op strabismus patients. The authors studied the relationship between binocular summation and stereoacuity. The authors point out that many strabismic patients have deficits in fusional tasks and impaired depth perception, and that there is an increased interest in determining how both eyes working together may be synergistic in the brain due to neural summation. In this study, the authors excluded patients under 3, older
than 65, patients with dissociated deviations, nystagmus, neurologic disease or amblyopia. They did not exclude patients based on when the strabismus began or based on their post op eye alignment. Stereoacuity was evaluated using the Randot Stereotest at both near and far. Sloan acuity was tested using the ETDRS protocol with low contrast levels of 2.5% and 1.25% at 3 meters. High contrast acuity was tested using the ETDRS protocol at distance. The authors found that patients with stereoacuity had statistically significantly more binocular summation in 2.5% low contrast acuity than those without stereoacuity. The authors point out that there is no causal relationship proven in this study nor did they compare pre and post surgical results, however they conclude that stereopsis and binocular summation are significantly correlated in patients who have had strabismus surgery.

10. STRABISMUS SURGERY

*Horizontal muscle surgeries*

*Long-term surgical outcomes and factors for recurrence after unilateral lateral rectus muscle recession*


This is an observational study to evaluate long-term surgical outcomes and risk factors for recurrence after unilateral lateral rectus muscle recession (ULR) in children with small to moderate angle basic type of intermittent exotropia (IXT) defined as 15-24 PD. The main outcome measure was success rate at 2 years after surgery and at final follow-up. Postoperative alignment was considered satisfactory if the alignment was between 8 PD exophoria/tropia and 5 PD esophoria/tropia. Recurrence was defined as >8 PD of exophoria/tropia and overcorrection was defined as >5 PD of esophoria/tropia. The risk factors related to recurrence were evaluated using univariable and multivariable logistic regression analyses. The authors found that the success rate at postoperative 2 years was 92.5% and 83.2% at final examination after a mean follow-up of 3.9 years. No overcorrection was observed. Preoperative exodeviation of 20–24 PD was a significant risk factor for recurrence according to both univariable (OR=3.577, p=0.022) and multivariable analysis (OR=3.265, p=0.034). In conclusion, long-term success of ULR for 15-24 PD of IXT was good. However, recurrence risk of subjects with 20–24 PD of exotropia was about 3 times higher than among subjects with less than 19 PD of exodeviation.

*Transposition surgeries*

This article describes a new surgical modified procedure in patients with chronic total oculomotor nerve palsy as well as the results of the procedure. Eight eyes of 6 consecutive patients who underwent strabismus surgery due to chronic total oculomotor nerve palsy were enrolled in the study. The lateral rectus muscle was split into two halves and disinserted from the sclera. The upper half of the muscle was passed under the superior rectus muscle and the inferior half of the muscle was passed under the inferior rectus muscle. The two halves of the muscle were moved to the medial rectus muscle insertion area and were sutured to sclera near the insertion. Additional medial rectus resections were made in the undercorrected patients. The mean age was 21.8 ± 12.1 years (range: 11 to 42 years). Postoperatively, 4 of 6 patients had stable horizontal deviations; 1 had orthophoria, 2 had 10 prism diopters (PD) of exotropia, and 1 had 10 PD of esotropia. However, 2 cases had 25 and 30 PD of undercorrection. Additional medial rectus resections were made in these undercorrected patients and horizontal deviations reduced to 15 and 20 PD of exotropia, respectively. The mean primary position horizontal deviation, which was 74.1 ± 10.2 PD before the surgeries, reduced to 10.8 ± 6.6 PD after the surgeries ($P < .001$). The authors concluded that this procedure might be an option in the treatment of chronic total third nerve palsy but that a larger sample is needed in order to reach safe conclusions.

### 11. ANTERIOR SEGMENT

### 12. CATARACT

Factors associated with stereopsis and a good visual acuity outcome among children in the Infant Aphakia Treatment Study S R Lambert, L DuBois, G Cotsonis, E E Hartmann and C Drews-Botsch for the Infant Aphakia Treatment Study Group *Eye* September 2016; 30: 1221-1228; advance online publication, July 29, 2016; doi:10.1038/eye.2016.164

In this IATS study the authors examine the factors associated with the development if good acuity and stereopsis. 112 children with unilateral cataract had 5 year followup and patching compliance was measured using 7 day diaries and phone interviews. They found that 27% of the patients had 20/40 vision or better. Of these children 50% had stereopsis, and those with stereopsis they more more
like to orthophoric and had LESS patching (3.4 hours/day in first year tapering to 1.8 hours by age 4). In contrast the group with no stereopsis showed an INCREASE in patching over 4 years (4.8 in first year increasing to 6.5 hours by age 3. There was no statistical difference in the IOL vs contact lens group. The authors conclude that the following patching regimen be applied to children who demonstrate good acuity and good compliance: year 1 - 4 hours/day, years 2-3 - 3 hours per day, year 4 -2 hours per day.

13. Cataract Surgery

Lens regeneration using endogenous stem cells with gain of visual function.

The repair and regeneration of tissues using endogenous stem cells represents an ultimate goal in regenerative medicine. This is the first study demonstrating the regeneration of a human lens. The authors isolate lens epithelial stem/progenitor cells (LECs) in mammals and show that Pax6 and Bmi1 are required for LEC renewal. They design a surgical method of cataract removal that preserves endogenous LECs and achieves functional lens regeneration in rabbits and macaques. They then perform this technique in 12 infants (24 eyes) ages <24 months with bilateral congenital cataracts. The control group was 25 infants (50 eyes) who underwent standard cataract surgery with either intraocular lens implantation or aphakia. In the new technique, the authors perform a 1.0-1.5 mm peripheral anterior capsulorrhexis and remove the cataractous lens through this small opening, leaving most of the anterior capsule and posterior capsule intact, and leaving most of the LECs. Then, over the next three to six months, they observe the LECs recreate a lens with refractive power and some accommodating ability. The small peripheral anterior capsular opening heals, leaving a peripheral scar in the lens. They use Teller acuity cards to measure postoperative visual acuity, showing approximately 20/200 average acuity six months later. They show slit lamp photographs and clear fundus photographs through the regenerated lenses, proving relatively normal lens shape and clarity. The authors harness what we previously deemed a complication of infantile cataract surgery: Soemmering’s ring formation and visual axis opacification, and use the ability of LECs to proliferate to an advantage. This approach demonstrates a novel treatment strategy for infantile cataracts, and it’s exciting to envision whether this approach could even be utilized in adult eyes. This study is a breakthrough for medicine in general, showing functional tissue regeneration using endogenous stem cells. Finally, the study is an exceptional example of translational research, truly taking what is learned from the laboratory bench to the bedside!

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

14. GLAUCOMA

Pediatric glaucoma – other topics

Long-term home monitoring of intraocular pressure in pediatric glaucoma


Diurnal fluctuation of intraocular pressure (IOP), implicated in progression of adult glaucoma, has been reported in children only in the context of office and short-term home monitoring. The purpose of this prospective study was to evaluate long-term patterns of IOP fluctuation and changes resulting from outflow-enhancing intervention in pediatric glaucoma. Parent-measured home-based rebound tonometry (Icare, Finland Oy) in pediatric glaucoma patients was used to monitor IOP for more than 1 month, with requested measurements at least 3 times daily. IOP was recorded at home on electronic data sheets. It was then evaluated for trends including mean overall IOP, IOP pre- and post-planned IOP-lowering interventions, and IOP spikes over determined time intervals. IOP was measured in 14 eyes of 7 children (mean age, 9.3 +/- 2.4 years) over a mean of 164.3 days (range, 75-341), with a mean of 2.46 readings daily. Six eyes of 5 children underwent attempted outflow improvement, with improved mean IOP before versus after intervention (26.6 vs 15.5 mm Hg, P < 0.0001) and decreased mean daily IOP fluctuation (8.4 vs 4.6 mm Hg, P < 0.001) for each. The likelihood of measuring an IOP spike (20% greater than mean for an individual eye over the entire period) was found to be 19.3 ± 6.7% over 1 day, 62.9 ± 18.0% over 3 days, 80.8 ±12.2% over 7 days, and 92.9 ± 9.4% over 14 days. The authors concluded that long-term home monitoring in pediatric glaucoma proved feasible in this study population and often demonstrated large IOP fluctuations. A
14-day period of home monitoring provided >90% chance of identifying an IOP spike. Successful outflow improvement lowered both mean IOP and mean daily IOP fluctuations. This study was intended to be a pilot on long-term home tonometry and was limited to motivated families of cooperative children with glaucoma. Included patients had post cataract surgery glaucoma and juvenile open-angle glaucoma; other types of pediatric glaucoma were not included. The cost-effectiveness of this type of home-monitoring of intra-ocular pressure in pediatric glaucoma has yet to be established. Yet this interesting and well-designed study gives us some insight into the IOP fluctuations in pediatric glaucoma.

15. REFRACTIVE SURGERY

16. GENETICS

Novel PEX11B Mutations Extend the Peroxisome Biogenesis Disorder 14B Phenotypic Spectrum and Underscore Congenital Cataract as an Early Feature.

Peroxisomes perform complex metabolic and catabolic functions essential for normal growth and development. Mutations in 14 genes cause a spectrum of peroxisomal disease in humans. Most recently, PEX11B was associated with an atypical peroxisome biogenesis disorder (PBD) in a single individual. In this study, the authors identify further PEX11B cases and delineate associated phenotypes. Probands from three families underwent next generation sequencing (NGS) for diagnosis of a multisystem developmental disorder. Autozygosity mapping was conducted in one affected sibling pair. ExomeDepth was used to identify copy number variants from NGS data and confirmed by dosage analysis. Biochemical profiling was used to investigate the metabolic signature of the condition. All patients presented with bilateral cataract at birth but the systemic phenotype was variable, including short stature, skeletal abnormalities, and dysmorphism-features not described in the original case. Next generation sequencing identified biallelic loss-of-function mutations in PEX11B as the underlying cause of disease in each case (PEX11B c.235C>T p.(Arg79Ter) homozygous; PEX11B c.136C>T p.(Arg46Ter) homozygous; PEX11B c.595C>T p.(Arg199Ter) heterozygous, PEX11B ex1-3 del heterozygous). Biochemical studies identified very low plasmalogens in one patient, whilst a mildly deranged very long chain fatty acid profile was found in another. The findings expand the phenotypic spectrum of the condition and underscore congenital cataract as the consistent prima-
Biochemical measurements of peroxisome function may be disturbed in some cases. Furthermore, diagnosis by NGS is proficient and may circumvent the requirement for an invasive skin biopsy for disease identification from fibroblast cells.

**Characterization of CDH3-Related Congenital Hypotrichosis With Juvenile Macular Dystrophy.**


Congenital hypotrichosis with juvenile macular dystrophy (HJMD) is a rare disorder presenting in childhood and adolescence with central visual disturbance and sparse scalp hair. Reported retinal imaging is lacking, and whether the condition is progressive remains unclear. The authors investigate a series of patients with HJMD due to balleic mutations in CDH3 and thereby characterize the disorder. Ten patients from 10 families underwent detailed clinical assessment, including serial retinal imaging and electrophysiologic evaluation, at Moorfields Eye Hospital, St James's University Hospital, and Calderdale Royal Infirmary. Patients ranged in age from 3 to 17 years at onset and 5 to 57 years at last assessment. The molecular genetic investigation included bidirectional Sanger sequencing of all exons and intron-exon boundaries of CDH3 and whole-exome sequencing in 2 patients. The study was conducted from June 5, 2013, to January 15, 2016, with final follow-up completed on December 15, 2015. All 10 patients (7 male and 3 female) presented with central visual disturbance in childhood and had lifelong sparse scalp hair with normal facial hair. Fundus examination revealed chorioretinal atrophy of the posterior pole contiguous with the disc in all but 1 patient that was associated with marked loss of autofluorescence on fundus autofluorescence imaging. Optical coherence tomography (OCT) demonstrated variable degrees of atrophy of the outer retina, retinal pigment epithelium, and choroid, with outer retinal tubulations frequently observed. One patient had mild disruption of the inner segment ellipsoid band on OCT and additional mild digit abnormalities. Electrophysiologic evaluation in 5 patients demonstrated macular dysfunction with additional mild, generalized retinal dysfunction in 2 patients. Eight patients had more than 1 evaluation; of these, 5 patients showed deterioration of visual acuity over time, 1 patient remained stable, and 2 patients had severe visual loss at presentation that precluded assessment of visual deterioration. The area of atrophy did not progress with time, but retinal thickness decreased on OCT. Electrophysiologic evaluation in 1 patient found deterioration of macular function after 13 years of follow-up, but the mild, generalized photoreceptor dysfunction remained stable. Biallelic mutations were identified in all patients, including 6 novel mutations. The disease is readily distinguished from other juvenile macular dystrophies by the universally thin and sparse scalp hair. Patients may have additional limb abnormalities.
Characterization of Chorioretinopathy Associated with Mitochondrial Trifunctional Protein Disorders: Long-Term Follow-up of 21 Cases.


Authors aim to assess, through a retrospective case series, the long-term effects of genotype on chorioretinopathy severity in patients with mitochondrial trifunctional protein (MTP) disorders. Participants are consecutive patients with MTP disorders evaluated at a single center from 1994 through 2015, including 18 patients with long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHADD) and 3 patients with trifunctional protein deficiency (TFPD). Local records from all visits were reviewed. Every participant underwent a complete ophthalmic examination and was evaluated by a metabolic physician and dietitian. Nine patients underwent ancillary funduscopic imaging including optical coherence tomography (OCT) and OCT angiography. The primary outcome measure was best-corrected visual acuity at the final visit. Secondary outcome measures included spherical equivalent refraction, visual fields, electroretinography B-wave amplitudes, and qualitative imaging findings. Participants were followed up for a median of 5.6 years (range 0.3-20.2 years). The median age of LCHADD participants at initial and final visits was 2.3 and 11.9 years, whereas that for TFPD participants at initial and final visits was 4.7 and 15.5 years, respectively. Four long-term survivors older than 16 years were included (3 with LCHADD and 1 with TFPD). The LCHADD participants demonstrated a steady decline in visual acuity from an average of 0.23 logarithm of the minimum angle of resolution (logMAR; Snellen equivalent, 20/34) at baseline to 0.42 logMAR (Snellen equivalent, 20/53) at the final visit, whereas TFPD patients maintained excellent acuity throughout follow-up. Participants with LCHADD, but not TFPD, showed an increasing myopia with a mean decrease in spherical equivalent refraction of 0.24 diopters per year. Visual fields showed sensitivity losses centrally associated with defects on OCT. Multimodal imaging demonstrated progressive atrophy of the outer retina in LCHADD, often preceded by the formation of outer retinal tubulations and choriocapillaris dropout. Electroretinography findings support the more severe clinical profile of LCHADD patients compared with TFPD patients; the function of both rods and cones are attenuated diffusely in LCHADD patients, but are within normal limits for TFPD patients. Authors conclude that Multimodal imaging is most consistent with choriocapillaris loss exceeding photoreceptor loss.

17. TRAUMA

Epidemiology of Sports-Related Eye Injuries in the United States
Sports related eye injuries, especially in children, can have a lifelong impact on numerous visual functions such as visual acuity, depth perception, and the need for regular monitoring of eye health, as in angle recession. This study examined data from the National Emergency Department Sample to determine the characteristics of eye trauma related to sports injury. The database contains information from 30 million ER visits annually in 900 hospitals nationwide. A three year period, 2010 through 2013 was studied and data extracted regarding age, sex, mechanism of injury, related activity, and factors associated with short-term impaired vision. 120,847 individuals presented with sports-related eye trauma. This was the primary diagnosis in 71% and injuries in males comprised 81% of the cohort. More than half of the males (41,775 [59.8%]) and females (10,814 [67.1%]) who sustained sports-related primary ocular injuries were 18 years or younger. The sports most commonly associated with eye injury were playing basketball (22.6%; 95%CI, 21.7%-23.6%), playing baseball or softball (14.3%; 95%CI, 13.7%-14.9%), and shooting an air gun (11.8%; 95%CI, 10.8%-12.8%). The most common type of eye injuries were open wounds of the adnexa (ICD-9-CM code 870.x; 33.5%) contusions of the eye and adnexa (ICD-9-CM code 921.x; 30.1%) and superficial injuries of the eye and adnexa (ICD-9-CM code 918.x; 21.1%). Impaired vision on presentation to the ER was most likely with paintball and air gun injuries relative to football-related injuries (odds ratio, 4.75; 95%CI, 2.21-10.19 and 3.71; 95%CI, 2.34-5.88, respectively; P < .001).

Conclusion: There are approximately 30,000 sport-related eye injuries to the emergency room each year in the United States. Injury with a projectile was most likely to cause short-term vision impairment, although long-term sequelae was unable to be determined from this study. This study is useful to help plan eye injury prevention strategies.

Association of Football Subconcussive Head Impacts With Ocular Near Point of Convergence

Recent attention to traumatic brain injury suffered during football play has increased awareness about safety. This article examines the effect of subconcussive head impacts on near point of convergence (NPC). The aim was to determine if there were changes in NPC, and perhaps to use change in NPC as a surrogate for severity of subconcussive head impact. This was a prospective observational study of 29 football players in the National Collegiate Athletic Association Division I. Information was gathered baseline and preseason practices (1 non-contact and 4 contact) as well as post-season. An accelerometer-embedded mouth guard measured head impact kinematics. Players participated in regular practices, and all head impacts greater than 10g from the 5 practices were recorded using the i1Biometerics Vector mouthguard (i1 Biometrics Inc). Based on
the sum of head impacts from all 5 practices, players were categorized into lower (n = 7) or higher (n = 22) impact groups. Linear and angular acceleration as well as number of impacts were, as expected, different between the 2 groups. Outcome measures were measure of near point of convergence and symptom scores. In the higher-impact group, there was a linear increase in NPC over time that plateaued and resolved post-season. In the lower-impact group, there was no change in NPC over time.

Importance: Playing football results in head impacts with significant force. In this study, 29 players received a total of 1193 head impacts, for an average of 41.1 impacts per player. Interestingly, players were asymptomatic, but this study suggests that repetitive subconcussive head impacts were associated with changes in NPC. Changes in NPC may become a useful clinical tool in assessing the severity of brain injury.

**NON-ACCIDENTAL HEAD TRAUMA**

**The natural history of retinal hemorrhage in pediatric head trauma**


This study determined the natural history of RH in infants and young children with suspected abuse or accidental head trauma and to identify helpful patterns which might suggest chronicity or help determined timing. This was an eight year retrospective review of children <2 years of age diagnosed with abusive or accidental head trauma. Ninety-one eyes of 52 children were included (abusive head trauma (AbHT) n=45 and accidental head trauma (AcHT) n=7). Mean subject age was 6.7 months. All 91 eyes had intra-retinal hemorrhages (IRH) at presentation and of these 62 eyes had IRH too numerous to count (TNTC). Sixty-eight eyes (75%) also had pre-retinal hemorrhages (PRH). Therefore at presentation, 25% only had IRH and none had only PRH. PRH only was not seen prior to a 1-week examination, and this pattern increased with further follow-up examinations (IRH clears faster than PRH). By the 1-week examination, no eyes had TNTC IRH. The longest an isolated single IRH persisted was 32 days. The longest isolated PRH persisted 111 days. This paper can help determine the timing of the injury and see if the clinical findings corroborate with the clinical history. This is an excellent paper which provides key data regarding retinal hemorrhages. The only assumptions that need to be made is that the abusive head trauma event occurred shortly before presentation (reasonable) and that the classification of AbHT versus AcHT was accurate (also reasonable).

18. **RETINA**
The New Pretender: A Large UK Case Series of Retinal Injuries in Children Secondary to Handheld Lasers.

Reports of retinal injury from handheld lasers have increased recently. Many of these lasers look like laser pointers and some are marketed as toys, and while there are attempts to regulate the sales of such devices, many can be purchased online. The purpose of this study is to describe a large cohort of 16 children, 24 eyes, with retinal injuries due to handheld lasers and to describe the eye exam and OCT findings. This was a retrospective study over 4 years at one institution. The authors found that many of these injuries were in males and the age ranged from 9-16 years old. 1/3 of the patients were initially diagnosed with a retinal dystrophy by outside eye doctors. 11/16 patients had mild injuries with focal retinal disruption at the photoreceptor layer on OCT and a better prognosis with a mean acuity at presentation of 20/25. Three eyes of 2 children had moderate injuries with diffuse outer retinal layer disruption on OCT and 3 patients (4 eyes) had severe injuries with loss of retinal architecture and overlying hyper reflective material extending to the inner retina. Many children did not admit to being exposed to the laser when asked with only half of the children admitting to this mechanism initially. The authors concluded that these injuries are likely underreported and difficult to diagnose. The vision in the patients did not improve over the somewhat short follow up time of 5 months. This is an important study for the pediatric ophthalmologist because it highlights a growing new public health concern and also helps the ophthalmologist better understand the OCT and exam findings so that laser retinal injury can be added to the differential diagnosis in cases where this mechanism might not be suspected.

Clinical and Genetic Features of Choroideremia in Childhood

In this retrospective case series, the authors describe the earliest features of choroideremia and to identify biomarkers useful for monitoring disease progression. 29 patients were identified with a mean age at referral of 9 years (range, 3-16 years). CHM mutations were identified in 15 of 19 patients tested. Nyctalopia was the predominant symptom (66%). Five of 29 patients were asymptomatic at presentation. At the final follow-up visit (mean age, 16 years; range, 7-26 years), most maintained excellent visual acuity (mean, 0.98-0.13 decimalized Snellen acuity). The first sign of retinopathy was widespread pigment clumping at the level of the retinal pigment epithelium (RPE). This later evolved to chorioretinal atrophy, most marked in the mid-peripheral retina. Peripapillary atrophy also was an early feature and was progressive in nature. Three different zones of FAF change were visible. Persistence of the inner retinal layers, detected by SD OCT,
was visible at presentation in 15 of 27 patients. Subfoveal choroidal thickness decreased with age, whereas central retinal thickness increased over a similar interval. Four patients in whom visual acuity decreased over the follow-up period recorded a reduction in central retinal thickness. The authors concluded that progressive structural changes occur initially while central visual function is maintained. Pigmentary changes at the level of the RPE occur early in the disease. Peripapillary chorioretinal atrophy, central retinal thickness, and subfoveal choroidal thickness are likely to be valuable in monitoring disease progression and should be considered as potential biomarkers in future therapeutic trials.

Comment: Wide-field fundus images and fundus autofluorescence in this paper nicely complement the authors’ descriptions of clinical findings.

Retinal and Optic Nerve Hemorrhages in the Newborn Infant
One-Year Results of the Newborn Eye Screen Test Study
Callaway NF, Ludwig CA, Blumenkranz MS, Jones JM et al. Ophthalmology May 2016;123:1043-1052

In this study, the authors prospectively evaluated 202 full term infants to report prevalence, risk factors, characteristics, and location of fundus hemorrhages (FHs) of the retina and optic nerve present in newborns at birth. The birth prevalence of FH in this study was 20.3% (41 infants). Of the group with FH, 95% involved the periphery, 83% involved the macula, and 71% involved multiple layers of the retina. The fovea was involved in 15% of FH cases (birth prevalence, 3.0%). No cases of bilateral foveal hemorrhage were found. Fundus hemorrhages were more common in the left eye than the right. Fundus hemorrhages were most commonly optic nerve flame hemorrhages (48%) and white-centered retinal hemorrhages (30%). Retinal hemorrhages were found most frequently in all 4 quadrants (35%) and more often were multiple than solitary. Macular hemorrhages most often were intraretinal (40%). Among the risk factors examined in this study, vaginal delivery compared with cesarean section (odds ratio [OR], 9.34) greatest level of association with FH. Self-identified ethnicity as Hispanic or Latino showed a protective effect (OR, 0.43). Other study factors were not significant.

Comment: Retcam image of FH included in this publication nicely illustrate the morphology of this common phenomenon.

Diagnosis of retinopathy in children younger than 12 years of age: implications for the diabetic eye screening guidelines in the UK
A Hamid, H M Wharton, A Mills, J M Gibson, M Clarke and P M Dodson Eye July 2016; 30: 949-951; advance online publication, April 15, 2016;
As the incidence of diabetes in children increases, there will be increasing need to screen children and young adults for the presence of diabetic retinopathy. In this study conducted in the UK, 143 children with Type 1 diabetes were examined and BDR was found in 9.6%. No retinopathy was seen in any child who had diabetes less than 6 years duration. The authors conclude that screening for retinopathy should begin 6 years after the diagnosis of diabetes is first established.

19. RETINOBLASTOMA / INTRAOCULAR TUMORS

RETINOBLASTOMA

Ocular Pharmacology of Chemotherapy for Retinoblastoma

This paper reviewed 21 studies to assess the preclinical and clinical pharmacokinetics of carboplatin, topotecan, and melphalan delivered by intravenous, periorcular, ophthalmic artery, and intravitreal routes. Some preclinical studies were done before translation to the clinics. Others, despite favorable preclinical data such as that reported for periorcular tepotecan, did not correlate with clinical use. In addition, some routes of drug delivery are clinically effective despite nonfavorable preclinical information, such as melphalan delivered as ophthalmic artery chemosurgery. The authors report that complete knowledge of the pharmacokinetics of these medications is lacking and additional study may guide retinoblastoma therapy in favor of safety and efficacy. However, they emphasize that results obtained in preclinical models must be translated to the clinics with caution.

NON-RETINOBLASTOMA

20. ORBIT
Isolated schwannoma involving extraocular muscles

Progressive strabismus initially considered idiopathic may be caused by isolated schwannomas of motor nerves to extraocular muscles, detectable only on careful imaging. This retrospective case series study reviewed the clinical experience of a referral
practice in identifying schwannomas on magnetic resonance imaging (MRI). Of 647 cases imaged for strabismus, schwannomas were identified by gadodiamide-enhanced, high-resolution surface coil orbital MRI and thin-section cranial MRI, as fusiform intraneural enlargements in 8 cases: 1 affecting the trochlear nerve; 2, the abducens nerve; and 5 the oculomotor nerve. Involved muscles were atrophic. Both abducens schwannomas, 1 superior oblique, and 1 oculomotor schwannoma were subarachnoid; 3 were intraorbital, and with one bilateral case of oculomotor lesions, which extended from the cavernous sinus to orbit. Associated strabismus progressed for 3-17 years. Abducens schwannoma caused esotropia; trochlear schwannoma caused hypertropia and cyclotropia. Intracranial oculomotor schwannoma caused mydriasis and exotropia. Intraorbital schwannoma caused exotropia with or without hypertropia. Since lesion diameters were 3-9 mm, 6 had been previously missed on routine MRI. Progressive, acquired strabismus may be caused by isolated cranial nerve schwannomas, representing about 1% of strabismus cases in this cohort, involving the oculomotor more than abducens nerve. Because most schwannomas are small and deep in the orbit, findings could be readily missed by routine imaging, leading to a possible diagnosis of idiopathic strabismus. The authors conclude that schwannomas should be suspected when extraocular muscles are atrophic. Targeted, high resolution MRI is necessary to identify these small lesions, which are nodular or fusiform hyperintense neural lesions in on T2-weighted and contrast-enhanced T1-weighted MRI. This small case series raises schwannomas as a possible diagnosis in clinical situations with progressive clinical course, atrophy of involved muscles, and highly selective involvement of cranial nerves.

**Orbital/Periorbital Plexiform Neurofibromas in Children with Neurofibromatosis Type 1 Multidisciplinary Recommendations for Care**


This consensus statement provides recommendations for ophthalmologic monitoring, outlines treatment indications and forthcoming biologic therapy. Comprehensive ophthalmic evaluation is recommended every 6 months until visual maturity. After that, frequency of examination should be guided by the clinical course. Patients with OPPN confined to the upper eyelid may not need to undergo neuroimaging. For patients with orbital, periorbital, or facial involvement, high-resolution magnetic resonance imaging (MRI) with and without contrast of the orbit, face, and cavernous sinus should be performed. Treatment for related ophthalmic issues, such as ptosis, lacrimal involvement, or amblyopia, is supportive.
Early intervention is recommended with the exception of strabismus surgery. Strabismus caused by orbital or periorbital tumor involvement while the tumor is in its rapid growth phase carries a high risk for recurrence after strabismus surgery. Associated problems such as amblyopia and refractive error should be managed aggressively and surgery deferred until the tumor growth has stabilized, if clinically appropriate. Debulking surgery may be indicated for the following: visual decline, progressive tumor growth involving a vital structure, progressive disfigurement or functional decline. Debulking is more successful in older patients and adults. Younger patients have a high risk of recurrent progression and need for more surgery. Clinical trials using biologic agents (i.e., MEK inhibitors) are underway, but no definitive recommendations can be made at this time. Comment: This paper provides a concise description of current evaluation and management priorities. Unless vision threatening, surgical interventions for neurofibroma are typically deferred until after tumor growth has ceased.

Risk of optic pathway glioma in children with neurofibromatosis type 1 and optic nerve tortuosity or nerve sheath thickening


Optic nerve tortuosity and nerve and sheath thickening are observed on MRI in some patients with neurofibromatosis type 1 (NF-1). This study aimed to determine if tortuosity and thickening are associated with the development of optic pathway glioma (OPG) and subsequent vision loss. Children with NF-1 who underwent brain MRI between 1992 and 2005, and had at least 1 year of subsequent visual acuity (VA) follow-up, were identified retrospectively. The baseline MRI was blinded and independently reviewed by three neuroradiologists for consensus assessment using validated criteria. Tortuosity was identified using validated operational criteria. Optic nerve and sheath thicknesses and VA at last follow-up were directly measured. Of 132 evaluable children, seven (5%) had tortuosity on baseline MRI. Twenty subjects (15%) ultimately developed OPG at a median of 1.9 years (range 7 months–8.0 years) following the baseline MRI. Subjects with tortuosity were significantly more likely to develop OPG than those without tortuosity (57% vs 13%, p=0.01). In subjects who developed OPG, the prevalence of tumor-related vision loss was not significantly different between those with and without baseline tortuosity (14% vs 4%, p=0.28). No difference existed between mean baseline optic nerve (2.3 vs 2.2 mm) or sheath (5.2 vs 5.4 mm) thicknesses comparing subjects who did and did not develop OPG. Optic nerve tortuosity at baseline is associated with OPG development among patients with NF-1, but does not predispose to aggressive OPG with associated vision loss. Neither nerve nor sheath thickening at baseline was associated with OPG development. The study time period of 1992 to 2005 was chosen to allow for 10 years of follow-up data that is deemed to be the critical period vision deterioration due to OPG. The authors point out that at the time the study was designed, any nerve with enhancement or enlargement was considered to be an OPG. However, there is ongoing debate in the NF-1 field regarding the minimal thickness cri-
Pediatric Idiopathic Orbital Inflammation: Clinical Features of 30 Cases

While Idiopathic Orbital Inflammation (IOI) is well described in adults, it has a low incidence in children and therefore little is known about the spectrum of the disease in the pediatric population. The authors performed a retrospective chart review of 30 patients diagnosed with IOI. In this study 13% of cases were bilateral. Previous studies have reported 1/3 of pediatric IOI cases present bilaterally. Post-treatment recurrence was found in 37% of cases. Recurrence was more likely to be associated with bilateral disease and had a female preponderance. The most common ophthalmic findings were periorbital edema and blepharoptosis. All patients had orbital radiography with common findings of dacryoadenitis, orbital mass, or myositis. Having an orbital mass on radiography was significantly related to the clinical presence of blepharoptosis. The most common treatment was steroid therapy, but a few patients were treated with steroid sparing therapy including IVIG and Rituximab with good results.

Rebound Growth of Infantile Hemangioma After Propranolol Therapy

Propranolol has become the first line therapy for treatment of infantile hemangiomas. Rebound growth occurs after discontinuation between in 19-25% of patients. This large, multi-center, retrospective cohort study aimed to identify the rate of rebound growth and predictive factors for rebound growth. The study enrolled 997 patients and found an incidence 25% rebound growth. Treatment was determined to be effective in 81% of patients after 12 months. The mean age of rebound growth was 17.1 months of age which is different from the natural progression of typical infantile hemangiomas. Significant risk factors for rebound growth include female gender, a deep component of the infantile hemangioma, and discontinuation of propranolol prior to 9 months of age. Limitations of the study include a possible referral bias because the patient population derives from tertiary care centers and patients that require systemic therapy. The findings of this study may help guide treatment decisions and counseling for the specific needs of each individual patient.

Safety of Oral Propranolol for the Treatment of Infantile Hemangioma: A Systematic Review
With the recent and widespread usage of propranolol for infantile hemangiomas, it is important to understand the safety profile of this medication. This study performed an in depth literature search revealing 83 studies that matched inclusion criteria which included a total of 5862 propranolol treated patients. These studies included clinical trials for the medication, compassionate use programs, and medical literature. The most common propranolol-related events included sleep disorders, diarrhea, peripheral coldness, and agitation. Most are not serious, transient, and manageable with appropriate education provided to caregivers. The article identifies pre-treatment screening for cardiovascular and pulmonary problems, risks for heart block, arrhythmia, reactive airways, or pulmonary abnormalities. These adverse events occurred very rarely in these studies. Routine echocardiography and EKG’s are not considered necessary prior to starting therapy but it is recommended to monitor blood pressure and heart rate after the first dose for at least 2 hours. The studies did not suggest monitoring glucose at the time of treatment but to give medication during or right after feeding and to stop the medication during times of fasting or vomiting. With these precautions, patients can prevent hypoglycemia and seizures related to low blood sugar. Oral propranolol appears to be well-tolerated and safe medication if medical providers appropriately screen patients for the potential serious adverse events and perform within-treatment monitoring.

21. **OCULOPLASTICS**

**Success Rates of Conventional Versus Endoscope-Assisted Probing for Congenital Duct Obstruction in Children 12 years and Youngers.**
Alicia Galindo-Ferreiro, Patricia Akaishi, Augisto Cruz, Rajiv Khandekar et al.

In this retrospective, nonrandomized case series, the success rates for congenital nasolacrimal duct obstruction (CNLDO) treated with conventional probing versus endoscope-assisted probing were compared. A total of 200 eyes were included in the study (n= 198 conventional probing group, n=72 endoscope-assisted group). The success of the procedure was evaluated with a subjective method (observations of the parents on tearing) and objective method (fluorescein dye disappearance test after 5 min). The subjective and objective success rates were 76.1% and 75.9% respectively in the conventional probing group and 95.7 % and 95.7% in the endoscope-assisted probing group (p<.005) The success rate decreased in older children in the conventional probing group but remained the same in the endoscope-assisted probing group. The au-
The authors suggest that endoscope assisted probing provides significantly higher success rates mainly in older children and in bilateral cases. The use of stents does not improve the success rates of either procedure. The study is limited by the fact that is retrospective, non-randomized. Although the use of an endoscope significantly increase the cost of the procedure and requires a learning curve from the physician’s perspective, the high success rates might justify the use of endoscope-assisted probing.

**22. INFECTIONS**

**Optical Coherence Tomography of Retinal Lesions in Infants With Congenital Zika Syndrome**


Zika virus (ZIKV), a neurotropic flavivirus, transmitted to humans mainly via mosquito bites, has rapidly spread across the globe. In utero ZIKV exposure may result in an infant born with congenital ZIKV syndrome (CZS), characterized by microcephaly, ocular involvement, hearing loss and limb anomalies. The authors look at the effect of the virus on the retina and choroid and describe their experience in evaluating these lesions using optical coherence tomography (OCT).

This is a cross sectional consecutive case series of 8 infants (3-5 months of age) born with CZS. ZIKV was confirmed by enzyme linked immunofluorescence analysis (ELISA) to detect IgM in the cerebrospinal fluid of 7/8 infants. Eleven of the 16 eyes had retinal lesions seen on indirect ophthalmoscopy and 9 of these eyes were imaged with OCT. The main OCT findings in the affected eyes included discontinuation of the ellipsoid zone and hyperreflectivity underlying the retinal pigment epithelium in 9 eyes (100%), retinal thinning in 8 eyes (89%), choroidal thinning in 7 eyes (78%), and colobomatous-like excavation involving the neurosensory retina, retinal pigment epithelium, and choroid in 4 eyes (44%).

Conclusion: The ocular findings in CZS include destructive effects on the retina and choroid. This is confirmed on OCT, which more so than a fundus photograph, elucidates the specific layers of the retina affected. This appearance is seen in other conditions such as toxoplasmosis and cytomegalovirus, so the authors caution using this OCT data to confirm ZKV infection. One limitation of the study is the lack of point-to-point correspondence between the fundus photos and OCT images.

**23. PEDIATRICS/ INFANTILE DISEASE/ SYNDROMES**
A cross-sectional examination of visual acuity by specific type of albinism


Reports of best-corrected visual acuity (BCVA) in albinism are often based on overlapping clinical phenotypes. BCVA in albinism has been shown to improve with age. This retrospective study reports a large cross-sectional investigation to determine whether BCVA differs by specific type of albinism when age-corrected. Included in the study 170 individuals with a specific type of albinism identified by mutation(s) in a gene known to cause albinism (for OCA1, OCA2, and Hermansky-Pudlak syndrome ([HPS]) or a specific phenotype (white hair and no melanin pigment in OCA1A; pigmentary mosaicism in the obligate carriers for males with OA1). Optotype binocular BCVA at final follow-up was recorded. Patients were age-grouped (2-5 years, 6-14 years, and >/=15 years) for comparison. Their results showed the greatest visual acuity deficit was found for OCA1A in all age groups. At age >/=15 years (n = 79), mean BCVA was 20/128 for OCA1A, 20/37 for OCA1B, 20/59 for OCA2, 20/63 for OA1, and 20/121 for HPS. Significant differences between BCVA at >/=15 years were found in the following: OCA1A vs OCA1B, OCA1A vs OCA2, OCA1A vs OA1, OCA1B vs HPS, OCA2 vs HPS, and OA1 vs HPS (P </= 0.02). Authors conclude that BCVA varies by albinism type, and there is overlap in BCVA, particularly in the younger age groups. For ages >/=15 years, there are significant differences in BCVA between several types of albinism. Even though this study provides a large sample size, it has several limitations in its design. We could not find data on length of follow-up. Would have been interesting to know the correlation of the BCVA with other clinical findings such as foveal hypoplasia and nystagmus.

Anesthesia and Developing Brains- Implications of the FDA Warning


This perspective reviews what is known and unknown about the effects of general anesthesia on developing brains and discusses the implications of an FDA warning. Data from studies in animals and in vitro research demonstrate that under experimental conditions, all general anesthetics tested, including both N-
methyl-d-aspartate (NMDA) antagonists and gammaaminobutyric acid (GABA) agonists, have immediate neuroanatomical consequences and associated long-lasting, if not permanent, functional effects in species ranging from roundworms to nonhuman primates. Clinical data are more difficult to interpret. Studies of brief, single exposures for relatively minor procedures have been reassuring. The long-term adverse neurodevelopmental effects that have been observed after prolonged or repeated anesthesia administration are difficult to interpret because of confounding by indication. Otherwise healthy young children do not undergo lengthy (longer than 3 hours) or repeated procedures under general anesthesia. And the brains of children born prematurely or with cyanotic congenital heart disease may have been injured by inflammation or chronic hypoxia before the children underwent the surgery that required general anesthesia. The interim analysis of the General Anesthesia vs. Spinal Anesthesia (GAS) study and the Pediatric Anesthesia and Neurodevelopment Assessment (PANDA) study, both of which involved formal neurodevelopmental testing, revealed that a brief, single exposure to general anesthesia was not associated with poorer neurodevelopmental outcomes. On December 14, 2016, the FDA issued a “Drug Safety Communication” warning that general anesthesia and sedation drugs used in children less than 3 years of age or in pregnant women in their third trimester who were undergoing anesthesia for more than 3 hours or repeated use of anesthetics “may affect the development of children’s brains.” Texas Children’s Hospital has changed its practice in response to the FDA warning. The hospital has adopted the warning’s recommendation that a discussion occur among parents, surgeons and other physicians, and anesthesiologists about the duration of anesthesia, any plan for multiple general anesthetics for multiple procedures, and the possibility that the procedure could be delayed until after 3 years of age; parent-education materials will also cover these topics. Indicated procedures in pregnant women and young children that can safely be delayed are rare. Until reassuring new information from well-designed clinical trials is available, the authors express concern that the FDA warning will cause delays for necessary surgical and diagnostic procedures that require anesthesia, resulting in adverse outcomes for patients. They urge parents, patients, and physicians to carefully consider the risks of delaying indicated procedures. In pediatric ophthalmology practice, this FDA warning may come up for discussion when anesthesia could potentially be delayed beyond age 3 years: should surgery for infantile esotropia patients who are brought to medical attention late (after age 2 years) be delayed an additional year; should surgery for the toddler with constant exotropia at distance fixation but intermittent exotropia or exophoria at near be delayed; should the toddler with acute/acquired esotropia who is otherwise developmentally and neurologically normal undergo a brain MRI? However, general anesthesia for pediatric ophthalmology indications is almost always shorter than 3 hours.

24. UVEITIS/ SYSTEMIC
Risk of Hypotony in Juvenile Idiopathic Arthritis-Associated Uveitis.

Juvenile idiopathic arthritis (JIA) associated uveitis can be complicated by hypotony, which can carry a worse visual prognosis. This is a retrospective study of 196 eyes of 108 patients at the Wilmer Eye Institute over 30 years with JIA-associated uveitis. The goal of this study was to evaluate the prevalence, incidence, and visual outcomes of patients with hypotony in the setting of JIA-associated uveitis. The authors defined hypotony as ≤5mmHg and low IOP from 6-8mmHg. They found a rate of hypotony at presentation in 9.3% of patients. 78% of patients were seen in follow up with a mean follow up of 5.3 years. During follow up, 26 of the 137 at-risk eyes developed hypotony. 12 patients (20 eyes) had hypotony prior to presentation, 10 patients (14 eyes) presented with hypotony, 4 patients presented with bilateral hypotony and 1 patient had bilateral low IOP. Most hypotonous eyes (12 of 14) were legally blind on presentation. All patients with hypotony were over 14 years old and most were older (over 18). Male sex was a risk factor for hypotony but this was not statistically significant. Other risk factors for hypotony included >10 of duration of arthritis prior to presentation, patients referred to tertiary care clinic 4 or more years after being treated elsewhere, a younger diagnosis of arthritis, and other signs of increased severity of uveitis. More than half of the eyes with hypotony had vitreous or posterior pole involvement and those eyes were 17 times more likely to have hypotony than eyes with anterior uveitis. Oral steroid use, previous periocular steroid injection and legal blindness at presentation were also statistically significantly correlated with hypotony and lower IOP. The authors note that the rate of patients referred to their center who were already receiving immunosuppressive drug therapy increased 4-fold over the timeline of this study and most importantly that the use of immunosuppressing drug therapy was associated with a substantial decrease in the rate of hypotony further supporting early and aggressive treatment of this blinding disease. The key findings of this large retrospective study were that prolonged inflammation, posterior involvement, and lack of systemic immunosuppressant were all risk factors for hypotony in patients with JIA associated uveitis.

25. PRACTICE MANAGEMENT/HEALTH CARE SYSTEM

Malpractice Litigation in Pediatric Ophthalmology

A survey by the AMA found that in any given year, 5 % of ophthalmologists had an open malpractice lawsuit. The authors searched the Westlaw Database for search terms, ophthalmology, ophthalmologist and malpractice from January 1, 1930 through 2014. 68 cases involving plaintiffs who were 18 years of age or less at the time of the occurrence were identified. This is a database of verdicts and settlements, not claims. Cases involving retinopathy of prematurity were the most common and had the highest awards. In cases resolved in favor of the plaintiff, the reason for the malpractice was insufficient follow up of the disease. This included failure to properly transfer care between specialists, loss to follow-up, and failure to ensure that follow-up visits and treatment are conducted within current guidelines for follow-up and treatment. In a comparison with adult malpractice cases, the study confirms that the plaintiff was more likely to win if he or she was a child. Also, the plaintiff was more likely to win if the alleged injury resulted in legal blindness. Failure to diagnose or failure to treat comprised 61.5% of cases which were ruled in the plaintiff’s favor. All cases involving endophthalmitis were ruled in favor of the plaintiff.

Conclusion: According to the authors, this is the largest study of pediatric malpractice cases in the literature. Focusing on the types of cases and outcomes of cases brought to court can help ophthalmologists who care for children understand unique risk factors for a verdict or settlement in favor of the plaintiff.